Manual of

Pediatric Nutrition

Fifth Edition

Kendrin Sonneville
Christopher Duggan

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CONTENTS

APPENDICES

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PREFACE

Eight years have passed since the publication of the fourth edition of the *Manual of Pediatric Nutrition*, and awareness of the critical importance of nutrition in determining health and wellness in children has only increased. This has been reflected in the growing knowledge base of evidence-based practice in nutrition and dietetics and a greater recognition of the influence of nutritional status and diet of children throughout the lifecourse on adult health.

This fifth edition of the *Manual of Pediatric Nutrition* provides a practical basis for pediatric nutritional assessment and therapy for dietitians, pediatricians, house officers, fellows, and students. We have maintained the organization of the book in three parts: Part 1, "Nutrition and the Well Child," covers the basics of nutrition assessment: nutritional requirements; feeding guidelines for healthy infants, children, and adolescents; and dietary supplements. Part 2, "Nutrition and the Hospitalized Child," reviews nutritional assessment in sick children, as well as the use of specialized enteral and parenteral products. Part 3, "Nutrition and Specific Disease States," provides updated information on the nutritional management of a wide range of pediatric clinical disorders. New and expanded sections for this edition include a new chapter on dysphagia and feeding/swallowing difficulties, a new section on eosinophilic esophagitis, and updated DRI tables and formulary.

We are grateful to our many colleagues who have reviewed the literature and written concise, practical chapters for this edition. We also acknowledge the excellent assistance of Linda Mehta of People's Medical Publishing House—USA, Ltd. in completing this edition. Finally, we wish to thank

Drs. Kristy Hendricks and W. Allan Walker for their invaluable contribution on previous editions and whose leadership in the field of nutrition helped begin this *Manual of Pediatric Nutrition* nearly 30 years ago.

Kendrin Sonneville, ScD, RD
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1 Nutritional Assessment: Food and Nutrition-Related History

Vanessa Kane-Alves, RD, LDN

Nutritional assessment is the first step in the nutrition care process. The data collected as part of a nutrition assessment typically include a food/nutrition-related history, anthropometric measurements, biochemical data, medical tests and procedures, nutrition-focused physical findings, and client history.[1] This chapter focuses on the food/nutrition-related history; the remaining parts of nutrition assessment are discussed in Chapters 2–4. Nutrition assessment data can come directly from the patient/caregiver through interview, observation and measurement, medical record, and/or another health care provider involved in the patients' care.[1]

Food and nutritional inadequacy or excess is frequently the cause of under- or overnutrition and often precedes biochemical, anthropometric, or clinical signs. This has special significance in the US pediatric and adolescent population where under- and overnutrition remain prevalent in hospital and community settings.[2,3] A nutrition assessment can lead

to early screening, detection, and treatment of these issues and can serve as a preventive strategy against long-term consequences and complications in adulthood.

The major component of the food/nutrition-related history is determining a typical dietary pattern. A number of nutrition assessment methods are used in pediatrics to determine a typical dietary pattern including the 24-hour recall or 3- to 7-day food records completed by the patient or their caregiver being the most common in clinical practice.[4] Consideration must be given to the under- or over-reporting of dietary intake. This can vary depending on the method used, the interviewer's technique, the patient/care provider ability to recall dietary details, and the day being evaluated.[5]

In addition to a typical dietary pattern, the following information is part of a comprehensive food and nutrition-related history: knowledge, beliefs, attitudes and behaviors, medication and herbal supplement use, factors affecting access to food and food/nutrition-related supplies, and physical activity and function.[6] Table 1–1 includes commonly collected food and nutrition-related data by age.

The conclusion of each food/nutrition-related history consists of a brief summary of the clinicians' impression of the adequacy of the nutrition intake. The information contained in this summary will vary by practice setting, but often includes the adequacy of calories, macro- or micronutrients, fluids, and/or food groups. Nutritional assessment findings are then compared with established criteria, comparative standards, and relevant norms to provide a basis for the identification of nutrition-related problems and objective recommendations for medical nutrition therapy.

Table 1–1 Common Food/Nutrition-Related History Data Collection

Full-Term Infant
If infant is breastfed: Breastfeeding frequency, duration, and patterns Exclusive breastfeeding Infant formula supplementation of breast milk Medication, vitamin/mineral, and/or herbal supplement intake for baby or mother *If infant is formula-fed:* Infant formula preparation (according to manufacturer directions or special instructions from another health care provider) Infant formula preparation and storage safety and sanitation Fluid/beverage or food intake in addition to the infant formula (juice, rice cereal, or water) Feeding frequency, duration, and patterns *In addition to the above:* Division of responsibility in feeding between parent/caregiver and infant[6] Hunger/satiety cue recognition skills of parent Dentition and oral–muscular development Developmental readiness for solids Food/nutrition program participation
Toddler *Interview all caregivers if possible (parents, grandparents, etc)*
Family and child food and nutrient intake (type, amount, patterns, and juice) Division of responsibility in feeding between parent/caregiver and toddler Eating environments Mealtime behavior Grazing on food or drinks in between mealtime Developmental feeding milestones Parent short-order cooking Cultural or religious beliefs affecting family eating practices Food/nutrition program participation Medication, vitamin/mineral, and/or herbal supplement intake

(*Continued*)

Table 1–1 Common Food/Nutrition-Related History Data Collection (*Continued*)

Preschooler *Interview all caregivers if possible (parents, grandparents, etc)*
Family and child food and nutrient intake (type, amount, patterns, and sugar-sweetened beverages/juice) Food preferences Division of responsibility in feeding between parent/caregiver and preschool-aged child Eating environments (family meals, foods outside of the home) Mealtime behavior Grazing on food or drinks Developmental feeding milestones Parent catering to child's food preferences Cultural or religious beliefs affecting family eating practices Food/nutrition program participation Physical activity TV/screen time, TV in the bedroom Medication, vitamin/mineral, and/or herbal supplement intake
School-Aged Child
Family and child food and nutrient intake (type, amount, patterns, and sugar-sweetened beverages/juice) Food preferences Eating environments (family meals, foods outside of the home including fast food/school) Division of responsibility between parent/caregiver and school-aged child Food avoidance, special dietary practices (vegetarian), dieting, hiding/sneaking foods Mealtime behavior Grazing on food or drinks in between meals Developmental eating milestones Parent short-order cooking Food/nutrition program participation (school breakfast or lunch program) Cultural or religious beliefs affecting family eating practices Child and parent food and nutrition knowledge Physical activity TV/screen time, TV in the bedroom Medication, vitamin/mineral, and/or herbal supplement intake Weight-related teasing Food avoidance

Adolescent *Interview parent or caregiver and adolescent separately; however, parent/caregiver should be involved*
Adolescent and family food and nutrient intake (type, amount, patterns, sugar-sweetened beverages/juice, and sports drinks) Food preferences Eating environments (family meals, foods outside of the home including fast food/school, and eating alone) Division of responsibility in feeding adolescents (teenager's self-sufficiency in feeding themselves outside of the home, around sports, cooking skills, etc.) Cultural or religious beliefs affecting teenager's/family eating practices Adolescent food and nutrition knowledge Physical activity, sports TV/screen time, TV in the bedroom Medication, vitamin/mineral, and/or herbal supplement intake Food avoidance, special dietary practices (vegetarian), dieting, and hiding/sneaking foods Alcohol, caffeine intake Preoccupation with weight, disordered eating Weight-related teasing Food/nutrition program participation

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2 Nutritional Assessment: Anthropometrics and Growth

Lori J. Bechard, MEd, RD, LDN and Kendrin Sonneville, ScD, RD, LDN

Growth is, from conception to maturity, a complex process influenced by nutrition, environment, and genetics. Anthropometry, the study of human body measurements on a comparative basis, includes the measurement of physical dimensions at different ages and is widely used to monitor growth and health.[1] Comparison with standard references for age and sex helps determine abnormalities in growth and development that may have resulted from nutrient deficiencies or excesses. Accurate assessment of growth requires an appropriate growth reference, accurate measures, accurate calculation of age, and appropriate interpretation of the scale used to describe the variable.[1] Various scales are used in the pediatric population to describe and evaluate anthropometric indicators. These measures are most frequently described as percentiles, z-scores, and percent of the median.

Although evaluating growth over time is more useful than a single measurement, single measurements can be used to screen children who may be at nutritional risk and determine the need for a more complete nutrition assessment. Errors in

the comparison of measurements taken at different times can be caused by poor techniques and equipment.[1] A basic description of anthropometric measurement technique is found in Table 2–1. Detailed descriptions of standardized techniques and equipment for anthropometry are available elsewhere.[1]

Table 2–1 Measurement Technique

Weight

The subject stands, lies, or sits in the center of a balance scale platform. Minimal clothing and no shoes should be worn. Weight is taken to the nearest 0.1 kg or 1.0 oz in children and to the nearest 0.01 kg or 0.5 oz. in infants.

Length/Height

Measurement of length is frequently erroneous because of improper technique or equipment. Children younger than 2 years of age should be measured recumbent on a length board; after this age, standing height should be measured if possible.[1] For standing height measurements, the patient should be standing erect, without shoes, on the scale platform or on the floor. Shoulders should be straight and the subject should look straight ahead. Measurements should be to the nearest 0.1 cm or 0.125 in.

Head Circumference

A flexible, narrow tape measure is placed firmly around the head above the supraorbital ridges and over the frontal bulge, where the circumference is greatest. Measurements should be taken to the nearest 0.5 cm or 0.25 in.[1]

Skinfold Thickness

Measurement of triceps skinfold thickness is taken at the midpoint between the acromion and olecranon on the relaxed right arm at the same level as the arm circumference. The layer of skin and subcutaneous tissue is pulled away from the underlying muscle and held until measurement with the calipers at the midpoint has been taken. Readings should be taken to 0.5 mm, 3 s after application of calipers. Other skinfold sites may also be used; techniques are described in the Centers for Disease Control Manual of Anthropometry.[1] High-quality skinfold calipers (Lange or Harpenden) are recommended for accurate measurements.[1]

Arm Circumference

Arm circumference is measured at the posterior aspect of the midpoint of the upper arm between the acromion and olecranon on the right arm. The measurement is taken perpendicular to the long axis of the upper arm while the patient is standing upright and relaxed.

GROWTH CHARTS

Growth charts contain a series of percentile graphs including weight-for-age, length/height-for-age, weight-for-length/height, and body mass index (BMI)-for-age for boys and girls birth to 20 years. The Centers for Disease Control and Prevention (CDC) and the American Academy of Pediatrics recommend the use of the WHO growth standards for infants and children from birth to 2 years of age,[2] and the use of the CDC growth charts for children 2–20 years of age.[3] All charts are available for downloading from the CDC website (www.cdc.gov/growthcharts) and are included in Appendix 3. Recommended indicators to assess nutritional status using the growth charts are provided in Table 2–2.

Weight

Body weight is a reproducible growth parameter and a good index of acute and chronic nutritional status. Accurate age, sex, and reference standards are all necessary for evaluation of weight.

Interpretation. Weight is evaluated using growth charts in three ways: weight-for-age, weight-for-height, and BMI. Weight-for-age compares the individual to reference data for weight attained at any given age, whereas weight-for-height evaluates the appropriateness of the individual's weight compared with his or her own height. *Weight velocity* evaluates change in rate of weight gain over a specified time

Table 2–2 Indicators of Nutritional Status[2,3,8,9,16]

	Stunting	Underweight	Wasting	Overweight	Obesity
Growth Chart Percentiles					
BMI-for-age			<5th percentile	85th to >95th percentile	>95th percentile
Weight-for-length			<5th percentile		
Height-for-age	<5th percentile				
Weight-for-age		<5th percentile			
Z-score	*Height-for-age* Moderate: <−2 Severe: <−3	*Weight-for-age* Moderate: <−2 Severe: <−3	*Weight-for-length or BMI-for-age* Moderate: <−2 Severe: <−3	*BMI-for-age* >+1	*BMI-for-age* >+2
% Median	Mild: 87%–98% Moderate: 80%–87% Severe: <80%	Mild: 75%–90% Moderate: 60%–74% Severe: <60%	Mild: 80%–90% Moderate: 70%–80% Severe: <70%		

period. Reference data for increments of weight from 0 to 24 months of age are shown in Table 2–3.

Recent change in weight (loss or gain) is also important to note, as it is often an indicator of acute nutritional problems.

$$\text{Percent weight change} = \frac{\text{Usual weight} - \text{Current weight}}{\text{Usual weight}} \times 100$$

Length/Height

Measured with appropriate equipment and technique, length is a simple and reproducible growth parameter that provides, in conjunction with weight, significant information. Length

Table 2–3 Growth Velocity[2,3]

WHO			CDC		
Age (mo)	Boys (g/d)	Girls (g/d)	Age (mo)	Boys (g/d)	Girls (g/d)
0–1	34.1	31.3	0–3	28	24
1–2	39.8	33.7			
2–3	27.1	23.9			
3–4	20.5	19.5	3–6	21	19
4–5	17.4	16.3			
5–6	14	13.3			
6–7	11.9	11.5	6–9	15	14
7–8	10.5	10.3			
8–9	9.5	9.1			
9–10	8.6	8.2	9–12	11	11
10–11	8.1	7.8			
11–12	8	7.7			
12–24	6–7	6–7	12–18	8	8
			18–36	5	5

or height assesses growth failure and chronic undernutrition, especially in early childhood and adolescence.

Interpretation. Length/height is evaluated using length/height-for-age growth charts. Length/height-for-age below the 5th percentile suggests a severe deficit, and measurements that range between the 5th and 10th percentiles should be evaluated further. Predicted mature height may also be considered when interpreting length/height. *Mature height* estimation may be helpful in evaluating short stature. Due to genetic influences, some children may be taller or shorter than average. The growth patterns of other family members may also be helpful in determining the correct diagnosis in such instances. Short stature during childhood and adolescence should be evaluated to determine whether it is a normal variation or indicates an underlying energy deficiency or disease. The corrected mid-parental height method (Tanner method) is one of several methods available for prediction of mature height.[6]

Height (cm) at maturity (male) = (Father's height + mother height + 13 cm)/2

Height (cm) at maturity (female) = (Father's height + mother's height – 13 cm)/2

Head Circumference

Head circumference can be influenced by nutritional status until 36 months of age, but deficiencies manifest in weight and height before being seen in brain growth. Routine examination also serves to screen for other possible influences on brain growth.

Interpretation. Head circumference is also interpreted using growth charts. Measurements below the 5th percentile may indicate chronic undernutrition during fetal life and early childhood.

Weight-for-Length/Height

This ratio more accurately assesses body build and distinguishes wasting (acute malnutrition) from stunting (chronic malnutrition).

Interpretation. Measurements that fall near the 50th percentile indicate appropriate weight-for-length/height; the greater the deviation, the more over- or undernourished the individual.

Body Mass Index

BMI is determined by dividing the person's weight in kilograms by their height in meters squared. In adolescents, BMI-for-age correlates with total body fatness.[4]

Interpretation. BMI percentiles are available for children older than 2 years.[3] BMI-for-age is the only indicator that allows plotting a measure of weight and height with age on the same chart. It is recommended that percentiles be used rather than an absolute number because this value changes throughout periods of growth, thus BMI is gender and age specific until adulthood.[5] A BMI at the 95th percentile may range from 18 to 30 depending on the age and sex of the child. BMI is a screening tool, used to identify over- or underweight individuals (Table 2–1). A BMI at or above the 95th percentile for age and sex indicates the need for evaluation and treatment for overweight. Physical examination, and possibly further assessment of body composition, may be warranted to confirm that a high BMI denotes excess body fat (BF).

◆ INDICATORS OF NUTRITIONAL STATUS

Three different classification systems can be used to distinguish *normal* from *abnormal* growth in childhood: percentiles, z-scores, and percent of median.

Percentiles

Percentiles are the common, clinically used method of comparison that graphically indicates on the growth charts where the child fits compared to the reference standard. Percentiles rank the position of the child's growth parameter(s), indicating what percent of the population would be less or greater than the individual child.

Z-Score

An alternative way to interpret height, weight, weight-for-height and BMI is z-score, which denotes units of standard deviation from the median.[7] It allows the clinician to detect movement toward or away from the median that is more sensitive and precise than percentile changes. This is especially useful in cases that lie outside the percentile curves (i.e., below the 5th or above the 95th percentile). Although percentiles are typically used in the United States, the WHO recommends using z-scores, especially when describing groups of subjects.[7] Z-scores are calculated using the growth chart data and are commonly included in electronic growth chart programs.

Percent of the Median

The third commonly used scale to compare anthropometric measures is percent of the median. Methods vary widely in classification of malnutrition, but most of them use percent standard (percent of the median) for various measures including weight-for-height, weight-for-age, and height-for-age.[8,9].

An anthropometric measure can be calculated as a percentage of standard (the 50th percentile for age and sex) as follows:

$$\% \text{ Standard} = \frac{\text{Actual measure}}{\text{Standard measure (50th percentile)}} \times 100$$

Examples of common classifications are shown in Table 2–2. The classification of the indices measured into discrete categories such as either wasting or stunting is important as the etiology and treatment may vary.

BODY COMPOSITION ANALYSIS

A determination of BF and fat free mass (lean body mass) is useful for comparison to age and sex adjusted normal values.[10] Changes associated with growth, activity, disease, and treatment may be observed. Methodology for children often relies on the use of constants or age ranges that may not be specific to the patient or group being studied; careful consideration of the relevant calculations are important. Three of the more common methods used in clinical practice and research are described in Table 2–4.

Table 2–4 Body Composition Assessment in Children[8]

Method	Advantages	Disadvantages
Bioelectrical impedance analysis (BIA)	• Rapid • Inexpensive • Easy to use • Portable	• Questionable accuracy • Sensitive to hydration status, temperature, and humidity
Dual energy x-ray absorptiometry (DXA)	• Noninvasive • Accurate and precise • Also measures bone density	• Some exposure to radiation • May not be appropriate for infants and young children
Air-displacement plethysmography (ADP)	• Rapid • Noninvasive • Easy to use • No radiation exposure	• Expensive equipment • Assumes constant density of fat-free mass

Skinfold Thickness

Measurements of the subcutaneous layer correlate with total BF and can be used to estimate fat stores. Skinfold thickness measurements are simple, inexpensive, and portable, which when performed with reliable technique, can be used to monitor BF changes. Skinfold thickness measurements assess current nutritional status and body composition; they provide an index of body energy stores and can be used in conjunction with weight or height to determine chronic undernutrition and to better define the athletic child who may be overweight but not over fat.

Interpretation. An estimate of BF can be calculated using one or more skinfold measurements and a variety of tested equations.[11] The Slaughter equation, shown here, has been widely used in the United States.[12]

BF % for children with triceps and subscapular skinfolds <35 mm:
Boys = 1.21 (sum of 2 skinfolds) – 0.008 (sum of 2 skinfolds^2) – 1.7
Girls = 1.33 (sum of 2 skinfolds) – 0.013 (sum of 2 skinfolds^2) – 2.5
BF % for children with triceps and subscapular skinfolds >35 mm:
Boys = 0.783 (sum of 2 skinfolds) – 1.7
Girls = 0.546 (sum of 2 skinfolds) + 9.7

Measurements of triceps skinfold (TSF) from childhood through adult life were compiled by Frisancho using large samples of American children throughout the United States[13] (Table 2–5). Measurements are most useful on children who are followed over a period of time.

Table 2–5 Percentile for Triceps Skinfold (mm²)[a]

	Male								Female							
Age Group	*n*	*5*	*10*	*25*	*50*	*75*	*90*	*95*	*n*	*5*	*10*	*25*	*50*	*75*	*90*	*95*
1–1.9	228	6	7	8	10	12	14	16	204	6	7	8	10	12	14	16
2–2.9	223	6	7	8	10	12	14	15	208	6	8	9	10	12	15	16
3–3.9	220	6	7	8	10	11	14	15	208	7	8	9	11	12	14	15
4–4.9	230	6	6	8	9	11	12	14	208	7	8	8	10	12	14	16
5–5.9	214	6	6	8	9	11	14	15	219	6	7	8	10	12	15	18
6–6.9	117	5	6	7	8	10	13	16	118	6	6	8	10	12	14	16
7–7.9	122	5	6	7	9	12	15	17	126	6	7	9	11	13	16	18
8–8.9	117	5	6	7	8	10	13	16	118	6	8	9	12	15	18	24
9–9.9	121	6	6	7	10	13	17	18	125	8	8	10	13	16	20	22
10–10.9	146	6	6	8	10	14	18	21	152	7	8	10	12	17	23	27
11–11.9	122	6	6	8	11	16	20	24	117	7	8	10	13	18	24	28
12–12.9	153	6	6	8	11	14	22	28	129	8	9	11	14	18	23	27

(*Continued*)

Table 2–5 Percentile for Triceps Skinfold (mm^2)[a] (*Continued*)

	Male								*Female*							
Age Group	*n*	*5*	*10*	*25*	*50*	*75*	*90*	*95*	*n*	*5*	*10*	*25*	*50*	*75*	*90*	*95*
13–13.9	134	5	5	7	10	14	22	26	151	8	8	12	15	21	26	30
14–14.9	131	4	5	7	9	14	21	24	141	9	10	13	16	21	26	28
15–15.9	128	4	5	6	8	11	18	24	117	8	10	12	17	21	25	32
16–16.9	131	4	5	6	8	12	16	22	142	10	12	15	18	22	26	31
17–17.9	133	5	5	6	8	12	16	19	114	10	12	13	19	24	30	37
18–18.9	91	4	5	6	9	13	20	24	109	10	12	15	18	22	26	30
19–24.9	531	4	5	7	10	15	20	22	1060	10	11	14	18	24	30	34
25–34.9	971	5	6	8	12	16	20	24	1987	10	12	16	21	27	34	37
35–44.9	806	5	6	8	12	16	20	23	1614	12	14	18	23	29	35	38
45–54.9	898	6	6	8	12	15	20	25	1047	12	16	20	25	30	36	40
55–64.9	734	5	6	8	11	14	19	22	809	12	16	20	25	31	36	38
65–74.9	1503	4	6	8	11	15	19	22	1670	12	14	18	24	29	34	36

[a]Data collected from whites in the United States Health and Nutrition Examination Survey 1 (1971–1974).

Source: Adapted from Frisancho.[13]

Arm Circumference

In conjunction with the triceps skinfold thickness, mid-arm circumference (MAC) can be used to determine cross-sectional mid-arm muscle and fat areas. Mid-arm circumference correlates well with more sophisticated measures of body composition, as well as mortality.[14]

Interpretation. Percentiles for arm circumference, arm muscle circumference, arm fat area, and arm muscle area were also compiled by Frisancho[13] (Tables 2–6 and 2–7). Calculations for arm muscle circumference, arm muscle area, and arm fat area (AFA) are provided below. It is to be noted that the units will need to be converted to millimeters and millimeters squared for comparison with Tables 2–6 and 2–7.

$$\text{MAMC (cm)} = \text{MAC (cm)} - [\pi \times \text{TSF (cm)}]$$

$$\text{MAMA (cm}^2\text{)} = [\text{MAC (cm)} - \pi \times \text{TSF (cm)}]^2/4\pi$$

$$\text{AFA (cm}^2\text{)} = [\text{MAC (cm)}^2/4\pi] - \text{MAMA}$$

BONE AGE

Epiphyseal closure is a measure of skeletal maturation. Radiographs of the hand and wrist are generally used for convenient determination of this measure. The percentage of maturity can be used to estimate potential for "catch up" growth. Measurements for epiphyseal closure can be found in the *Radiographic Atlas of Skeletal Development of the Hand and Wrist* by Greulich and Pyle.[15] Skeletal age is generally advanced in overnutrition and retarded in any condition in which linear growth is slowed secondary to malnutrition. The success of catch up growth depends on the duration and age at which slowed growth occurs and the adequacy of nutritional repletion. Appropriate treatment of underlying

Table 2–6 **Percentiles of Mid-Arm Circumference and Estimated Mid-Arm Muscle Circumference**[a]

	Arm Circumference (mm)							Arm Muscle Circumference (mm)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
Male														
1–1.9	142	146	150	159	170	176	183	110	113	119	127	135	144	147
2–2.9	141	145	153	162	170	178	185	111	114	122	130	140	146	150
3–3.9	150	153	160	167	175	184	190	117	123	131	137	143	148	153
4–4.9	149	154	162	171	180	186	192	123	126	133	141	148	156	159
5–5.9	153	160	167	175	185	195	204	128	133	140	147	154	162	169
6–6.9	155	159	167	179	188	209	228	131	135	142	151	161	170	177
7–7.9	162	167	177	187	201	223	230	137	139	151	160	168	177	190
8–8.9	162	170	177	190	202	220	245	140	145	154	162	170	182	187
9–9.9	175	178	187	200	217	249	257	151	154	161	170	183	196	202
10–10.9	181	184	196	210	231	262	274	156	160	166	180	191	209	221
11–11.9	186	190	202	223	244	261	280	159	165	173	183	195	205	230
12–12.9	193	200	214	232	254	282	303	167	171	182	195	210	223	241
13–13.9	194	211	228	247	263	286	301	172	179	196	211	226	238	245

	Arm Circumference (mm)							Arm Muscle Circumference (mm)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
14–14.9	220	226	237	253	283	303	322	189	199	212	223	240	260	264
15–15.9	222	229	244	264	284	311	320	199	204	218	237	254	266	272
16–16.9	244	248	262	278	303	324	343	213	225	234	249	269	287	296
17–17.9	246	253	267	285	308	336	347	224	231	245	258	273	294	312
18–18.9	245	260	276	297	321	353	379	226	237	252	264	283	298	324
19–24.9	262	272	288	308	331	355	372	238	245	257	273	289	309	321
25–34.9	271	282	300	319	342	362	375	243	250	264	279	298	314	326
35–44.9	278	287	305	326	345	363	374	247	255	269	286	302	318	327
45–54.9	267	281	301	322	342	362	376	239	249	265	281	300	315	326
55–64.9	258	273	296	317	336	355	369	236	245	260	278	295	310	320
65–74.9	248	263	285	307	325	344	355	223	235	251	268	284	298	306

(*Continued*)

Table 2–6 **Percentiles of Mid-Arm Circumference and Estimated Mid-Arm Muscle Circumference[a] (*Continued*)**

	Arm Circumference (mm)							Arm Muscle Circumference (mm)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
						Female								
1–1.9	138	142	148	156	164	172	177	105	111	117	124	132	139	143
2–2.9	142	145	152	160	167	176	184	111	114	119	126	133	142	147
3–3.9	143	150	158	167	175	183	189	113	119	124	132	140	146	152
4–4.9	149	154	160	169	177	184	191	115	121	128	136	144	152	157
5–5.9	153	157	165	175	185	203	211	125	128	134	142	151	159	165
6–6.9	156	162	170	176	187	204	211	130	133	138	145	154	166	171
7–7.9	164	167	174	183	199	216	231	129	135	142	151	160	171	176
8–8.9	168	172	183	195	214	247	261	138	140	151	160	171	183	194
9–9.9	178	182	194	211	224	251	260	147	150	158	167	180	194	198
10–10.9	174	182	193	210	228	251	265	148	150	159	170	180	190	197
11–11.9	185	194	208	224	248	276	303	150	158	171	181	196	217	223
12–12.9	194	203	216	237	256	282	294	162	166	180	191	201	214	220

	Arm Circumference (mm)							Arm Muscle Circumference (mm)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
13–13.9	202	211	223	243	271	301	338	169	175	183	198	211	226	240
14–14.9	214	223	237	252	272	304	322	174	179	190	201	216	232	247
15–15.9	208	221	239	254	279	300	322	175	178	189	202	215	228	244
16–16.9	218	224	241	258	283	318	334	170	180	190	202	216	234	249
17–17.9	220	227	241	264	295	324	350	175	183	194	205	221	239	257
18–18.9	222	227	241	258	281	312	325	174	179	191	202	215	237	245
19–24.9	221	230	247	265	290	319	345	179	185	195	207	221	236	249
25–34.9	233	240	256	277	304	342	368	183	188	199	212	228	246	264
35–44.9	241	251	267	290	317	356	378	186	192	205	218	236	257	272
45–54.9	242	256	274	299	328	362	384	187	193	206	220	238	260	274
55–64.9	243	257	280	303	335	367	385	187	196	209	225	244	266	280
65–74.9	240	252	274	299	326	356	373	185	195	208	225	244	264	279

[a]Data collected from the whites in the United States Health and Nutrition Examination Survey 1 (1971–1974).

Source: Adapted from Frisancho.[13]

Table 2–7 Percentiles for Estimates of Mid-Arm Fat Area and Mid-Arm Muscle Area[a]

	Arm Muscle Area Percentiles (mm^2)							Arm Fat Area Percentiles (mm^2)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
Male														
1–1.9	956	1014	1133	1278	1447	1644	1720	452	486	590	741	895	1036	1176
2–2.9	973	1040	1190	1345	1557	1690	1787	434	504	578	737	871	1044	1148
3–3.9	1095	1201	1357	1484	1618	1750	1853	464	519	590	736	868	1071	1151
4–4.9	1207	1264	1408	1579	1747	1926	2008	428	494	598	722	859	989	1085
5–5.9	1298	1411	1550	1720	1884	2089	2285	446	488	582	713	914	1176	1299
6–6.9	1360	1447	1605	1815	2056	2297	2493	371	446	539	678	896	1115	1519
7–7.9	1497	1548	1808	2027	2246	2494	2886	423	473	574	758	1011	1393	1511
8–8.9	1550	1664	1895	2089	2296	2628	2788	410	460	588	725	1003	1248	1558
9–9.9	1181	1884	2067	2288	2657	3053	3257	485	527	635	859	1252	1864	2081
10–10.9	1930	2027	2182	2575	2903	3486	3882	523	543	738	982	1376	1906	2609
11–11.9	2016	2156	2382	2670	3022	3359	4226	536	695	754	1148	1710	2348	2574
12–12.9	2216	2339	2649	3022	3496	3968	4640	544	650	874	1172	1558	2536	3580
13–13.9	2363	2546	3044	3553	4081	4502	4794	475	570	812	1096	1702	2744	3322
14–14.9	2830	3147	3586	3963	4575	5368	5530	453	563	786	1082	1608	2746	3508

	Arm Muscle Area Percentiles (mm^2)							Arm Fat Area Percentiles (mm^2)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
15–15.9	3138	3317	3788	4481	5134	5631	5900	521	595	690	931	1423	2434	3100
16–16.9	3625	4044	4352	4951	5753	6576	6980	542	593	844	1078	1746	2280	3041
17–17.9	3998	4252	4777	5286	5950	6886	7726	598	698	827	1096	1636	2407	2888
18–18.9	4070	4481	5066	5552	6374	7067	8355	560	665	860	1264	1947	3302	3928
19–24.9	4508	4777	5274	5913	6660	7606	8200	594	743	963	1406	2231	3098	3652
25–34.9	4694	4963	5541	6214	7067	7847	8436	675	831	1174	1752	2459	3246	3786
35–44.9	4844	5181	5740	6490	7265	8034	8488	703	851	1310	1792	2463	3098	3624
45–54.9	4546	4946	5589	6297	7142	7918	8458	749	922	1254	1741	2359	3245	3928
55–64.9	4422	4783	5381	6144	6919	7670	8149	658	839	1166	1645	2236	2976	3466
65–74.9	3973	4411	5031	5716	6432	7074	7453	573	753	1122	1621	2199	2876	3327
Female														
1–1.9	885	973	1084	1221	1378	1535	1621	401	466	578	706	847	1022	1140
2–2.9	973	1029	1119	1269	1405	1595	1727	469	526	642	747	894	1061	1173
3–3.9	1014	1133	1227	1396	1563	1690	1846	473	529	656	822	967	1106	1158
4–4.9	1058	1171	1313	1475	1644	1832	1958	490	541	654	766	907	1109	1236

(*Continued*)

Table 2–7 Percentiles for Estimates of Mid-Arm Fat Area and Mid-Arm Muscle Area[a] (*Continued*)

	Arm Muscle Area Percentiles (mm^2)							Arm Fat Area Percentiles (mm^2)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
5–5.9	1238	1301	1423	1598	1825	2012	2159	470	529	647	812	991	1330	1536
6–6.9	1354	1414	1513	1683	1877	2182	2323	464	508	638	827	1009	1263	1436
7–7.9	1330	1441	1602	1815	2045	2332	2469	491	560	706	920	1135	1407	1644
8–8.9	1513	1566	1808	2034	2327	2657	2996	527	634	769	1042	1383	1872	2482
9–9.9	1723	1788	1976	2227	2571	2987	3112	642	690	933	1219	1584	2171	2524
10–10.9	1740	1784	2019	2296	2583	2873	3093	616	702	842	1141	1608	2500	3005
11–11.9	1784	1987	2316	2612	3071	3739	3953	707	802	1015	1301	1942	2730	3690
12–12.9	2092	2182	2579	2904	3225	3655	3847	782	854	1090	1511	2056	2666	3369
13–13.9	2269	2426	2657	3130	3529	4081	4568	726	838	1219	1625	2374	3272	4150
14–14.9	2418	2562	2874	3220	3704	4294	4850	981	1043	1423	1818	2403	3250	3765
15–15.9	2426	2518	2847	3248	3689	4123	4756	839	1126	1396	1886	2544	3093	4195
16–16.9	2308	2567	2865	3248	3718	4353	4946	1126	1351	1663	2006	2598	3374	4236
17–17.9	2442	2674	2996	3336	3883	4552	5251	1042	1267	1463	2104	2977	3864	5159
18–18.9	2398	2538	2917	3243	3694	4461	4767	1003	1230	1616	2104	2617	3508	3733

	Arm Muscle Area Percentiles (mm^2)							Arm Fat Area Percentiles (mm^2)						
Age Group	**5**	**10**	**25**	**50**	**75**	**90**	**95**	**5**	**10**	**25**	**50**	**75**	**90**	**95**
19–24.9	2538	2728	3026	3406	3877	4439	4940	1046	1198	1596	2166	2959	4050	4896
25–34.9	2661	2826	3148	3573	4138	4806	5541	1173	1399	1841	2548	3512	4690	5560
35–44.9	2750	2948	3359	3783	4428	5240	5877	1336	1619	2158	2898	3932	5093	5847
45–54.9	2784	2956	3378	3858	4520	5375	5974	1459	1803	2447	3244	4229	5416	6140
55–64.9	2784	3063	3477	4045	4750	5632	6247	1345	1879	2520	3369	4360	5276	6152
65–74.9	2737	3018	3444	4019	4739	5566	6214	1363	1681	2266	3063	3943	4914	5530

[a]Data collected from the whites in the United States Health and Nutrition Examination Survey 1 (1971–1974).

Source: Adapted from Frisancho.[13]

medical problems may also increase the likelihood of maximum growth potential. During catch up growth, height velocity may be twice average for age and sex, and weight velocity may be four times average for age and sex; the rate of skeletal maturation also increases.[15]

SEXUAL MATURATION

During adolescence, growth in height and weight is accelerated. Following sexual maturation, a rapid deceleration of growth occurs. Clinical evaluation of sexual maturation is helpful in determining the level of progression through adolescence. Expectations for growth velocity and body composition are dependent on pubertal status and lend specificity to a comprehensive pediatric nutrition assessment. Tanner's stages of sexual development provide a clinical rating scale (1 = preadolescent, 5 = mature) for comparison of development. Considerable variability exists as to the age at which these events occur. The sequence, however, is fairly uniform. See Chapter 8 for further information on adolescent assessment.

CLASSIFICATION OF MALNUTRITION

Malnutrition is a pathologic state of varying severity; its clinical features are caused by a deficiency, or imbalance of essential nutrients. The cause may be primary (insufficient quantity or quality of food) or secondary (increased requirements or inadequate utilization). Development of *marasmus* occurs after severe deprivation primarily of energy, and it is characterized by growth retardation and wasting of muscle and subcutaneous fat. In *kwashiorkor*, protein deficiency exceeds energy deficiency; edema accompanies muscle wasting resulting from acute protein deprivation or

loss of protein caused by stress and/or inadequate provision of calories. Indifference, lethargy, and fatigue are present in children with these conditions, and psychological alterations may be profound. Severe anorexia, apathy, and irritability make children with these conditions difficult to feed and manage. Many of the clinical signs (changes in hair and skin) lack specificity and are identical to symptoms of other nutrient deficiencies listed in Table 2–8.[8] The morbidity and mortality associated with malnutrition are more closely correlated with the degree of malnutrition than with sex, age, or specific clinical factors, although some studies show a higher mortality rate in infancy than in older age groups. A higher

Table 2–8 Clinical Signs of Severe Malnutrition[7]

	Marasmus	Kwashiorkor
Growth retardation (linear)	++	+
Muscle wasting	++	+
Edema	–	+
Apathy, fatigue	+	++
Irritability	+	+
Electrolyte imbalance (hypokalemia)	+	+
Hypoalbuminemia	–	+
Anemia	+	++
Fatty liver	–	+
Low body temperature	+	++
Flakey paint dermatitis	–	+

– = not seen, + = seen, ++ = seen more frequently or is more marked.

mortality rate is seen with *kwashiorkor* than with *marasmus*; electrolyte and fluid imbalances, increased risk of infections, and underlying disease increase the death rate significantly.

Malnutrition was first defined in terms of a deficit in weight for a child's age[8,9]; however, height-for-age and weight-for-height are often more useful tools. For example, a low weight-for-height is seen in acute malnutrition. The WHO defines moderate acute malnutrition (MAM) as a weight-for-height z-score <−2 but >−3 and severe acute malnutrition (SAM) as a weight-for-weight z-score <−3. In chronic undernutrition, there are frequently no clinical signs other than a low height and weight-for-age. Children with chronic malnutrition may present with an appropriate weight-for-height or BMI-for-age, but with lower than expected height-for-age because their linear growth is stunted.

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3 Nutritional Assessment Clinical Evaluation

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Assessment of nutritional status is an essential part of clinical evaluation in the pediatric setting because patients are undergoing growth and development.[1] Severe nutritional deficiencies are often easily detectable, while less severe chronic or subacute deficiencies typically present with more subtle or nonspecific physical signs. Results of physical examination for signs suggestive of nutrient deficiency or excess should be recorded and described as precisely as possible and confirmed by biochemical, anthropometric, or dietary evaluation. Table 3–1 describes the major physiologic functions, deficiency signs, excess signs, important food sources, potential causes of deficiency, and status assessment for all essential nutrients. Recommended intakes of all nutrients are detailed in Chapter 5.

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Macroutrients						
Carbohydrate	Supplies energy at an average of 4 kcal/g (sparing protein) and is the major energy source for CNS function; unrefined, complex carbohydrates supply fiber that aids in normal bowel function	Ketosis	Obesity	Bread, cereals, crackers, potatoes, corn, simple sugar (sugar, honey), fruits and vegetables, milk, breast milk, infant formula	Malabsorption	Blood sugar, OGTT
Fat	Concentrated calorie source at an average of 9 kcal/g; constitutes part of the membrane structure of every cell; supplies essential fatty acids; provides and carries fat-soluble vitamins (A, D, E, and K)	Essential fatty acid deficiency (dry, scaly skin, poor weight gain, and hair loss); requirements are increased by cell turnover	Atherosclerosis may be affected by excessive intakes of certain dietary fats; altered blood lipid levels	Shortening, oil, butter, margarine, protein-rich foods (meat, dairy, nuts), breast milk, infant formula	Cystic fibrosis, biliary disease, short bowel syndrome, hereditary lipoprotein disorders	Total cholesterol, LDL, HDL

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Protein	Supplies energy at an average of 4 kcal/g; regulates body processes as part of enzymes, hormones, body fluids, and antibodies that increase resistance to infection; provides nitrogen; constitutes part of the membrane structure of every cell	Dry, depigmented, easily pluckable hair; bilateral, dependent edema, cirrhosis, fatty liver, decreased visceral proteins; skin is dry with pellagroid dermatosis in severe cases	Azotemia, acidosis, hyperammonemia	Meat, poultry, fish, legumes, eggs, cheese, milk and other dairy products, nuts, breast milk, infant formula	Protein-losing enteropathy, liver disease, gastrointestinal disease, renal disease	Albumin, retinol-binding protein, prealbumin
Fat soluble vitamins						
Vitamin A	Formation and maintenance of skin and mucous membranes; necessary for the formation of rhodopsin of the rods governing vision in dim light; regulation of membrane structure and function; necessary for growth and normal immune function	Night blindness, degeneration of the retina, xerophthalmia, follicular hyperkeratosis, poor growth, keratomalacia, Bitot's spots	Fatigue, malaise, lethargy, abdominal pain, hepatomegaly, alopecia, headache with increased intracranial pressure	Carrots, liver, green vegetables, sweet potatoes, butter, margarine, apricots, melons, peaches, broccoli, cod liver oil, breast milk, infant formula	Liver disease, cystic fibrosis, short bowel syndrome, protein deficiency (alters transport)	Plasma retinol (HPLC), plasma retinol-binding protein, relative dose response, dark adaptation test, liver biopsy concentration

Vitamin D	Promotes intestinal absorption of calcium and phosphate and renal conservation of calcium and phosphorus	Rickets, osteomalacia, costochondral beading, epiphyseal enlargement, cranial bossing, bowed legs, persistently open anterior fontanel	Hypercalcemia, vomiting, anorexia, diarrhea, convulsions	Cod liver oil, fish, eggs, liver, butter, fortified milk, sunlight (activation of 7-dehydrocholesterol in the skin), infant formula	Liver disease, cystic fibrosis, short bowel syndrome, renal disease	Plasma 25-hydrooxyvitamin D (HPLC), serum alkaline phosphatase, calcium and phosphate, radiography, bone densitometry
Vitamin E	Acts as an antioxidant and free radical scavenger to prevent peroxidation of polyunsaturated fatty acids in the body; neuromuscular function	Hemolytic anemia in the premature and newborn, enhanced fragility of red blood cells, increased peroxidative hemolysis	In anemia, suppresses the normal hematologic response to iron	Oils high in polyunsaturated fatty acids, milk, eggs, breast milk, infant formula	Cystic fibrosis, short bowel syndrome, liver disease	Plasma tocopherol (HPLC) (corrected for total or LDL-cholesterol), hydrogen peroxide hemolysis

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Vitamin K	Necessary for prothrombin and the three blood clotting factors VII, IX, and X; half of the vitamin K in humans is of intestinal origin, synthesized by gut flora; necessary for bone mineralization	Hemorrhagic manifestations (especially in newborns), prolonged clotting	Hemolytic anemia, nerve palsy	Green leafy vegetables, fruits, cereals, dairy products, soybeans, breast milk, infant formula	Liver disease, antibiotic therapy	Prothrombin time (prolonged), plasma phylloquinone, clotting factor levels, protein-induced by vitamin K absence or antagonists-II (PIVKA-II)
Water soluble vitamins						
Ascorbic acid (vitamin C)	Forms collagen cross-linkage of proline hydroxylase, thus strengthening tissue and improving wound healing and resistance to infection; aids absorption of iron	Joint tenderness, scurvy (capillary hemorrhaging), impaired wound healing, acute periodontal gingivitis, petechiae, purpura, anemia	Documentation of a chronic high intake may result in "rebound" deficiency symptoms	Heat-labile; broccoli, papaya, orange, mango, grapefruit, strawberries, tomatoes, potatoes, leafy vegetables, breast milk, infant formula	Stress	Plasma level (enzyme assay/HPLC), leukocyte concentration (longer term), whole blood concentration, urine concentration

Biotin	Component of several carboxylating enzymes; plays an important role in the metabolism of fat and carbohydrate	Anorexia, nausea, vomiting; glossitis; depression; dry, scaly dermatitis; thin hair; loss of eyebrows		Liver, kidney, egg yolk, breast milk, infant formula	Certain inborn errors of metabolism	Plasma (microbiologic plasma lactate, assay), urine organic acids, lymphocyte carboxylase
Cobalamin (B12)	Cobalamin-containing coenzymes function in the degradation of certain odd-chain fatty acids and in the recycling of tetrahydrofolate	Megaloblastic anemia, neurologic deterioration		Animal products, breast milk, infant formula	Ileal disease, strict vegetarian, lack of intrinsic factor	Plasma level (radioimmune assay (RIA) or microbiologic), Schilling test, plasma homocysteine, deoxyuridine suppression test
Folacin	Utilized in carbon transfer and nucleotide synthesis	Megaloblastic anemia, stomatitis, glossitis, neural tube defects in pregnancy		Liver, leafy vegetables, fruit, yeast, breast milk, infant formula	Liver disease, alcoholism, celiac disease, inflammatory bowel disease	Plasma level (RIA or microbiologic), red cell level

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Niacin	Aids in energy utilization as part of a coenzyme (NAD^+ and $NADP^+$) in fat synthesis, tissue respiration, and carbohydrate utilization; aids digestion and fosters normal appetite; synthesized from amino acid tryptophan	Pellagra (dermatitis, diarrhea, dementia, death), cheilosis, angular stomatic inflammation of mucous membranes, weakness	Dilation of the capillaries, vasomotor instability, "flushing" (utilization of muscle glycogen, serum lipids, mobilization of fatty acids during exercise)	Liver, meat, fish, poultry, peanuts, fortified cereal products, yeast, breast milk, infant formula	B6 deficiency (impairs conversion of tryptophan to niacin)	Urine ratio of metabolites (*N*-methylnicotinamide/2-pyridone), tryptophan load, red cell NAD or NAD:NADP ratio
Pantothenic acid	Component of coenzyme A; plays a role in release of energy from carbohydrates and in synthesis and degradation of fatty acids	Infertility, abortion, slow growth, depression, vomiting, malaise, abdominal stress	Diarrhea, water retention	Meat, fish, poultry, whole grains, legumes, breast milk, infant formula	Severe malnutrition	Urine excretion, whole blood level (RIA/microbiologic)

Pyridoxine (B6)	Coenzyme component for many of the enzymes of amino acid metabolism; all compounds implicated as neurotransmitters are synthesized and/or metabolized in B6-dependent reactions	Convulsions, weight loss, abdominal distress, vomiting, hyperirritability, depression, confusion, hypochromic and macrocytic anemia	Neuropathy	Fish, poultry, meat, wheat, breast milk, infant formula	Elderly, high protein intake	Red cell aminotransferase activity, pyridoxal phosphate (HPLC), tryptophan load test, urine 4-pyridoxic acid
Riboflavin (B2)	Functions primarily as the reactive portion of flavoproteins concerned with biologic oxidations (cellular metabolism)	Cheilosis, glossitis, photophobia, angular stomatitis, corneal, vasculation, scrotal skin changes, seborrhea, magenta tongue		Dairy products, liver, almonds, lamb, pork, breast milk, infant formula	Alcoholism, starvation, chronic diarrhea, malabsorption	Erythrocyte glutathione reductase activity (EGR), red cell flavin adenine dinucleotide, urine riboflavin:creatinine ratio

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Thiamine (B1)	Aids in energy utilization as part of coenzyme component to promote the utilization of carbohydrate; promotes normal functioning of the nervous system; coenzyme for oxidative carboxylation of 2-keto acids	Beriberi, neuritis, cardiac failure, anorexia, restlessness, confusion, loss of vibration sense and deep tendon reflexes, calf tenderness, edema		Lean pork, nuts, whole grain and fortified cereal products, breast milk, infant formula	Alcoholism, refeeding syndrome, prolonged dialysis	Red cell transketolase activity, whole blood level (HPLC), urine thiamine:creatinine ratio
Minerals						
Calcium	Essential for calcification of bone (matrix formation); assists in blood clotting; functions in normal muscle contraction and relaxation and in normal nerve transmission	Osteomalacia, osteoporosis	Hypercalcemia, vomiting, anorexia, lethargy	Dairy products (milk, cheese), sardines, oysters, salmon, herring, greens, breast milk, infant formula	Renal disease, liver disease	Plasma total calcium, plasma free calcium in altered protein binding (e.g., hypoalbuminemia), acidosis, radiographs, computed tomography, photon densitometry

Magnesium	Essential part of many enzyme systems; important for maintaining electrical potential in nerves and muscle membranes and for energy turnover	Tremor, convulsions, hyperexcitability (hypocalcemic tetany)	Diarrhea, transient hypocalcemia	Widely distributed, especially in food of vegetable origin; breast milk, infant formula	Protein calorie malnutrition, refeeding syndrome	Plasma total or free magnesium, magnesium loading test
Phosphorus	Important intracellular anion; involved in many chemical reactions within the body; necessary for energy turnover (ATP)	Weakness, anorexia, malaise, bone pain, growth arrest	Hypocalcemia (when parathyroid gland not fully functioning)	Dairy products, fish, legumes, pork, breast milk, infant formula	Renal disease, liver disease, refeeding syndrome	Plasma concentration, alkaline phosphatase activity, radiography, densitometry, renal tubular excretion threshold
Trace elements						
Chromium	Maintenance of normal glucose metabolism, cofactor for insulin	Disturbed glucose metabolism (lower glucose tolerance caused by insulin resistance)		Brewer's yeast, meat products, cheeses	Protein calorie malnutrition, elderly	Plasma chromium, glucose tolerance

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Copper	Constituent of proteins and enzymes, some of which are essential for the proper utilization of iron; immunity; skeletal development	Anemia (hemolytic), neutropenia, bone disease	Excess accumulation in the liver, brain, kidney, and cornea; anemia, diarrhea	Oysters, nuts, liver, kidney, corn oil margarine, dried legumes	Menkes kinky hair syndrome Excess: Wilson's disease	Plasma copper, plasma ceruloplasmin (ferrochelatase), liver biopsy concentration, superoxide dismutase activity
Fluoride	The main target organs of fluoride in man are the enamel of teeth and bones, where fluoride is incorporated into the crystalline structure of hydroxyapatite and produces increased caries resistance	Poor dentition, caries, osteoporosis	Mottling, brown staining of teeth (in excess of 4 ppm); fluorosis occurs after prolonged (10–20 yr) ingestion of 20–80 mg/d	Fluoridated water; depends on the geochemical environment and therefore amount in food varies widely	Unfluoridated water, bottled water	

Iodine	Component of thyroid hormones triiodothyronine and thyroxine; important in regulation of cellular oxidation and growth	Goiter, depressed thyroid function, cretinism	Thyroid suppression (thyrotoxicosis)	Iodized table salt, salt water, fish, shellfish (content of most other foods geographically dependent), breast milk, infant formula	Endemic goiter in low iodine areas	Thyroid hormones, TSH, urinary iodide:creatinine ratio
Iron	Part of hemoglobin molecule; prevents nutritional anemia and fatigue; increases resistance to infection; functions as part of enzymes involved in tissue respiration	Anemia, malabsorption, irritability, anorexia, pallor, lethargy	Hemosiderosis, hemochromatosis	Red meat, liver, dried beans and peas, enriched farina, breast milk, infant formula, infant cereal	Protein-losing enteropathy, malabsorption, acute or chronic blood loss Excess: hemochromatosis	Plasma iron and ferritin, total iron-binding capacity, hemoglobin/hematocrit, red cell indices, RBC zinc protoporphyrin:heme ratio, bone marrow aspirate stain

(*Continued*)

Table 3–1 Clinical Examination in Nutritional Deficiencies and Excesses (*Continued*)

	Major Physiologic Functions	Deficiency Signs	Excess Signs	Important Food Sources	Potential Causes of Deficiency	Status Assessment
Manganese	Essential part of several enzyme systems involved in protein and energy metabolism and in the formation of mucopolysaccharide	Impaired growth, skeletal abnormalities, lowered reproductive function, neonatal ataxia	In extremely high exposure of contamination: severe psychiatric and neurologic disorders	Nuts, whole grains, dried fruits, fruits, leafy vegetables		Plasma level, whole blood level, mitochondrial superoxide dismutase
Molybdenum	Essential for the function of flavin-dependent enzymes involved in the production of uric acid and in the oxidation of aldehydes and sulfites		Acts as an antagonist to the essential element copper; gout like syndrome associated with elevated blood levels of molybdenum, uric acid, and xanthin oxidase	Varies considerably depending on growing environment; main contributions come from meat, grains, and legumes		

Selenium	Functions as a part of the enzyme glutathione peroxidase, which protects cellular component from oxidative damage	Cardiomyopathy, probably secondary to oxidative damage	In animals: blindness, abdominal pain	Seafoods, kidney, liver meat, grains (depending on growing environment)	Cystic fibrosis	Plasma concentration, glutathione peroxidase activity, nail/hair selenium
Zinc	Constituent of enzymes involved in most major metabolic pathways (specifically nucleic acid synthesis for growth and repair)	Growth failure, skin changes, delayed wound healing, hypogeusia, sexual immaturity, hair loss, diarrhea	Acute gastrointestinal upset, vomiting, sweating, dizziness, copper deficiency	Whole grains, legumes, beef, lamb, pork, poultry, nuts, seeds, shellfish, eggs, some cheeses, breast milk, infant formula	Malabsorption, chronic diarrhea, liver disease, sickle-cell disease	Plasma concentration, alkaline phosphatase activity, urinary excretion, leukocyte concentration

Abbreviations: CNS, central nervous system; OGTT, oral glucose tolerance test; LDL, low-density lipoprotein; HDL, high-density lipoprotein; HPLC, high-performance liquid chromatography; TSH, thyroid-stimulating hormone.

Source: Adapted from Table I-9 of Duggan et al.[1]

Reference

1. Duggan C, Watkins JB, Walker, WA, eds. *Nutrition in Pediatrics: Basic Science and Clinical Applications*. 4th ed. Hamilton, ON: BC Decker Inc; 2008.

4 Laboratory Assessment of Nutritional Status

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INTRODUCTION

Nutritional assessment in pediatrics largely rests on the food/nutrition-related history and anthropometric measurement methods outlined in the preceding chapters. However, biochemical data, medical tests, and procedures play a complementary role, which may be critical in (1) diagnosing subclinical micronutrient deficiencies, (2) confirming nutritional deficiency suggested by clinical assessment, and (3) providing baseline and serial data with which to monitor response to nutritional interventions, particularly important in the prevention of the refeeding syndrome (see Chapter 13).

PROTEINS

Plasma Proteins

Proteins synthesized by the liver have long been used to assess protein status, because decreased blood concentrations presumably reflect a reduced supply of amino acid precursors or decreased hepatic (and other visceral) mass. However, plasma proteins are subject to influences other than nutritional status, particularly the presence of an

inflammatory state, and also fluid shifts. Plasma proteins may be classified according to whether their concentration increases or decreases in the setting of acute infection or catabolism (see Table 4-1). The concentrations of positive acute-phase proteins are increased in infectious or other catabolic illnesses due to preferential secretion by the liver. Conversely, negative acute-phase proteins, made up of labile protein stores that are catabolized early in starvation complicated by metabolic stress, are decreased in these circumstances. The magnitude of a positive acute-phase response is attenuated in protein–energy malnutrition.[1]

Albumin. Albumin is the most abundant protein in blood, the least expensive and easiest to measure, and therefore the most commonly used biochemical marker to assess protein status. As more than half of body albumin is extravascular (primarily in skin and muscle), maintenance of normal plasma levels can occur from mobilization of these stores, despite prolonged energy or protein inadequacy. Combined with its long half-life of 20 days, these factors make serum albumin a relatively insensitive marker of nutritional status and an insensitive measure of nutritional recovery. Nonetheless, hypoalbuminemia continues to be a reasonable predictor of morbidity and mortality in hospitalized patients.

Table 4–1 Plasma Proteins and Acute Illness

Positive Acute-Phase Proteins	Negative Acute-Phase Proteins
C-reactive protein	Albumin
Fibrinogen	Prealbumin
Haptoglobin	Retinol-binding protein
Ferritin	Transferrin
Ceruloplasmin	
Alpha-1-antitrypsin	
Alpha-1-glycoprotein	

Hypoalbuminemia is not specific for malnutrition and can also be seen in situations of decreased synthesis (e.g., in people with liver disease or >70 years of age), increased losses (e.g., nephrosis, protein-losing enteropathy, and burn injuries), or increased losses to extravascular spaces (e.g., acute catabolic stress with capillary leak). Fluid overload can also dilute albumin concentrations, and bed rest can decrease levels by 0.5 g/dL over several days due to redistribution into tissues.

Prealbumin. Prealbumin, so named because of its proximity to albumin on an electrophoretic strip, is a transport molecule for thyroxine, hence its alternative name, transthyretin. It circulates in plasma in a 1:1 ratio with retinol-binding protein (RBP). Its short half-life (2 days), small body pool, and high ratio of essential to nonessential amino acids make it a good measure of visceral protein status, more sensitive than albumin as a measure of nutritional recovery.

Retinol-Binding Protein. RBP has properties similar to prealbumin in that it has a small body pool and a rapid response to protein–energy depletion and repletion. Its half-life is 12 hours. As RBP is excreted by the kidneys, levels are high in renal failure. RBP levels drop in vitamin A deficiency and, as with albumin and prealbumin, with infectious or other catabolic stresses.

Transferrin. Transferrin is another plasma protein sometimes used to assess visceral protein status. It is synthesized primarily in the liver and has a half-life of 8 days. Transferrin concentrations are decreased in all situations that depress serum albumin, as well as with steroid therapy, iron overload, and anemia of chronic disease. Increased concentrations are seen in pregnancy, oral contraceptive use, and iron-deficiency anemia.

Reference ranges for these plasma proteins are given in Table 4-2.

Table 4–2 **Typical Reference Ranges of Select Nutritional Laboratory Values (Ranges are method- and population-dependent: please refer to local laboratory for accurate ranges.)**

Nutrient	Age	Males	Either	Females
Albumin (g/dL)	<5 d (<2.5 kg)		2.0–3.6	
	<5 d (>2.5 kg)		2.6–3.6	
	1–3 y		3.4–4.2	
	4–6 y		3.5–5.2	
	>6 y		3.7–5.6	
Alkaline phosphatase (U/L)	1–30 d	75–316		48–406
	31–365 d	82–383		124–341
	1–3 y	104–345		108–317
	4–6 y	93–309		96–297
	7–9 y	86–315		69–325
	10–12 y	42–362		51–332
	13–15 y	74–390		50–162
	16–18 y	52–171		47–119
Ammonia, plasma (umol/L)	Newborn		<50	
	Child and adult		<35	
Calcium (mg/dL)	1–30 d	8.5–10.6		8.4–10.6
	31–365 d	8.7–10.5		8.9–10.5
	1–3 y	8.8–10.6		8.5–10.4
	4–6 y	8.8–10.6		8.5–10.6
	7–9 y	8.7–10.3		8.5–10.3

Nutrient	Age	Males	Either	Females
	10–12 y	8.7–10.2		8.6–10.2
	13–15 y	8.5–10.2		8.4–10.0
	16–18 y	8.4–10.3		8.6–9.8
Calcium, ionized whole blood (mmol/L)	0–1 mo		1.0–1.5	
	1–6 mo		0.95–1.5	
	1–17 y		1.22–1.37	
Carnitine, total, fasting (umol/L)	1–12 mo		15–39	
	1–7 y		18–37	
	7–15 y		31–43	
Cerulosplasmin (mg/L)	1–30 d	77–253		33–275
	31–365 d	154–484		154–429
	1–3 y	253–561		286–539
	4–6 y	286–561		264–539
	7–9 y	253–517		231–484
	10–12 y	209–506		209–484
	13–15 y	198–495		209–462
	16–18 y	198–451		220–495
Cholesterol (mg/dL)	0–1 mo	54–151		62–155
	2–6 mo	81–147		62–141
	7–12 mo	76–179		76–216
	1–3 y	85–182		108–193
	4–6 y	110–217		106–193
	7–9 y	110–211		104–210
	10–12 y	105–223		105–218
	13–15 y	91–204		108–205
	16–18 y	82–192		92–234

(*Continued*)

Table 4-2 Typical Reference Ranges of Select Nutritional Laboratory Values (*Continued*)

Nutrient	Age	Males	Either	Females
Copper (µg/dL)	0–6 mo		38–104	
	6–12 mo		24–152	
	1–2 y		76–193	
	2–4 y		87–187	
	4–6 y		56–191	
	6–10 y		117–181	
	10–14 y		87–182	
	14–18 y		75–187	
Ferritin ug/mL	1–6 mo	6–410		6–340
Folic acid (nmol/L)	0–1 y	16.3–50.8		14.3–51.5
	2–3 y	5.7–34.0		3.9–35.6
	4–6 y	1.1–29.4		6.1–31.9
	7–9 y	5.2–27.0		5.4–30.4
	10–12 y	3.4–24.5		2.3–23.1
	13–18 y	2.7–19.9		2.7–16.3
Glucose (mg/dL)	Outside neonatal period		70–126	
Growth hormone (ug/L)				
Unstimulated	0–6 y		<1–13.6	
	7–10 y		<1–16.4	
	11–14 y		<1–14.4	
	15–18 y		<1–13.4	
Stimulated			>5	
After stimulation			>6	

Nutrient	Age	Males	Either	Females
Hemoglobin (g/dL)	1–3 d	12.5–16.6		12.7–16.4
	4–7 d	12.5–16.3		12.6–15.3
	8–14 d	11.9–15.7		12.7–14.9
	15–30 d	11.6–14.2		11.6–14.3
	31–60 d	10.2–12.7		11.1–13.7
	2–6 mo	10.4–13.0		10.7–13.4
	6 mo to 2 y	10.4–12.5		10.8–12.6
	2–5 y	11.0–12.8		11.1–12.9
	6–11 y	11.0–13.3		11.3–13.4
	12–17 y	11.0–14.3		11.3–13.4
	≥18 y	11.4–15.1		10.9–13.4
Hemoglobin A1c (%)				
Nondiabetic		<6.5		
mmol/mol creatinine		<48		
Homocysteine, total (umol/L)	2 mo to 10 y		3.3–8.3	
	11–15 y		4.7–10.3	
	16–18 y		4.7–11.3	
Iron (µg/dL)	1–5 y		22–136	
	6–9 y		39–136	
	10–14 y	28–134		45–145
	15–19 y	34–162		28–184
Iron–binding capacity (µg/dL)	1–5 y		268–441	
	6–9 y		240–508	
	10–14 y	302–508		318–575
	15–19 y	290–570		302–564

(*Continued*)

Table 4-2 Typical Reference Ranges of Select Nutritional Laboratory Values (*Continued*)

Nutrient	Age	Males	Either	Females
Magnesium (mg/dL)	1–30 d	1.7–2.4		1.7–2.5
	1–12 mo	1.6–2.5		1.9–2.4
	1–3 y	1.7–2.4		1.7–2.4
	4–6 y	1.7–2.4		1.7–2.2
	7–9 y	1.7–2.3		1.6–2.3
	10–12 y		1.6–2.2	
	13–15 y		1.6–2.3	
	16–18 y		1.5–2.2	
Mean corpuscular volume, MCV (um^3)	1–3 d	94.0–106.3		89.7–105.4
	4–7 d	87.1–96.5		86.5–93.8
	8–14 d	87.1–94.8		87.4–92.2
	15–30 d	88.0–95.2		88.4–93.3
	31–60 d	86.5–92.1		85.7–91.6
	2–6 mo	79.6–86.3		82.0–87.0
	6 mo to 2 y	75.6–83.1		76.6–83.2
	2–5 y	76.8–83.3		77.7–84.1
	6–11 y	78.2–83.9		79.5–85.2
	12–17 y	80.8–86.6		82.1–87.7
	≥18 y	83.5–90.2		82.7–89.4
Osmolality (plasma) (mOsm/kg)	1 mo to 18 y		280–300	
Phosphate (mg/dL)	1–30 d	3.9–6.9		4.3–7.7
	1–12 mo	3.5–6.6		3.7–6.5
	1–3 y	3.1–6.0		3.4–6.0
	4–6 y	3.3–5.6		3.2–5.5

Nutrient	Age	Males	Either	Females
	7–9 y	3.0–5.4		3.1–5.5
	10–12 y	3.2–5.7		3.3–5.3
	13–15 y	2.9–5.1		2.8–4.8
	16–18 y	2.7–4.9		2.5–4.8
Prothrombin time			11–15 s	
Prealbumin (transthyretin) (mg/dL)	1–40 d	3.2–15.9		4.2–14.4
	41–90 d	2.7–17.6		2.5–21.9
	3–9 mo	7.3–27.9		5.3–25.0
	10–24 mo	6.7–28.5		7.3–33.7
	2–10 y	6.9–31.2		8.0–35.2
	11–15 y	6.3–33.5		8.6–40.7
	16–18 y	8.0–41.6		13.7–44.1
Protein, total (g/dL)	0–2 mo	4.0–7.6		3.6–7.0
	>2–6 mo	4.0–7.0		4.0–7.6
	>6–12 mo	4.2–7.9		4.6–7.8
	1–6 y	6.0–8.0		6.0–7.8
	7–9 y	6.3–8.1		6.3–8.1
	10–19 y	6.4–8.6		6.4–8.6
Retinol-binding protein (RBP) (mg/dL)	0–30 d	0.91–5.6		1.01–5.75
	1 mo to 18 y	1.09–8.7		0.98–6.76
Selenium (µg/dL)	0–<6 mo		0.8–4.4	
	6–<12 mo		0–6.9	
	1–<2 y		1.5–7.3	
	2–<4 y		0.9–10.4	

(*Continued*)

Table 4-2 Typical Reference Ranges of Select Nutritional Laboratory Values (*Continued*)

Nutrient	Age	Males	Either	Females
	4–<6 y		0.6–12.5	
	6–<10 y		2.4–11.8	
	10–<14 y		2.4–11.4	
	14–<18 y		2.1–11.8	
	1–30 d	0.84–1.78		0.80–1.81
	1–6 mo	0.92–2.83		1.11–2.69
	>6–12 mo	1.55–3.11		1.27–3.17
	1–3 y	1.71–3.18		1.30–3.32
Transferrin (g/L)	4–6 y	1.76–3.05		1.51–3.47
	7–9 y	1.30–3.07		1.62–3.20
	10–12 y	1.51–3.31		1.61–3.28
	13–15 y	1.49–3.25		1.68–3.40
	16–18 y	1.69–3.03		1.57–3.62
	0–7 d	21–182		28–166
	8–30 d	30–184		30–165
	31–90 d	40–175		35–282
	91–180 d	45–291		50–355
	181–365 d	45–501		36–431
Triglycerides (mg/dL)	1–3 y	27–125		27–125
	4–6 y	32–116		32–116
	7–9 y	28–129		28–129
	10–11 y	24–137		39–140
	12–13 y	24–145		37–130
	14–15 y	34–165		38–135
	16–19 y	34–140		37–140

Nutrient	Age	Males	Either	Females
Urea nitrogen (mg/dL)	1–30 d	4–12		3–17
	1–12 mo	2–13		4–14
	1–3 y	3–12		3–14
	4–6 y	3–16		4–14
	7–9 y	4–16		4–16
	10–12 y	5–18		5–16
	13–15 y	7–18		4–15
	16–18 y	5–20		4–15
Vitamin A (retinol) (μg/dL)	Preterm neonates		13–46	
	Term neonates		18–50	
	1–6 y		20–43	
	7–12 y		20–49	
	13–19 y		26–72	
Vitamin B_1 (thiamine) (μg/dL)			1.6–4.0	
Vitamin B_6 (pyridoxine) (ug/L)			3.6–18.0	
Vitamin B_{12} (cyanocobalamin) (pmol/L)	0–1 y	216–891		168–1117
	2–3 y	195–897		307–892
	4–6 y	181–795		231–1038
	7–9 y	200–863		182–866
	10–12 y	135–803		145–752
	13–18 y	158–638		134–605
Vitamin C (ascorbic acid) (mg/dL)			0.2–2.0	

(*Continued*)

Table 4-2 Typical Reference Ranges of Select Nutritional Laboratory Values (*Continued*)

Nutrient	Age	Males	Either	Females
Vitamin D (as 25-hydroxy D) (ug/L)	1–30 d	3.3–33.4		1.9–32.0
	1 mo to 1 y	7.4–53.3		11.6–48.2
	1–3 y	6.9–46.8		11.3–48.9
	4–12 y	4.6–37.4		2.8–36.7
	13–18 y	2.0–31.4		1.8–28.3
Vitamin D (as 25-OH vitamin D_3) ug/L	0–<3 mo		5–42	
	3–<6 mo		9–60	
	6mo –<12mo		18–58	
	1–<3y		15–54	
	3–<10 y		14–46	
	10–<13y		11–50	
	13–<15y		10–44	
	15–<18y		8–45	
	18y		8–56	
Vitamin D (as 1,25-dihydroxy D) (pg/mL)			15–60	
Vitamin E (α tocopherol) (ug/mL)	Preterm neonates		0.5–3.5	
	Full–term neonates		1.0–3.5	
	2–5 mo		2.0–6.0	
	6–12 mo		3.5–8.0	
	1–6 y		3.0–9.0	
	7–12 y		4.0–9.0	
	13–19 y		6.0–10.1	

Nutrient	Age	Males	Either	Females
Zinc (μg/dL)	0–5 d		65–140	
	1–5 y		67–118	
	6–9 y		77–107	
	10–14 y	76–101		79–118
	15–19 y	64–104		60–101

Source: Adapted from Soldin et al.[9]

Other Biochemical Indicators of Protein Status

Somatic Protein. Assessment of lean body mass is most readily carried out by anthropometric measures such as mid-arm muscle circumference. Because muscle creatine is directly metabolized to creatinine, which is freely excreted in urine, however, urinary creatinine has been used as a biochemical indicator of total muscle mass. Analysis of 24-hour excretion of creatinine is compared to height-standardized reference values to give a creatinine height index (CHI), expressed as a percentage of the reference value. This quick and inexpensive test has been widely used as a marker of muscle protein status, although it is also influenced by factors that cause increased protein catabolism and by impaired renal function. A deficit of <15% is classed as mild, 15%–30% moderate, and >30% as severe depletion in muscle mass.

Nitrogen Balance. Nitrogen (N) balance is one of the oldest methods of assessing nutritional status and has classically been used to define amino acids requirements, because negative N balance will ensue if an essential amino acid is ingested in inadequate amounts. Children and others who should be actively gaining lean body mass should normally be in positive N balance, whereas healthy adults may be said

to be in nitrogen equilibrium if N loss is within 5% of N intake. It should be noted, however, that the mere demonstration of positive N balance disclose any information neither about N distribution throughout the body nor about the accumulation of lean body mass.

Urea, which is the main excretory product of N metabolism, appears in both urine and sweat; approximately 85% of the body's N is lost in the urine. Other sources of N loss include fecal losses, integumental losses (e.g., desquamating skin, sweat, hair, and nail growth), and miscellaneous losses (e.g., tissue fluid, saliva, vomitus, blood drawing, and menstrual losses). These losses can be high in patients with wounds or burn injuries. As most proteins contain 16% N, dietary protein intake is customarily divided by a factor of 6.25 to estimate N intake.

The equation for calculating N balance is therefore:

$$\begin{aligned}\text{N balance} &= \text{N intake} - \text{N output}\\ &= \left(\text{24h dietary protein intake in grams} \;/\; 6.25\right)\\ &\quad - \text{24h UUN} - \text{factor}\end{aligned}$$

where UUN = urine urea nitrogen (in grams), and factor = allowance made for uncollected N loss in stool, skin, and miscellaneous sources. In adults, this factor is 2–4 g/day, and in children an estimate of 10 mg/kg/day may be used.

Negative N balance can result from inadequate energy intake, inadequate protein intake, or catabolic stress and lean body mass breakdown. Positive N balance implies adequate energy and/or protein intake.

Amino Acid Profiles. Quantitative amino acid analysis can be carried out by laboratories that possess an amino acid analyzer. In practice, actual amino acid concentrations

in plasma are not as helpful as they might seem, because individual amino acids are subject to a wide range of physiological variation and their levels poorly reflect release or uptake by tissues. However, concentrations of the essential branched-chain amino acids leucine, isoleucine, and valine tend to be lower in protein–energy malnutrition and relatively higher in infection and injury. This may reflect the fact that branched-chain amino acids, unlike most others, are only minimally metabolized by the liver and are therefore available for muscle protein synthesis, which is not prominent in infection or injury.

Citrulline

The amino acid citrulline is not incorporated into proteins, nor is it commonly present in food, and thus, plasma concentrations are independent of nutritional status.[2] It is generated predominantly by small bowel enterocytes. Plasma concentrations have been shown to be highly correlated with the functioning enterocyte mass and an effective marker of intestinal failure, although it increases in renal failure and decreases with the acute phase response. In the first month of life, plasma citrulline levels are low but progressively increase with adaption to food diversification, to reach levels of around 30–50 μmol/L. In patients with short bowel syndrome, a cut-off of 20 μmol/L is predictive of long-term intestinal failure in both adults and children.

LIPIDS

Essential Fatty Acids

Fatty acids are classified according to carbon chain length, the presence or absence of one or more double bonds. Long chain fatty acids (LCFAs), which have a backbone of

12–20 carbon atoms, are the most common fatty acid configuration found in nature. LCFAs are further classified as ω-9, ω-6, or ω-3, depending on the number of carbon atoms between the terminal methyl group and its nearest double bond. Mammals can introduce double bonds in the ω-9 position only; ω-6 and ω-3 fatty acids must be supplied preformed in the diet and thus the essential fatty acids (EFA) in humans are linoleic acid ($C_{18:2}$ω-6) and linolenic acid ($C_{18:3}$ω-3). Three common clinical scenarios of EFA deficiency are (1) prolonged fasting or reliance on lipid-free parenteral nutrition, (2) extended use of a formula with a predominance of medium chain fatty acids, and (3) fat malabsorption. The clinical signs of linoleic acid deficiency include poor growth and a desquamating skin rash or redness and oozing in skin creases (deficiencies of zinc and biotin should also be considered with such skin features); however, it is much more common to diagnose EFA deficiency by biochemical profile.

Laboratory assessment of fatty acid status is complex. Most individual fatty acids can now be measured using sophisticated chromatographic techniques; results are generally expressed as a percentage of the total fatty acids. When EFA deficiency occurs, the non-EFA eicosatrienoic acid ($C_{20:3}$ω-9) increases in serum; its three double bonds make it a "triene." Conversely, arachidonic acid ($C_{20:4}$ω-9, i.e., a "tetraene") is reduced. A triene to tetraene ratio of >0.4 is consistent with EFA deficiency. Clinical features may however be apparent at this level, and some laboratories use a lower cut-off.

Carnitine. Carnitine is a small water-soluble molecule recognized to play two major physiological roles[3]: (1) facilitating the transport of long-chain fatty acids, as acylcarnitines, into the mitochondrion for the generation of energy and (2) facilitating the removal of short- and medium-chain fatty

acids that accumulate inside the mitochondrion. The main dietary sources of carnitine are red meat and dairy products, but it can be synthesized endogenously from peptide-bound lysine and methionine. In strict vegetarians, this latter source provides more than 90% of the total available carnitine. It is stored mainly in muscle (98%); liver stores comprise 1.6% and a very minor proportion exists in extracellular fluid.

Carnitine is generally considered a conditionally essential nutrient, although a clinical deficiency state has not yet been well defined in subjects who do not possess one of the rare primary inherited defects. Acquired carnitine deficiency is most likely to develop where there is reduced intake, reduced synthesis, increased requirements, or increased excretion. Both strict and lact-ovo vegetarian children have lower plasma carnitine than their omnivorous peers (approximately 30% and 20%, respectively). Newborn infants, who depend heavily on lipids as a concentrated fuel source for rapid growth in early life, also have relatively low plasma and tissue carnitine, probably due to immature synthetic pathways and a lower renal threshold for excretion. This may be of particular relevance in preterm infants, whose carnitine stores are very low compared to term infants. Critical illness has been reported to cause increased carnitine excretion, and parenteral nutrition formulas do not normally contain carnitine. Thus, the preterm sick infant who is maintained exclusively on intravenous feeding is likely to be at greatest risk for functional carnitine deficiency, which may conceivably manifest with defective energy-dependent processes (e.g., hypoglycemia, respiratory distress, delayed growth, hyperlipidemia, and developmental delay). However, administration of carnitine to preterm infants has not been shown to result in improved weight gain compared to controls.

Plasma carnitine, constituting a minute proportion of total body stores, does not necessarily reflect tissue levels,

although plasma and urine are the most amenable to sampling. Carnitine is both present as free carnitine and bound to fatty acids as acylcarnitine esters. Both total and free carnitine must be measured, because reductions in total and/or free acylcarnitines, as well as altered ratios, have been described in both hereditary and acquired carnitine deficiencies. The recent advent of tandem mass spectrometry has enabled the identification of abnormal acylcarnitines, which has been of great value in expanded newborn screening for inherited metabolic disorders, and may also help broaden our understanding of disordered carnitine metabolism.

MICRONUTRIENTS

Clinical assessment of vitamin and mineral status is indicated in Table 3-1. Reference ranges of vitamins and minerals, as well as various other laboratory nutritional parameters, are given in Table 4-1. When interpreting plasma micronutrient levels, it is important that care is exercised with results obtained during metabolic stress. It is widely accepted that acute illness results in redistribution of vitamins and trace elements for various reasons, including acute-phase response of some carrier molecules (see Table 4-3).[4–6] Monitoring of trends and magnitude of the acute-phase response (e.g., by measuring C-reactive protein concentrations) will facilitate interpretation of blood micronutrient levels. It has been suggested that plasma micronutrient concentrations can only be reliably interpreted if the C-reactive protein is <20 mg/L (plasma zinc), <10 mg/L (plasma selenium and vitamins A and D), or <5 mg/L (vitamins B_6 and C).[4]

In circumstances that make interpretation of serum concentrations difficult, indicators of function may be better predictors of the status. For example, although serum iron and transferrin (or iron-binding capacity) fall, the main

Table 4–3 Effects on Plasma Concentrations of Micronutrients by Metabolic Stress

Micronutrient	Direction of Change	Reason for Change
Iron	Decreased	↓ Transferrin
Copper	Increased	↑ Ceruloplasmin
Zinc	Decreased	↓ Albumin; redistribution
Selenium	Decreased	↓ Selenoprotein P
Vitamin A	Decreased	↓ Retinol-binding protein
Vitamin B_6	Decreased[5]	? Redistribution[5]
Vitamin C	Decreased	↑ Transfer into tissues
Vitamin D	Decreased[6]	?
Vitamin E	Decreased	↓ LDL cholesterol

storage form of iron, ferritin, rises during the acute-phase response as it is released from the liver. Conventional iron studies are therefore very difficult to interpret in the presence of acute inflammation, and it may be more helpful to look at mean red cell volume and hemoglobin concentration as indicators of iron status. Alternatively, the soluble transferrin receptor (sTfR) is a newer marker of cellular iron need and may be used either on its own or as part of the sTfR/log ferritin index.[7]

The serum concentration of vitamin B_{12} that constitutes true insufficiency is poorly defined. Macrocytosis is a well-known but late sign of B_{12} deficiency. Vitamin B_{12} is a cofactor in the remethylation of homocysteine, and a raised plasma homocysteine can be used to demonstrate a metabolic "block" due to B_{12} deficiency. However, B_{12} is not the

only cofactor involved in this pathway; folate deficiency in the presence of a common genetic polymorphism will also result in a raised homocysteine. A more specific functional test of B_{12} deficiency is urinary methylmalonic acid; this metabolite is not normally seen but appears in urine if there is a block in the conversion of methylmalonyl CoA to succinyl CoA, for which B_{12} is the only cofactor.

Other Laboratory Indicators of Nutritional Status

A complete blood count with differential white cell count is perhaps the most useful and least expensive laboratory measure of nutritional status. Lymphopenia is a well-known feature of protein–energy malnutrition due to a reduction in circulating T lymphocytes. Total lymphocyte count (TLC) can be calculated as follows:

$$\text{TLC (cells / mm}^3\text{)} = \text{white blood count} \times \text{percentage of lymphocytes}$$

With mild malnutrition, TLC is <1500; with moderate malnutrition, TLC is 800–1200; and with severe malnutrition, TLC is <800. However, TLC is both a nonspecific and an insensitive measure of nutritional status.

Another common functional test of immunocompetence and, therefore, adequate nutritional status is delayed-type hypersensitivity testing. Cutaneous anergy, a delayed or absent response to intradermal injection of antigens, is a consistent finding in moderate to severe malnutrition and has been associated with an increased risk of complications of surgery. It may result in false-negative skin testing for tuberculin, and thus failure to assess accurately for tuberculosis, of particular relevance in population screening in developing countries.[8]

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5 Nutritional Requirements: The Dietary Guidelines, MyPlate, and Dietary Reference Intakes

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The US Department of Agriculture's (USDA) Center for Nutrition Policy and Promotion (CNPP) was established in 1994 to improve the health and well-being of Americans by developing and promoting dietary guidance, bearing in mind the research and nutrition needs of consumers. CNPP's core projects support the Dietary Guidelines for Americans and the USDA Food Guidance System (MyPlate, MyPyramid, and Food Guide Pyramid). More information on CNPP or these and other projects can be found on www.cnpp.usda.gov.

The Dietary Guidelines are designed to provide easily understood, science-based information on how Americans can choose diets that promote good health (www.dietaryguidelines.gov). In 2010, the Department of Health and Human Services (HHS) and the USDA released the seventh edition of the Dietary Guidelines for Americans, which introduced three key messages:

- Balance calories with physical activity to manage weight
- Consume more of certain foods and nutrients such as fruits, vegetables, whole grains, fat-free and low-fat dairy products, and seafood

- Consume fewer foods with sodium (salt), saturated fats, trans fats, cholesterol, added sugars, and refined grains

These messages came with 23 specific recommendations (Table 5–1). *Nutrition and Your Health: Dietary Guidelines for Americans, Seventh Edition* is available to the public and can be accessed at http://www.health.gov/dietaryguidelines/dga2010/DietaryGuidelines2010.pdf. The eighth edition will be released in 2015. Table 5–2 lists federal government resources that provide reliable, science-based information on nutrition and physical activity, as well as an evolving array of tools to facilitate Americans' adoption of healthy choices.

In June 2011, MyPlate (Figure 5–1) replaced MyPyramid as a tool to promote healthy eating to consumers based on messages from the 2010 Dietary Guidelines for Americans. MyPlate includes five food groups and promotes variety and portion control in its icon, which recommends consumers build a healthy plate that is half fruits and vegetables, a quarter lean protein, and a quarter grains or starchy vegetables.

Table 5–1 Dietary Guidelines for Americans

Balancing calories to manage weight

- Prevent and/or reduce overweight and obesity through improved eating and physical activity behaviors
- Control total calorie intake to manage body weight. For people who are overweight or obese, this will mean consuming fewer calories from foods and beverages
- Increase physical activity and reduce time spent in sedentary behaviors
- Maintain appropriate calorie balance during each stage of life—childhood, adolescence, adulthood, pregnancy and breastfeeding, and older age

(*Continued*)

Table 5–1 Dietary Guidelines for Americans (*Continued*)

Food and food components to reduce

- Reduce daily sodium intake to <2300 mg and further reduce intake to 1500 mg among persons who are 51 and older and those of any age who are African-American or have hypertension, diabetes, or chronic kidney disease. The 1500-mg recommendation applies to about half of the US population, including children, and the majority of adults.
- Consume <10% of calories from saturated fatty acids by replacing them with monounsaturated and polyunsaturated fatty acids
- Consume <300 mg per day of dietary cholesterol
- Keep trans-fatty acid consumption as low as possible by limiting foods that contain synthetic sources of trans fats, such as partially hydrogenated oils, and by limiting other solid fats
- Reduce the intake of calories from solid fats and added sugars
- Limit the consumption of foods that contain refined grains, especially refined grain foods that contain solid fats, added sugars, and sodium
- If alcohol is consumed, it should be consumed in moderation—up to one drink per day for women and two drinks per day for men—and only by adults of legal drinking age.

Foods and nutrients to increase

Individuals should meet the following recommendations as part of a healthy eating pattern while staying within their calorie needs.

- Increase vegetable and fruit intake
- Eat various vegetables, especially dark green and red and orange vegetables and beans and peas
- Consume at least half of all grains as whole grains. Increase whole grain intake by replacing refined grains with whole grains
- Increase intake of fat-free or low-fat milk and milk products, such as milk, yogurt, cheese, or fortified soy beverages[6]
- Choose various protein foods, which include seafood, lean meat and poultry, eggs, beans and peas, soy products, and unsalted nuts and seeds

- Increase the amount and variety of seafood consumed by choosing seafood in place of some meat and poultry
- Replace protein foods that are higher in solid fats with choices that are lower in solid fats and calories and/or are sources of oils
- Use oils to replace solid fats where possible
- Choose foods that provide more potassium, dietary fiber, calcium, and vitamin D, which are nutrients of concern in American diets. These foods include vegetables, fruits, whole grains, and milk and milk products.

Building healthy eating patterns

- Select an eating pattern that meets nutrient needs over time at an appropriate calorie level.
- Account for all foods and beverages consumed and assess how they fit within a total healthy eating pattern. Follow food safety recommendations when preparing and eating foods to reduce the risk of foodborne illnesses.

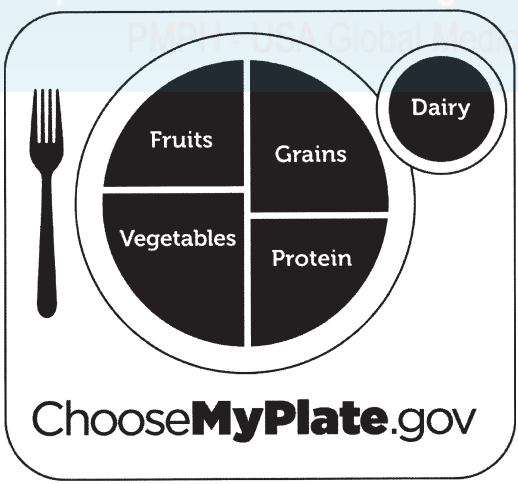

Figure 5–1: MyPlate. Accessed at www.choosemyplate.gov

The breakdown of the different food groups, examples of those foods, practical tips, and printable materials can be found on the Myplate website at www.choosemyplate.gov.

The Healthy Eating Plate (Figure 5–2), created by faculty members at the Harvard School of Public Health, has been proposed as an alternative to MyPlate. The Healthy Eating Plate visually emphasizes the importance of weight management through exercise and encourages the consumption of whole grains and plant oils rather than refined grains and animal fats. It also makes the distinction of starchy vegetables as counting toward grains. The Nutrition Source also recommends 10 nutrition tips for eating right. More information can be found on their website at http://www.hsph.harvard.edu/nutritionsource/.

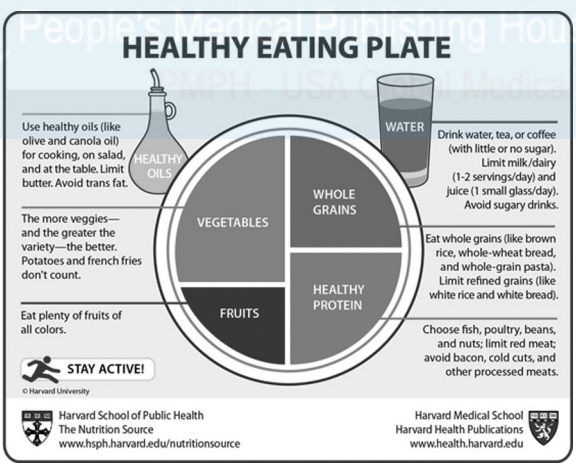

Figure 5–2: Harvard School of Public Health "Healthy Eating Plate." © 2012 The President and Fellows of Harvard College. Accessed at http://www.hsph.harvard.edu/nutritionsource/

NUTRITIONAL REQUIREMENTS/DIETARY REFERENCE INTAKES

The dietary reference intakes (DRIs) are a comprehensive set of nutrient reference values established by the Food and Nutrition Board (FNB) of the Institute of Medicine, National Academy of Sciences, in collaboration with Health Canada. The DRIs expand and replace the series of Recommended Dietary Allowances that have been published since 1941 by the FNB. Since then, an interactive guide for professionals was developed and can be accessed at http://fnic.nal.usda.gov/interactiveDRI/. The DRIs are the result of a vast expansion in our understanding of nutrients and other food components, including their role in chronic disease prevention and possible adverse effects of over consumption.

The DRIs consist of five reference intakes:

1. Recommended dietary allowance (RDA): a nutrient intake level that is used as a goal for the individual; a level sufficient to meet the nutrient requirements of nearly all (97%–98%) healthy individuals in the group. The population recommendations are broken into gender, life cycle groups (infants, elderly, etc.) with more specific age subgroups.
2. Estimated average requirement (EAR): a nutrient intake level that is estimated to meet the requirements of half of the healthy individuals in a group; a level used to assess the intake adequacy of population groups. The EAR is used along with knowledge of the distribution of requirements to develop RDAs; RDA is calculated as EAR + 2 standard deviations.
3. Adequate intake (AI): a level that is felt to meet the needs of all individuals in the group but for which there exists much less clinical data than is necessary to establish an RDA (underscoring the need for continued research on requirements for these nutrients).

4. Tolerable upper intake level (UL): the maximum level of daily nutrient intake that is unlikely to cause adverse health effects to almost all individuals of the group. These guidelines should be used to prevent consumption of too much of a nutrient.
5. Acceptable macronutrient distribution range (AMDR): the range of intake for a particular energy source that is associated with reduced risk of chronic disease while providing intakes of essential nutrients.

To date, the DRIs for six nutrient groups have been established:

1. Calcium, vitamin D (published 2011),[1] phosphorus, magnesium, fluoride (published 1997)[2])
2. Folate and other B vitamins (published 1998)[3]
3. Antioxidants (published 2000)[4]
4. Trace elements (published 2001)[5]
5. Macronutrients (published 2002; updated 2005)[6]
6. Electrolytes and water (published 2004; updated 2005)[7]

DRIs are summarized for vitamins, elements, macronutrients, and fluids and electrolytes in Tables 5–3 through 5–7.

The estimated energy requirement (EER) is defined as the dietary energy intake that is predicted to maintain energy balance in a healthy individual of a defined age, gender, weight, height, and physical activity level (PAL). EERs were determined using prediction equations developed from data on total daily energy expenditure measured by the doubly labeled water technique. In children and pregnant or lactating women, the EER includes the needs in association with the deposition of tissues or the section or milk at rates consistent with good health. EER equations and a description of PAL categories are listed in Table 5–7.

Table 5–2 Resource List from Dietary Guidelines 2010

Dietary Guidelines for Americans	http://www.dietaryguidelines.gov
Physical Activity Guidelines for Americans	http://www.health.gov/paguidelines
Healthfinder.gov	http://www.healthfinder.gov
Health.gov	http://health.gov
US Department of Agriculture (USDA) Center for Nutrition Policy and Promotion	http://www.cnpp.usda.gov
Food and Nutrition Service	http://www.fns.usda.gov
Food and Nutrition Information Center	http://fnic.nal.usda.gov
National Institute of Food and Agriculture	http://www.nifa.usda.gov
Office of Disease Prevention and Health Promotion, US Department of Health and Human Services (HHS)	http://odphp.osophs.dhhs.gov
Food and Drug Administration	http://www.fda.gov
Centers for Disease Control and Prevention	http://www.cdc.gov
National Institutes of Health	http://www.nih.gov
Let's Move!	http://www.letsmove.gov
Healthy People	http://www.healthypeople.gov
U.S. National Physical Activity Plan	http://www.physicalactivityplan.org
Nutrition.gov	http://www.nutrition.gov

The US National Physical Activity Plan is not a product of the Federal Government. However, a number of Federal offices were involved in the development of the Plan.

Table 5–3 Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals and Tolerable Upper Intake Levels, Vitamins—Food and Nutrition Board, Institute of Medicine, National Academy of Sciences

		Infants		Children		Males			
		0–6 Mo	7–12 Mo	1–3 Y	4–8 Y	9–13 Y	14–18 Y	19–30 Y	31–50 Y
Biotin (µg/d)	**RDA**/AI*	5*	6*	8*	12*	20*	25*	30*	30*
	UL	ND	ND	ND	ND	ND	ND	ND	ND
Choline (mg/d)	**RDA**/AI*	125*	150*	200*	250*	375*	550*	550*	550*
	UL	ND	ND	1000	1000	2000	3000	3500	3500
Folate (µg/d)	**RDA**/AI*	65*	80*	**150**	**200**	**300**	**400**	**400**	**400**
	UL	ND	ND	300	400	600	800	1000	1000
Niacin (mg/d)	**RDA**/AI*	2*	4*	**6**	**8**	**12**	**16**	**16**	**16**
	UL	ND	ND	10	15	20	30	35	35
Pantothenic Acid (mg/d)	**RDA**/AI*	1.7*	1.8*	2*	3*	4*	5*	5*	5*
	UL	ND	ND	ND	ND	ND	ND	ND	ND
Riboflavin (mg/d)	**RDA**/AI*	0.3*	0.4*	**0.5**	**0.6**	**0.9**	**1.3**	**1.3**	**1.3**
	UL	ND	ND	ND	ND	ND	ND	ND	ND
Thiamin (mg/d)	**RDA**/AI*	0.2*	0.3*	**0.5**	**0.6**	**0.9**	**1.2**	**1.2**	**1.2**
	UL	ND	ND	ND	ND	ND	ND	ND	ND
Vit A (µg [IU]/d)	**RDA**/AI*	400* [1320]	500* [1650]	**300 [1000]**	**400 [1320]**	**600 [2000]**	**900 [3000]**	**900 [3000]**	**900 [3000]**
	UL	600 [2000]	600 [2000]	600 [2000]	900 [3000]	1700 [5610]	2800 [9240]	3000 [10000]	3000 [10000]
Vit B_6 (mg/d)	**RDA**/AI*	0.1*	0.3*	**0.5**	**0.6**	**1.0**	**1.3**	**1.3**	**1.3**
	UL	ND	ND	30	40	60	80	100	100
Vit B_{12} (µg/d)	**RDA**/AI*	0.4*	0.5*	**0.9**	**1.2**	**1.8**	**2.4**	**2.4**	**2.4**
	UL	ND	ND	ND	ND	ND	ND	ND	ND
Vit C (mg/d)	**RDA**/AI*	40*	50*	**15**	**25**	**45**	**75**	**90**	**90**
	UL	ND	ND	400	650	1200	1800	2000	2000
Vit D (µg [IU]/d)	**RDA**/AI*	10 [400]	10 [400]	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**
	UL	25 [1000]	38 [1500]	63 [2500]	75 [3000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]
Vit E (mg [IU]/d)	**RDA**/AI*	4* [6]	5* [7.5]	**6 [9]**	**7 [10.4]**	**11 [16.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**
	UL	ND	ND	200 [300]	300 [450]	600 [900]	800 [1200]	1000 [1500]	1000 [1500]
Vit K(µg/d)	**RDA**/AI*	2.0*	2.5*	30*	55*	60*	75*	120*	120*
	UL	ND	ND	ND	ND	ND	ND	ND	ND

Abbreviations: AI, adequate intake; ND, not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts;
RDA, recommended dietary allowance.RDAs are represented in bold type. AIs are represented in regular type and are followed by an asterisk (*).
Source: Adapted from the DRI reports.[1-5]

Males		Females						Pregnancy		Lactation	
51–70 Y	**>70 Y**	**9–13 Y**	**14–18 Y**	**19–30 Y**	**31–50 Y**	**51–70 Y**	**>70 Y**	**≤ 18 Y**	**19–50 Y**	**≤ 18 Y**	**19–50 Y**
30*	30*	20*	25*	30*	30*	30*	30*	30*	30*	35*	35*
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
550*	550*	375*	400*	425*	425*	425*	425*	450*	450*	550*	550*
3500	3500	2000	3000	3500	3500	3500	3500	3000	3500	3000	3500
400	**400**	**300**	**400**	**400**	**400**	**400**	**400**	**600**	**600**	**500**	**500**
1000	1000	600	800	1000	1000	1000	1000	800	1000	800	1000
16	**16**	**12**	**14**	**14**	**14**	**14**	**14**	**18**	**18**	**17**	**17**
35	35	20	30	35	35	35	35	30	35	30	35
5*	5*	4*	5*	5*	5*	5*	5*	6*	6*	7*	7*
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
1.3	**1.3**	**0.9**	**1.0**	**1.1**	**1.1**	**1.1**	**1.1**	**1.4**	**1.4**	**1.6**	**1.6**
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
1.2	**1.2**	**0.9**	**1.0**	**1.1**	**1.1**	**1.1**	**1.1**	**1.4**	**1.4**	**1.4**	**1.4**
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
900 [3000]	**900 [3000]**	**600 [2000]**	**700 [2310]**	**700 [2310]**	**700 [2310]**	**700 [2310]**	**700 [2310]**	**750 [2500]**	**770 [2565]**	**1200 [4000]**	**1300 [4300]**
3000 [10000]	3000 [10000]	1700 [5610]	2800 [9240]	3000 [10000]	3000 [10000]	3000 [10000]	3000 [10000]	2800 [9240]	3000 [10000]	2800 [9240]	3000 [10000]
1.7	**1.7**	**1.0**	**1.2**	**1.3**	**1.3**	**1.5**	**1.5**	**1.9**	**1.9**	**2.0**	**2.0**
100	100	60	80	100	100	100	100	80	100	80	100
2.4	**2.4**	**1.8**	**2.4**	**2.4**	**2.4**	**2.4**	**2.4**	**2.6**	**2.6**	**2.8**	**2.8**
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
90	**90**	**45**	**65**	**75**	**75**	**75**	**75**	**80**	**85**	**115**	**120**
2000	2000	1200	1800	2000	2000	2000	2000	1800	2000	1800	2000
20 [800]	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**	**20 [800]**	**15 [600]**	**15 [600]**	**15 [600]**	**15 [600]**
100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]	100 [4000]
15 [22.4]	**15 [22.4]**	**11 [16.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**	**15 [22.4]**	**19 [28.4]**	**19 [28.4]**
1000 [1500]	1000 [1500]	600 [900]	800 [1200]	1000 [1500]	1000 [1500]	1000 [1500]	1000 [1500]	800 [1200]	1000 [1500]	800 [1200]	1000 [1500]
120*	120*	60*	75*	90*	90*	90*	90*	75*	90*	75*	90*
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

Table 5–4 Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals and Tolerable Upper Intake Levels, Minerals—Food and Nutrition Board, Institute of Medicine, National Academy of Sciences

		Infants		Children		Males					
		0–6 Mo	7–12 Mo	1–3 Y	4–8 Y	9–13 Y	14–18 Y	19–30 Y	31–50 Y	51–70 Y	>70 Y
Boron (mg/d)	**RDA**/AI*	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	UL	ND	ND	3	6	11	17	20	20	20	20
Calcium (mg/d)	**RDA**/AI*	210*	270*	500*	800*	1300*	1300*	1000*	1000*	1200*	1200*
	UL	1000	1500	2500	2500	3000	3000	2500	2500	2000	2000
Chromium (µg/d)	**RDA**/AI*	0.2*	5.5*	11*	15*	25*	35*	35*	35*	30*	30*
	UL	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Copper (µg/d)	**RDA**/AI*	200*	220*	**340**	**440**	**700**	**890**	**900**	**900**	**900**	**900**
	UL	ND	ND	1000	3000	5000	8000	10,000	10,000	10,000	10,000
Fluoride (mg/d)	**RDA**/AI*	0.01*	0.5*	0.7*	1*	2*	3*	4*	4*	4*	4*
	UL	0.7	0.9	1.3	2.2	10	10	10	10	10	10
Iodine (µg/d)	**RDA**/AI*	110*	130*	**90**	**90**	**120**	**150**	**150**	**150**	**150**	**150**
	UL	ND	ND	200	300	600	900	1100	1100	1100	1100
Iron (mg/d)	**RDA**/AI*	0.27*	**11**	**7**	**10**	**8**	**11**	**8**	**8**	**8**	**8**
	UL	40	40	40	40	40	45	45	45	45	45
Magnesium (mg/d)	**RDA**/AI*	30*	75*	**80**	**130**	**240**	**410**	**400**	**420**	**420**	**420**
	UL	ND	ND	65	110	350	350	350	350	350	350
Manganese (mg/d)	**RDA**/AI*	0.003*	0.6*	1.2*	1.5*	1.9*	2.2*	2.3*	2.3*	2.3*	2.3*
	UL	ND	ND	2	3	6	9	11	11	11	11
Molybdenum (µg/d)	**RDA**/AI*	2*	3*	**17**	**22**	**34**	**43**	**45**	**45**	**45**	**45**
	UL	ND	ND	300	600	1100	1700	2000	2000	2000	2000
Nickel (mg/d)	**RDA**/AI*	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	UL	ND	ND	0.2	0.3	0.6	1.0	1.0	1.0	1.0	1.0
Phosphorus (mg/d)	**RDA**/AI*	100*	275*	**460**	**500**	**1250**	**1250**	**700**	**700**	**700**	**700**
	UL	ND	ND	3000	3000	4000	4000	4000	4000	4000	3000
Selenium (µg/d)	**RDA**/AI*	15*	20*	**20**	**30**	**40**	**55**	**55**	**55**	**55**	**55**
	UL	45	60	90	150	280	400	400	400	400	400
Vanadium (mg/d)	**RDA**/AI*	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
	UL	ND	ND	ND	ND	ND	ND	1.8	1.8	1.8	1.8
Zinc (mg/d)	**RDA**/AI*	2*	**3**	**3**	**5**	**8**	**11**	**11**	**11**	**11**	**11**
	UL	4	5	7	12	23	34	40	40	40	40

Abbreviations: AI, adequate intake; ND, not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts;
RDA, recommended dietary allowance; UL, tolerable upper intake level.RDAs are represented in bold type. AIs are represented in regular type and are followed by an asterisk (*).
Source: Adapted from the DRI reports.[1,2,4,5] ©The National Academy of Sciences. Complete reports can be accessed at www.nap.edu.

Females						Pregnancy			Lactation		
9–13 Y	**14–18 Y**	**19–30 Y**	**31–50 Y**	**51–70 Y**	**>70 Y**	**≤ 18 Y**	**19–30 Y**	**31–50 Y**	**≤ 18 Y**	**19–50 Y**	**31–50 Y**
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
11	17	20	20	20	20	17	20	20	17	20	20
1300*	1300*	1000*	1000*	1200*	1200*	1300*	1000*	1000*	1300*	1000*	1000*
3000	3000	2500	2500	2000	2000	3000	2500	2500	3000	2500	2500
21*	24*	25*	25*	20*	20*	29*	30*	30*	44*	45*	45*
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
700	**890**	**900**	**900**	**900**	**900**	**1000**	**1000**	**1000**	**1300**	**1300**	**1300**
5000	8000	10,000	10,000	10,000	10,000	8000	10,000	10,000	8000	10,000	10,000
2*	3*	3*	3*	3*	3*	3*	3*	3*	3*	3*	3*
10	10	10	10	10	10	10	10	10	10	10	10
120	**150**	**150**	**150**	**150**	**150**	**220**	**220**	**220**	**290**	**290**	**290**
600	900	1100	1100	1100	1100	900	1100	1100	900	1100	1100
8	**15**	**18**	**18**	**8**	**8**	**27**	**27**	**27**	**10**	**9**	**9**
40	45	45	45	45	45	45	45	45	45	45	45
240	**360**	**310**	**320**	**320**	**320**	**400**	**350**	**360**	**360**	**310**	**320**
350	350	350	350	350	350	350	350	350	350	350	350
1.6*	1.6*	1.8*	1.8*	1.8*	1.8*	2.0*	2.0*	2.0*	2.6*	2.6*	2.6*
6	9	11	11	11	11	9	11	11	9	11	11
34	**43**	**45**	**45**	**45**	**45**	**50**	**50**	**50**	**50**	**50**	**50**
1100	1700	2000	2000	2000	2000	1700	2000	2000	1700	2000	2000
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
0.6	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
1250	**1250**	**700**	**700**	**700**	**700**	**1250**	**700**	**700**	**1250**	**700**	**700**
4000	4000	4000	4000	4000	3000	3500	3500	3500	4000	4000	4000
40	**55**	**55**	**55**	**55**	**55**	**60**	**60**	**60**	**70**	**70**	**70**
280	400	400	400	400	400	400	400	400	400	400	400
ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
ND	ND	1.8	1.8	1.8	1.8	ND	ND	ND	ND	ND	ND
8	**9**	**8**	**8**	**8**	**8**	**12**	**11**	**11**	**13**	**12**	**12**
23	34	40	40	40	40	34	40	40	34	40	40

Table 5–5 Dietary Reference Intakes (DRIs): Acceptable Macronutrient Distribution Ranges, Macronutrients—Food and Nutrition Board, Institute of Medicine, National Academy of Sciences

		Infants		Children		Males		
		0–6 Mo	7–12 Mo	1–3 Y	4–8 Y	9–13 Y	14–18 Y	19–30 Y
Carbohydrate (g/d)	**RDA**/AI*	60*	95*	**130**	**130**	**130**	**130**	**130**
	AMDR	ND	ND	45–65	45–65	45–65	45–65	45–65
Total fiber (g/d)	**RDA**/AI*	ND	ND	19*	25*	31*	38*	38*
Fat (g/d)	**RDA**/AI*	31*	30*	ND	ND	ND	ND	ND
	AMDR	ND	ND	30–40	25–35	25–35	25–35	20–35
Linoleic acid (g/d)	**RDA**/AI*	4.4*	4.6*	7*	10*	12*	16*	17*
	AMDR	ND	ND	5–10	5–10	5–10	5–10	5–10
α-Linolenic acid (g/d)	**RDA**/AI*	0.5*	0.5*	0.7*	0.9*	1.2*	1.6*	1.6*
	AMDR	ND	ND	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2
Protein (g/d) [a]	**RDA**/AI*	9.1*	**11**	**13**	**19**	**34**	**52**	**56**
	AMDR	ND	ND	5–20	10–30	10–30	10–30	10–35

Abbreviations: AI, adequate intake; AMDR, acceptable macronutrient distribution range; ND, not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts; RDA, recommended dietary allowance.RDAs are represented in bold type. AIs are represented in regular type and are followed by an asterisk (*).

[a] Based on 1.5 g/kg/d for infants, 1.1 g/kg/d for 1–3 y, 0.95 g/kg/d for 4–13 y, 0.85 g/kg/d for 14–18 y, 0.8 g/kg/d for adults, and 1.1 g/kg/d for pregnant (using pre-pregnancy weight) and lactating women.

Source: Adapted from the DRI report.[6] ©The National Academy of Sciences. Complete report can be accessed at www.nap.edu.

Males		Females					Pregnancy	Lactation
31–50 Y	>50 Y	9–13 Y	14–18 Y	19–30 Y	31–50 Y	>50 Y	14–50 Y	14–50 Y
130	**130**	**130**	**130**	**130**	**130**	**130**	**175**	**210**
45–65	45–65	45–65	45–65	45–65	45–65	45–65	45–65	45–65
38*	30*	26*	26*	25*	25*	21*	28*	29*
ND	ND	ND	ND	ND	ND	ND	ND	ND
20–35	20–35	25–35	25–35	20–35	20–35	20–35	20–35	20–35
17*	14*	10*	11*	12*	12*	11*	13*	13*
5–10	5–10	5–10	5–10	5–10	5–10	5–10	5–10	5–10
1.6*	1.6*	1.0*	1.1*	1.1*	1.1*	1.1*	1.4*	1.3*
0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2	0.6–1.2
56	**56**	**34**	**46**	**46**	**46**	**46**	**71**	**71**
10–35	10–35	10–30	10–30	10–35	10–35	10–35	10–35	10–35

Table 5–6 Dietary Reference Intakes (DRIs): Recommended Intakes for Individuals and Tolerable Upper Intake Levels, Fluids, and Electrolytes—Food and Nutrition Board, Institute of Medicine, National Academy of Sciences

		Infants		Children		Males				
		0–6 Mo	7–12 Mo	1–3 Y	4–8 Y	9–13 Y	14–18 Y	19–30 Y	31–50 Y	51–70 Y
Sodium (g/d)	AI	0.12	0.37	1.0	1.2	1.5	1.5	1.5	1.5	1.3
	UL	ND	ND	1.5	1.9	2.2	2.3	2.3	2.3	2.3
Chloride (g/d)	AI	0.18	0.57	1.5	1.9	2.3	2.3	2.3	2.3	2.0
	UL	ND	ND	2.3	2.9	3.4	3.6	3.6	3.6	3.6
Potassium (g/d)	AI	0.4	0.7	3.0	3.8	4.5	4.7	4.7	4.7	4.7
	UL	No UL [a]	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL
Water (L/d)	AI	0.7	0.8	1.3	1.7	2.4	3.3	3.7	3.7	3.7
	UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL

Abbreviations: ND, not determinable due to lack of data of adverse effects in this age group and concern with regard to lack of ability to handle excess amounts; UL, tolerable upper intake level.

[a]In the absence of ULs, extra caution may be warranted in consuming levels above recommended intakes.

Source: Adapted from the DRI report.[7] ©The National Academy of Sciences. Complete report can be accessed at www.nap.edu.

Males	Females						Pregnancy		Lactation	
>70 Y	9–13 Y	14–18 Y	19–30 Y	31–50 Y	51–70 Y	>70 Y	≤ 18 Y	19–50 Y	≤ 18 Y	19–50 Y
1.2	1.5	1.5	1.5	1.5	1.3	1.2	1.5	1.5	1.5	1.5
2.3	2.2	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3	2.3
1.8	2.3	2.3	2.3	2.3	2.0	1.8	2.3	2.3	2.3	2.3
3.6	3.4	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6
4.7	4.5	4.7	4.7	4.7	4.7	4.7	4.7	4.7	5.1	5.1
No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL
3.7	2.1	2.3	2.7	2.7	2.7	2.7	3.0	3.0	3.8	3.8
No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL	No UL

Table 5–7 Dietary Reference Intakes (DRIs): Estimated Energy Requirements—Food and Nutrition Board, Institute of Medicine, National Academy of Sciences

Category	Estimated Energy Requirements (kcal/d)
Infants and children (0–2 y)	
0–3 mo	(89 × wt [kg] – 100) + 175
4–6 mo	(89 × wt [kg] – 100) + 56
7–12 mo	(89 × wt [kg] – 100) + 22
13–35 mo	(89 × wt [kg] – 100) + 20
Males	
3–8 y	88.5 – 61.9 × age [y] + PA[a] × (26.7 × wt [kg] + 903 × ht [m]) + 20
9–18 y	88.5 – 61.9 × age [y] + PA × (26.7 × wt [kg] + 903 × ht [m]) + 25
≥19 y	662 – 9.53 × age [y] + PA × (15.91 × wt [kg] + 539.6 × ht [m])
Females	
3–8 y	135.3 – 30.8 × age [y] + PA × (10.0 × wt [kg] + 934 × ht [m]) + 20
9–18 y	135.3 – 30.8 × age [y] + PA × (10.0 × wt [kg] + 934 × ht [m]) + 25
≥19 y	354 – 6.91 × age [y] + PA × (9.36 × wt [kg] + 726 × ht [m])
Pregnancy	
14–18 y	
1st trimester	Adolescent EER
2nd trimester	Adolescent EER + 340
3rd trimester	Adolescent EER + 452
19–50 y	
1st trimester	Adult EER
2nd trimester	Adult EER + 340
3rd trimester	Adult EER + 452

Category	Estimated Energy Requirements (kcal/d)
Infants and children (0–2 y)	
Lactation	
14–18 y	
First 6 mo	Adolescent EER + 330
Second 6 mo	Adolescent EER + 400
19–50 y	
First 6 mo	Adult EER+ 330
Second 6 mo	Adult EER+ 400

[a]PA = physical activity coefficient based on physical activity level (PAL)
PA = 1.00 if PAL is estimated to be ≥ 1.0 < 1.4 (sedentary)
PA = 1.12 if PAL is estimated to be ≥ 1.4 < 1.6 (low active)
PA = 1.24 if PAL is estimated to be ≥ 1.6 < 1.9 (active)
PA = 1.45 if PAL is estimated to be ≥ 1.9 < 2.5 (very active)
Source: Adapted from the DRI report.[6] © The National Academy of Sciences. Complete report can be accessed at www.nap.edu.

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6 Breastfeeding and Human Milk

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Human milk is the preferred primary source of infant nutrition throughout the first year of life. Extensive research in the past 20 years has advanced the science of human lactation into a field supported by evidence-based practice. Breastfeeding advocates can now shift their efforts from promoting the benefits of breast milk (Table 6–1) to supporting mothers to ensure breastfeeding success and duration.

Table 6–1 Benefits of Breast Milk

Nutrition Components
Protein
• Whey predominant ratio to casein (60:40 in mature milk), easily digestible
• Promotes rapid gastric emptying
• High biological value protein
• Provides immunological defense

(*Continued*)

Table 6–1 Benefits of Breast Milk (*Continued*)

Nutrition Components
Fat • Provides 40%–50% calories • Hindmilk may contain twice as much fat as foremilk • Preterm mother's milk has 30% higher fat concentration • Bile salt–stimulated lipase and lipoprotein lipase readily break down triglycerides • Contains essential fatty acids • Long-chain fatty acids: docosahexanoic acid and arachadonic acid may improve vision and cognition • Cholesterol: essential for central nervous system development, may influence cholesterol metabolism **Carbohydrate** • Lactose: enhances calcium absorption, breaks down into galactose and glucose for energy to the brain • Amylase: aids in the digestion of starch, may also aid with glucose polymers **Nonprotein Nitrogen** • free amino acids for growth, higher percentage found in colostrum
Vitamins, Minerals, and Recommendations for Supplements
Vitamin D • Infants born to vitamin D–deficient mothers are at risk for vitamin D deficiency • The vitamin D content of human milk is related to the lactating mother's vitamin D status • High-dose vitamin D supplementation in the lactating mother results in increased vitamin D levels in human milk; universal supplementation has not yet been validated • Though not common, rickets may occur in the breastfed infant • Risk of rickets increases for infants with dark skin, little exposure to sunlight (due to sunscreen, cold weather climates, and heavy clothing)

- AAP recommends supplementation of 400 IU vitamin D per day to all infants and children, including adolescents, beginning soon after birth to prevent deficiency[4]

Fluoride

- Breast milk has low fluorine content
- Every child should begin to receive oral health risk assessments by 6 mo of age by a qualified pediatric health care professional
- Infants who breastfeed throughout the night should be referred to a dentist as early as 6 mo of age and no later than 6 mo after the first tooth erupts or 12 mo, whichever comes first[5]
- Supplementation:[6]
  - < 6 months: none
  - 6 mo to 3 y: 0.25 mg if local water fluoride content is deficient

Iron

- Iron content: 0.5–1.0 mg/L
- Absorption from breast milk is efficient
- Term infants should have sufficient iron stores for first 6 mo of life
- Additional iron is received from iron-rich solids in the second 6 mo of life
- Iron supplementation usually not necessary and may decrease anti-infective properties of lactoferrin in breast milk
- Preterm infants may require iron supplementation

Vitamin K

- All infants, breastfed or not, must receive vitamin K at birth

Water

- Breast milk contains 87.5% water, will provide adequate hydration with adequate intake
- Supplements not recommended, even in hot/humid climates
- Water supplements are nutritionally void and may exacerbate hyperbilirubinemia in the newborn

(*Continued*)

Table 6–1 Benefits of Breast Milk (*Continued*)

Protection Against Infection and Allergy
• Secretory immunoglobulin A (sIgA): passive immunologic protection through the enteromammary immune system • Lactoferrin: iron-binding protein, reduces the iron-binding sites available for iron-dependent pathogens • Lysozyme: antimicrobial factor • ***Lactobacillus bifidus***: promotes the growth of beneficial bacteria, inhibits growth of enteropathogens • Leukocytes: includes macrophages and lymphocytes to fight infection • Low risk of contamination of feeding if fed directly from breast
Reduced incidence and/or severity of the following: • Diarrhea • Otitis media • Respiratory tract infection • Bacteremia • Bacterial meningitis • Late-onset sepsis in preterm infants • Urinary tract infection • Necrotizing enterocolitis (NEC)
Possible protection against the following: • Sudden infant death syndrome (SIDS) • Insulin-dependent and non-insulin dependent diabetes mellitus • Crohn's disease • Ulcerative colitis • Lymphoma, leukemia, and Hodgkin's disease • Allergic diseases, asthma • Overweight, obesity, hypercholesterolemia • Other chronic digestive diseases
Physiologic
• Low renal solute load: aids in kidney function • Aids in intestinal maturation (through growth factors and hormones)

- Infant self-regulates intake based on need through "feeding on demand"

Breast milk composition changes based on infant need

- Colostrum, transitional and mature milk, preterm vs. term milk
- Changes occur during each feeding (foremilk to hindmilk), from am to pm, throughout entire breastfeeding course (newborn though older infant or toddler)

Psychological

- Bonding between mother and infant
- Mutual caregiving

Maternal Health Benefits

- Increased levels of oxytocin that lead to less postpartum bleeding, rapid uterine involution
- Earlier return to prepregnancy weight
- Increased child spacing and decreased menstrual bleeding due to delayed resumption of ovulation
- Improved bone re-mineralization postpartum
- Reduction in hip fractures and osteoporosis in the postmenopausal period
- Reduced risk of ovarian cancer
- Reduced risk of premenopausal breast cancer

Community

- Parents have more time available for infant/siblings (no need to obtain and prepare formula and decreased infant illness)
- Reduced parental employee absenteeism secondary to decreased infant and child illness
- Reduced lost family income secondary to less absenteeism at work
- Decreased annual health care costs
- Decreased costs for public health programs such as Women, Infant and Children Nutrition Program (WIC)—a government subsidized free program that provides healthy foods, nutrition, and health information to families who qualify
- Decreased environmental burden and energy demands for production, transport, and disposal of formula products

(*Continued*)

Table 6–1 Benefits of Breast Milk (*Continued*)

Community
• Cost savings could be put toward breastfeeding education and support programs • Improved retention of experienced employees who are provided with workplace lactation support programs and the ability to express milk with a pump after returning from maternity leave

Source: Adapted in part from American Academy of Pediatrics, Section on Breastfeeding.[2]

The World Health Organization recommends infants receive breast milk exclusively through the first 6 months of life and continue to receive breast milk along with nutritionally adequate and safe complementary foods for up to two years of life or beyond.[1] The American Academy of Pediatrics supports exclusive breast milk feeding to approximately six months of life, recognizing infants may be developmentally ready to take complementary foods between 4 and 6 months of age, with continued breastfeeding through the first year of life and beyond.[2]

In January 2011, Surgeon General Regina M. Benjamin released *The Surgeon General's Call to Action to Support Breastfeeding* that identifies ways to improve breastfeeding rates and increase support for breastfeeding.[3] It is the responsibility of every health care provider who works with mothers and infants to educate them to provide breastfeeding support or to refer to experts such as International Board Certified Lactation Consultants to help their families meet their breastfeeding goals. The following tables, recommended reading, and resources provide easy reference to assist families toward successful, exclusive breastfeeding (Tables 6–2 through 6–9).

Table 6–2 Initiating Breastfeeding

Perinatal

- Choose a midwife, OB-GYN, and pediatrician who support breastfeeding
  - Discuss with health care provider any prior breastfeeding history or difficulties, clarify concerns, and dispel myths
  - Request health care provider perform breast examination to identify anatomical concerns that may affect latch or milk production
  - Request prenatal referral to lactation consultant for anticipatory guidance, if needed
- Choose a birth center/hospital that strives to be "baby-friendly" (Table 6–8)
  - Employs clinical staff who are knowledgeable and supportive of breastfeeding
  - Encourages breastfeeding as soon as possible after delivery
  - Lactation consultant will be available soon after birth and later as needed until breastfeeding is well established
  - Rooming-in of mother and infant is practiced
  - Hospital staff will not provide formula unless medically necessary
  - Birth facility does not distribute "Formula Company Discharge Bags"[7]
- Attend prenatal classes and read about breastfeeding
- Observe another mother successfully breastfeeding her infant to visualize latch and positioning
- Identify support person(s): family or friends with positive breastfeeding experience, new mothers group, or breastfeeding peer counselors for help after birth
- Obtain quality breast pump if mother plans to return to work/school while breastfeeding

Postpartum

- Initiate breastfeeding as soon as possible after birth, preferably within first half hour

(*Continued*)

Table 6–2 Initiating Breastfeeding (*Continued*)

- Encourage feeding "on demand," as frequent as every hour, no more than 4 hours between feeds
- Help mother identify changes in infant state and hunger cues: rooting, sucking on hand, fussiness, awake state; crying is a late cue for hunger
- Intermittent assessment of mother and infant breastfeeding by clinical staff is essential to observe positioning, infant latch, suck, swallow, and milk transfer (Table 6–3)
- Referral to International Board Certified Lactation Consultant to resolve problems or for ongoing support after discharge

Separation of mother and infant

- Initiation of breast milk expression as soon as possible if infant unable to feed from the breast (Table 6–4)
- Teach manual expression of colostrum to provide small volumes in first several days before the onset of milk production and to support increased milk production later
- Recommend mother pump every 3 h, including through the night, to establish milk supply
- Instruct mother on proper storage and handling techniques for expressed breast milk (Table 6–5)

Alternative methods of feeding breast milk

- Suggest alternatives when mother not available to provide every feeding at breast or infant unable to sustain effective latch
- Methods include spoon, syringe, cup feeding, finger feeding or a supplemental nursing system
- Spoon or syringe/eye dropper can provide small amounts of colostrum to newborn to entice infant to breast, stimulate hunger, and provide nutrition/hydration
- Methods should be used judiciously and with proper instruction
- May prevent nipple preference for bottle feeding in healthy newborn while learning to breastfeed
- May aid transition from tube feeding to feeding at breast

Establishing milk production

- Milk supply is dependent on regular milk removal, either by infant or breast pump
- Mother should offer breast 8–12 times per 24 h, waking newborns if more than 4 h have passed
- Newborn infants initially breastfeed every 1–3 h, may go longer between feedings in later infancy
- Mother must breastfeed or express milk during the night
- Alternate initial breast offered at each breastfeeding session to stimulate milk production equally in both breasts
- Note that most breastfed infants initially breastfeed more frequently than formula-fed infants take their bottle

Causes of inadequate breast milk production

- Ineffective milk removal due to poor latch, insufficient duration, and/or infrequent breastfeeding are common and preventable causes of low milk volume
- Hesitation/failure to wake sleeping baby to feed after long duration between feeds
- Excessive use of a pacifier may mask feeding cues and cause missed feeds
- "Sleepy" or "good" baby demands fewer feedings, difficult to wake to feed
- Jaundiced infant—infrequent feeds, increasing bilirubin levels, decreased demand
- Mother unaware of necessity of frequent feeds, especially early postpartum
- Intermittent formula feeding leads to missed opportunities to breastfeed and produce more milk
- Maternal intrapartum blood loss, trauma, excessive intravenous fluids during delivery
- Maternal stress, dehydration, rapid weight loss
- Maternal medication or herbal therapy that inhibits milk supply
- Primary, congenital insufficient glandular tissue of mother
- History of maternal breast reduction surgery

(*Continued*)

Table 6–2 Initiating Breastfeeding (*Continued*)

Premature infants[8]

- Colostrum or breast milk should be the first enteral feeding for premature infants
- If mother's own milk is unavailable, consider the use of donor human milk from a human milk bank
- Provide lactation support to mother to initiate and maintain milk supply with long-term pumping
- Fortification of human milk may begin before full feeding volumes are achieved
- Consider provision of higher calorie hindmilk to promote infant growth
- Encourage skin to skin (Kangaroo) care with mother to promote physiologic stability in infant, increased maternal breast milk volumes, passive immunity through breast milk, and increased duration of breastfeeding
- Encourage infant's first feeding by mouth to be at breast; this may be non-nutritive suckling concurrent with tube feeding of expressed breast milk
- Weighing infant before and after feedings, use of nipple shields or alternative feeding methods (cup, syringe, and supplemental nursing system) may help transition to breast
- Late preterm infants (34–37 wk gestation) are at increased risk of breastfeeding difficulties and hospital readmission for inadequate weight gain, jaundice, and feeding problems

Table 6–3 Assessment of Breastfeeding

Positioning, latch, and milk transfer (swallowing) are key components to effective breastfeeding

Positioning

- Mother should be comfortable, supported with pillows and/or foot rest to keep her body position relaxed

- Infant may be positioned in a cradle, cross-cradle or modified clutch, side-lying, clutch or "football" hold; or mother may be in a semi-reclining or "laid back" position with infant prone
- Mother's hand should be positioned on infant's back at upper shoulders, gently supporting base of head (occiput) but NOT holding head and forcing it toward breast
- Infant should be at the level of the breast to prevent neck strain
- Mother may need to support breast—U-hold, C-hold, scissor or V-hold, dancer-hand hold

Latch

- Tickle infant's middle upper lip (philtrum) with nipple to elicit rooting reflex (infant opens mouth wide)
- As infant opens mouth wide, draw infant to breast in one quick movement—do not push on the back of the head
- Lips should be flanged wide and flipped outward taking in as much of the nipple and areola into the mouth as possible
- Latch should be asymmetrical with chin in deep to breast and infant nose/head slightly tipped back
- If latch is not right the first time, release latch and try again (place finger in corner of baby's mouth to break seal)

Important: Breastfeeding should not hurt. Refer to International Board Certified Lactation Consultant if mother expresses pain, soreness, cracked nipples, or bleeding.

Milk transfer (swallowing)

- When suckling, deep intermittent jaw excursions are visible along the jaw toward the ear
- Audible swallowing is heard; soft "puffs" of air to loud gulping
- Infant appears satiated after the feeding: relaxed posture, soft facies, and sleeps between feeds
- Mother's breast feels softer after feeding
- Urine output—after the onset of milk production and approximately on day 5, infant should have six or more wet diapers per day; urine is clear to light yellow; urine is not dark, concentrated, or foul smelling

(*Continued*)

Table 6–3 Assessment of Breastfeeding (*Continued*)

- Stool output—stools transition from meconium dark to brown to green to yellow over first several days; after day 5, infant has three or more yellow seedy stools, loose, small volume; frequency of stools changes as infant grows
- Weight gain—approximately 5–7 oz/wk after initial weight loss in first days

Inadequate milk intake

- Infant is lethargic, not waking on own to feed, or is difficult to wake for feeding
- Infant is feeding <8–12 times per 24 h in first weeks
- Little or no swallowing is heard at breast
- Mother reports sore nipples, develops creased or cracked nipples
- Mother has engorged, painful breasts making latch difficult
- Breasts are not relieved (softened) by feeding baby
- Infant's urine output is scant, dark in color, concentrated, or absent
- Infant's stools are minimal (<3/d after day 3) and do not turn yellow by day 4 or 5
- Infant continues to lose weight
- Infant is jaundiced—may be physiologic, but need to rule out exaggerated jaundice

If infant is not receiving sufficient breast milk, supplementation is necessary

- Mother should initiate breast milk expression with a pump to increase or maintain milk supply (Table 6-4)
- Provide colostrum or breast milk to infant through syringe, cup, and bottle
- If mother unable to express milk, give appropriate infant formula, not water
- Water or dextrose water will not prevent hyperbilirubinemia
- Close follow-up for weight monitoring and breastfeeding assistance is essential

Table 6–4 Expression of Breast Milk

Breast milk expression or removal with a breast pump is necessary to initiate or maintain milk production whenever the infant is unable to feed directly at the breast due to the following:

- Maternal or infant illness requiring hospitalization
- Infant prematurity
- Infant unable to breastfeed (i.e., neurological problems and anatomical problems such as cleft palate)
- Infant/child requires surgery (temporarily unable to feed by mouth and ventilator dependent)
- Mother has returned to work or school
- Mother needs to travel away from baby (pleasure or work, short or long term)
- Mother has temporary need for a medicine that is contraindicated for breastfeeding
- To relieve engorgement from delayed or missed breastfeeding
- Or to increase mother's milk supply when baby has poor latch, inadequate suck, or decreased ability to remove milk from breast

Types of breast pumps

- Manual (hand) expression—no cost, requires practice to be effective, excellent for occasional relief and milk removal when away from baby or to entice infant to breastfeed
- Manual breast pump—low cost ($20–$50), requires no batteries or electricity, effective for occasional milk removal, separation from breastfed infant for short periods of time (<6 h) or to relieve engorgement and draw out nipple to facilitate latch; not for maintenance of milk supply
- Battery-operated or small electric pump—moderate cost ($75–$150), requires batteries or electricity to use, portable, excellent for short-term separations, part-time work or school, not for maintenance of milk supply or long-term separation

(*Continued*)

Table 6–4 Expression of Breast Milk (*Continued*)

- Professional quality electric breast pump for single or double breast expression—higher cost ($200–$350), preferred for full-time work or school, longer separations from infant, possible use for hospitalized infant after milk supply established, may be covered by health insurance
- Multi-User electric breast pump (resources in Table 6–9) — available for use in hospitals or for rent from durable medical supply stores, private lactation consultants, and maternity specialty stores; effective for initiating and maintaining milk supply for extended periods of time when unable to breastfeed directly and may be covered by health insurance for medically necessary separation. Each user requires individual attachment kit for use of breast pump.

Use of a breast pump

- Read all instructions before use, clean breast pump attachment pieces before use
- Wash hands before pumping
- Find a clean area to express milk; pumping should NOT occur in a bathroom facility
- Use only clean bottles or storage containers; single-use containers are preferred for hospital use; breast milk storage bags should not be used in the hospital setting
- Begin with breast massage to initiate let-down and start milk flowing
- Center breast pump flanges/funnels over nipples and start pump; larger size flanges may be needed for larger nipples/areola to remove milk and prevent discomfort when pumping
- Start with low suction and increase suction strength and rate to maintain comfort and to maximize milk flow
- If pumping one breast at a time, massage breast while pumping to help increase flow, and alternate breasts every 5 min
- Pump each breast 10–15 min (or both together for 10–15 min) or until milk flow decreases

- Double pumping preferred for long-term expression to maximize supply, decrease time needed to pump
- For exclusive pumping, pump every 3 h, including during the night until milk supply is established, then individualize schedule according to milk production

Goals for milk expression

- Exclusive pumping—milk expression of 6–8 times daily (or more), or minimum 100 min of pumping time in 24 h
- Part-time pumping—milk expression once for every 3 h of separation from infant (i.e., 2 times in 8-h work day)
- Volume—500 mL/d after day 5 or onset of milk production, >500 mL/24 h after first week, increasing to750–1000 mL/24 h

Handling and storage of breast milk

- In hospitals and day care settings: all milk should be labeled with infant's name, the date and time mother expressed the milk, and expiration date if previously frozen
- To retain highest level of anti-infective and nutritional properties of breast milk, always provide baby with freshly pumped milk first, then refrigerated-only, and then previously frozen (thawed)
- When giving stored milk, provide colostrum first, then oldest dated milk
- To thaw breast milk, place in refrigerator overnight, or use a warm water bath (do not submerge top of container to avoid water leaking in and contamination)
- NEVER microwave breast milk, as it can negatively affect immune properties of breast milk; uneven heating causes hot spots and can burn infant mouth

Refer to **Table 6–5** for storage times and utilize the Human Milk Banking Association of North America guidelines for more detailed information about storing and handling human milk.[9]

Table 6–5 Breast Milk Storage Guidelines

	Room Temperature	Refrigerator	Freezer (Standard (20°C)
Fresh breast milk	At home ≤6 h Refrigerate milk immediately if not to be used within 6 h	≤5 d Do not store on door	Ideal: 3 mo Optimal: ≤6 mo Acceptable: ≤12 mo Place milk toward back of freezer, not in door; shorter storage times preserve fat content of human milk
	In hospital ≤4 h Refrigerate milk immediately if possible For continuous tube feedings, use an enteral syringe feeding pump and change syringe of breast milk every 4 hours	2–4 d	Ideal: 1 mo Optimal: 3 mo Acceptable: ≤ 12 mo
Thawed breast milk	At home 1 h (left over warmed milk should be discarded after the feed)	24 h Re-label after thawing with date and time thawed	DO NOT REFREEZE
	In hospital ≤4 h at room temperature	≤ 24 h	DO NOT REFREEZE

Source: Adapted from HMBANA Guidelines[9] 2011.

Table 6–6 Weaning

Weaning is initiated when other foods or fluids are introduced to the breastfed infant and ends with the last breastfeeding. Timing of weaning varies according to cultural and social influences and individual mother and infant needs. Continued partial breastfeeding into the second year of life and worldwide breastfeeding duration of 2–4 y with gradual weaning are normal. Weaning can be an emotional experience. Many mothers feel sad, guilty, or uncertain about the many changes weaning brings to their relationship with their baby.

Gradual weaning

- Preferred method, occurs over weeks, months, or years
- Allows milk supply to taper off and maintains maternal comfort
- Child continues to breastfeed a few times daily while learning new feeding skills
- If intentional: eliminate one feed every 3 d until no longer breastfeeding
  - Skip feeding the child is least interested at first; this is often when the child eats solids
  - Distract child with other activities, like reading a story or going for a walk, at times when he/she is used to breastfeeding
  - Infants under 1 y require an alternative source of infant milk
- Younger infants may have continued sucking needs after weaning; offer a bottle, pacifier, or thumb depending on the age of the baby
- Avoid weaning when a child is sick or going through other changes (new sibling, daycare) as it will be more difficult and stressful to wean

Abrupt weaning

- Emergent, unplanned, outside influence, or forced by mother or infant
- If temporary wean, mother should pump and save or discard milk as appropriate

(*Continued*)

Table 6–6 Weaning (*Continued*)

- If a mother needs to wean unexpectedly and quickly, it is important not to stop all at once; mother's breasts may become swollen and painful, and she can develop a breast infection
  - If baby is unable to breastfeed, use a breast pump to remove milk
  - Skip every other feeding the first day; if mother usually feeds her baby or pumps 8 times a day, then decrease to 4 times
  - Skip another 1 or 2 feedings the next day
  - On the third day, pump or breastfeed only 1 or 2 times
  - Continue until no longer breastfeeding
- Pump only enough milk to relieve the breast fullness not enough to drain completely; sometimes hand expressing a small amount of milk is all that is needed
- Use cold compresses to relieve the discomfort and swelling
- Wear a bra that fits comfortably for support; do not bind breasts tightly
- Some women can squeeze out a few drops of milk for several months after weaning is complete

Mothers who wean after their baby has died may choose to donate their expressed breast milk to a milk bank. For more information on this process, see the Human Milk Banking Association website www.hmbana.org

Table 6–7 Conditions for Which Breastfeeding May Be Contraindicated

Although most women are able to breastfeed their infants, certain situations exist when breastfeeding must be temporarily halted, limited, discontinued, or avoided

Galactosemia

Infants with galactosemia must receive a lactose-free formula

PKU (Phenylketonuria)

Although low in phenylalanine, provision of breast milk should be given in conjunction with prescribed levels of Phenalalanine-free formula for infants with PKU

Tuberculosis
Women with untreated, active tuberculosis should not breastfeed. The tubercle bacillus are present in breast milk. Mother should initiate pumping to maintain supply and discard milk until 2 or more weeks of treatment is complete and mother is no longer contagious, then breastfeeding can resume.

Hepatitis
Hepatitis A—mother can breastfeed after receiving gamma globulin
Hepatitis B—infant should receive hepatitis B immune globulin (HBIG) and first dose of Hep B immunization before discharge from hospital; breastfeeding can occur from delivery
Hepatitis C—breastfeeding NOT contraindicated unless co-infected with HIV

HIV/AIDS[10]
In developed countries, mothers with HIV should avoid breastfeeding and feed their infants with formula
In low- and middle-income countries where formula feeding is not affordable or safe, the World Health Organization recommends national authorities decide on an infant feeding practice that will be supported by Maternal Child Health services:

1. breastfeeding with the protection of antiretroviral (ARV) medication to reduce transmission
2. or avoidance of all breastfeeding

Breastfeeding and ARV intervention together have the potential to significantly improve infants' chances of HIV-free survival.
For mothers known to be HIV-infected, ***exclusive*** breastfeeding for the first 6 mo of life (no addition of water or food) and continued breastfeeding up to the age of 12 mo with complementary feedings is recommended.

HTLV-1
Mothers with human T-lymphotropic virus 1 should not breast-feed their babies due to risk of vertical transmission

Maternal medications
Most medications are considered compatible with breastfeeding
Consult appropriate scientific literature not manufacturer/pharmacy inserts to assess risk of infant exposure to medication
Weigh risks to infant of NOT breastfeeding and support ongoing breastfeeding whenever possible

(*Continued*)

Table 6–7 Conditions for Which Breastfeeding May Be Contraindicated (*Continued*)

Minimize effects of medications

- Administer medication immediately after breastfeeding to minimize exposure to infant by allowing time for absorption and excretion before the next feeding
- Choose short-acting medications not long-acting doses
- Choose an alternative medication or delay treatment if able
- Mother can pump and discard milk until medication therapy is complete

Resources for medications and breastfeeding

- Infant Risk Center at Texas Tech University http://www.infantrisk.com/category/breastfeeding
- National Library of Medicine, Drugs and lactation database (LACTMED) http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT
- *Medications and Mother's Milk*. Thomas Hale; published every 2 y[11]

Drugs of abuse

Drugs of abuse for which adverse effects on the infant during breastfeeding have been reported are amphetamine, heroin, phencyclidine (PCP), cocaine, marijuana

Must evaluate risk of mother continuing to use these drugs; if mother not likely to remain drug-free, infant should not be breastfed

Mothers receiving treatment with Methadone maintenance may breastfeed; neonates may show withdrawal symptoms related to *in-utero* exposure regardless of breastfeeding

Table 6–8 The Ten Steps to Successful Breastfeeding

The Baby-Friendly Hospital Initiative is a global program sponsored by the World Health Organization and the United Nations Children's Fund to encourage and recognize hospitals and birthing centers that offer an optimal level of care for infant feeding (from www.babyfriendlyusa.org). Implementation of the following 10 steps can earn an institution the designation of "Baby-Friendly Hospital":

1. Have a written breastfeeding policy that is routinely communicated to all health care staff

2. Train all health care staff in skills necessary to implement this policy
3. Inform all pregnant women about the benefits and management of breastfeeding
4. Help mothers initiate breastfeeding within an hour of birth
5. Show mothers how to breastfeed and how to maintain lactation, even if they should be separated from their infants
6. Give newborn infants no food or drink other than breast milk, unless medically indicated
7. Practice "rooming in" by allowing mothers and infants to remain together 24 h a day
8. Encourage breastfeeding on demand
9. Give no pacifiers or artificial nipples to breastfeeding infants
10. Foster the establishment of breastfeeding support groups and refer mothers to them on discharge from the hospital or birthing center

Table 6–9 Breastfeeding Information, Advocacy, and Professional Education

International Lactation Consultant Association (ILCA)
1-888-ILCA-IS-U (452-2478)
http://www.ILCA.org
Maintains a database to "Find a Lactation Consultant," resources for professional lactation education and lactation consultant certification requirements

International Board of Lactation Consultant Examiners (IBLCE)
703-560-7330
http://www.iblce.org
An independent international certification body conferring the International Board Certified Lactation Consultant (IBCLC) credential and examination requirements. Maintains list of education providers and registry of IBCLCs.

La Leche League International (LLLI)
1-800-LALECHE (525-3243)
http://www.LaLecheLeague.org
Peer support and breastfeeding resources. Local chapter listings.

(*Continued*)

Table 6–9 Breastfeeding Information, Advocacy, and Professional Education (*Continued*)

Human Milk Banking Association of North America (HMBANA)
817-810-9984
http://www.hmbana.org
Healthy People 2020 Objectives for Improving Health: Maternal, Infant and Child Health Indicators MICH-21.1–21.5.
http://www.healthypeople.gov/2020

National Alliance for Breastfeeding Advocacy (NABA)
http://www.naba-breastfeeding.org

Infant Feeding Action Coalition (INFACT) Canada
http://infactcanada.ca/

World Alliance for Breastfeeding Action (WABA)
http://www.waba.org.my/

Breast Pump Information:
Ameda (Evenflo Company, Inc.)
1-866-99-AMEDA
http://www.Ameda.com

Medela, Inc. Breastfeeding US
1-800-435-8316
http://www.medela.us/

Hygeia II Medical Group, Inc.
1-888-PUMP-4-MOM (786-7466)
www.hygeiababy.com

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7 Feeding Guidelines for Infants, Toddlers, and Children

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Infants, toddlers, and children need good nutrition for growth and development. Each child grows at a unique rate and therefore has unique nutritional needs. This chapter reviews feeding guidelines from infancy through school age. The following are general guidelines to follow when feeding infants and children; they should not be viewed as precise.

INFANT NUTRITION

Breast milk is the ideal food for most infants, because it has the right balance of nutrients. It also has many benefits for mother and child (see Chapter 6 for more details). Iron-fortified infant formula can be a good alternative to human milk for those women who cannot breast-feed or choose not to. During the first 4–6 months, breastfeeding or infant formula should be the only source of nutrition. Infants should progress to complementary foods between the ages of 4 and 6 months.

The transition to solid foods is based on multiple factors including developmental signs of readiness. Texture, consistency, type, and amount of solid food offered should

complement the infant's feeding skills and the development of the gastrointestinal tract (see Table 7–1, which outlines the normal development of sucking and chewing skills).

Table 7–1 Oral Motor and Feeding Development[1]

Age	Feeding & Oral Motor Development	Food Types & Textures	Tips for Successful Eating
0–4 mo	• Roots in search of nipple • Sucking and tongue thrusting are reflexes	• *Liquids*: breast milk or formula	• If baby is gassy, recommend an angled bottle
4–6 mo	• Reflexive suck diminishes • Opens mouth for spoon but tongue thrust still present • May gag easily with purees • May put things in mouth to practice biting	• *Liquids*: breast milk or formula • *Smooth purees*: infant cereal, stage 1 or 2 purees	• Use a baby spoon; allow baby to suck off the spoon instead of "dumping" food into mouth or scraping food off the roof of mouth
6–8 mo	• Spoon feeding improves and baby can tolerate thicker purees • Craves a variety of textures including hard teething foods and dissolvable solids • Tongue moves side to side and tongue thrust disappears	• *Liquids:* breast milk or formula • *Smooth purees*: infant cereal, stage 1 or 2 purees • *Thick purees:* homemade or blenderized purees	• Use long, stick-shaped foods, so that the baby can put the food to the molar area to practice biting and munching

(*Continued*)

Table 7–1 Oral Motor and Feeding Development[1] (*Continued*)

Age	Feeding & Oral Motor Development	Food Types & Textures	Tips for Successful Eating
	• Learns to drink from a ***sippy*** cup (training cup with a spout)	• *Teething biscuits* • *Crunchy dissolvable solids*	• Early *sippy* cups should allow liquid to flow through the spout easily; the valve can be replaced once the baby learns to suck from a *sippy* cup
8–10 mo	• Refines biting and munching • Can eat most soft and dissolvable foods but may gag frequently as child experiments with more mature foods • Wants to self-feed	• *Liquids:* breast milk or formula • *Smooth purees* • *Thick purees* • *Crunchy dissolvable solids* • *Soft well-cooked vegetables* • *Very well-cooked or ground meat*	• Cut solids into an appropriate size (cubed or stick shape), so that little fingers and mouths can manipulate them easily • If the baby gags easily, that particular food may still be too advanced for skill level
10–12 mo	• Eats a variety of table foods • Begins to show more efficient chewing of most soft table foods • Still gags with harder to chew foods	• *Liquids:* breast milk or formula • *Smooth purees* • *Thick purees* • *Crunchy dissolvable solids*	• Encourage self-feeding as much as possible • Keep offering the baby new foods even if baby refuses it

Age	Feeding & Oral Motor Development	Food Types & Textures	Tips for Successful Eating
		• *Soft well-cooked vegetables* • *Very well-cooked or ground meat*	• Baby may spit food out when learning how to eat and chew that food successfully
12–16 mo	• Refines self-feeding skills, preferring to use utensils • Can drink from a straw cup	Mostly all table foods including some raw fruits and vegetables	• Provide utensils with short handles and cups with handles

Table 7–2 American Academy of Pediatrics' Infant Feeding Recommendations[2]

- Introduce solid foods when the infant is developmentally ready, between 4 and 6 mo. Iron-, zinc-, and protein-rich foods, such as iron-fortified cereals or pureed meats as first food to offer
- Single-ingredient food should be offered every 3–5 d to observe any adverse reactions. When each single-item food is tolerated, the infant can begin consuming mixed foods that contain only these previously tolerated items
- To establish healthy eating patterns during childhood, it is important to introduce a variety of foods by the first year of life. It can take 8–15 tries for infant or child to accept a new food
- Juices may be introduced after 6 mo of age to the infant; if introduced, 100% juices should be used, and juice should be limited to 4–6 oz daily for 1–6 y olds in a cup
- Delay introduction of cow's milk until 1 y of age; cow's milk should be whole milk during the second year of life

The American Academy of Pediatrics (AAP) recommendations for general infant feeding practices is listed in Table 7–2.

Amount of solid foods consumed varies by infant. General recommendations for feeding solid foods to infants are included in Table 7–3.

Table 7–3 General Feeding Guidelines for Infants

0–4 mo	Frequent feedings or nursing (8 or more per day, 16–32 oz in total)
4–6 mo	Frequent feedings or nursing (5 or more per day, 24–40 oz in total) 2–3 teaspoons boxed iron-fortified infant cereal (rice, oatmeal, or barley) mixed with formula, breast milk, or water, or stage 1 or 2 purees
6–8 mo	On demand feedings or nursing (5 or more per day, 24–32 oz total) 4–6 tablespoons iron-fortified cereal 1 small serving of crackers, toast, dry unsweetened cereal, or other dissolvable solid 3–7 tablespoons of soft, cooked, mashed fruit 3–7 tablespoons of soft, cooked, mashed vegetables
8–10 mo	On demand feedings or nursing (16–32 oz total) 8–12 tablespoons iron-fortified cereal 1 small serving of crackers, toast, or dry unsweetened cereal 8 tablespoons potato, pasta, rice, or other starch 7–8 tablespoons Junior, soft, cooked, or mashed fruit 7–8 tablespoons Junior, soft, cooked, or mashed vegetables 3–4 tablespoons Junior, chopped, or strained meats or other protein foods
10–12 mo	On demand feedings or nursing (16–32 oz total) 8–12 tablespoons iron-fortified cereal 1 small serving of crackers, toast, or dry unsweetened cereal 8 tablespoons potato, pasta, rice, or other starch 8–9 tablespoons Junior, soft, cooked, or mashed fruit 8–9 tablespoons Junior, soft, cooked, or mashed vegetables 3–4 tablespoons Junior, chopped, or strained meats or other protein foods

Table 7–4 Vitamin D supplementation for infants[2]

- Breast-fed and partially breast-fed infants should be supplemented with 400 IU of vitamin D daily
- All non-breast-fed infants, as well as older children, who are consuming <1 quart per day of vitamin-D-fortified formula or milk should receive vitamin supplement of 400 IU daily

The AAP supports exclusive breastfeeding for a minimum of 4 months, with preference for 6 months. After 6–8 months, exclusive breastfeeding may lead to insufficient intake of iron, zinc, and vitamins D and K. Complementary feeding will help the infant meet these needs, although it is recommended that all breast-fed infants receive a vitamin D supplement (see Table 7–4 for vitamin D supplementation recommendations for infants).[2]

TODDLER/CHILDHOOD NUTRITION

It is important to offer a variety of foods that can provide children with the proper intake of carbohydrates, protein, healthy fats, minerals, and vitamins. Each child's behaviors and food preferences are unique; thus, the nutritional needs of children should be balanced with their food likes and dislikes. It is important to recognize that children eat differently every day and that they should be allowed to follow their own internal hunger and satiety cues. Principle of "normal eating,"[3] in which parents are expected to prepare a variety of nutritious foods in ways the child will eat and the child is allowed to decide how much of and which food to eat, should be applied throughout childhood. Table 7–5 provides feeding guidelines for toddlers.

Table 7–5 Feeding Recommendations for Toddlers

Food Group	Total Amount/ Day	Serving Sizes and Food Sources	Important Contents
Whole milk and milk substitutes	4 servings (same as 2 cups of milk)	• ½ cup of whole milk or ½ cup of calcium-fortified soy milk • ½ cup yogurt, 1 oz cheese, ½ cup custard or pudding; 1 slice cheese pizza	Calcium, riboflavin, protein, and vitamins
Meat, fish, poultry, peanut butter, cooked or dried beans, and other protein foods	2 servings with total 3½ oz a day	• 1 oz is the same as 1 egg; 1 slice of cheese; ½ cup of cooked dried beans, peas, or lentils; 2 tablespoons peanut butter; 1 slice turkey or lean meats; 2 slices luncheon meat; 1 hotdog; 1 slice small cheese pizza; ¼ cup cottage cheese; ¼ cup drained tuna; ½ cup tofu; or 1 soy burger patty • 3 oz is the same as ¼ chicken (½ breast, leg, or thigh); 1 piece of meat or fish in the size and thickness of a deck of cards	Protein, niacin, iron, and thiamin

Food Group	Total Amount/ Day	Serving Sizes and Food Sources	Important Contents
Grains: breads, cereals, rice, pasta, and other starches (emphasize whole grain products)	4–6 servings	• 1 serving is the same as ½ slice of bread (any kind of bread); ½ small bagel; ½ English muffin; ½ biscuit (roll or muffin); 3 crackers; ½ hamburger bun; ½ hotdog bun; ¼ cup cooked rice or pasta; ¼ cup cooked cereal, ½ oz ready-to-eat cereal, unsweetened	B vitamins, iron, minerals, and fiber
Fruits	2 servings	• 1 serving is the same as ½ piece fresh fruit or ¼–½ cup of canned or frozen fruit • Suggestions: oranges, berries, melons, apricots, nectarines, peaches, tangerines, and banana slices	Vitamins A, potassium, and fiber

(*Continued*)

Table 7–5 Feeding Recommendations for Toddlers (*Continued*)

Food Group	Total Amount/ Day	Serving Sizes and Food Sources	Important Contents
Vegetables	3 servings	• 1 serving is the same as ¼ cup of fresh, frozen, or canned vegetables • Suggestions: tomatoes, peppers, cabbage, spinach, carrots, peas, beans, squash, sweet potatoes, broccoli, and potatoes	Vitamins A, C, folate, potassium, and fiber

HEALTHY EATING FOR CHILDREN

Children require adequate amounts of a balanced variety of foods. These include fruits, vegetables, whole and enriched grains and cereals, milk and other dairy products, and meat, fish, poultry, and other protein products.

Fruits and vegetables are the primary sources of vitamins A and C and contain other nutrients such as B vitamins, trace minerals, and fiber. They are also rich in antioxidants. Whole grain breads and cereals are excellent sources of B vitamins and, if enriched, iron. Whole grain breads and cereals are also good sources of fiber, vitamin E, and trace elements such as magnesium. It is recommended that the majority of breads and cereals in the diet be whole grain. Refined grain products should be consumed only on occasion, if at all, as they provide fewer micronutrients and less fiber. Dairy products, especially milk, provide protein and serve as primary dietary sources of

calcium and vitamin D. Milk provides the primary source of protein in early childhood. When the child makes the transition to table foods toward the end of the first year, more protein will be obtained from meat, fish, poultry, or other protein foods in the diet. These foods then begin to supplement milk as a source of protein and should thus be offered on a regular basis. Foods from the meat group are good sources of protein, iron, and trace elements such as zinc.[3,4]

When planning three scheduled meals, a variety of foods should be offered at each meal. The meal should provide lean protein (in the form of meat, fish, poultry, eggs, or legumes), whole grains, fruit and/or vegetables, and milk (see Tables 7–3, 7–5, and 7–6 for feeding recommendations for infants, toddlers, and children aged 6–12 years). Fat in moderate amounts is an essential component of any diet. It is recommended that total fat intake stay between 30% and 35% for children 2–3 years of age and between 25% and 35% of calories for children 4 years of age and over. Also, added sugar should not exceed 25% of total calories to ensure sufficient intake of micronutrients[5] (see Table 7–6 for healthy eating guidelines for children).

Table 7–6 Daily Food Guide for 6- to 12-Year-Old Child

Food Groups	Recommended Foods	Foods Not Recommended
Grains	Choose whole grains (whole wheat pasta, multigrain bread, and brown rice)	Refined grains (white bread, white pasta, and white rice) and sugar-sweetened cereals
Vegetables	Fresh, canned, or frozen vegetables without butter, cheese, or sauces	Vegetables with added butter, cheese, or sauce

(*Continued*)

Table 7–6 Daily Food Guide for 6- to 12-Year-Old Child (*Continued*)

Food Groups	Recommended Foods	Foods Not Recommended
Fruits	Fresh, whole fruits; frozen or canned fruits without added sugar; unsweetened juice (limit to 4 oz/d)	Fruit with added sugar or syrup
Meat and protein	Lean meat, skinless chicken, fish, beans/legumes, and eggs Nuts and nut butters	Fried foods (chicken fingers, French fries, fried chicken, and mozzarella sticks) Processed deli meats, bacon, and sausage
Milk and milk products	Skim milk, low-fat or nonfat yogurt, low-fat cheese, and frozen yogurt	Whole milk, cream, full-fat yogurt, regular cheese, full-fat ice cream, or frozen yogurt
Fats and oils	Limited amounts of oils (olive and canola), trans-fat free butter or margarine, and avocado	Butter, margarine, lard, and gravy

Children become hungry between meals, making snacks an important part of their daily intake. Snacks should be planned, so that the child does not continually graze. They should be spaced to ensure the child is hungry at meals, with the interval between meals and snacks tailored to the child's hunger and satiety cues. Parents are responsible for choosing the snack, when it is eaten and where it is eaten. The child is responsible for how much to eat and whether or not they eat the snack. Filling and satisfying snacks should contain at least two of the three macronutrients (carbohydrate, protein, and healthy fat). Carbohydrates provide bulk and some energy value, whereas protein and fat provide satiety value. Snacks can also help to

stabilize energy levels and moods. Snacks can provide valuable calories for those children experiencing growth spurts who have difficulty consuming their required calories at mealtimes. Table 7–7 lists ideas for nutritious snacks.

Table 7–7 Nutritious Snack Choices

Snack Ideas
• Cereal bar or granola bar and milk • Hummus with pita or veggies • Light microwave popcorn or air-popped popcorn and parmesan cheese • Crackers (such as Melba® toast, Saltines, or Triscuits®) and a cheese slice • Beans and tortillas • Peanut butter, almond butter, or soy nut butter on celery, apple, or crackers • 1/2 peanut butter sandwich • Deli meat (turkey) and whole wheat bread • Pudding made with low-fat milk and graham crackers • Graham crackers and peanut butter • Canned fruit in juice and cottage cheese • Animal crackers and milk • Celery with cream cheese • Carrots or pepper strips and ranch dip • String cheese and fresh fruit • Baked tortilla chips with salsa • Cereal with milk
Kid-Friendly Snack Recipes
• *Cereal parfait*: layer low-fat yogurt with cereal and frozen berries
• *Trail mix*: mix ingredients like dried fruit, low-sugar cereal (such as Kix®, Shredded Wheat®, Cheerios®, or Kashi®), nuts, and soy nuts with some mini chocolate chips or M&M's®

(*Continued*)

Table 7–7 Nutritious Snack Choices (*Continued*)

Snack Ideas
• *Smoothie*: blend low-fat milk and fruit like bananas and berries (fresh or frozen). Add frozen yogurt to make a fruit milkshake
• *Rabbit bag*: keep cut up fruits and veggies in small plastic bags in your refrigerator. If you are adding apples, also add orange slices to keep them from turning brown
• *Pizza bagel*: add tomato sauce and low-fat cheese to half of a whole grain bagel (or an English muffin). Bake or microwave it until the cheese melts

Children generally enjoy starchy foods and thus do not have to be persuaded to eat them. A diet that is too high in carbohydrates, however, is likely to be unsatisfying. High carbohydrate snacks may lead to excessive caloric consumption between meals, which could lead to both weight gain and the concomitant decreased intake of nutrient-dense foods at meal times. This is an important principle in which to educate parents and caregivers, especially in those children who are, or at risk of becoming, overweight.

ORAL HEALTH FOR CHILDREN

It is important to offer healthy food and drink choices for infants, toddlers, and children as nutrition plays a vital role in oral health. Tooth decay is the most common infectious diseases in children.[6] Early childhood caries are often thought to be caused by inappropriate use of a bottle or cup containing breast milk, formula, or juice while sleeping or frequent use during the day with a liquid other than water. The frequency of eating and drinking also plays a role in dental caries. Routine daily cleaning with a moist cloth or infant toothbrush should begin as soon as any tooth erupts, by 6 months of age. In children over the age of two, daily brushing with fluoridated toothpaste, only a pea-sized amount, is needed. It is recommended that all

Table 7–8 Dietary Fluoride Supplement Recommendations[7]

	Fluoride Ion Level in Drinking Water (ppm)		
Age	<0.3 ppm	0.3–0.6 ppm	>0.6 ppm
Birth to 6 mo	0	0	0
6 mo to 3 y	0.25 mg/d	0	0
3–6 y	0.50 mg/d	0.25 mg/d	0
6–16 y	1.0 mg/d	0.50 mg/d	0

infants by 6 months of age obtain an oral health risk assessment and to see a dentist by 12 months of age.[7]

The fluoride content of drinking water varies from town to town; parents should contact their local town office and discuss with pediatrician whether there is a need for fluoride supplementation (see Table 7–8 for fluoride supplementation information). It should be noted that excessive ingestion of fluoride results in mottled enamel (chronic endemic dental fluorosis).

Optimal nutrition and oral hygiene are essential for the prevention of oral disease and to the development and maintenance of oral health.

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8 Adolescent Nutrition

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FEEDING GUIDELINES FOR ADOLESCENTS

Adolescence is a time of biologic, physical, emotional, and cognitive transition. With these changes come new nutritional challenges related to increased independence, increased nutrient needs, peer pressure, and changing food preferences. Dietary patterns established during teenage are frequently carried through to adulthood,[1] so it is important to promote the development of a healthy lifestyle through diet and exercise to prevent chronic disease later in life.

The most common nutritional concerns in adolescence include low consumption of fruits and vegetables, whole grains, calcium and low-fat dairy and frequent consumption of sugar-sweetened beverages and fast food,[2] leading to deficiencies in folate, vitamins A, E, and B_6, calcium, iron, zinc, and magnesium, as well as high intake of fat, saturated fat, sodium, cholesterol, and sugar.[3] Dieting and unhealthy weight control behaviors are common among adolescents and are associated with excess weight gain.[1,4] These issues, combined with the increased nutrient needs of teenagers, can

lead to a wide range of physical manifestations including iron deficiency anemia, poor bone mineralization, micronutrient deficiencies, eating disorders, obesity, and the development of chronic diseases such as type 2 diabetes, heart disease, and osteoporosis later in life. Please refer to other chapters in this manual for more information on nutrition assessment in teenagers and the management of obesity, eating disorders, sports nutrition, and vegetarianism. This chapter will focus on age-specific development, assessment, and disease states including general nutritional recommendations, sexual maturity ratings (SMRs), bone health, and polycystic ovary syndrome (PCOS).

Feeding recommendations for adolescents are found in Table 8–1. For best results, nutritional counseling for teenagers should focus on[2,5]:

- Empowering them to take control of their own health and well-being
- Establishing concrete, attainable goals
- Directing conversation at the patient instead of the parents, including patient in decision making and goal setting
- Discouraging meal skipping
- Discouraging dieting and unhealthy weight control behaviors
- Encouraging family meals at home in a supportive environment
- Educating family on healthy food choices
- Encouraging high availability of healthy foods at home
- Providing ideas for affordable, healthy, quick meals
- Encouraging patient to be involved in food shopping, meal planning, and cooking

- Encouraging parents to model desirable behavior, make healthy choices, and avoid weight talk
- Educating patients on the dangers of dieting and unhealthy weight control measures

Table 8–1 Feeding Recommendations in Adolescence

Food Group	Servings/D	Examples/Notes
Fruits and vegetables	2–3 cups vegetables 1.5–2 cups fruit	Encourage whole fruits over juice Variety of colors Include in all meals Have available for snacking
Grains	5–8 servings total 3–4 servings should be whole grains	Encourage whole grain cereal, popcorn, hot breakfast cereal, etc. Educate on how to identify whole grains Recipe ideas including whole grains
Milk and Dairy	3 servings of low-fat or fat-free	Encourage parents to model behavior Encourage breakfast consumption Drink milk at meals Include in healthy snacks
Protein	5–6.5 oz	Emphasize lean proteins
Fats and oils	5–6 tsp	Encourage healthy fats (fish, nuts, vegetable oils) Discourage saturated fat and *trans* fat
Sweets (sugar-sweetened beverages)	Minimize	Provide acceptable drink alternatives
Fiber	25–35 g a day	Emphasize fruits, vegetables, and whole grains

Source: Adapted from www.myplate.gov.

SEXUAL MATURITY RATINGS

Puberty occurs during adolescence and is a time of major increases in height, when adolescents attain approximately 15% of their final adult height. The age of onset, duration, and speed of puberty differ for each individual: adolescents of a given chronological age may vary widely in physiological development, and, because of this, age is a poor indicator of physiological maturity and nutrition needs. SMR, also known as Tanner Staging, is a better indicator to evaluate growth and developmental age during adolescence. Tanner stages are based on the development of secondary sexual characteristics, and are rated on a scale of 1 (prepubertal) to 5 (adult). For girls, this is based on breast maturity and pubic hair development; for boys, it is based on the progression of genital and pubic hair development (Tables 8–2 and 8–3).[6] The mean age of pubertal milestones attainment of White, Hispanic, and Black youth is shown in parenthesis.[7]

Table 8–2 Tanner Stages of Development in Boys

Tanner Stages	Genitalia/Pubic Hair/Other	Growth
1	Prepubescent	About 5–6 cm/y
2	Enlargement of testes and scrotum, reddening of scrotum (11.0 y) First appearance of pubic hair (11.8 y) Increased activity of sweat glands	About 5–6 cm/y
3	Growth of penis, mostly length, further growth of testes/scrotum (12.5 y) Pubic hair darker cover pubis (13.1 y) Voice begins to change	About 7–8 cm/y

Tanner Stages	Genitalia/Pubic Hair/Other	Growth
4	Growth of penis and scrotal skin darker (15.2 y) Adult type pubic hair—no spread to the thighs (15.1 y) Axillary and facial hair Voice deepens	About 10 cm/y
5	Adult genitalia (16.6 y) Adult type pubic hair—extends to the thighs (16.9 y)	Deceleration and cessation at about 17 y

Source: Adapted from Tanner.[6]

Table 8–3 Tanner Stages of Development in Girls

Tanner Stages	Genitalia/Pubic Hair/Other	Growth
1	Prepubescent	About 5–6 cm/y
2	Small breast bud under enlarged aerola (10.7 y) Small amount of pubic hair (10.8 y) Increased activity of sweat glands	About 7–8 cm/y
3	Breasts grow larger—no separation of the nipple and the aerola (12.5 y) Pubic hair is increased, darker, coarser, and curled (12.2 y) Axillary hair	About 8 cm/y
4	Projection of aerola and nipple from secondary mound (14.3 y) Adult type pubic hair—no spread to medial thighs (14.5 y) Menarche	Deceleration < 7 cm/y
5	Adult breast contour (16.1 y) Adult type pubic hair—extends to medial thighs (16.4 y)	Cessation at about 16 y

Source: Adapted from Tanner.[6] Development of Reproductive System.

Linear growth occurs at different periods of development for boys and girls.[6] Females begin the linear growth spurt during Tanner stage 2, with peak height velocity occurring at the end of stage 2 through stage 3 (about 8 cm a year). Their growth spurt occurs on an average from age 10½–13, two years earlier than for boys. Girls will have completed the majority of growth by the onset of menarche at Tanner stage 4. An average of only two inches of linear growth will be added after menarche. However, girls who enter puberty early (before age 11) may have more linear growth after menarche than those who enter puberty later. In United States, the average age when girls reach menarche is between 12½ and 13½ years.[7,8] Peak height velocity in boys is between Tanner 3 and 4 (about 7–8 cm a year and about 10 cm per year, respectively) and correlates with peak energy needs.[6] The growth spurt for boys lasts an average from age 12½ to 15. In males, peak weight velocity coincides with peak height velocity. In contrast, in females, peak weight velocity occurs 6–9 months before height rate changes.

Teenagers with severely restricted energy intakes during this phase are likely to experience delayed or slow linear growth, and attainment of full adult height may be affected.[8] In the prepubertal period, the proportion of fat and muscle in boys and girls tends to be similar. But under the influence of testosterone, boys proportionately gain more muscle mass than fat, with muscle mass doubling between the ages of 10 and 17. Boys have more lean body mass per unit height than girls.[8]

BONE HEALTH

Bone is a living tissue. The process of bone formation and resorption (bone turnover) in the body is continuous. During adolescence, the rate of bone formation predominates

over resorption. The goal is to reach the optimum peak bone mass, which is defined as the stage at which individuals reaches their maximum bone density and strength, by allowing maximum bone mass development. Approximately 45%–50% of total skeletal mass is completed during adolescence. Ninety percent of peak bone mass is achieved by around age 18 for girls and age 20 for boys, when growth usually ceases. The remaining 10% of peak bone mass is accrued at a slower rate, into the third decade of life.[9] Maximizing bone mass will protect against osteoporosis, a major public health problem whose incidence is increasing in adults in the Western countries.

CONTRIBUTORS TO THE PROCESS OF SKELETAL DEVELOPMENT

Indicators of Bone Metabolism

Levels of bone turnover markers appear to reach peak values during midpuberty (Tanner stages 2 and 3) and decrease markedly in late puberty (Tanner 4 and 5). The increase in urinary bone markers is an indicator of higher bone mass, as well as of more active bone turnover. Several studies have shown that osteocalcin, a protein synthesized by the osteoblasts, which is a sensitive marker of bone formation, increases significantly during puberty, both in boys and girls.

Estrogen

Estrogen is central to the growth and development of bone in girls during childhood as well as for maintenance of bone integrity during adulthood. Estrogen is directly involved along with growth hormone and insulin like growth factor in bone modeling. Indirectly, estrogen stimulates production of 1,25-dihydroxycholecalciferol from hydroxyvitamin D, which enhances gastrointestinal (GI) absorption

of calcium, and restricts excretion of calcium from the kidney. With increased total body retention of calcium, production of parathyroid hormone (PTH) is suppressed. Estrogen also increases the number of vitamin D receptors on the bone cell, which enhances the impact of vitamin D on the bone cell, especially the osteoblast, and 1,25 $(OH)_2D$ appears to stimulate secretion of osteocalcin. Estrogens are an important determinant of bone mineral density in girls during puberty.[10]

Diet and Lifestyle

Bone mass is 70%–80% genetically determined, but 20%–30% of peak bone mass depends on the quality of diet and lifestyle. Some of the key nutrition and lifestyle factors that have been identified are: adequate calcium intake, adequate vitamin D status, appropriate weight-bearing activity, and appropriate body weight. Calcium is the most abundant mineral in the human body, and 99% is found in bones and teeth. Calcium and phosphorus are the main minerals for bone strength as they are deposited into the porous protein structure of the bone, thereby increasing density and therefore strength. Phosphorus is abundant in many foods but adequate amounts of calcium are usually not met in the adolescent population; however, calcium absorption is enhanced during puberty. Vitamin D sufficiency enhances calcium and phosphorus absorption by 30%–40% and 80%, respectively. Without vitamin D, only 10%–15% of dietary calcium and about 60% of phosphorus is absorbed. The major source of vitamin D is from solar exposure, less from dietary intake/food fortification. Known risk factors for deficiency are darker skin pigmentation, topical application of sunscreen, winter season, latitude above 35° north, and inadequate dietary intake.

The Dietary Reference Intakes for calcium and vitamin D are found in Chapter 5, although The Endocrine Society's recommendation of 600–1,000 IU for adolescents of 9- to 18-year-old[11] is higher than the 600 IU recommended by the Institute of Medicine.[12]

Threshold values for 25-hydroxyvitamin D levels are found in Table 8–4. Vitamin A task force of The Endocrine Society has developed guidelines for the evaluation, treatment, and prevention of vitamin D deficiency with an emphasis on patients who are at high risk for vitamin D deficiency (Table 8–5). Treatment recommendations for vitamin D deficiency are in Table 8–6, although clinical experience shows that it is not uncommon to need a repeat treatment course. Although vitamin D clinical trials are very limited in children, one study of infants and toddlers showed that subjects receiving either 50,000 D2 weekly, 2000 IU daily of Vitamin D2, or 2000 IU daily of Vitamin D3 for 6 weeks all attained normal vitamin D levels with no significant differences, and no one had hypercalcemia as an associated risk.[13] For Vitamin D insufficiency (25OHD: 20–29 ng/mL), there is no consensus as to what is the adequate amount of vitamin D3 (cholecalciferol) supplementation. It is common practice to supplement with 1000 per day for 2–3 months, and recheck levels after that. Clinical judgment is strongly encouraged, especially when someone is at higher risk for vitamin D deficiency (Table 8–5).

Table 8–4 Vitamin D Thresholds

Deficiency 25OHD	<20 ng/mL
Insufficiency 25OHD	20–29 ng/mL
Normal 25OHD	>30 ng/mLMl

Table 8–5 Patients Risk for Deficiency

- Bone disease (rickets, osteopenia)
- Hepatic failure
- Malabsorption syndromes (cystic fibrosis; inflammatory bowel disease, Crohn's disease, Bariatric surgery)
- Chronic kidney disease
- Lymphoma
- Medication (seizure meds, glucocorticoids, HIV medication, antifungals, cholestyramine)
- Obese children (BMI > 30 kg/m^2)
- AA and Hispanic children

Source: Partial list from the Endocrine Society 2011 Clinical Practice Guidelines.

Table 8–6 Recommendations for Treatment (25OHD:<20ng/mL)

- Ergocalciferol (Vitamin D2) 50,000 IU weekly for 6–8 wk
- Calcium per recommended dietary allowance , divided over day
  - 9–18 y: 1300 (UL 3000 mg)
- Check follow-up 25OHD at approximately 8–10 wk (to obtain an accurate level, should be rechecked 2 wk after the treatment is over as vitamin D is a reflection of stores)
- Followed by maintenance therapy of 800–1000 IU/d

In adults, maximal suppression of serum PTH has been commonly used to determine the sufficiency of serum 25OHD. The inflection point 25OHD for maximal suppression of PTH in children and adolescents is unknown.

POLYCYSTIC OVARY SYNDROME

PCOS is an endocrine disorder affecting 5%–10% of adolescent girls. It is characterized mainly by irregular

menses, acne, hirsutism, and obesity. Teenagers with PCOS will also frequently exhibit insulin resistance and hypothalamic–pituitary dysfunction, and are at higher risk of developing impaired glucose tolerance and type 2 diabetes.

The first line of treatment for overweight and obese teenagers with PCOS is lifestyle modification and weight loss. Although studies in adolescents are limited, research conducted in adult women and teenagers with PCOS suggests that weight loss of 5%–10% can help regulate menses, lower testosterone levels, improve lipid profiles, improve insulin sensitivity, reduce diabetes and cardiovascular risks, improve hirsutism and acne, and have positive effects on mood and self-esteem.[14]

Nutrition counseling of adolescent girls with PCOS should include:

- Incorporate low GI foods to help with insulin resistance
- Reduce fast food intake (decrease saturated fat intake)
- Incorporate more whole grains and vegetables (increase fiber intake)
- Emphasis on lean proteins
- Encourage daily breakfast consumption
- Limit soda and juice
- Increase in physical activity to 150 minutes per week
- Recommend oral glucose tolerance test every 2 years

It is important to recognize that patients with PCOS will typically also be managed with pharmacologic agents such as oral contraceptives, insulin-sensitizing agents such as metformin, and/or antiandrogens such as spironolactone. Long-term follow-up is important for best results.[14]

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9 Vegetarian Diets

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Vegetarians do not include meat, fish, or fowl in their diet and typically base their diet on fruits, vegetables, grains (preferably whole grains), legumes, and nuts. Lacto-ovo vegetarians permit eggs and dairy products. Lacto-vegetarians exclude eggs, as well as meat, fish, and fowl, but permit dairy products. Vegans, also known as total vegetarians, eat only plant-based foods.[1,2] Even within defined types of vegetarian diets, eating patterns may vary tremendously. Vegetarian diet adherents are motivated by reasons including health concerns, religious beliefs, animal welfare, or environmental considerations. Interest in vegetarianism appears to be increasing. An estimated 3% of 8- to 18-year-old children and adolescents are vegetarian and close to 1% are vegan.[1]

Appropriately planned vegetarian diets have been shown to be healthful, nutritionally adequate, and beneficial in the prevention and treatment of certain diseases.[1,2] Vegetarian diets in childhood and adolescence can foster the development of lifelong healthy eating patterns and can provide nutritional advantages.[1] Vegetarian children and adolescents have lower intakes of cholesterol, saturated fat, and total fat and higher

intakes of fruits, vegetables, and fiber than nonvegetarians.[1] Vegetarian children have also been reported to be leaner and to have lower serum cholesterol levels.[1] Vegetarian diets are appropriate for all stages of the life cycle, although specific menu planning considerations are needed depending on the type of vegetarian diet followed. To help guide vegetarian food choices, U.S. Department of Agriculture's MyPlate can be used as visual tool to choose well-balanced meals and appropriate portion sizes. The MyPlate website (www.choosemyplate.gov) also includes "Tips for Vegetarians" with specific nutrient information and meal ideas.[3] A vegetarian food guide has been developed by the Academy of Nutrition and Dietetics and Dietitians of Canada with recommended servings of each food group and of calcium-rich foods (Table 9–1).[4]

Table 9–1 Recommended Servings[a] of Vegetarian Foods

		Calcium-rich foods Child (4–8 y): 6 servings Adolescent (9–18 y): 10 servings
Fats 2 servings	Oil, mayonnaise, or soft margarine (1 tsp)	
Fruits 2 servings	Medium fruit (1 piece) Cut up or cooked fruit (1/2 cup) Fruit juice (1/2 cup) Dried fruit (1/4 cup)	Fortified fruit juice (1/2 cup) Figs (5)
Vegetables 4 servings	Cooked vegetables (1/2 cup) Raw vegetables (1 cup) Vegetable juice (1/2 cup)	Bok choy, broccoli, collards, Chinese cabbage, kale, mustard greens, or okra (1 cup cooked or 2 cups raw) Fortified tomato juice (1/2 cup)

(*Continued*)

Table 9–1 Recommended Servings[a] of Vegetarian Foods (*continued*)

Legumes, nuts, and other protein-rich foods 5 servings	Cooked beans, peas, or lentils (1/2 cup) Tofu or tempeh (1/2 cup) Nut or seed butter (2 tbsp) Nuts (1/4 cup) Meat analog (1 oz) Egg (1)	Cow's milk or yogurt or fortified soymilk (1/2 cup) Cheese (3/4 oz) Tempeh or calcium-set tofu (1/2 cup) Almonds (1/4 cup) Almond butter or sesame tahini (2 tbsp) Cooked soybeans (1/2 cup) Soynuts (1/4 cup)
Grains 6 servings	Bread (1 slice) Cooked grain or cereal (1/2 cup) Ready-to-eat cereal (1 oz)	Calcium-fortified breakfast cereal (1 oz)

[a]The number of servings in each group is for minimum daily intakes.
Source: Adapted from: Messina et al.[4]

Although vegetarian diets can satisfy nutrient needs and promote normal growth of infants and children, caregivers must be mindful of recommended food alternatives. Vegetarian infants should be breast-fed or given a commercial infant formula. Breast-fed infants of vegan mothers might need a B-12 supplement, if the mother's diet is low in B-12,[1] and may benefit from docosahexaenoic acid (DHA)–fortified foods or supplements because of increased requirements of DHA. Guidelines for the introduction of solid food are the same for vegetarian infants; however, the types of protein-rich food, such as pureed tofu, legumes, soy or dairy yogurt, cooked egg, cottage cheese, cubed tofu, cheese or soy cheese, and bite-size pieces of veggie burgers, offered will differ. When assessing vegetarian diets, particular attention should be paid to nutrients that are most abundant in foods of animal origin and vegetarian sources (Table 9–2) should be encouraged.

Table 9–2 Vegetarian Food Sources of Select Nutrients

Nutrient	Vegetarian Food Sources
Protein	Eggs[a], milk[a], cheese[a], yogurt[a], soy milk, soy cheese, soy yogurt, tofu, beans and legumes, seeds, nuts, nut butter, hummus, vegetarian burgers, vegetarian meat substitutes made with textured vegetable protein, tempeh, and grains and grain products.
Iron	Soybeans, soy nuts, tofu, beans (pinto, lima, navy, kidney, garbanzo), lentils, cashews, almonds, pumpkin seeds, sunflower seeds, sesame tahini, fortified cereals, cream of wheat, fortified cereal, dried fruit, prune juice, potatoes, and blackstrap molasses, green leafy vegetables (spinach, collard greens, kale, Swiss chard).
Calcium	Milk[a], cheese[a], yogurt[a], soy yogurt, soybeans, soy milk, tofu (processed with calcium), calcium-fortified orange juice, tempeh, beans (black, garbanzo, navy, pinto), blackstrap molasses, almonds, almond butter, sesame tahini, fortified cereals, figs, and green leafy vegetables (kale, broccoli, turnip greens, mustard greens, collard greens, bok choy).
Vitamin D	Eggs[a], milk[a], soymilk, and fortified cereals.
Vitamin B-12	Eggs[a], milk[a], soymilk, fortified cereals, nutritional yeast, and fortified vegetarian meat substitutes.
n-3 Fatty Acids	Ground flaxseeds, flaxseed oil, canola oil, walnuts, walnut oil, tofu, soybeans, and soybean oil.

[a]May not be consumed by some vegetarians.

PROTEIN

Plant protein can meet protein requirements when a variety of plant foods are consumed and energy needs are met.[1] At one time, it was believed that vegetarians have to carefully combine certain plant-based foods to receive the appropriate amino acids comprising a complete protein. Research indicates that a diet consisting of a variety of plant foods

eaten over the course of a day can provide all essential amino acids and adequate nitrogen retention.[1]

IRON

Iron in plant food is nonheme iron, which is sensitive to both inhibitors and enhancers of iron absorption.[1,2] Inhibitors of iron absorption include phytates, calcium, and the polyphenolics in tea, coffee, herbal tea, and cocoa.[1,2] Research now indicates that fiber only slightly inhibits absorption.[1] Vitamin C and other organic acids found in fruits and vegetables substantially enhance iron absorption and reduce the effects of phytate and should be included in vegetarian diets.[1,2] Recommended intakes of iron for vegetarians are 1.8 times those of nonvegetarians because of the decreased bioavailability of iron.[1,2] However, incidence of iron deficiency anemia, among vegetarians is similar to that of nonvegetarians.[1,2]

CALCIUM

Calcium is found in many plant-based and fortified foods. Oxalates found in some foods reduce calcium absorption; so, vegetables high in oxalates, such as spinach, beet greens, and Swiss chard, are not good sources of usable calcium.[1] Vegetables low in oxalates, such as bok choy, broccoli, Chinese cabbage, and collards, and juices fortified with calcium citrate malate have good calcium bioavailability.[1,2] Calcium intakes of lacto-vegetarians are comparable with or higher than those of nonvegetarians, whereas intakes of vegans tend to be lower than both groups.[1,2] Vegans may find it easier to meet their calcium needs if fortified foods or supplements are included.

VITAMIN D

Vitamin D status depends on sunlight exposure and intake of vitamin D–fortified foods or supplements. Low vitamin

D levels and reduced bone mass have been observed in some vegan populations.[1,2] In addition to the role in maintaining bone health, vitamin D has also been found to play a role in supporting immune function, by reducing inflammation and the risk of chronic diseases.[2] If sun exposure and intake of fortified foods are insufficient, vitamin D supplements are recommended.

VITAMIN B-12

Most plant-based foods are rich in vitamins, with the exception of vitamin B-12. Although some plant foods may be contaminated with this vitamin, there are no reliable nonanimal sources of B-12. All vegans should obtain a regular, reliable source of the vitamin, either from fortified foods (such as cereals, meat alternatives, soy or vegetable milk, or nutritional yeast) or from a daily B-12 supplement.[1,2]

n-3 FATTY ACIDS

Vegetarian diets are typically rich in n-6 fatty acids, but may be low in n-3 fatty acids, which are important for cardiovascular health and infant brain development.[1,2]

The bioconversion of alpha-linolenic acid (ALA), a plant-based n-3 fatty acid, to eicosapentaenoic acid (EPA) is generally less than 10% in humans, and the bioconversion of ALA to DHA is substantially less.[1,2] Studies have shown lower blood levels of these n-3 fatty acids in vegetarians, particularly vegans.[1] High or excessive intake of n-6 fatty acids decreases conversion rates of ALA.[1,2] Vegetarians should include good sources of ALA in their diets. For vegans, certain microalgae and fortified foods provide DHA, and oil from brown algae (kelp) provides EPA. Chickens fed n-3 fatty acids in their diet produce eggs that contain EPA and DHA.

ZINC

The bioavailability of zinc is lower in vegetarian diets compared with nonvegetarian diets, mainly due to higher phytic acid content.[1,2] According to studies, zinc intake varies from marginal to falling below recommendations.[1,2] For vegetarians who eat a diet rich in phytates and unrefined grains and legumes, zinc requirements may exceed the recommended dietary allowance.[1,2] Organic acids, such as citric acid, and food preparation techniques, such as soaking and sprouting beans, grains, and seeds, as well as leavening bread, can increase zinc bioavailability.[1,2] Zinc sources include soy products, legumes, grains, cheese, and nuts.[1]

IODINE

Plant-based diets are typically low in iodine and some studies suggest that some vegans may be at risk for iodine deficiency.[1] Key sources of iodine include iodized salt and sea vegetables. Sea salt, kosher salt, and salt seasonings such as tamari are often not iodized.

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10 Sports Nutrition

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Sports participation continues to become increasingly popular. Individuals of all ages and abilities train and compete for enjoyment, achievement, and physical fitness. Success in sports is multifactorial. Not only genetics and training are important but also nutrition contributes to success. As an athlete's needs change throughout the life cycle, it is important to consider the ideal diet to support the short-term goals of training and performance, as well as the mid- and long-term goals of optimal growth and development, and a healthy adulthood. The purpose of this chapter is to offer recommendations for the assessment, nutrition, and hydration of athletes.

◆ ASSESSMENT

A complete nutrition assessment of an athlete should include a survey of all available nutritional, medical, biochemical, clinical, and psychosocial data. Dietary assessment analyzes the diet for total caloric intake and intake of macronutrients and micronutrient.[1] It is important that the diet recall reflects the athlete's typical intake, with both weekdays and weekend

days represented. Underreporting of energy intake is widespread among some athletes, and overreporting may be common among those with restrictive eating disorders.[2] Thus, both possibilities should be addressed when interpreting the assessment. Other issues that should be assessed are knowledge and adequacy of portion sizes, frequency of snacking, fluid intake, use of vitamin, mineral, and alternative nutrition supplements, weight-control practices, and seasonality of sport activities and food consumption.[1,3]

Once the diet assessment has been completed, it is then analyzed and evaluated. This typically involves comparing the data to nutrient standards and offering recommendations to enhance the athlete's nutrition status.[1] A more comprehensive assessment may incorporate the following questions to help formulate individualized and sports-specific recommendations:

- Does the athlete desire to reduce body weight to enhance performance?
- Is the athlete at risk for disordered eating and inadequate nutrition related to overemphasis on low body weight? Furthermore, is the athlete at risk for menstrual disturbances, female athlete triad, and/or low bone mineral density[4]?
- Is the athlete at risk for low iron status? This is especially important in the assessment and design of a nutrition plan for female and/or vegetarian athletes.[5]
- Has energy restriction affected the athlete's growth? This is particularly important if the athlete is in the critical period of growth around puberty.[4]
- Does the athlete fear body changes during maturation and adolescence[4]?
- Does the athlete have difficulties in consuming sufficient energy on a typical day with or without exercise?

- Does the athlete have optimal food and fluid intake during both short and long training sessions, as well as for optimal recovery after and between training sessions[1]?
- Does the athlete use ergogenic aids or performance-enhancing supplements[6]?
- Does the athlete ingest adequate protein intake to preserve and/or increase lean body mass during resistance training and to repair muscle in recovery[4]?

CARBOHYDRATES

Athletes have essentially the same nutrition needs as nonathletes with some differences. The total amount of calories for athletes may be slightly to much greater depending on the sport.[7] When counseling an athlete about the how to design a diet with optimal total calories, the current diet should be analyzed and then compared with a recent weight history, the athlete's sport and training regimen, and the frequency and intensity of exercise.[1,7] Furthermore, the percentages of macronutrients may differ depending on the sport and the stage of growth of the athlete, as well as whether the athlete is designing a nutrition plan for training, competition, pre-event, and/or postevent recovery nutrition.[7]

An athlete needs a healthful mix of carbohydrate, protein, and fat to ensure proper energy levels. The general guidelines for athletes recommend 50% to 65% calories from carbohydrate, with endurance athletes needing as much as 70% of total calories from carbohydrate.[7]

The typical daily diet in the United States provides approximately 4 to 5 g of carbohydrate per kilogram of body weight. Carbohydrate recommendations for athletes range from 6 to 10 g/kg/d, with an average intake of 5 to 7g/d for

general training, increased to 7 to 10 g/d for those athletes training for endurance events. Using an absolute value such as 5 to 7g of carbohydrate per kilogram per day is a good method of determining what is best for an athlete as it takes into account body weight. A more muscular athlete with a higher body weight who has a very intense training schedule may require more total energy with a lower amount of absolute carbohydrate than an athlete with a lower body weight and a less intense training regimen.[7] Each athlete's carbohydrate prescription is best determined individually, based on body weight, sports-specific considerations, energy balance, and adequacy of macronutrients and micronutrients.[7]

Carbohydrates should be consumed before, during, and after exercise. Prior to exercise, carbohydrates provide energy to maintain daily activities of living, as well as a pool of calories to spare, or make available protein for muscle growth and repair.[7] During exercise, muscles use more glucose, even up to 30 times more, depending on the intensity and duration of the exercise.[7,8] Athletes should consume 1 to 4 g of carbohydrate per kilogram body weight, one to four hours prior to exercise. High-intensity athletes such as wrestlers and body builders may require 5 to 8 g/kg of body weight. Recommendations are higher for endurance athletes who need on average 7 to 10 g of carbohydrate per kilogram of body weight.[7]

Athletes with more intense training regimens or higher body weights may not be able to consume enough solid food per day to meet daily caloric and carbohydrate needs. In this case, a high calorie sports beverage may be helpful. Liquid supplements with a high percentage of carbohydrate (18% to 24%), as well as glucose polymers, may be helpful if an athlete has trouble meeting caloric needs with solid foods.[1]

These supplements are not designed to replace food intake, but are for additional calories, carbohydrate, and fluid during heavy training.[1]

Daily consistent carbohydrate intake helps maintain optimal muscle glycogen stores. Many athletes focus on daily needs and neglect the pre-exercise meal. As liver glycogen stores may be reduced during sleep, the pre-exercise meal is important to ensure sustained fuel for exercise. It is best to consume carbohydrates one to four hours before exercise.[7,8] The pre-exercise meal provides energy for exercise that lasts for one hour or longer. Many athletes participate in events that occur very early in the day and prefer not to eat this early. In these cases, a second option would be to ensure a snack prior to bedtime.

There is considerable research on the ideal pre-exercise meal. Carbohydrates should be portable, palatable, and easily digested. A good way to avoid gastrointestinal distress prior to exercise is to consume less carbohydrate just prior to exercise.[7] Whereas an average of 4 to 5 g carbohydrate per kilogram should be consumed four hours prior to exercise, only 1 g of carbohydrate per kilogram is optimal in the last hour before exercise.[7] This may help to avoid any gastrointestinal side effects.

It is best to avoid pre-exercise meals that are high in protein as they may take longer to digest and absorb. The protein content of the pre-exercise meal should be approximately 10% to 15%.[7,8] Furthermore, this meal should also not be high in fat as fat tends to leave the stomach slowly, thereby delaying the absorption of carbohydrates. Only about 15% to 20% of the calories in the pre-exercise meal should come from fat.[7] An example of a favorable pre-exercise meal would be whole-wheat toast with peanut, or other nut butter, or oatmeal with fruit and milk (Table 10–1).

Table 10–1 Sample Meal Plans for Event Fueling

The Night Before the Event

- Pasta with Vegetarian or Bolognese sauce served with garlic bread, steamed broccoli (or other vegetable), fresh fruit, and low-fat dairy or soy milk.
- Grilled, marinated chicken breast served with mashed white or sweet potatoes, green beans, fresh fruit salad, and low-fat dairy or soy milk.
- Chicken, pork, or beef and vegetable stir-fry served with white or brown rice, orange, and grapefruit slices and low-fat dairy or soy milk.
- Deep dish pizza served with a side garden salad and olive oil dressing and low-fat dairy or soy milk.

The Morning of the Event

2 to 3 h before: Small to regular-size meal and liquids

- Pancakes or waffles, served with Canadian bacon, banana slices, and low-fat dairy or soy milk.
- Oatmeal with raisins or dates, served with low-fat dairy or soy milk, toast with jam and water.
- Two eggs, any style served with an English muffin, jam, fruit, and water.

1 to 2 h before: Small snack and liquids

- Cereal bar
- Banana
- One-half bagel with peanut or other nut butter
- One-half turkey sandwich

30 min to 1 h before

- Mostly liquids

During the Event

- Remember to stay well hydrated. Have water and sports drinks available and drink 6 to 12 oz every 15 min.
- Use sports drinks, bars, and gels, alternating with water to ensure optimal hydration.
- During breaks between events (1 to 2 h or less) have on hand cereal bars, low-fat granola, pretzels, graham crackers, oatmeal cookies, animal crackers, trail mix, fig bars, yogurt, and bananas.

- During longer breaks of more than 2 h, have on hand turkey, ham, or chicken sandwiches, peanut butter and jam, fluff or Nutella sandwiches, oranges, apples and/or grapes, cheese sticks, pudding cups, and squeeze yogurts, as well as the above options.

After the Event: Consume recovery snacks with an approximate ratio of 4 to 5 g of protein to 1 g of protein.

- Chocolate milk
- Fast food milkshake
- Cereal and low-fat dairy or soy milk
- Low-fat dairy or soy milk and a banana
- Peanut butter sandwich and milk
- Baked potato and cheddar or cottage cheese

Carbohydrates are classified in several ways. Formerly, carbohydrates were referred to as either simple or complex. Simple carbohydrates are basic sugars that are single or one-unit sugars and include foods such as honey, raw sugar, syrup, candy, jelly, and table sugar. Complex carbohydrates contain mostly glucose units that are joined together in compounds called polysaccharides and include starch, fiber, and glycogen.[7] Another classification of carbohydrates is called the glycemic index (GI). This is a more comprehensive explanation of the quality of carbohydrates. GI is a relative number that describes the potential of a food to raise blood glucose and subsequently insulin. Foods are compared to white bread or pure glucose to obtain a number called the GI.[9] In general, a food with a GI has a greater potential to raise blood glucose and be rapidly absorbed, whereas one with a lower GI has a slower the rate of digestion and absorption.[7,9]

Increasingly, athletes are using GI to make food choices that may enhance performance (Table 10–2). Some propose that lower GI foods are best before exercise to promote

sustained and slower absorption of carbohydrates for longer lasting energy. Moderate-to-high GI foods with faster carbohydrate absorption may be recommended during and after exercise to ensure optimal muscle glycogen stores and enhance recovery.[7,9] GI may be useful to help guide carbohydrate choices; however, further studies are warranted. In determining which foods are most beneficial for training and competition, athletes would be wise not only to consider GI but also to take into account the nutrient value, taste, cost, preparation, and portability of the food.[7,9] Refer to Table 10–3 for a list of recommended sports nutrition websites.

Table 10–2 Examples of Low, Medium, and High Glycemic Index Foods

High Glycemic Index

- Glucose and sucrose
- Corn Flakes, Cheerios[a], Rice Krispies[a]
- Waffles, pancakes, and bagels
- White bread
- Baked potato
- Honey
- Banana
- Rice cakes
- English muffins
- Pop-tarts[a]
- White bread

Medium Glycemic Index

- Raisins
- Sweet potato
- Pasta
- Peas
- Apple
- Orange juice
- Oatmeal

Low Glycemic Index

- Milk
- Yogurt
- Raw celery, peppers, and carrots
- Peanuts and tree nuts
- Beans
- 100% bran cereals
- Bulgur and barley
- Ice cream

Source: Adapted from the International Tables of Glycemic Index and Glycemic Load Values: 2008.[10]

Table 10–3 Recommended Sports Nutrition Websites

- American Dietetic Association
- SCAN (Sports and Cardiovascular Nutritionists)
  www.eatright.org
- International Journal of Sport Nutrition and Exercise Metabolism
  www.humankinetics.com
- Gatorade Sports Science Institute
  www.gssiweb.com
- Sports and Nutrition: The Winning Connection (This website is particularly good for meal planning.)
  www.urbanext.uiuc.edu/hsnut
- Nutrition Science and the Olympics
  http://btc.montana.edu/olympics/nutrition/
- Nutrition on the Move
  www.eatnmove.com

Carbohydrates during exercise serve to maintain blood glucose stores at higher levels, thus increasing the use of blood glucose when muscle glycogen stores may be lower.

Carbohydrates during exercise are especially important for endurance sports such as running, but also with sports such as tennis, basketball, soccer, and cycling that require repeated periods of high-intensity, short-duration efforts.[8] During exercise, it is recommended that athletes consume 30 to 60 g of carbohydrate per hour. This translates to 120 to 240 calories of carbohydrate per hour. The carbohydrate can be obtained from either solid or liquid foods, depending on the athlete's preference.[7]

Energy bars are one of the most popular options for snacks during exercise. The ideal bar is one that has at least 80% carbohydrate and less than 10% fat, to help prohibit the delayed absorption of carbohydrates.[7] Some protein is also helpful, particularly for endurance athletes, as up to 10% of the energy during exercise may come from protein stores in the body. Some athletes prefer to consume liquid supplements. Most sports beverages provide about 15 to 20 g of carbohydrate per 8 to 12 ounces, thus at least 8 ounces every half hour should help maintain an adequate supply of carbohydrates. Both liquid and solid carbohydrates will supply adequate energy during exercise. By comparison, sports gels provide an average of 25 g of carbohydrate, an average sports bar provides 66 g, and one large banana provides 30 g.[7,8]

Carbohydrates should also be consumed after exercise. This is particularly important in restoring muscle glycogen stores to ensure optimal performance for consecutive exercise sessions. Athletes who train hard over a period of days or several times in one day, as well as those who are competing in events that last more than one day, need to ensure that they have a recovery snack after each exercise session. Research shows that consuming carbohydrates within 15 to 30 minutes after exercise will provide optimal muscle glycogen re-synthesis, whereas delaying the ingestion of carbohydrates by over an hour may reduce muscle glycogen

stores up to 50% or greater.[8] The amount of carbohydrate recommended after exercise is 1.0 to 1.5 g/kg of body weight within 30 minutes after exercise with continued intake of carbohydrate over several hours for a total of 1.0 g/kg of body weight per hour.[7,8]

Foods that are moderate-to-high in GI are rapidly absorbed and, thus, promote optimal restoration of muscle glycogen.[7,9] Common recovery foods include pasta, granola, oatmeal raisin cookies, fig bars, potatoes, bananas, and chocolate milk (Tables 10–1 and 10–2). The optimal carbohydrate to protein ratio for a recovery snack is 4 to 1 g. Although no conclusive data have been found that suggest that the addition of protein aids in restoring muscle glycogen, it may enhance muscle repair.[7]

Carbohydrates are very important to optimal sports nutrition. Below is a summary of the basic sports nutrition carbohydrate prescriptions:

- One to four hours prior to exercise, athletes should consume 1 to 4 g of carbohydrate per kilogram.
- During exercise, 30 to 60 g of carbohydrate should be consumed every hour.
- 1.0 to 1.5 g/kg of body weight within 30 minutes after exercise with continued intake of carbohydrate over several hours for a total of 1.0 g/kg of body weight per hour.[7]

PROTEIN

The Dietary Reference Intake (DRI) for protein is 0.95 g/kg for individuals 4–13 years of age, 0.85 g/kg for individuals 14–18 years of age, and 0.8 g/kg/d for individuals above 18 years of age. These amounts do not take into account the amount of physical activity. The American College of

Sports Medicine, the Academy of Nutrition and Dietetics, and the Dietitians of Canada all have agreed that active individuals have higher protein requirements. The position statement on "Nutrition and Athletic Performance" recommends that endurance athletes should consume 1.2 to 1.4 g of protein per kilogram per day and that strength, or resistance-trained athletes, may need to consume up to 1.6 to 1.7 g/kg/d.[11]

One of the reasons that athletes may require more protein than sedentary individuals is that it may contribute from 5% to 15% of the fuel during exercise. Exercise may cause muscle breakdown which may increase the amount of protein needed. Endurance athletes may need more protein as some lose a small amount of protein in the urine, whereas protein is typically not lost this way in a healthy person who engages in little to no exercise.[7] Other athletes who may require more protein are those who restrict food intake to achieve a desirable weight or those who practice some form of vegetarianism.[4,7] Athletes who are still growing especially those who have not had their pubertal growth spurt may also require more protein.[7]

Protein requirements remain somewhat controversial among athletes. Many falsely believe that they need more protein than they actually do and consider using protein supplements. These supplements are often marketed as ways to gain extra muscle quickly. However, the primary reason protein supplements help an athlete gain muscle is by contributing extra calories, which thereby spares the dietary protein consumed through food for growth and repair of muscle. The average American diet generally provides ample protein.[5,7] Excess protein may be detrimental to optimal performance and may lead to complications such as impairment of kidney function.[7] A high-protein diet may also indicate a high-fat diet, especially saturated fat. The additional fat may

increase the risk of certain diseases such as cardiovascular disease.[5] In summary, adequate protein, and not excessive protein, should be encouraged for all athletes.

FAT

Dietary fat serves several functions for the athlete. It provides essential fatty acids, which the body cannot synthesize on its own, facilitates the absorption of fat-soluble vitamins, and is an energy source that not only helps to meet daily energy needs but also supplies energy when other sources of readily available energy such as glucose are depleted.[5] The extent to which fat supplies energy depends on the duration and intensity of the exercise. The amount of fat in an athlete's diet will vary depending on the amount of total calories consumed, the type of sport, and the level of training. However, in general, athletes should follow the same guidelines as the general public with 20% to 35% of total calories from fat, with saturated fat less than 10% of the total calories. This equates to about 1 g of fat per kilogram of body weight.[5,7] As with all macronutrients, dietary fat should be individualized, taking into account an athlete's growth stage, nutrition needs, taste preference, physical activity level, energy expenditure, and sports-specific considerations.[7]

Athletes in appearance sports, such as gymnastics and figure skating may have much lower intakes of fat, and even go well below the recommended range, particularly if they are trying to achieve lower body fat levels.[2,5] Very low-fat diets such as those lower than 20% of the total calories are not optimal. Athletes trying to achieve lower body weight or body fat may increase the intake of carbohydrates and/or protein at the expense of consuming adequate dietary fat. For some athletes, especially those who are still growing, a low-fat diet may not provide sufficient energy to meet both the needs of

growth and training. Furthermore, athletes consuming very low-fat diets may avoid dairy products, meat, fish, poultry, and eggs, leading to deficiencies of calcium, iron, and zinc. Female athletes may compromise estrogen production with accompanying menstrual dysfunction.[2,5]

VITAMINS AND MINERALS

Vitamins and minerals are necessary for the proper functioning of all body tissues. They are essential for the release of energy from macronutrients by serving as enzymes and cofactors for metabolism. They are called micronutrients, or small nutrients, as although each vitamin and mineral has an important role in maintaining normal cell and body function, they are only needed in small amounts.[7] Many athletes take a low-dose multivitamin and mineral supplement to ensure they are getting enough of each vitamin and mineral. Other athletes mistakenly think they need to take megadoses of vitamins and minerals to achieve optimal performance.[7,8] Athletes who consume enough total calories, in a varied diet, to support regular daily activities, as well as sports-specific increased caloric needs, will most likely have sufficient vitamins and minerals for optimal performance.

Athletes who may require more of certain vitamins and/or minerals include individuals with monotonous and/or restrictive diets, vegetarians, or those with certain medical conditions such as food allergies, or malabsorptive disorders such as lactose intolerance, inflammatory bowel disease, and celiac disease.[5,7] Iron supplementation may be necessary in adolescent females with restrictive eating issues or athletes who are vegetarian. Iron deficiency anemia is often a concern with these athletes and may require appropriate use of a multivitamin and mineral supplement with iron or iron supplementation alone.[5] In these, and potentially all cases, it is best

to consult with a registered dietitian to determine whether or not a supplementation regimen is necessary.

Athletes may seek dietary supplements other than vitamins and/or minerals to enhance performance. These supplements may include energy bars, sports drinks, and other substances claiming to enhance athletic performance such as amino acids, protein powders, and weight loss or muscle gaining supplements. In ideal circumstances, supplements should not be used as a substitute for an optimal diet. Health risks of supplements, particularly in a pediatric population, continue to be investigated with no concrete guidelines for safety or efficacy. Thus, these supplements are contraindicated. Proper nutrition and hydration as well as consultation with a sports dietitian should be encouraged for all athletes.[6,7]

HYDRATION

Proper hydration is essential to good sports nutrition. Water functions to regulate body temperature, transport waste products and nutrients, and assist with many biochemical reactions for energy production.[7] Athletes should make a conscious effort to drink fluids throughout the day. As with all macronutrients, total calories, and vitamins and minerals, fluid needs should be individualized. The amount of fluid necessary depends on the individual's age, size, level of physical activity, and the environmental temperature. Athletes should drink before, during, and after exercise. In general, most athletes need one to two cups prior to exercise and one-half to one cup every 15 to 20 minutes during exercise.[5]

Fluids may include plain water, juice, sports beverages, caffeinated and decaffeinated beverages, and soups. Many athletes prefer the taste of sports drinks to water. However, a sports drink is really no better than water, unless exercise

lasts more than 90 minutes or occurs in hot weather. In these conditions, carbohydrates and electrolytes in sports beverages may help to improve performance. Drinking carbonated drinks or juice is not recommended as they may cause cramping, bloating, or diarrhea.[5,7]

A simple way to gauge fluid needs is to weigh before and after a workout. A minimal weight loss usually means that there is adequate fluid and fluid-replacement. A weight loss of more than two pounds probably indicates inadequate fluid intake and possibly dehydration. For every pound of body weight lost during exercise, 16 to 20 ounces of fluid should be consumed to appropriately replace lost fluids. Gaining weight during exercise may be a sign of excessive drinking, or overhydration, indicating the need to reduce the amount of fluid during exercise.[5,7]

Thirst is not a reliable indication of the need for hydration and may actually indicate dehydration. Symptoms of dehydration may include cramping, dizziness, and, in severe cases, heat stroke. Therefore, it is important for an athlete to drink before thirst occurs to maintain proper hydration.[7,11] An athlete should drink often during exercise and monitor hydration by checking urine for its color. If urine is straw colored, then the athlete is most likely properly hydrated. However, if it is dark, the urine may still be concentrated and indicative of inadequate hydration. One exception to this is if a multivitamin is consumed, as it may cause urine to be yellow. In this case, monitor hydration by the volume of urine.[5,7]

WEIGHT CONSIDERATIONS

Although some sports require an athlete to lose or maintain weight to optimize performance, other sports and sports positions require weight gain for a greater competitive

advantage. Conversely, athletes participating in "appearance sports" (e.g., gymnastics, figure skating, dance, and swimming) may feel pressure to lose weight to achieve an ideal thinness. In these athletes, restrictive eating and the use of unsafe dieting practices may not only compromise the athlete's ability to perform, but more concerning, their health.[2,5]

Female Athlete Triad is a syndrome in which restrictive eating (or low energy availability), amenorrhea, and decreased bone mineral density are present. This condition is seen in females participating in sports emphasizing leanness or low body weight. The triad is a serious illness with lifelong health consequences and can potentially be fatal.[2] A multidisciplinary approach to the treatment of this disorder is recommended and includes a medical doctor, dietitian, and a therapist.[7]

Weight gain is important for those who are underweight or who require greater strength, as it increases energy and endurance. Endurance affects an athlete's ability to cope with intense and frequent exercise.[5] Weight gain is achieved by ensuring that each meal and snack has healthful, higher calorie foods. The overall goal is to gain about one-half to one pound per week. The speed at which weight gain occurs may depend on an athlete's genetic make-up, calories consumed in excess of metabolic and training needs, number of rest and recovery days per week, and the training program.[7] Athletes trying to gain weight should consume three meals and two to three snacks each day. Skipping meals such as breakfast may make it more difficult to obtain the necessary calories needed to gain weight. Portions should be larger than normal and calorically dense foods should be encouraged. If extra calories are needed, nutrition supplement drinks contain extra calories and are marketed specifically for weight gain.[5]

SUMMARY

In summary, proper nutrition and hydration can positively affect growth, as well as sports training and performance. Despite the abundance of nutrition supplements and ergogenic aids, food should be encouraged as the optimal fuel for exercise. Athletes are urged to consider constructing their diets carefully and professional help from a registered dietitian is advised. Dietitians formulate individualized nutrition and hydrations prescriptions, as well as provide guidance on proper and improper use of supplements. A dietitian can assess growth, identify athletes who are overweight or underweight, monitor athletes with overuse injuries related to poor nutrition, and identify those who have or are at risk for disordered eating. Daily exercise, including participation in organized sports, is recommended for all children and adolescents. A healthful diet will support these activities as well as optimal growth.

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11 Dietary Supplements

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Dietary supplements are products that include vitamins, minerals, prebiotics, probiotics, or herbs. Supplements are available in various forms, which can include tablets, capsules, liquids, powders, as well as those simulating candies and gums. Supplementation for vitamins and minerals is generally not necessary if a child is eating a wide variety of foods. However, if a child is not eating well, is on a restricted diet, or has a chronic illness (e.g., cystic fibrosis, inflammatory bowel disease, and short bowel syndrome), supplementation may be necessary. The decision to use a single-nutrient supplement, versus a multivitamin with minerals, should be based on the child's individual needs. Supplementation should be done to meet science-based standards such as the Dietary Reference Intake (DRI) while not exceeding tolerated upper intake levels (UL). It is best to administer vitamins and minerals with meals to improve absorption and minimize gastric upset.

Prebiotics are nutrients that are preferentially used to stimulate the growth of healthy intestinal bacteria.

For example, fructooligosaccharides (FOS) are a type of prebiotic because they stimulate the growth of healthy bacteria in the colon and result in the production of short-chain fatty acids (SCFAs). SCFAs are a preferential fuel source of colonic cells, help to maintain GI tract integrity, inhibit the growth of harmful bacteria, and may help reduce diarrhea.

Probiotics are mono or mixed cultures of live bacteria that may have healthful effects on the host by improving properties of indigenous flora. Probiotics are available as supplements or may be added to foods, as in some brands of yogurt. Some studies have shown that probiotics help to optimize healthy gut flora, may help with immunity, food allergy, irritable bowel syndrome, control diarrhea or constipation, prevent further recurrence of *Clostridium difficile*–associated diarrhea, and may also help control yeast overgrowth syndrome. Because probiotics contain live cultures, stability of the product is important to monitor. Most probiotics should be given with meals and should also be given 2 hours apart from antibiotics, with the exception of *Saccharomyces boulardii*, which is not inhibited by antibiotics and is best given in-between meals.

Herbal supplements can originate from herbaceous plants as well as bark, roots, leaves, seeds, flowers and fruit of trees, shrubs, and woody vines. They are available in variable forms such as fresh or dried herbs, tablets, capsules, herbal teas, essential oils, and extracts. Herbs have played a role in maintaining health for thousands of years, and many medications have their origin from plant extracts. Herbal remedies may

also interact with other medications. Before considering taking any herbal remedy, consult expert advice.

The tables that follow summarize the composition of oral multivitamin and multivitamin/mineral products in common use in pediatrics, as well as any inactive ingredients and other information. When taken according to the manufacturer's guidelines, these agents provide or exceed the DRI for most of the nutrients listed. Each table notes the dose for the appropriate age group. Table 11–1 lists the vitamin and mineral of common supplements, as well as any inactive ingredients and miscellaneous information that may be of value to the practitioner. Table 11–2 lists common parenteral and oral electrolyte supplementation products. Information regarding the composition of parenteral multivitamin and trace element products may be found in Chapter 10. Table 11–3 lists common pre- and probiotics, potential benefits of these products, and some commercial products available. Table 11–4 lists information regarding herbal supplements. Table 11–5 summarizes the different vitamin D analogues and metabolites.

The use of any type of supplementation should be communicated to a child's physician. The information provided should include the specific dietary supplement, dosage regimen, and any potential dietary interactions.

Table 11–1 Vitamin and Mineral Supplements

	AquADEKs® Chewable Tablets (per 2 tablets)	AquADEKs™ Pediatric Liquid (per mL)	AquADEKs™ Softgels (per softgel)	Centrum Kids® (per tablet)	Flintstones™ Complete Gummies (per 2 gummies)	Flintstones™ Plus Bone Building Support Gummies (per 2 gummies)	Flintstones™ Plus Bone Building Support (per tablet)	Flintstones™ Plus Immunity Support Gummies (per 2 gummies)	Flintstones™ Plus Immunity Support (per tablet)	Flintstones™ Plus Iron (per tablet)	Flintstones™ Plus Omega-3 DHA Gummies (per 2 gummies)	Flintstones™ Sour Gummies (per 2 gummies)	Flintstones™ Toddler Chewable (per 1 tablet)
Vitamin A	18,167 IU	5751 IU	18,167 IU	3500 IU	2000 IU	1600 IU	2500 IU	2000 IU	2500 IU	2500 IU	2000 IU	2000 IU	1600 IU
Vitamin C	70 mg	45 mg	75 mg	60 mg	30 mg	30 mg	60 mg	125 mg	250 mg	60 mg	30 mg	30 mg	
Vitamin D	800 IU	400 IU	800 IU	400 IU	800 IU	400 IU	400 IU	200 IU	400 IU	400 IU	400 IU	600 IU	600 IU
Vitamin E	100 IU	50 IU as D-a tocopherol and 15 mg as mixed tocopherols	150 IU as D-a tocopherol and 80 mg as mixed tocopherols	30 IU	18 IU	20 IU	15 IU	20 IU	15 IU	15 IU	20 IU	18 IU	10 IU
Vitamin K	150 mcg	400 mcg	700 mcg	10 mcg									
Thiamin (B_1)	1.5 mg	0.6 mg	1.5 mg	1.5 mg			1.05 mg		1.05 mg	1.05 mg			0.7 mg
Riboflavin (B_2)	1.7 mg	0.6 mg	1.7 mg	1.7 mg			1.2 mg		1.2 mg	1.2 mg			0.8 mg
Niacin	10 mg	6 mg	10 mg	20 mg			13.5 mg		13.5 mg	13.5 mg			6 mg
Folic acid	200 mcg		100 mcg	400 mcg	200 mcg		300 mcg	200 mcg	300 mcg	300 mcg	200 mcg	200 mcg	100 mcg
Vitamin B_6	1.9 mg	0.6 mg	1.9 mg	2 mg	1 mg	1 mg	1.05 mg	1 mg	1.05 mg	1.05 mg	1 mg	1 mg	0.7 mg
Vitamin B_{12}	12 mcg		12 mcg	6 mcg	3 mcg	3 mcg	4.5 mcg	5 mcg	4.5 mcg	4.5 mcg	5 mcg	3 mcg	3 mcg
Biotin	100 mcg	15 mcg	100 mcg	45 mcg	75 mcg	75 mcg		75 mcg			75 mcg	75 mcg	150 mcg
Pantothenic acid	12 mg	3 mg	12 mg	10 mg	5 mg	5 mg		5 mg				5 mg	2.5 mg
Calcium				108 mg		100 mg	200 mg						80 mg
Iron				18 mg						15 mg			
Phosphorus				50 mg									

(*Continued*)

Table 11–1 Vitamin and Mineral Supplements (*Continued*)

	AquADEKs® Chewable Tablets (per 2 tablets)	AquADEKs™ Pediatric Liquid (per mL)	AquADEKs™ Softgels (per softgel)	Centrum Kids® (per tablet)	Flintstones™ Complete Gummies (per 2 gummies)	Flintstones™ Plus Bone Building Support Gummies (per 2 gummies)	Flintstones™ Plus Bone Building Support (per tablet)	Flintstones™ Plus Immunity Support Gummies (per 2 gummies)	Flintstones™ Plus Immunity Support (per tablet)	Flintstones™ Plus Iron (per tablet)	Flintstones™ Plus Omega-3 DHA Gummies (per 2 gummies)	Flintstones™ Sour Gummies (per 2 gummies)	Flintstones™ Toddler Chewable (per 1 tablet)
Iodine				150 mcg	30 mcg	40 mcg		40 mcg				30 mcg	70 mcg
Magnesium				40 mg									
Zinc	10 mg	5 mg	10 mg	15 mg	2.5 mg	2.5 mg		2.5 mg				2.5 mg	1.6 mg
Selenium	75 mcg	10 mcg	75 mcg										
Copper				2 mg									
Manganese				1 mg									
Chromium				20 mcg									
Molybdenum				20 mcg									
Potassium													
Sodium							10 mg		25 mg	10 mg			
Coenzyme Q10	10 mg	2 mg	10 mg										
Choline													
Fluoride													
Inositol								20 mcg					
Manufacturer	Aptalis Pharma	Aptalis Pharma	Aptalis Pharma	Centrum	Bayer	Bayer	Bayer	Bayer	Bayer	Bayer	Bayer	Bayer	Bayer
Comments	92% of vitamin A is beta carotine, 8% is palmitate, gluten and casein free	87% of vitamin A is beta carotene; gluten and casein free	92% of vitamin A is beta carotene; gluten and casein free	Contains phenylalanine, contains milk, soy, wheat products	Contains wheat and tree nuts (coconut)	Contains tree nuts (coconut)	Contains phenylalanine and soy products	Contains wheat and tree nuts (coconut)	Contains phenylalanine soy products	Contains phenylalanine soy products	With 32 mg DHA (vegetarian source); contains wheat and tree nuts (coconut)	Contains treenut (coconut), wheat	Contains soy products

	Gummy Bear Essentials® Multivitamin Multimineral (per 3 gummies)	Kids' One MultiStars™ (per tablet)	Kirkman® Super Nu-Thera® Liquid (per tsp)	L'il Critters® Gummy Vites (per 2 gummies)	L'il Critters® Calcium Gummy Bears (per 2 gummies)	L'il Critters® Vitamin D Gummy Bears
Vitamin A	5000 IU	4000 IU	2500 IU	2100 IU		
Vitamin C	60 mg	100 mg	200 mg	20 mg		
Vitamin D	400 IU	400 IU	100 IU	400 IU	220 IU	800 IU
Vitamin E	30 IU	10 IU	2.5 IU	16.5 IU		
Vitamin K		20 mcg				
Thiamin (B_1)	75 mcg	2 mg	7.5			
Riboflavin (B_2)		2 mg	7.5			
Niacin	10 mg	13 mg	12.5			
Folic acid	400 mcg	200 mcg		260 mcg		
Vitamin B_6	2 mg	2 mg	225	2 mg		
Vitamin B_{12}	6 mcg	1 mcg	5	6 mcg		
Biotin	300 mcg	25 mcg	25	60 mcg		
Pantothenic acid	10 mg	4 mg	10	5.2 mg		
Calcium	20 mg	100 mg			200 mg	
Iron		5 mg				
Phosphorus					100 mg	
Iodine	150 mcg	25 mcg		42 mcg		
Magnesium	20 mg	50 mg	75 mg			
Zinc	3 mg	2.5 mg	5 mg	2.7 mg		
Selenium		20 mcg	25 mcg			
Copper		250 mcg				
Manganese		1.5 mg	0.75 mg			
Chromium		30 mcg				

(*Continued*)

Table 11–1 Vitamin and Mineral Supplements (*Continued*)

	Gummy Bear Essentials® Multivitamin Multimineral (per 3 gummies)	Kids' One MultiStars™ (per tablet)	Kirkman® Super Nu-Thera® Liquid (per tsp)	L'il Critters® Gummy Vites (per 2 gummies)	L'il Critters® Calcium Gummy Bears (per 2 gummies)	L'il Critters® Vitamin D Gummy Bears
Molybdenum		30 mcg				
Potassium		15 mg				
Sodium					10 mg	
Coenzyme Q10						
Choline				40 mcg		
Fluoride						
Inositol				40 mcg		
Manufacturer	Rainbow Light	Rainbow Light	Kirkman	Northwest Natural Products	Northwest Natural Products	Northwest Natural Products
Comments	Free of artificial colors, flavors, sweeteners and preservatives; gluten, and free; contains soy	Contains 25 mg citrus bioflavonoid complex, 10 mg organic spirulina, 50 mg 2:1 herbal tonics, 12.5 mg 4:1 vegetable juice complex, and 15 million cfus *Lactobacillus sporogenes*; gluten, yeast, milk, eggs, soy, nuts, fish/ shellfish.	No sucrose, yeast, casein, gluten, soy, egg, milk, peanuts, treenuts, gelatin, artificial colors or flavors.	Gluten free; dairy free; peanut free; soy free egg	Gluten free; dairy free; peanut free; soy free egg and treenut	Gluten free; dairy free; soy free; peanut free

	NanoVM 1–3Y (per 2 level scoops)	NanoVM 4–8Y (per 2 level scoops)	NanoVM t/f (per 41 mL)	Natrol Liquid Kid's Companion® (per 2 mL)	NutriStart Multivitamin Powder™ (per packet)	One A Day® Kids Jolly Rancher™ Gummies (per 2 gummies)	One A Day® Kids Scooby-Doo!™ Complete	One A Day® Kids Scooby-Doo!™ Gummies (per 2 gummies)	One A Day™ Teen Advantage for Her (per tablet)	One A Day™ Teen Advantage for Him (per tablet)	One a Day Women's Prental (per tablet)	Phlexy Vits (per 7 g packet)	Poly-Vi-Sol® (per 1 mL)	Poly-Vi-Sol® With Iron (per 1 mL)
Vitamin A	1000 IU	1332 IU	350 mcg	2500 IU	2500 IU	2000 IU	3000 IU	2000 IU	2500 IU	2500 IU	4000 IU	2664 IU	1500 IU	1500 IU
Vitamin C	15 mg	25 mg	32.5 mg	100 mg	100 mg	30 mg	60 mg	30 mg	120 mg	120 mg	60 mg	50 mg	35 mg	35 mg
Vitamin D	400 IU	400 IU	5 mcg	400 IU	400 IU	200 IU	400 IU	200 IU	800 IU	400 IU	400 IU	400 IU	400 IU	400 IU
Vitamin E	9 IU	10 IU	7.5 mg	30 IU	20 IU	20 IU	30 IU	20 IU	30 IU	30 IU	30 IU	13.5 IU	5 IU	5 IU
Vitamin K	30 mcg	55 mcg	37.5 mcg		50 mcg				25 mcg	25 mcg		70 mcg		
Thiamin (B_1)	0.5 mg	0.6 mg	0.5 mg	1 mg	1 mg		1.5 mg		2.3 mg	3.75 mg	1.7 mg	1.2 mg	0.5 mg	0.5 mg
Riboflavin (B_2)	0.5 mg	0.6 mg	0.5 mg	1 mg	1.2 mg		1.7 mg		2.6 mg	4.25 mg	2 mg	1.4 mg	0.6 mg	0.6 mg
Niacin	6 mg	8 mg	7 mg	12 mg	16 mg		15 mg		30 mg	30 mg	20 mcg	20 mg	8 mg	8 mg
Folic acid	150 mcg	200 mcg	200 mcg	100 mcg	200 mcg	200 mcg	400 mcg	200 mcg	400 mcg	400 mcg	800 mcg	700 mcg		
Vitamin B_6	0.5 mg	0.6 mg	0.6 mg	1.4 mg	800 mcg	1 mg	2 mg	1 mg	3 mg	5 mg	2.5 mg	1.6 mg	0.4 mg	0.4 mg
Vitamin B_{12}	0.9 mcg	1.2 mcg	1.2 mcg	2.5 mcg	4 mcg	5 mcg	6 mg	5 mcg	9 mcg	15 mcg	8 mcg	5 mcg	2 mcg	
Biotin	8 mcg	12 mcg	12.5 mcg	20 mcg	150 mcg	75 mcg	40 mcg	75 mcg	300 mcg	300 mcg	300 mcg	150 mcg		
Pantothenic acid	2 mg	3 mg	2.5 mg	6 mg	6 mg	5 mg	10 mg	5 mg	10 mg	10 mg	10 mg	5 mg		
Calcium	500 mg	800 mg	650 mg		200 mg		100 mg		300 mg	200 mg	300 mg	1000 mg		
Iron	7 mg	10 mg	5.5 mg		4 mg		18 mg		18 mg	9 mg	28 mg	15.1 mg		10 mg
Phosphorus	460 mg	500 mg	625 mg				100 mg					775 mg		
Iodine	90 mcg	90 mcg	75 mcg			40 mcg	150 mcg	40 mcg			150 mcg	150 mcg		
Magnesium	65 mg	110 mg	175 mg		100 mg		20 mg		50 mg	100 mg	50 mg	300 mg		
Zinc	3 mg	5 mg	4.5 mg		10 mg	2.5 mg	12 mg	2.5 mg	15 mg	15 mg	15 mg	11.1 mg		
Selenium	20 mcg	30 mcg	27.5 mcg		25 mcg				20 mcg	20 mcg		75 mcg		
Copper	340 mcg	440 mcg	445 mcg				2 mg		2 mg	2 mg	2 mg	1505 mcg		

(*Continued*)

Table 11–1 Vitamin and Mineral Supplements (*Continued*)

	NanoVM 1–3 Y (per 2 level scoops)	NanoVM 4–8 Y (per 2 level scoops)	NanoVM t/f (per 41 mL)	Natrol Liquid Kid's Companion® (per 2 mL)	NutriStart Multi-vitamin Powder™ (per packet)	One A Day® Kids Jolly Rancher™ Gummies (per 2 gummies)	One A Day® Kids Scooby-Doo!™ Complete	One A Day® Kids Scooby-Doo!™ Gummies (per 2 gummies)	One A Day® Teen Advantage for Her (per tablet)	One A Day® Teen Advantage for Him (per tablet)	One a Day Women's Prental (per tablet)	Phlexy Vits (per 7 g packet)	Poly-Vi-Sol® (per 1 mL)	Poly-Vi-Sol® With Iron (per 1 mL)
Manganese	1.2 mg	1.5 mg	0.8 mg						2 mg	2 mg		1.5 mg		
Chromium	11 mcg	15 mcg	12 mcg						120 mcg	120 mcg		30 mcg		
Molybdenum	17 mcg	22 mcg	21.5 mcg									70 mcg		
Potassium	575 mg	775 mg	1170 mg									<1.4 mg		
Sodium							10 mg					8.8 mg		
Coenzyme Q10														
Choline					20 mg	30 mcg		30 mcg						
Fluoride														
Inositol						20 mcg		20 mcg						
Manufacturer	Solace Nutrition	Solace Nutrition	Solace Nutrition	Natrol	Rainbow Light	Bayer	Bayer	Bayer	Bayer	Bayer	Bayer	Nutricia	Mead Johnson	Mead Johnson
Comments	Carbohydrate free (0.006 g); free from egg, milk, wheat, walnut, almond, and peanut; free from additives, sweeteners, flavorings, gluten and casein.	Carbohydrate free (0.006 g); free from egg, milk, wheat, walnut, almond, and peanut; free from additives, sweeteners, flavorings, gluten and casein.	For individuals who are exclusively tube fed; Free from egg, milk, wheat, walnut, almond and peanut; free from corn derived ingredients; free from additives, sweeteners, flavorings, gluten and casein soy, fish, and shellfish under the free from section	Contains soy and corn; gluten free	Contains 25 mg antioxidant fruit blend, 500 mg organic apple powder and 500 mg organic banana powder no gluten, yeast, milk, egg, soy, nut, fish, shellfish	contains tree nuts (coconut) and wheat	Contains phenylalanine	Contains wheat and tree nuts (coconut)	Contain soy	Contain soy	contains soy	Also contains <0.35 mg of chloride; indicated for individuals 11 y and older that have restricted therapeutic diets	does not contain ingredients derived from milk, egg, peanut, treenut, fish, shellfish, soy, wheat Gluten free	does not contain ingredients derived from milk, egg, peanut, treenut, fish, shellfish, soy, wheat Gluten free

	Schiff® Children's Chewable Vitamins with Minerals	Source of Life® Animal Parade® GOLD Liquid	Tri-Vi-Sol® (per 1 mL)	Yummi Bears® Multivitamin & Minerals Gummies (per 3 bears)
Vitamin A	2500 IU	5000 IU	1500 IU	2500 IU
Vitamin C	30 mg	60 mg	35 mg	30 mg
Vitamin D	200 IU	500 IU	400 IU	150 IU
Vitamin E	15 IU	30 IU		15 IU
Vitamin K		40 mcg		
Thiamin (B_1)	0.75 mg	1.5 mg		
Riboflavin (B_2)	0.85 mg	1.7 mg		
Niacin	10 mg	20 mg		2.5 mg
Folic acid	200 mcg	10 mcg		200 mcg
Vitamin B_6	1 mcg	2 mg		1 mg
Vitamin B_{12}	3 mcg	6 mcg		3 mcg
Biotin		50 mcg		70 mcg
Pantothenic acid		10 mg		5 mg
Calcium	20.5 mg	50 mg		9.2 mg
Iron	9 mg	5 mg		
Phosphorus				
Iodine		100 mcg		75 mcg
Magnesium		10 mg		8 mg
Zinc	1 mg	3 mg		7.5 mg
Selenium		35 mcg		
Copper		1 mg		
Manganese	3 mg	1 mg		

(*Continued*)

Table 11–1 Vitamin and Mineral Supplements (*Continued*)

	Schiff® Children's Chewable Vitamins with Minerals	Source of Life® Animal Parade® GOLD Liquid	Tri-Vi-Sol® (per 1 mL)	Yummi Bears® Multivitamin & Minerals Gummies (per 3 bears)
Chromium		60 mcg		
Molybdenum				
Potassium		1 mg		
Sodium				
Coenzyme Q10				
Choline		10 mcg		15 mcg
Fluoride				
Inositol		10 mcg		15 mcg
Manufacturer	Schiff	Nature's Plus	Mead Johnson	Hero Nutritionals
Comments		0.5 mg lutein, 2mg essential fatty acid complex, free of yeast, wheat, soy, milk	does not contain ingredients derived from milk, egg, peanut, treenut, fish, shellfish, soy, wheat Gluten free	Contains no yeast, wheat, milk, egg, soy, gluten, salt, peanuts, shellfish, artificial colors, artificial flavors, salicylates and preservatives

Table 11–2 Comparison of Mineral and Electrolyte Products

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
Enteral products					
Calcium	Acetate	25	12.7	1 g calcium acetate = 250 mg elemental calcium = 12.7 mEq calcium PhosLo® Gelcaps 667 mg (8.45 mEq elemental Ca^{2+}) Eliphos™ Tablets 667 mg (8.45 mEq elemental Ca^{2+}) PhosIrya™ Solution 667 mg/5 mL (8.45 mEq elemental Ca^{2+})	May cause constipation or dry mouth
	Carbonate	40	20	1 g calcium carbonate = 400 mg elemental calcium = 20 mEq calcium Calci-Mix® Capsule 1250 mg (500 mg elemental Ca^{2+}) Florical® Capsule 364 mg (145 mg elemental Ca^{2+}) Caltrate®, Nephro-Calci®, Super Calcium Tablets 1500 mg (600 mg elemental Ca^{2+}) Oystercal™ and Oysco Tablets 1250 mg (500 mg elemental Ca^{2+}) Children's Pepto and Maalox® Children's Chewable Tablets 400 mg (160 mg elemental Ca^{2+}) Maalox® Regular Strength 600 mg (240 mg elemental Ca^{2+})	Florical® contains fluoride Must be taken with meals or glass of acidic (orange) juice May cause gas or constipation

(*Continued*)

Table 11–2 Comparison of Mineral and Electrolyte Products (*Continued*)

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
				Tums® 500 mg (200 mg elemental Ca^{2+}) Tums® E-X and Tums® Smoothies 750 mg (300 mg elemental Ca^{2+}) Tums® Ultra 1000 mg (400 mg elemental Ca^{2+})	
	Citrate	21	10.6	1 g calcium citrate = 211mg elemental calcium = 10.6 mEq calcium Cal-C-Caps Capsule 180 mg elemental Ca^{2+} Cal-Citrate™ Capsule 225 mg elemental Ca^{2+} Cal-Cee Tablet 250 mg elemental Ca^{2+} Calcitrate Tablet 200 mg elemental Ca^{2+}	Most easily absorbed Most expensive form of oral calcium supplements
	Glubionate	6.5	3.3	1 g calcium glubionate = 64 mg elemental calcium = 3.2 mEq calcium Calcionate Syrup 1.8 g/5 mL (115 mg/5 mL elemental Ca^{2+})	
	Gluconate	9	4.5	1 g calcium gluconate = 90 mg elemental calcium = 4.5 mEq calcium Cal-G Capsule 700 mg (65 mg elemental Ca^{2+}) Cal-GLU Capsule 515 mg (50 mg elemental Ca^{2+}) Various, Tablet 500 mg (45 mg elemental Ca^{2+}) Various, Tablet 648 mg (60 mg elemental Ca^{2+})	Cal-G gluten Free Cal-GLU dye free, sugar free

Mineral	Salt Form	% Cation	mEq/ gram	Representative Products	Com- ments
	Lactate	13	6.5	1 g calcium lactate = 130 mg elemental calcium = 6.5 mEq calcium	
				Various, Tablet 648 mg and 650 mg (84.5 mg elemental Ca^{2+})	
	Phosphate	39	19.3	1 g calcium phosphate, tribasic = 390 mg elemental calcium = 19.3 mEq calcium Caplet: Posture® 600 mg calcium and 280 mg phosphorus (as tricalcium phosphate)	Easily absorbed Does not cause gas or constipa- tion More expen- sive than calcium carbonate salts
Iron	Carbonyl iron	100		1000 mg/g Suspension: Icar® Pediatric 15 mg (iron)/ 1.25 mL Tablets: Feosol caplets 45 mg (iron)/caplet	Carbonyl iron is elemental iron, not an iron salt
	Fumarate	33		Femiron® 63 mg (20 mg elemental Fe) Ircon® 200 mg (66 mg elemental Fe) Ferrocite™ and Hemo- cyte® 324 mg (106 mg elemental Fe) Ferro-Sequels® Timed Release Tablets 150 mg (50 mg elemental Fe)	

(*Continued*)

Table 11–2 Comparison of Mineral and Electrolyte Products (*Continued*)

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
	Gluconate	11.6		Various: Tablets 240 mg (27 mg elemental Fe) 246 mg (28 mg elemental Fe) 300 mg (34mg elemental Fe) 320 mg (37 mg elemental Fe) 324 mg (36 mg elemental Fe) 325 mg (38 mg elemental Fe)	
	Sulfate	20		Elixir 220 mg/5 mL (44 mg elemental Fe/5 mL) Fer-In-Sol® and Fer-iron 75 mg/mL (15 mg elemental Fe/mL) MyKidz Iron 75 mg/1.5 mL (15 mg elemental Fe/1.5 mL) Tablet 324 mg and 325 mg (65 mg elemental Fe) also available in enteric coated Extended Release Tablet 140 mg (45 mg elemental Fe) Slow FE® Slow Release Tablet 142 mg (45 mg elemental Fe)	
Magnesium	Carbonate	28	23.4	Only used in antacids in combination with aluminum hydroxide	

Mineral	Salt Form	% Cation	mEq/ gram	Representative Products	Com- ments
	Chloride	11.8	9.8	Magnesium chloride 500 mg = 59 mg elemental Mg^{2+}= 4.9 mEq elemental Mg^{2+} Tablet, controlled released: Mag 64™ and Mag Delay Delayed Release Enteric Coated tablet 535 mg (elemental Mg^{2+} 64 mg) Tablet, enteric coated Slow-Mag® 535 mg (64mg elemental Mg^{2+})	
	Gluconate	5.9	4.5	Magnesium gluconate 500 mg = 27 mg elemental Mg^{2+}= 2.4 mEq elemental Mg^{2+} Magonate® 1000 mg/ 5 mL liquid (54 mg/5 mL Mg^{2+}) Magonate®, Magtrate®, Mag®-G 500 mg tablet (27 mg elemental Mg^{2+})	
	Oxide	60	49.6	Magnesium oxide 500 mg = 302 mg elemental Mg^{2+}= 25 mEq elemental Mg^{2+} Uro-Mag® 140 mg Capsule (84.5 mg elemental Mg^{2+}) Mag-Ox® and MAGnesium-Oxide™ 400 mg tablet (240 mg Mg^{2+})	
Potassium	Bicarbonate	39.1	9.99	Effervescent Tablet for Solution Potassium 25 mEq	

(*Continued*)

Table 11–2 Comparison of Mineral and Electrolyte Products (*Continued*)

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
	Chloride	52.4	13.4	microK® Extended Release, microencapsulated capsule 8 mEq, 10 mEq Epiklor™ and Klor-Con® Powder for Solution 20 mEq/packet and 25 mEq/packet Oral Solution 20 mEq/15 mL and 40 mEq/15 mL Extended Release Tablet 10 mEq Klor-Con® Extended Release, microencapsulated tablet 10 mEq (750 mg), 15 mEq (1125 mg), and 20 mEq (1500 mg) Klor-Con® Extended Release, wax matrix tablet 8 mEq (600 mg) K-Tab®, Kaon-CL®, and Klor-Con® Extended Release, wax matrix tablet 10 mEq (750 mg)	Morton Lite Salt (¼ teaspoon = 290 mg Na^+ 350 mg K^+)
	Citrate	38.3	9.26	Urocit®-K Extended Release Tablet 5 mEq (540 mg), 10 mEq (1080 mg) 15 mEq (1620 mg)	
	Gluconate	16.7		Capsule, Caplet, and Tablet 595 mg (99 mg K^+) Tablet 550 mg (90 mg K^+) Timed Release tablet 95 mg (strength expressed as base)	

Mineral	Salt Form	% Cation	mEq/ gram	Representative Products	Com- ments
Sodium	Bicarbonate	27.4	12	Brioschi® Effervescent Granules for solution 2.69 g/capful and 2.69 g/packet (770 mg Na^+) Tablet 325 mg (3.8 mEq) 650 mg (7.6 mEq)	
	Chloride	39.3	17.1	Tablet 650mg (11.3 mEq Na^+) 1gm (17 mEq Na^+) 2.25gm(38.5mEq Na^+) Slow release tab 600mg(10.3 mEq Na^+) Enteric coated tab 1gm (17 mEq Na^+)	Regular table salt (1 teaspoon = 2300 mg Na^+) Morton Lite Salt (¼ teaspoon = 290 mg Na^+ 350 mg K^+)
	Phosphate	19.2 (mono- basic) 32.4 (dibasic)		Oral solution monoba- sic sodium phosphate monohydrate 2.4 g and dibasic sodium phos- phate heptahydrate 0.9 g per 5 mL (556 mg/5 mL Na^+) OsmoPrep® and Visi- col® tablet, monobasic sodium phosphate monohydrate 1.102 g and dibasic sodium phosphate anhydrous 0.398 g (1.5 g Na^+)	Osmo- Prep® and Visicol® tablet gluten free
Parenteral products					
Calcium	Chloride	27	14	10% solution for injec- tion 100 mg/mL (27.2 mg/mL elemental Ca^{2+}) (1.36 mEq/mL elemen- tal Ca^{2+})	

(*Continued*)

Table 11–2 Comparison of Mineral and Electrolyte Products (*Continued*)

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
	Gluconate	9	4.5	10% solution for injection 100 mg/mL (9.3 mg/mL elemental Ca^{2+}) (0.465 mEq/mL elemental Ca^{2+})	
Iron	Dextran			Dexferrum® and INFeD® elemental iron 50 mg/mL elemental iron	Dexferrum high-molecular-weight iron dextran INFed low-molecular-weight iron dextran Test dose required Adverse reactions usually occur more with the high-molecular-weight formulation compared to the low-molecular-weight product Absorption: I.M.: 60% absorbed after 3 d; 90%

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
					after 1–3 wk, the balance is slowly absorbed over months
	Gluconate			Ferrlecit® solution for injection 12.5 mg elemental iron/mL Nulecit™ 12.5 mg elemental iron/mL	Contains benzyl alcohol, sucrose 20%
	Sucrose			Venofer® solution for injection Elemental iron 20 mg/mL	
Magnesium	Chloride	11.8	9.8	Chloromag® solution for injection 200 mg/mL (1.97 mEq elemental Mg^{2+}/mL)	
	Sulfate	9.9	8.12	Solution for injection 500 mg/mL (49.3 mg/mL elemental Mg^{2+}) (4.06 mEq/mL elemental Mg^{2+})	
Potassium	Acetate	39.8	10.2	Solution for injection 2 mEq/mL Solution for injection 4 mEq/mL	
	Chloride	52.4	13.4	Solution for injection 2 mEq/mL	
	Phosphate	28.7 (monobasic) 44.9 (dibasic)	7.3 (monobasic) 11.5 (dibasic)	Solution for injection Potassium 4.4 mEq/mL (170 mg/mL K^+) (3 mM phosphorus/mL)	

(*Continued*)

Table 11–2 Comparison of Mineral and Electrolyte Products (*Continued*)

Mineral	Salt Form	% Cation	mEq/gram	Representative Products	Comments
Sodium	Acetate	28	7.3	Solution for injection 2 mEq/mL 4 mEq/mL	
	Bicarbonate	27.4	12	Solution for injection 4% (0.48 mEq/mL) (Neut) 4.2% (0.5mEq/mL) 7.5% (0.892 mEq/mL) 8.4% (1 mEq/mL)	
	Chloride	39.3	17.1	Solution for injection 0.225% (38.5 mEq/1000 mL) 0.45% (77 mEq/1000 mL) 0.9% (154 mEq/l000 mL) 3% (513 mEq/1000 mL) Concentrate solution for injection 14.6% (2.5 mEq/mL) 23.4% (4 mEq/mL)	
	Lactate	20.5	8.92	Solution for injection 560 mg/mL (5 mEq/mL)	
	Phosphate	19.2 (monobasic) 32.4 (dibasic)		Solution for injection 92 mg/mL (4 mEq/mL) (3mM/mL phosphorus)	

Sources: Adapted from Calcium. *Facts & Comparison® eAnswers Clin-eguide.* Retrieved June 20, 2012; Iron Products. *Facts & Comparison® eAnswers Clin-eguide*. June 20, 2012; *Lexicomp Online™* Retrieved June 20, 2012; Potassium Salts. *Facts & Comparison® eAnswers Clin-eguide.* Retrieved June 20, 2012.

Table 11–3 Recommended Probiotics and Suggested Pediatric Doses

Single-Species Probiotics	Uses	Brand Names and Product Information
Lactobacillus (best studied are strains of *Lactobacillus rhamnosus, GG, Lactobacillus bulgaricus, Lactobacillus reuteri, and Lactobacillus acidophilus*)	• Can treat and prevent diarrhea, including infectious (rotavirus in children), traveler's diarrhea, and antibiotic-associated diarrhea • May help relieve infant colic • May reduce risk of necrotizing enterocolitis in very low weight preterm babies • May reduce symptoms of irritable bowel syndrome (IBS) • Can effect clearance of *Helicobacter pylori* in conjunction with standard therapy • May promote a "balanced" normal physiologic and bacterial flora of the intestinal tract[1–11]	Lactinex™: *Lactobacillus acidophilus* • *Children*: Take 4 chewable tablets or 1 packet of granules 3–4 times daily • *Adults*: Take 4 chewable tablets or 1 packet of granules 3–4 times daily • Keep products refrigerated • Tablets should be chewed and then followed by milk, water or juice, and the granules can be added to cereal, food, or milk • All Lactinex™ products are gluten free Do not take Lactinex™ if you are allergic to milk or sensitive to soy or lactose Culturelle®: *Lactobacillus GG* • *Children:* • For children with IBS: Take 1 capsule (10 billion cfu) by mouth 1–2 times daily • For infant colic: Give 1 "for Kids" packet (1 billion cfu) or 1 capsule(10 billion cfu) by mouth daily • For antibiotic associated diarrhea in children: 1 capsule (10 billion cfu) twice daily - Culturelle® has a dairy and gluten free formulation for patients with allergies • *Adults*: Take 1 capsule by mouth daily • The contents of the Culturelle® capsule can be opened and mixed into a cool drink or food. Do not mix into warm/hot foods or beverages • Store at room temperature

(*Continued*)

Table 11–3 Recommended Probiotics and Suggested Pediatric Doses (*Continued*)

Single-Species Probiotics	Uses	Brand Names and Product Information
Bifidobacterium (best studies are strains of *Bifidobacterium infantis, Bifidobacterium breve, Bifidobacterium longum)*	Demonstrated in trials to manage symptoms associated with irritable bowel syndrome (IBS) including symptoms of diarrhea, constipation, abdominal discomfort, urgency, gas, and bloating[12–15]	Align®: *Bifidobacterium Infantis strain 3526* • *Children*: Take 1 capsule (100 million cfu) by mouth daily • *Adults*: Take 1 capsule by mouth daily • Can be taken with or without food • Store at room temperature Align® is lactose free but does contain milk protein, so should not be used in patients with milk allergies
Saccharomyces (Saccharomyces boulardii)	• Shown to be efficacious in the treatment and prevention of infectious diarrhea, and antibiotic-associated diarrhea • Can prevent recurrent *Clostridium difficile* colitis • May help relieve symptoms of lactose intolerance[16–19]	Florastor®: • *Children 2 mo of age and older:* Take 1–2 capsules or packets by mouth twice daily - For antibiotic-associated diarrhea: Take 1 capsule (250 mg) by mouth twice daily • *Adults*: Take 1–2 capsules by mouth twice daily • Also available in "for kids" packets that contain the same 250 mg dose as the capsules • Can be taken with or without food • Swallow capsules whole. Do not chew • The contents of the capsules or packets can be emptied on the tongue or mixed into semi-solid food or beverages. Do not mix Florastor® with carbonated, very hot (above 122 °F), or alcohol-containing beverages • Florastor® is contraindicated in patients with a central line due to rare occurrences of fungemia

Single-Species Probiotics	Uses	Brand Names and Product Information
		• Store at room temperature • All Florastor® products are free from corn, egg protein, fish, gluten, latex, meat, milk protein, nuts, and shell fish • May contain traces of soy • Contains 33 mg of lactose but may help increase lactase production that helps break down lactose
Multiple Species Products	**Uses**	**Brand Names and Product Information**
VSL #3: A mixture of 8 live lactic acid probiotic species: *Bifidobacterium breve, Bifidobacterium longum, Bifidobacterium infantis, Lactobacillus acidophilus, Lactobacillus plantarum, Lactobacillus paracasei, Lactobacillus bulgaricus, and Streptococcus thermophilus.*	• Can help relieve the gas and bloating associated with irritable bowel syndrome (IBS) • May provide adjunct to anti-inflammatory therapy in patients with ulcerative colitis • May prevent recurrent pouchitis[20–26]	VSL #3®: • Children: - For IBS: Take 1 packet (ages 4–11) or 2 packets (ages 12–18) by mouth daily - For UC and pouchitis: Take 1–2 packets of VSL #3-DS daily - Specific dosing instructions for children by age and weight are available at http://www.vsl3.com/healthcare-recommended-daily-intake.asp • Adults: - For IBS: Take ½–1 packet or 2–4 capsules by mouth daily - For ulcerative colitis: Take 1–2 packets or 4–8 capsules by mouth daily - For active ulcerative colitis: Take 4–8 packets or 16–32 capsules by mouth daily - For pouchitis: Take 2–4 packets or 6–18 capsules by mouth daily

(*Continued*)

Table 11–3 Recommended Probiotics and Suggested Pediatric Doses (*Continued*)

Multiple Species Products	Uses	Brand Names and Product Information
		• The flavored power packets should be mixed in 4 oz of cold water, and the unflavored packets can be mixed in yogurt, ice cream, applesauce, or any cold food. Consume right after mixing • Do not mix with carbonated beverages or hot beverages/foods • Store VSL #3® in the refrigerator but may be stored at room temperature for up to 1 wk • Avoid taking with antibiotics • VSL #3® is Kosher and Halal certified • VSL #3® is an over-the-counter medication but needs to be ordered through the pharmacy or online. It is recommended to purchase through either amazon.com or drugstore.com since they sell VSL #3® at a discounted price • You can also order through www.vsl3.com or by calling 1-866-GET-VSL3 • Double strength (DS) packets are available by prescription only • VSL #3® is non-dairy and gluten free

Other Over-the-Counter Preparations	Uses	Brand Names and Product Information
Flora-Q®: Lactobacillus acidophilus, Bifidobacterium, Lactobacillus paracasei, and Streptococcus thermophilus	Claims to help maintain the balance of the gastrointestinal tract flora *Source*: Flora-Q® website[27]	Flora-Q®: • *Children*: Take 1 capsule by mouth daily • *Adults*: Take 1 capsule by mouth daily • Can be taken with or without food • Store at room temperature and do not store in the bathroom • May cause increased stomach gas • Also available as a double strength capsule • Flora-Q® is wheat/gluten, milk/lactose, eggs, fish, crustacean shellfish, soybean, tree nut, and peanut free • Flora-Q® is preservative free
Phillips' Colon Health®: Lactobacillus gasseri, Bifidobacterium bifidum, and Bifidobacterium longum	• Claims to help relieve constipation, gas, bloating, and diarrhea[28]	Phillips' Colon Health®: • *Children 3 y of age and older:* Take 1 capsule by mouth daily with food • *Adults*: Take 1 capsule by mouth daily with food • Keep at room temperature Inactive ingredients: potato starch, gelatin, and silicon dioxide

Disclaimer: These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease. Some probiotic usage information in the table is transcribed from company websites and promotional materials. It has not evaluated for its accuracy or validity.

Table 11–4 Herbal Product Considerations

Herbal Products With Appetite Stimulating Properties	
Angelica root	Fenugreek seed
Bitter orange peel	Galangal
Blessed thistle herb[a]	Gentian root
Bogbean leaf	Gingsing
Century herb	Goldenseal
Cinchona bark	Horehound herb
Cinnamon	Iceland moss
Codonopsis	Lemon balm
Condurango bark	Orange peel
Coriander seed	Pollen
Dandelion herb	Wormwood
Dandelion root with herb	Yarrow
Devil's Claw root	Yeast, medicinal
Herbal Products Contraindicated in Children	
Aloe (oral)	Fennel
Buckthorn bark	Horseradish
Buckthorn berry	Nasturtium
Cajeput oil	Rhubarb root
Camphor	Senna leaf
Cascara sagrada bark	Senna pod
Eucalyptus leaf	Scotch Broom
Eucalyptus oil	Watercress

[a]Not recommended for use in infants/young children.

Sources: University of Maryland Medical Center: Herbs and Supplements for Appetite Loss. Jim Meuninck. *Medicinal Plants of North America: A Field Guide*. Guilford, CT: Falcon Press Publishing, The Globe Pequot Press; 2008.

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Table 11–5 Comparison of Vitamin D Analogues/Metabolites

	Vitamin D_2	Vitamin D_3	1,25-Dihydroxyvitamin D_3
Generic name	Ergocalciferol	Cholecalciferol	Calcitriol
Brand name(s)	Calciferol™; Drisdol®	Enfamil® D-Vi-Sol; DDrops®; Bio-D-Mulsion®; Delta® D3	Calcijex®; Rocaltrol®
	1 mcg = 40 USP IU	1 mcg cholecalciferol = 40 USP IU	
Dosage	*Prevention of Vitamin deficiency*: Premature neonates: 10–20 mcg/d (400–800 IU), up to 750 mcg/d (30,000 IU) Breast-fed neonates (fully or partially): 10 mcg/d (400 IU/d) beginning in the first few days of life. Continue supplementation until infant is weaned to ≥1000 mL/d or 1 qt/d of vitamin D-fortified formula (after 12 mo of age) Formula-fed neonates ingesting <1000 mL of vitamin D-fortified formula: 10 mcg/d (400 IU/d) *Vitamin D-dependent rickets:* In addition to calcium supplementation: 25 mcg/d (1000 IU) for 2–3 mo; once radiologic evidence of healing is observed, dose should be decreased to 10 mcg/d (400 IU/d) *Vitamin D insufficiency or deficiency associated with CKD*:	*Prevention of Vitamin deficiency*: Premature neonates: 400–800 IU/d or 150–400 IU/kg/d Term neonates: 400 IU/d Infants: 400 IU/dy Children and adolescents: 600 IU/d *Treatment of Vitamin D deficiency and/or rickets*: Infants 1–12 mo: 1000–5000 IU/d for 2–3 mo; once radiologic evidence of healing is observed, dose should be decreased to 400 IU/d Children >12 mo: 5000–10,000 IU/d for 2–3 mo; once radiologic evidence of healing is observed, dose should be decreased to 400 IU/d	*Hypocalcemic tetany*: Neonates: I.V.: 0.05 mcg/kg once daily for 5–12 d; Oral: Initial 0.25 mcg/dose once daily, followed by 0.01–0.10 mcg/kg/d divided in 2 doses (maximum daily dose: 2 mcg) *Management of hypocalcemia in patients with CKD*: Children and adolescents CKD stages 2–4: Oral: <10 kg: 0.05 mcg every other day 10–20 kg: 0.1–0.15 mcg daily >20 kg: 0.25 mcg daily CKD Stage 5: Oral/IV:

(*Continued*)

Table 11–5 Comparison of Vitamin D Analogues/Metabolites (*Continued*)

	Vitamin D_2	Vitamin D_3	1,25-Dihydroxyvitamin D_3
	Serum 25(OH)D level 16–30 ng/mL Children: 2000 IU/d for 3 mo or 50,000 IU every month for 3 mo Serum 25(OH)D level 5–15 ng/mL Children: 4000 IU/d for 12 wk or 50,000 IU every other week for 12 wk Serum 25(OH)D level <5 ng/mL Children: 8000 IU/d for 4 wk then 4000 IU/d for 2 mo for total therapy of 3 mo or 50,000 IU/wk for 4 wk followed by 50,000 IU 2 times/month for a total therapy of 3 mo Maintenance dose [once repletion accomplished; serum 25(OH)D level >30 ng/mL]: 200–1000 IU/d *Hypoparathyroidism*: Children: 50,000–200,000 IU/d with calcium supplements Prevention and treatment of Vitamin D deficiency in cystic fibrosis: RDI Infants <1 y: 400 IU/d; Children >1 y: 400–800 IU/d *Nutritional rickets and osteomalacia*: Children and adults (with normal absorption) 1000–5000 IU/d for 6–12 wk Children with malabsorption: 10,000–25,000 IU/d	*Vitamin D insufficiency or deficiency associated with CKD*: Serum 25(OH)D level 16–30 ng/mL Children: 2000 IU/d for 3 mo or 50,000 IU every month for 3 mo Serum 25(OH)D level 5–15 ng/mL Children: 4000 IU/d for 12 wk or 50,000 IU every other week for 12 wk Serum 25(OH)D level <5 ng/mL Children: 8000 IU/d for 4 wk then 4000 IU/d for 2 mo for total therapy of 3 mo or 50,000 IU/wk for 4 wk followed by 50,000 IU 2 times/month for a total therapy of 3 mo Maintenance dose [once repletion accomplished; serum 25(OH)D level >30 ng/mL]: 200–1000 IU/d	iPTH 300–500 pg/mL: 0.0075 mcg/kg per dialysis session (3 times/wk); not to exceed 0.25 mcg daily iPTH >500–1000 pg/mL: 0.015 mcg/kg per dialysis session (3 times/wk); not to exceed 0.5 mcg daily iPTH >1000 pg/mL: 0.025 mcg/kg per dialysis session (3 times/wk); not to exceed 1 mcg daily *Hypoparathyroidism/pseudohypoparathyroidism*: Infants <1 y: 0.04–0.08 mcg/kg once daily Children 1–5 y: 0.25–0.75 mcg once daily Children >6 y and Adults: 0.5–2 mcg once daily *Vitamin D-dependent rickets*: Children and adults: Oral: 1 mcg once daily

	Vitamin D_2	Vitamin D_3	1,25-Dihydroxyvitamin D_3
	Familial hypophosphatemia: Children: Initial: 40,000–80,000 IU/d with phosphate supplements; daily dosage is increased at 3–4 mo intervals 10,000–20,000 IU increments	*Prevention and treatment of Vitamin D deficiency in cystic fibrosis*: RDI Infants <1 y: 400 IU/d Children >1 y: 400–800 IU/d	*Vitamin D-resistant rickets (familial hypophosphatemia)*: Children and adults: Oral: Initial: 0.015–0.02 mcg/kg once daily Maintenance: 0.03–0.06 mcg/kg once daily Maximum dose: 2 mcg once daily
Onset of maximal effect	30 d	Specific data for cholecalciferol is unavailable but initial response takes 10–14 d	Oral: 3–6 h Injection: 5 min
How supplied	*Capsule*: 50,000 IU *Tablet*: 400 IU *Solution*: 8000 IU/mL	*Capsule*: 1000 IU; 2000 IU; 5000 IU; 10,000 IU; 50,000 IU *Tablet*: 400 IU; 1000 IU *Solution*: 400 IU/drop; 2000 IU/drop; 400 IU/mL (D-Vi-Sol®)	*Capsule*: 0.25 mcg, 0.5 mcg (Rocaltrol®) *Solution for Injection*: 1 mcg/mL (Rocaltrol® and Calcijex®)
Monitoring parameters	Serum calcium, creatnine/BUN, and phosphate	Serum calcium, creatinine/BUN, and phosphate	Serum calcium, creatinine/BUN, phosphate, and intact parathyroid hormone (iPTH) concentrations

25-Hydroxyvitamin D_3 (Calcifediol): No single-ingredient product containing calcifediol currently available. Dihydrotachysterol (DHT): All DHT products are currently off the market.

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12 Community Nutrition Programs

Erin Keenan, MS, RD, LDN

Knowledge of age-appropriate feeding practices and good nutrition concepts cannot be implemented unless a caregiver has access to food, financial resources to buy food, or the resources to find assistance. The Food and Nutrition Information Center, (www.fnic.nal.usda.gov) as part of the US Department of Agriculture (USDA) offers nutrition and health educational materials on topics ranging from food safety, eating disorders, and herbal supplement use to child nutrition and health. Nutrition Assistance Programs (Table 12–1) are often USDA-directed programs. In addition, many state and local agencies, neighborhood health centers, and local schools and universities offer programs and services to promote the nutritional health of children. The Healthy Meals Resource System is an online information center allowing quick and easy access to wide variety of resources for USDA-based programs and nutrition professionals alike (http://healthymeals.nal.usda.gov).

Table 12–1 US Department of Agriculture Food Assistance Programs

Program	Description	Eligibility Components[a]
Supplemental Nutrition Assistance Program (SNAP)	Provides electronic benefit cards to buy food in approved stores	Gross income must be at or below 185% of federal poverty income guidelines; residency requirements
Special Supplemental Nutrition Program for Women, Infants, and Children (WIC)	Provides health referrals, nutrition education, and food assistance to women, infants, and children	Pregnant or postpartum women and children aged <5 y found to be at nutritional risk; gross income must be at or below 185% of federal poverty income guidelines
National School Lunch Program and School Breakfast Program; Afterschool Snacks	Provides low-cost or free lunches and breakfasts to children in public and nonprofit schools and residential child care institutions; schools are given reimbursement to help serve snacks to children after regular school day ends	Schools must participate in National School Lunch Program and offer an after-school care program to be eligible for afterschool snacks; gross income must be at or below 185% of federal poverty income guidelines
Special Milk Program	Provides milk to children in schools and child care institutions that do not participate in other federal child nutrition meal service programs	Gross income must be at or below 185% of federal poverty income guidelines

Program	Description	Eligibility Components[a]
Fresh Fruit and Vegetable Program	Provides all children in participating schools free fresh fruits and vegetables throughout the school day	Elementary schools in which at least 50% of students receive free or reduced meals; once a school is chosen to participate, all children are eligible to participate
Summer Food Service Program	Provides free, nutritious meals to low-income children during school vacations	Must live in a low-income area; may be required to be enrolled in a program at the site where the meals are served
Child and Adult Care Food Program	Provides low-cost or free healthy meals and snacks in daycare facilities, including eligible after-school care programs	Gross income must be at or below 185% of federal poverty income guidelines
Homeless Children Nutrition Program (HCNP)	Provides free food throughout the year to homeless children living in emergency/temporary shelters	Age criteria vary by state
Commodity Supplemental Food Program	Provides nutrition education and monthly packages of USDA foods to low-income infants and children up to 6 y of age; postpartum and breastfeeding women and elderly persons aged 60 and older are also eligible	Residency requirements and gross income must be at or below 185% of federal poverty income guidelines

(*Continued*)

Table 12–1 US Department of Agriculture Food Assistance Programs (*Continued*)

Program	Description	Eligibility Components[a]
Food Distribution Program Indian Reservations (FDPIR)	Provides a monthly package of USDA foods to low-income households on Indian reservations and to low-income Native Americans living near Indian reservations	Family must have at least one member who is of a federally recognized tribe; must follow net monthly income standards

[a]Refer to USDA guidelines for additional or more detailed eligibility requirements.

Local food assistance programs are typically found in churches and other places of worship. Also, they may be listed online or in telephone directories under food pantries, food assistance, food banks, or social and human services. Nationwide programs such as Feeding America (www.feedingamerica.org) or the Food Research and Action Center website (www.frac.org) offer information on regional programs throughout the country. Healthfinder.gov also offers links for food resources in the food assistance/food bank programs section of their health library.

The US Department of Health and Human Services, as well as local health departments, offers programs, services, and guidelines to improve the health and well-being of children and adolescents and aid in meeting Healthy People 2020 Nutrition-Related Goals for Children and Adolescents (www.healthypeople.gov). More specifically, Early Intervention programs can assist those meeting-specific criteria (Table 12-2) by accessing community resources to support, promote, and enhance childhood development.

In addition, Supplemental Security Income can provide financial support for those eligible (Table 12–3). Divisions for Children With Special Health Care Needs may also exist in Departments of Public Health at the state level.

Table 12–2 Nutrition-Related Eligibility Components for Early Intervention of Massachusetts

- *Birth weight*—must be <1200 g
- *Gestational age*—must be <32 wk
- *NICU admission*—stay in Neonatal Intensive Care Unit for >5 d
- *Apgar*—must be <5 at 5 min
- *Total hospital stay*—total number of days as inpatient in hospital or extended care facility must exceed 25 d in a 6-mo period
- *Intrauterine growth retardation (IUGR)/small for gestational age (SGA)*—diagnosis made at birth for IUGR or SGA
- *Weight for age and weight for height*—weight for age or weight for height <5th percentile or weight for age dropped more than 2 major centiles in 3 mo (for child under 12 mo of age) or in 6 mo (for child 12–36 mo of age)
- *Chronic feeding difficulties*—including any of the following: severe colic, stressful feedings, refusal or inability to eat, failure to progress with feeding

Source: Adapted from Massachusetts Department of Health and Human Services.

Table 12–3 Supplemental Security Income (SSI)

- Child must have chronic illness, blindness, disabling condition, or special medical needs
- Child is uninsured
- Child has private health insurance that only covers some costs of care
- Family has low to moderate income, or child is hospitalized more than 1 mo or is in a residential facility

Source: Adapted from Massachusetts Department of Public Health.

For Additional Information

1. Child nutrition programs. US Department of Agriculture. http://www.fns.usda.gov/child-nutrition-programs
2. Food and Nutrition Services. US Department of Agriculture. http://www.fns.usda.gov/fns/
3. Massachusetts Department of Public Health. http://www.mass.gov/eohhs/consumer/basic-needs/food/
4. Healthy People 2020. http://www.healthypeople.gov
5. National WIC Association. http://www.nwica.org

13 Nutritional Assessment in Sick or Hospitalized Children

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INTRODUCTION

Hospitalized children are subject to profound metabolic changes associated with acute and chronic illness that places them at increased risk of malnutrition.[1] Table 13–1 offers examples of common, yet undesirable, practices that occur in hospitalized patients, which can greatly affect their nutritional status.

Table 13–1 Nutritionally Undesirable Practices in the Hospitalized Patient

Failure to record and accurately plot anthropometric data
Failure to recognize altered nutritional needs
Withholding meals because of diagnostic tests
Frequent rotation of staff
Failure to help feed those in need of assistance
Failure to provide food in a timely and attractive manner
Delay in nutrition evaluation
Diffusion of responsibility of nutritional care of patient

Source: Adapted from Butterworth, CE. The skeleton in the hospital closet. *Nutr Today.* 1974;2:4.

Malnutrition is prevalent in hospitalized children and is associated with a variety of abnormalities that include physiologic instability, organ dysfunction, infection risk, and increased length of stay, which in turn, requires an increased use of hospital care resources.[1,2,3] Screening for existing malnutrition and completion of accurate nutritional assessment provide the foundation for effective nutrition interventions (Chapter 1). Unfortunately, despite advances in treating hospitalized children, completing nutrition assessments in this area remains a challenge. Table 13–2 lists standard methods of nutrition assessment and how their interpretation can be difficult in hospitalized patients.

Table 13–2 Assessment of Nutritional Status in Hospitalized Patients

Methodology	Usual Indication	Problem in Applying to Hospitalized Patients
History of weight loss	Standard risk factor for malnutrition	None
Weight for age	Standard growth reference	Difficult to obtain; falsely affected by acute hydration changes
Height for age	Standard growth reference	Difficult to obtain
Absolute lymphocyte count	Immune function	Falsely elevated with infection or other cause of leukocytosis
Hemoglobin	Iron status	Falsely low with phlebotomy, anemia of chronic disease
Anergy	Immune function	Many confounders (e.g., renal failure, burns, sepsis)

Methodology	Usual Indication	Problem in Applying to Hospitalized Patients
Serum albumin	Visceral protein stores	Falsely low due to bedrest, capillary leak syndrome, renal or gastrointestinal losses, or hepatic disease
Serum prealbumin	Visceral protein stores	Falsely low in hepatic disease
Serum retinol	Vitamin A status	Acute phase response depresses blood levels and may increase urine loss

As a result of these difficulties, additional steps are recommended in assessing a patient's nutritional status. Foremost is the completion of a careful physical examination of the patient, to identify evidence of edema or dehydration, as changes in body water distribution will impact body weight. Edema can also falsely elevate anthropometric measure of body composition such as triceps skinfold. Together with the physical exam, use of laboratory data plays a role in more accurately assessing a patient's nutritional status. Specifically, identifying gastrointestinal and hepatic disease, as well as assessing the acute phase response (e.g., serum C reactive protein, erythrocyte sedimentation rate), can help facilitate the interpretation of visceral protein and selection of micronutrient levels. It is important to keep in mind an individual patient's nutritional history, underlying diseases, and medication therapy when interpreting biochemical markers.[4]

NUTRITIONAL REQUIREMENTS OF HOSPITALIZED PATIENTS: ENERGY

The pediatric metabolic response during critical illness is proportional to the degree of severity/stress, causing an

increase in the turnover of proteins, fats, and carbohydrates. Thus, protein-energy malnutrition can result if nutritional requirements are not accurately assessed.[5] This metabolic response, however, has been shown to be highly variable, with the degree of hypermetabolism being unpredictable and unlikely to be sustained during a prolonged hospital course.[6] Important mechanisms by which nutritional requirements are affected by critical illness include anorexia associated with infection, decreased absorption of consumed nutrients, increased energy and protein requirements associated with the severity of illness or injury, drug–nutrient interactions, and reduced energy requirements related to the transient absence of growth during illness and certain medical therapies. It is important to be aware of these contributing factors as it has become apparent that the nutritional requirements of hospitalized pediatric patients differ compared to healthy children. It is also important to note that the majority of the predictive energy equations available are derived from measurements of energy expenditure in healthy children[6,7,8] (Chapter 5). Recent studies have underlined the standard practice not to use the published U.S. Recommended Dietary Allowances in estimating a hospitalized patient's nutritional requirements, as they may overestimate energy requirements in the intensive care unit (ICU) setting.[9]

Energy: When considering energy requirements in both the healthy and hospitalized patient, it is helpful to review the components of Total Energy Expenditure (TEE):

$$TEE = BMR + SDA + E_{activity} + E_{growth} + E_{losses}$$

where BMR = basal metabolic rate, which is the largest component of TEE (energy required by the body at rest while fasted, 60–70%),

SDA = specific dynamic action of food or thermic effect of food (energy produced as heat during digestion and metabolism of food, 8–10%),
$E_{activity}$ = energy required for physical activity,
E_{growth} = energy required for somatic growth, and
E_{losses} = obligatory energy lost in urine and stool because of inefficiencies of absorption and metabolism.

In the healthy, pediatric population, significant age-related changes in the components of TEE are seen (Figure 13–1). A1-month-old infant has relatively low energy requirements for activity (10 kcal/kg/d) but has significant needs to support age-appropriate growth (40–50 kcal/kg/d). In comparison, a 6-month-old infant's energy requirements are used differently, with greater energy expended for activity, while growth velocity is reduced.

Hospitalized pediatric patients generally have reduced total energy requirements when compared to healthy children. Of the five components of TEE, four are often significantly reduced in the critically ill. Energy required for

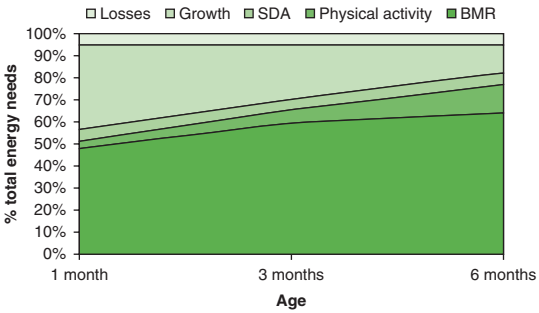

Figure 13–1: Factorial Estimates of Energy Requirements. Adapted from Tsang and Nichols.[17]

physical activity is minimal in hospitalized patients because of bedrest and use of sedative and paralytic agents. Energy required for growth is often reduced since the catabolic response following severe injury or illness results in a temporary halt to anabolism (accretion of lean body mass). The thermic effect of food is reduced in patients receiving parenteral nutrition support as opposed to patients receiving enteral nutrition. Also, in patients receiving parenteral nutrition, obligatory gastrointestinal losses of nutrients are minimized.

As a result of these metabolic factors, it is generally recommended to estimate the nutritional needs of hospitalized patients by (1) calculating or measuring BMR (see below for discussion of indirect calorimetry), and (2) determining a stress factor by which BMR should be multiplied to estimate TEE. Stress factors are highly variable, ranging from 0.9 to 2.0 based on disease process and are also subjective based on the clinician's experience.[3]

Multiple predictive energy equations have been published to calculate BMR from readily available anthropometric data, age, and sex. The oldest and most commonly used of these is the Harris–Benedict equation for adults (Table 13–3).[10] The Schofield equation is commonly used in assessing nutritional requirements in pediatrics; however, recent studies have suggested that the use of predictive energy equations with the indiscriminate use of variable stress factors are often inaccurate and place patients at risk for underfeeding or overfeeding.[2,11] BMR energy data is included in this chapter in two different forms: calculation via the equations of Schofield et al. (Table 13–4)[12] and tables that report BMR for children based on weight (Table 13–5).

Table 13–3 Harris Benedict Equations for Calculating Basal Metabolic Rate in Adults

Males: BMR = 66 + (13.7 × weight (kg)) + (5 × height (cm)) − (6.9 × age (y))
Females: BMR = 665 + (9.6 × weight (kg)) + (1.8 × height (cm)) − (4.7 × age (y))

Source: Adapted from Harris and Benedict.[16]

Table 13–4 Schofield Equations for Calculating Basal Metabolic Rate in Children

Males	
0–3 y	REE = 0.167W + 15.174H − 617.6
3–10 y	REE = 19.59W + 1.303H + 414.9
10–18 y	REE = 16.25W + 1.372H + 515.5
> 18 y	REE = 15.057W + 1.004H + 705.8
Females	
0–3 y	REE = 16.252W + 10.232H − 413.5
3–10 y	REE = 16.969W + 1.618H + 371.2
10–18 y	REE = 8.365W + 4.65H + 200
> 18 y	REE = 13.623W + 23.8H + 98.2

where REE = kcal/day, W = weight (kg), and H = height (cm).
Source: Adapted from Mehta NM and Compher C.[11]

Table 13–5 Assessment of Basal Energy Requirements in Hospitalized Pediatric Patients

Body Weight (kg)	Kcal/day	
	Male	Female
3.0	120	144
4.0	191	191
5.0	270	274

(*Continued*)

Table 13–5 **Assessment of Basal Energy Requirements in Hospitalized Pediatric Patients (*Continued*)**

Body Weight (kg)	Kcal/day	
	Male	Female
6.0	330	336
7.0	390	395
8.0	445	448
9.0	495	496
10.0	545	541
11.0	590	582
12.0	625	620
13.0	665	655
14.0	700	687
15.0	725	718
16.0	750	747
17.0	780	775
18.0	810	802
19.0	840	827
20.0	870	852
22.0	910	898
24.0	980	942
26.0	1070	984
28.0	1100	1025
30.0	1140	1063
32.0	1190	1101
34.0	1230	1137
36.0	1270	1173
38.0	1305	1207
40.0	1340	1241

Body Weight (kg)	Kcal/day	
	Male	Female
42.0	1370	1274
44.0	1400	1306
46.0	1430	1338
48.0	1460	1369
50.0	1485	1399
52.0	1505	1429
54.0	1555	1458
56.0	1580	1487
58.0	1600	1516
60.0	1630	1544
62.0	1660	1572
64.0	1690	1599
66.0	1725	1626
68.0	1765	1653
70.0	1785	1679
72.0	1815	1705
74.0	1845	1731
76.0	1870	1756
78.0	1900	1781
80.0	1935	1805
82.0	1970	1830
84.0	2000	1855

Source: Adapted from Schofield.[12]

Specific clinical circumstances among hospitalized pediatric patients in which energy requirements are substantially higher than might be predicted include thermal injuries and nutritional rehabilitation (i.e., catch-up growth).

Nutritional therapy of burn patients is discussed in Chapter 17 and that of patients recovering from malnutrition/growth failure in Chapter 26.

The gold standard for assessing energy balance continues to be weight changes over time. Serial monitoring of body weight during a patient's hospital course is the most effective measure when assessing if nutritional needs are being met.

INDIRECT CALORIMETRY

The use of indirect calorimetry in measuring a patient's resting energy expenditure (REE) remains the gold standard for establishing energy goals and avoiding the complications associated with both underfeeding and overfeeding. As the name applies (*calor* is the Latin word for heat), indirect calorimetry is the determination of heat production of a biochemical reaction by measuring uptake of oxygen and liberation of carbon dioxide. (This is in contrast to direct calorimetry, wherein the heat produced by the body at rest is measured.) Oxygen consumption (VO_2) and carbon dioxide production (VCO_2) measured by the calorimeter are entered into the Weir equation to calculate REE:

$$\text{REE} = (3.94 \times \text{VO}_2) + 1.06 \times \text{VCO}_2) - (2.17 \times \text{UUN})$$

where UUN = urinary nitrogen (N) excretion, used as a correction factor for protein oxidation.

Indirect calorimetry can also assist in determining whether a patient is being overfed. The ratio of VCO_2 to VO_2 is termed the respiratory quotient (RQ) and is used to estimate substrate oxidation. For example, in the case of pure glucose oxidation, one mole of carbohydrate reacts with six moles of oxygen to create six moles each of water and carbon dioxide:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O$$

The RQ would then be 6/6 = 1.0

When long-chain fat, such as palmitic acid is oxidized,

$$CH_3(CH_2CH_2)_7COOH + 23O_2 \rightarrow 16CO_2 + 16H_2O$$

the RQ = 16/23 = 0.695

Thus, the RQ in a fasted state is normally 0.70–1.00, with RQ in this range representing a mixed substrate oxidation. Although not yet fully supported, based on research available, the lower RQ noted for lipid oxidation has been used as a rationale for use of a higher fat diet compared to carbohydrate in patients with advanced lung disease to avoid an increased carbon dioxide load to emit.

However, when excess energy is provided and lipogenesis results,

$$9C_6H_{12}0_6 + 8O_2 \rightarrow 2CH_3(CH_2CH_2)7COOH + 22CO_2 + 22H_2O$$

the resulting RQ = 22/8 = 2.75

The finding of an RQ significantly greater than 1.0, is consistent with energy intake in excess of nutritional requirements. Other reasons for this occurrence may include hyperventilation (wherein CO_2 is excreted at high rates) or failure to achieve steady state in gas measurement.

Although REE measurements are usually taken to approximate BMR, REE actually includes BMR, in addition to nonshivering thermogenesis and stress hypermetabolism. The difference between REE and BMR is estimated to be 10%.

An alternative to indirect calorimetry is to calculate REE using the Fick equation:

$$REE = CO \times Hgb \times (SaO2 - SvO2) \times 95.18,$$

where CO = cardiac output (L/minute) as measured with a thermodilution pulmonary catheter,
Hgb = hemoglobin concentration (g/dL),
SaO_2 = oxygen saturation in arterial blood, and
SvO_2 = oxygen saturation in mixed venous blood.

Of note, this equation can only be applied to patients whose cardiac output is measured with a pulmonary artery catheter, which is not a routine pediatric ICU procedure.

Current critical care nutrition guidelines recommend that energy prescription in children should be guided by accurate measurement of energy expenditure using indirect calorimetry when possible.[11]

NUTRITIONAL REQUIREMENTS OF HOSPITALIZED PATIENTS: PROTEIN

Protein requirements in disease and critical illness are generally thought to be higher than in health because of the increased urinary N losses characteristic of the catabolic state, gastrointestinal and skin losses, and the increased requirement for protein synthesis.[13,14]

Children have reduced protein reserves available to account for increased protein catabolism following illness. Despite receiving what seems to be adequate protein, hospitalized patients often end up in net negative protein balance.[11] As reviewed in Chapter 4, Laboratory Assessment of Nutritional Status, measurement of N balance is the most direct way to measure whether the nutrition provided to an individual patient is adequate in protein. In the absence of N balance data, it is common for clinicians to rely on serum concentrations of visceral proteins such as albumin, prealbumin, and retinol-binding protein. Please refer to Chapter 17 for updated protein recommendations for critically ill, injured children.

Ideally, the protein provided to a patient in parenteral nutrition solutions should not be used as a primary fuel source per se, but as amino acid substrates for enzyme synthesis and lean body mass accretion. In cases where the parenteral nutrition is providing significantly less than the

BMR for energy, the amino acids will be used as a substrate, that is why this form of PN is referred to as an "expensive" and ineffective mode of nutrition support. Therefore, some institutions do not commonly include protein in the total energy sum provided from PN. Instead, the ratio of non-protein energy (kcal) to protein intake (grams of Nitrogen) is estimated as a measure of adequate energy and protein balance; ratios between 150:1 and 250:1 are acceptable. See Chapter 15 for details.

REFEEDING SYNDROME

Refeeding syndrome is characterized by a constellation of fluid, electrolyte, and metabolic abnormalities that are the result of a rapid provision of nutrients delivered to patients who have been in a starved, malnourished state.[15] During chronic malnutrition, lean body mass is broken down and total body stores of nitrogen, phosphorus (P), magnesium (Mg), and potassium (K) are depleted. Despite these changes, serum levels of P, Mg, and K are usually maintained within the normal range. On refeeding; however, intracellular protein synthesis and insulin released because of carbohydrate provision combine to drive cellular uptake of these cations leading to precipitous drops in serum concentrations. The clinical manifestations of hypophosphatemia include hemolytic anemia, muscle weakness (especially diaphragmatic muscle), and decreased cardiac output. In combination with hypokalemia and hypomagnesemia, cardiac failure and fluid overload may occur.

Pediatric patients at highest risk of refeeding syndrome include those with severe weight loss (e.g., anorexia nervosa, cancer cachexia, and other cases of severe malnutrition) as well as patients who have been maintained on prolonged intravenous hydration. Serial monitoring of

serum electrolytes up to twice per day in the early stages of nutritional repletion is indicated. If symptoms of refeeding syndrome are observed, nutritional prescriptions should be reduced or put on hold until the metabolic and clinical changes are corrected and resolved.[15]

MICRONUTRIENTS AND OTHER ESSENTIAL AND CONDITIONALLY ESSENTIAL NUTRIENTS

"Pharmaconutrition" and "Immunonutrition" describe current terminology that is being used to support the idea that certain nutrients, perhaps in pharmacologic amounts or with certain immunologically active components, may benefit patients who are hospitalized. The concept that certain nutrients, synthesized endogenously in adequate amounts while healthy, may become essential in conditions of illness continues to be widely studied. Glutamine, arginine, antioxidants, zinc, and omega-3 fatty acids are some examples of the nutrients studied for their role in modifying the inflammatory response. At this time, further studies are needed in this area to determine the efficacy and safety in the pediatric population.[1,11]

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14 Enteral Nutrition

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Enteral nutrition (EN) provides nutrients through the gastrointestinal (GI) tract, either orally or artificially through the use of a feeding tube to ensure that energy, macro, and micronutrient needs are being met. The GI tract should be the first choice for nutritional support, because EN is safer, more physiologic, and is associated with better nutritional and clinical outcomes than parenteral nutrition (PN) (Table 14–1). EN is indicated when an infant or child is unable to meet estimated nutritional needs orally (Table 14–2). It can provide total or supplemental nutrition and can be used for short- or long-term nutritional management.

Table 14–1 Advantages of Enteral Versus Parenteral Nutrition

- Reduced risk of infection and metabolic abnormalities
- Low-volume enteral feeds may promote GI maturation in premature infants
- Maintains and can help restore the integrity of GI mucosa
- May facilitate restoration of digestive enzymes
- Less expensive than parenteral nutrition
- Mimics standard human nutrition

Abbreviation: GI, gastrointestinal.

Table 14–2 Indications for Enteral Nutrition

Inability to meet full nutrient needs orally
Anatomic abnormalities
Congenital anomalies, (tracheoesophageal fistula (TEF))
Facial trauma
Tumor or other mass
Anorexia
Acute or chronic infection (pneumonia, diarrhea)
Cancer
Cyanotic heart disease
Endocrine disease
Micronutrient deficiency (vitamin B_{12}, iron, zinc)
Pregnancy
Psychosocial (chronic mental/emotional stress, depression, neglect/abuse)
Increased metabolic needs
Brain injury
Bronchopulmonary dysplasia
Burns
Chronic renal disease
Congenital heart disease
Cystic fibrosis
Sepsis
Trauma
Neurologic disorders
Cerebral palsy affecting oral motor skills
Coma
Dysphagia
Severe mental retardation
Prematurity
Psychosocial disorders
Anorexia nervosa
Nonorganic growth failure
Severe food aversion

Altered absorption or metabolism requiring modification of diet
Acquired Immunodeficiency Syndrome (AIDS)
Amino or organic acidopathies
Chronic diarrhea
Chronic intestinal pseudo-obstruction
Chronic liver disease, that is, biliary atresia
Glycogen storage disease (types I and III)
Inflammatory bowel disease
Pancreatitis
Short bowel syndrome
Solid organ transplant

Source: Adapted from Davis.[8]

ROUTES AND EQUIPMENT

Small bore silicone or polyurethane tubes (5–6 French) are placed nasally for anticipated usage of three months or less; larger bore tubes (8 French) for extended use are placed endoscopically or surgically.[1] Nasogastric (NG) tubes are easily placed and often the first consideration for short-term EN therapy.

EN can be provided by either gastric or postpyloric tubes. Choosing between these two methods depends on the function of the GI and risk for aspiration. Methods of gastric and postpyloric feedings are described in Tables 14–3 and 14–4. Gastric feeding is preferred as it easier to position the gastric tubes and is more physiological.[2] Gastric feeding is not intended when a patient has severe gastroesophageal reflux or poor gastric motility. Gastric feedings also allow the use of bolus feedings. Bolus feedings into the stomach can mimic typical meal patterns, whereas nocturnal feedings can supplement oral intake or provide additional calories.

Table 14–3 Gastric Feeding

	Advantages	Disadvantages
Orogastric	Avoids nasal passage obstruction Appropriate for infants < 34 weeks gestational age	Not appropriate for patients with gag reflex
Nasogastric	Easy intubation	Nasal or esophageal irritation Easily dislodged
Percutaneous endoscopic gastrostomy	Fewer occlusions with larger bore tube Appearance can be hidden under clothing Open surgery not required	Invasive technique for placement Site at risk for infection Appropriate anatomy required
Surgical gastrostomy	Endoscopy not required for placement Procedure directly accesses stomach	Risks of anesthesia/surgery Open surgical wound at risk for infection

Table 14–4 Postpyloric/Small Bowel Feeding

	Advantages	Disadvantages
Nasoduodenal/nasojejunal	Temporary access for small bowel feeding pH-guided placement available	Easily dislocated; may require radiographic evidence of appropriate placement
Gastrostomy–jejunostomy	Transpyloric tube may be passed through existing gastrostomy	Requires healing of gastrostomy tract prior to jejunostomy tube placement. Meticulous care

	Advantages	Disadvantages
	Intestinal access for feeding and gastric access for decompression and medications	of both ports necessary
Jejunostomy	Direct access to small bowel	Easily occluded

Postpyloric feeding is intended for patients with gastroparesis, or are at high risk of aspiration, to name a few indications. These feedings should be provided as a continuous feed only because the small intestine cannot expand to accommodate a bolus feeding.[2] Contraindications for small bowel feeding include nonfunctioning GI tract or inability to access the intestine.[3]

FORMULA SELECTION

It is important to complete a nutritional evaluation to ensure the proper formula is selected. Assessment of the following is necessary: energy and protein requirement, fluid and electrolyte status, digestive capacity, functional status of the GI tract, other organ system function, and any food allergies or macronutrient sensitivity.[4] Age is an important consideration in formula selection because certain formulas are specifically designed to meet the needs of children at specific ages (e.g., < 34 weeks gestation, up to 1 year, 1 to 10 years, and > 10 years). These formulas may differ in their nutrient composition and vitamin and mineral content (Tables 14–5 and 14–6). Tables 14–7 and 14–8 contain nutrient information for milk, milk alternatives, and other oral supplements.

Table 14–5 Enteral Product References: INFANT (per 100 mL)

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat g % kcals Source	Carbohydrate g % kcals Source	mEq mg/100 mL Na/K Ca/P Fe	Osm/kg Water	General Comments
Human milk, term, mature	0.67	1.0 / 5 whey and casein	3.90 / 55 long chain fatty acids high in palmitic, oleic, linoleic, and linolenic	7.2 / 38 lactose	.78 / 1.35 28 / 14 .04	255	Preferred nutrition in human infants
EleCare (Abbott)	0.67	2.0 / 15 free L-amino acids	3.2 / 42 high-oleic safflower oil, MCT oil, soy oil	7.2 / 43 corn syrup solids	1.3 / 2.6 73 / 55 1.2	335	100% free amino 33% fat as MCT oil
Enfamil A.R. (Mead Johnson)	0.67	1.7 / 10 nonfat milk	3.4 / 46 palm olein, soy oil, coconut oil, high-oleic sunflower oil	7.3 / 44 lactose, rice starch, maltodextrin	1.17 / 1.87 53 / 36 1.2	240	Thickened with rice cereal

Enfamil Enfacare 22 cal/oz (Mead Johnson)	0.74	2.1 / 11 whey protein concentrate and nonfat milk	3.9 / 46 high oleic vegetable oil, soy oil, MCT oil, coconut oil	7.7 / 43 liquid: maltodextrin-lactose powder: lactose, corn syrup solids	1.13 / 2 89 / 49 1.3	310	Designed for former premature infants contains extra Ca and P 20% fat MCT
Enfamil Gentlease (Mead Johnson)	0.67	1.56 / 9 partially hydrolyzed nonfat milk and whey protein concentrate solids	3.6 / 48 palm olein, soy, coconut, and high-oleic sunflower oils	7.3 / 43 corn syrup solids	1 / 1.87 55 / 31 1.2		

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat g % kcals Source	Carbohydrate g % kcals Source	mEq mg/100 mL Na K Ca P Fe	Osm/kg Water	General Comments
Enfamil Lipil 24 (Mead Johnson)	0.81	1.7 / 8.5 reduced minerals whey, nonfat milk	4.3 / 48 palm olein, soy, coconut, and high-oleic sunflower oils, DHA, ARA	8.8 / 43.5 lactose	.95 / 2.25 Na/K; 63 / 43 Ca/P; 1.46 Fe	360	
Enfamil Premature 20 Lipil (Mead Johnson)	0.67	2.0 / 12 whey protein concentrate nonfat milk	3.4 / 44 MCT, soy, and high-oleic vegetable oils, single cell oil blend rich in DHA and ARA	7.4 / 44 corn syrup solids, lactose	1.69 / 1.69 Na/K; 112 / 56 Ca/P; 1.22 Fe	240	Designed for premature or low birth weight infants. Increased level of Ca, P, vitamin D 40% MCT oil

Enfamil Premature 24 cal/oz (Mead Johnson)	0.81	2.4 / 12 whey protein concentrate nonfat milk	4.1 / 44 MCT, soy, and high-oleic vegetable oils, single cell oil blend rich in DHA and ARA	8.9 / 44 corn syrup solids, lactose	2.04 / 2.05	134 / 67	1.46	300	Designed for premature or low birth weight infants. Increased level of Ca, P, vitamin D 40% MCT oil
Enfamil PREMIUM Infant (Mead Johnson)	0.67	1.4 / 8.5 whey protein concentrate and nonfat milk	3.5 / 48 palm olein oil, soy oil, coconut oil, high-oleic sunflower oil	7.3 / 43 lactose, galactooligosaccharides, polydextrose	0.78 / 1.8	52 / 35	1.2	300	
Enfamil PREMIUM Newborn (Mead Johnson)	0.67	1.42 / 8.5 nonfat milk, whey protein concentrate	3.6 / 48 palm olein, coconut, soy, and high-oleic sunflower oils	7.6 / 43.5 lactose, galactooligosaccharides, polydextrose	0.8 / 1.9	53 / 29	1.22	300	Newborn to 3 months Higher in vitamin D (400 IU in 27 oz)

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g / % kcals / Source	Fat g / % kcals / Source	Carbohydrate g / % kcals / Source	mEq mg/100 mL Na K Ca P Fe	Osm/kg Water	General Comments
Enfamil Prosobee (Mead Johnson)	0.67	1.69 / 10 soy protein isolate	3.6 / 48 palm olein, soy, coconut, and high-oleic sunflower oils, single cell oil blend rich in DHA and ARA	7.2 / 42 corn syrup solids	Na 1.04, K 2.07, Ca 71, P 56, Fe 1.22	200	Lactose free
Enfaport (Mead Johnson)	1.01	3.6 / 14 calcium caseinate, sodium caseinate	5.5 / 45 MCT oil, soy oil, DHA, and ARA	10.3 / 41 corn syrup solids	Na 1.3, K 3, Ca 95, P 53, Fe 1.83	280	Ready to feed 30 cal/oz formula that can be modified to as low as 20 cal/oz

							84% fat as MCT oil includes all essential fatty acids
Gerber Good Start Soy (Nestle)	0.67	1.7/10 soy protein isolate	3.4/46 palm olein, soy, coconut, high-oleic safflower or sunflower oils	7.5/44 corn maltodextrin, sucrose	1.1/2.0 70/42 1.2	180	
Gerber Good Start Gentle (Nestle)	0.67	1.5/9 hydrolyzed whey protein concentrate	3.4/46 palm olein, soy, coconut, and high-oleic safflower or sunflower oils	7.8/45 lactose, corn maltodextrin	0.79/1.9 45/26 1.0	250	100 % whey protein
Monogen (Nutricia)	0.73	2/11 whey protein concentrate	2/25 oil blend (including coconut, walnut)	11.9/64 corn syrup solids	1.52/1.62 48/35 0.74	250	24% calories from fat, 80% of fat as MCT

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat g % kcals Source	Carbohydrate g % kcals Source	mEq mg/100 mL Na Ca Fe / K P	Osm/kg Water	General Comments
							complete profile vitamin and minerals including trace elements
Neocate infant DHA and ARA (Nutricia)	0.67	3.1pro eq / 12 free amino acids	4.5 / 41 high-oleic safflower oil, refined vegetable oil (coconut oil and/or palm kernel oil), MCT	11.7 / 47 corn syrup solids	1.6 / 4 Na; 124 / 93 Ca; 1.85 Fe	375	33% MCT oil Severe protein allergy Lactose free 100% free amino acids

Nutramigen with Enflora LGG (Mead Johnson)	0.67	1.89 / 11 casein hydrolysate L-cystine, L-tyrosine, L-tryptophan, taurine, L-carnitine	3.6 / 48 palm olein, soy, coconut, and high-oleic sunflower oils, DHA, ARA	7 / 41 corn syrup solids, modified corn starch	1.39 / 1.89 64 / 43 1.22	270	Lactose free Hypoallergenic, lactose-free and galactose-free
PurAmino (Mead Johnson)	0.67	1.89 / 11 amino acids	3.6 / 48 palm olein, soy, coconut, and high-oleic sunflower oils	7 / 41 corn syrup solids, tapioca starch	1.4 / 1.9 64 / 35 1.44	350	hypoallergenic, amino acid-based contains DHA and ARA
Pregestimil (Mead Johnson)	0.67	1.87 / 11 casein hydrolysate L-cystine L-tyrosine L-trytophan Taurine L-carnitine	3.7 / 48 liquid: MCT, soy oil, high-oleic safflower oils powder: MCT, soy oil, corn oil, high oleic oils	6.8 / 41 liquid: corn syrup solids, modified corn starch powder: corn syrup solids, dextrose, modified corn starch	1.35 / 1.9 77 / 50 1.2	320	Lactose free Hypoallergenic and lactose-free 55% of the fat from MCT oil

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g / % kcals Source	Fat g / % kcals Source	Carbohydrate g / % kcals Source	mEq mg/100 mL Na / K / Ca / P / Fe	Osm/kg Water	General Comments
Pregestimil 24 (Mead Johnson)	0.80	2.22 / 12 casein hydrolysate L-cystine L-tyrosine L-trytophan Taurine L-carnitine	4.5 / 48 liquid: MCT, soy oil, high-oleic safflower oils	8.1 / 41 liquid: corn syrup solids, modified corn starch	1.6 / 2.23 — 91 / 60 — 1.5	320	Lactose free
Similac Advance (Abbott)	0.67	1.4 / 8 nonfat milk and whey protein concentrate	3.7 / 49 high-oleic safflower oil, coconut oil, soy oil	7.3 / 43 lactose, galactooligosaccharides (GOS)	0.71 / 1.8 — 53 / 28 — 1.22	270	Prebiotic

Similac Expert Care Alimentum (Abbott)	0.67	1.86 / 11 casein hydrolysate, L-cystine, L-tryptophan, L-tyrosine	3.74 / 48 safflower oil, MCT oil, soy oil, DHA, ARA	6.9 / 41 corn malodextrin, sucrose	1.29 / 2.04 | 71 / 51 | 1.22	370	33% MCT oil lactose free Hypoallergenic
Similac Expert Care 24 with iron (Abbott)	0.80	2.19 / 11 nonfat milk	4.25 / 49 soy oil, coconut oil	8.5 / 42 lactose	1.5 / 2.6 | 73 / 57 | 1.45	380	
Similac Expert Care Neosure (Abbott)	0.74	2.08 / 11 nonfat milk and whey protein concentrate	4.1 / 49 soy oil, high-oleic safflower oil, MCT oil, coconut oil	7.5 / 40 lactose, corn syrup solids	1.07 / 2.70 | 78 / 46 | 1.34	250	Designed for former premature infants > 2 kg or > 40 weeks corrected age 25% of the fat blend as medium-chain triglycerides

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat g % kcals Source	Carbohydrate g % kcals Source	mEq mg/100 mL Na K Ca P Fe	Osm/kg Water	General Comments
Similac Sensitive (Abbott)	0.67	1.45 / 9 milk protein isolate	3.65 / 49 high oleic safflower, soy, and coconut oil	7.23 / 43 corn maltodextrin, sucrose, galactooligosaccharides (GOS)	0.88 / 1.85 57 / 38 1.22	180	Lactose free
Similac Soy Isomil (Abbott)	0.67	1.65 / 10 soy protein isolate, L-methionine	3.69 / 49 high-oleic safflower oil, coconut oil, soy oil, DHA, ARA	6.97 / 41 corn syrup, sucrose, fructooligosaccharides (FOS)	1.29 / 1.87 71 / 51 1.22	200	Lactose free
Similac Special Care 20 with iron (Abbott)	0.67	2.03 / 12 nonfat milk, whey protein concentrate	3.67 / 47 MCT oil, soy oil, coconut oil	7.0 / 41 corn syrup solids, lactose	1.26 / 22 121 / 68 1.22	235	designed for growing low-birth-weight and premature infants, additional

							Ca, P, vitamin A, vitamin D, folate, Zn Ca:P ratio of 2:1 High in protein
Similac Special Care 24 with iron (Abbott)	0.81	2.43/12 nonfat milk, whey protein concentrate	4.41/47 MCT oil, soy oil, coconut oil	8.4/41 corn syrup solids, lactose	1.51/2.66	145/81	1.45	280	Designed for growing low-birth-weight and premature infants, additional Ca, P, vitamin A, vitamin D, folate, Zn Ca:P ratio of 2:1 High in protein

(*Continued*)

Table 14–5 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat g % kcals Source	Carbohydrate g % kcals Source	mEq mg/100 mL Na/K Ca/P Fe	Osm/kg Water	General Comments
Similac Special Care 24 High Protein (Abbott)	0.81	2.7 / 13 nonfat milk, whey protein concentrate	4.4 / 47 MCT oil, soy oil, coconut oil	8.1 / 40 corn syrup solids, lactose	1.52 / 2.7 146 / 81 1.46	280	
Similac Special Care 30 with iron (Abbott)	1	3 / 12 nonfat milk, whey protein concentrate	6.7 / 57 MCT oil, soy oil, coconut oil	7.8 / 31 corn syrup solids, lactose	1.9 / 3.4 183 / 101 1.8	325	
Similac PM 60/40 (Abbott)	0.67	1.5 / 9 whey protein concentrate, sodium caseinate	3.78 / 50 high-oleic safflower, soy, and coconut oils	6.90 / 41 lactose	0.71 / 1.4 38 / 19 0.5	280	low iron Lower in Ca, P, maintaining 2:1 ratio Lower in K

Abbreviation: MCT, medium chain triglycerides.

Table 14–6 **Enteral Product References: NONINFANT (1000 mL)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na/K Ca/P	mOsm/ kg Water	General Com- ments
Boost (Nestle)	1.01	40/17 milk protein concentrate	16/16 canola, high-oleic sunflower and corn oils	173/67 corn syrup solids and sugar	24/43 1390/1310	610–670	85 % free water Gluten and lactose free, low residue and kosher
Boost Kid Essentials (Nestle)	1.0	30/12 sodium and calcium caseinates, whey protein concentrates	38/34 high-oleic sunflower oil, soybean oil, MCT oil	135/54 sugar, maltodextrin,	24/29 1181/886	550–600	84% free water 20% fat as MCT oil multiple flavors

(*Continued*)

Table 14–6 **Enteral Product References: INFANT (per 100 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/ kg Water	General Com- ments
							and fiber containing versions available lactose and gluten free, low residue, kosher
Boost Kid Essentials 1.5 (Nestle)	1.5	42 / 11 sodium and calcium caseinates, whey protein concentrates	75 / 45 high-oleic sunflower oil, soybean oil, MCT oil	165 / 44 sugar, maltodextrin,	30 / 33 1304 / 992	390	72% free water fiber containing versions available

							lactose and gluten free, low residue, kosher
Boost Plus (Nestle)	1.52	59/16 milk protein concentrate, calcium, and sodium caseinates	58/34 canola, high-oleic, sunflower and corn oils	200/50 corn syrup solids, sugar	31/41 1390/1310	720	78% free water Gluten and lactose free, kosher and low residue
EleCare Jr (Abbott)	1.0	30/15 free L-amino acids	48/42 high-oleic safflower oil, medium chain tri-glycerides, soy oil	109/43 corn syrup solids	20/39 1096/822	551	100% free amino 33% fat as MCT oil Unflavored Gluten, lactose, fructose, galactose, milk, and soy protein free

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/ kg Water	General Com- ments
Ensure (Abbott)	1.06	37 / 14 calcium caseinates, soy protein isolate, whey protein concentrate	26 / 22 high-oleic safflower oil, canola oil, corn oil	169 / 64 corn syrup, sucrose, maltodextrin	37 / 40 1266 / 1055	590	84% free water High protein and high calcium versions available Gluten and lactose free Kosher
Ensure Plus (Abbott)	1.5	54 / 17 sodium and calcium caseinates, soy protein isolates	49 / 29 corn oil, canola oil, high-oleic saf- flower oil	211 / 56 corn syrup, maltodextrin, sucrose	44 / 48 844 / 844	680	76% free water Gluten and lactose free Kosher

EO28 Splash (Nutricia)	1.0	25/10 free amino acids	35/32 canola oil, high-oleic safflower oil, coconut oil	146/58 maltodextrin, sucrose, corn syrup solids	8.5/24	620/620	820	3.4 g Gln/L 2.3g Arg/L flavored version available
Glucerna (Abbott)	1.0	42/17 sodium and calcium caseinates	54/49 high-oleic safflower oil, canola oil, soy lecithin	96/34 corn maltodextrin, fructose, soy fiber	40/40	705/705	355	85% free water Low carbohydrate content 14 g fiber/L Gluten and lactose free Kosher Comes in 1.2 and 1.5 cal/mL

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na Ca K P	mOsm/kg Water	General Comments
Hi-Cal (Abbott)	2.0	84 / 17 sodium and calcium caseinates	89 / 40 corn oil, soy lecithin	215 / 43 corn syrup solids, corn, maltodextrin, sucrose	63 / 62 Na K; 844 / 844 Ca P	705	70% free water gluten and lactose free low residue kosher
IsoSource HN (Nestle)	1.2	53 / 18 soy protein isolate	39 / 29 canola oil, MCT oil	160 / 53 corn syrup	48 / 49 Na K; 1200 / 1200 Ca P	490	82% free water 50% fat as MCT oil Higher calorie version available (1.5) Gluten and lactose free

Jevity (Abbott)	1.06	44/17 sodium and calcium caseinates	35/29 high-oleic safflower oil, canola oil, MCT oil, soy lecithin	154/54 maltodextrin, corn syrup, soy fiber	40/40	910/760	300	84% free water 20% fat as MCT oil 14.4 g fiber/L Higher calorie versions available (1.2, 1.5) luten and lactose free Kosher
Prebiotics (Nutricia)	1.0	30/13 free amino acids	50/45 fractionated coconut oil, MCT oil, canola oil, high-oleic safflower oil	104/42 corn syrup solids	18/35	1130/697	590–700	Free amino acid Severe protein allergy Vanilla or unflavored

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/ kg Water	General Com- ments
Nepro with Carb Steady (Abbott)	1.8	70 / 14 calcium, magnesium and sodium caseinates, milk protein isolate	96 / 43 high-oleic saf-flower oil, canola oil, soy lecithin	333 / 43 corn syrup, sucrose, FOS	37 / 27 1370 / 695	665	Gluten and lactose free Kosher
Nutren Junior (Nestle)	1.0	30 / 12 whey protein concentrate, milk protein concentrate	49.6 / 44 soybean, canola and MCT oil, soy lecithin	110 / 44 malto-dextrin, sugar,	20 / 33.8 1000 / 800	350	fiber containing version available contains MCT oil gluten and lactose free low resi-due and kosher

Nutren 1.0 (Nestle)	1.0	40/16 calcium–potassium caseinate	38/33 canola, MCT, corn oil, and soy lecithin	127/51 maltodextrin, sucrose	38/32 668/668	370	fiber containing version available contains MCT oil kosher, lactose and gluten free, low residue comes in 1.5, 2.0
Nutren 1.5 (Nestle)	1.5	60/16 calcium–potassium caseinate	68/39 MCT, canola, corn oil, soy lecithin	169/45 malto-dextrin	51/48 1000/1000	430–520	50 % MCT oil

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K	mEq mg/1000 mL Ca / P	mOsm/ kg Water	General Com- ments
Nutren 2.0 (Nestle)	2.0	80 / 16 calcium–potassium caseinate	104 / 45 MCT and canola oil, soy lecithin, corn oil	196 / 39 corn syrup solids, maltodextrin, sucrose	57 / 49	1340 / 1340	720	75 % of fat as MCT oil kosher, lactose and gluten free, low residue
Nutrihep (Nestle)	1.5	40 / 11 L- amino acids, whey protein con- centrate	21 / 12 MCT and canola oil, soy lecithin, corn oil	290 / 77 malto- dextrin	7 / 34	956 / 1000	790	70 % fat as MCT oil high in BCAA unflavored kosher, lactose and gluten free, low residue

Osmolite (Abbott)	1.06	44/17 sodium and calcium caseinates, soy protein isolate	35/29 canola oil, MCT oil, soy lecithin, corn oil	144/54 malto-dextrin, corn syrup solids	40/40	760/760	300	84% free water 20% fat as MCT oil unflavored high calorie version available (1.2, 1.5 cal/mL) kosher, lactose and gluten free, low residue
PediaSure Enteral formula (Abbott)	1.0	30/12 milk protein concentrate	40/35 high-oleic safflower oil, soy oil, MCT oil	133/53 Corn maltodextrin, sucrose	17/34	972/845	335	84% free water 20% fat as MCT oil kosher, lactose and gluten free, low residue

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/ kg Water	General Com- ments
PediaSure with Fiber Enteral formula (Abbott)	1.0	30 / 12 milk protein con- centrate	38 / 34 high-oleic safflower oil, soy oil, MCT oil	143 / 54 corn, maltodextrin, sucrose, dextrose, soy fiber, scFOS	17 / 34 1055 / 844	345	85% free water 20% fat as MCT oil 13g fiber/L kosher, lactose and gluten free
Pediasure 1.5 (Abbott)	1.5	58 / 16 milk protein con- centrate	67 / 41 high-oleic safflower oil, soy oil, MCT oil	158 / 43 corn, maltodextrin	16 / 42 1458 / 1042	370	Lactose and gluten free Fiber containing version

Pediasure Peptide	1.0	$\frac{30}{12}$ whey protein hydrolysate, hydrolysed caseinate	$\frac{40}{35}$ anola and MCT oils	$\frac{134}{53}$ corn, maltodextrin	$\frac{31}{34}$ $\frac{1060}{844}$	250	
Pepdite Junior (Nutricia)	1.0	$\frac{31}{12}$ free amino acids, hydrolyzed protein (pork, soy)	$\frac{50}{46}$ MCT, coconut oil, canola oil, safflower oil	$\frac{106}{42}$ corn syrup solids	$\frac{17}{35}$ $\frac{1130}{940}$	430–440	44% free amino acids 35% fat as MCT oil flavored version available
Peptamen (Nestle)	1.0	$\frac{40}{16}$ enzymatically hydrolyzed whey protein	$\frac{39}{33}$ MCT oil, soybean oil, soy lecithin	$\frac{127}{51}$ maltodextrin, corn starch	$\frac{24}{38}$ $\frac{800}{700}$	270–380	85% free water, flavored version available 70% of fat from MCT Also in 1.5

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/kg Water	General Comments
Peptamen Junior (Nestle)	1.0	30 / 12 enzymatically hydrolyzed whey protein	38 / 33 MCT oil, canola oil, soybean oil	138 / 55 maltodextrin, corn starch	20 / 34 1000 / 800	260–400	85 % free water, flavored version available
Peptamen Junior 1.5 (Nestle)	1.5	45 / 12 enzymatically hydrolyzed whey protein	68 / 33 MCT oil, canola oil, soybean oil	180 / 55 maltodextrin, corn starch	30 / 51 652 / 1352	450	77% free water 60% MCT 5.6 g/L PREBIO

Peptamen 1.5 (Nestle)	1.5	67.6 / 18 enzymatically hydrolyzed whey protein	56 / 33 MCT oil, soybean oil	188 / 49 maltodextrin, corn starch	44 / 48	1000 / 1000	550	77% free water, flavored version available
Promote (Abbott)	1.0	62.5 / 25 sodium caseinate, soy protein isolate	26 / 23 safflower oil, MCT oil, soy oil, and soy lecithin	130 / 52 corn maltodextrin, sucrose	43 / 51	1200 / 1200	340	84% free water 19% fat as MCT oil fiber containing version available kosher, high protein lactose and gluten free, low residue

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/kg Water	General Comments
Pulmocare (Abbott)	1.5	63 / 17 sodium and calcium caseinates	93 / 55 canola oil, MCT oil, corn oil, high-oleic safflower oil, soy lecithin	106 / 28 sucrose, corn malto-dextrin	57 / 50 1060 / 1060	475	79% free water 20% fat as MCT oil Low-carbohydrate formula kosher, lactose and gluten free, low residue
Resource Breeze (Nestle)	0.68	34 / 20 whey protein isolate	0	131 / 80 fructose, juice concentrate, sugar	9 / 25 630 / 1480	900–930	89% free water clear liquid, protein containing supplement

Carb Steady (Abbott)	1.8	30/6 milk protein isolates, sodium caseinate	96/43 high-oleic safflower oil, canola oil, soy lecithin	196/51 maltodextrin, sucrose	35/29 1055/717	780	Low-protein formula kosher, lactose and gluten free, low residue Low in phos, K, Ca, Na
Tolorex (Nestle)	1.0	21/8 free amino acids	1.5/1.0 safflower oil	230/91 maltodextrin, modified food starch	20/30 560/560	550	84% free water free amino acid, high carbohydrate, low-fat formula flavor packets available lactose and gluten free, low residue

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na / K Ca / P	mOsm/ kg Water	General Com- ments
TwoCal HN (Abbott)	2.0	84 / 17 sodium and calcium caseinates	90 / 40 high-oleic saf-flower oil corn oil, MCT oil, canola oil, soy lecithin	218 / 43 corn syrup solids, maltodextrin, sucrose, FOS	63 / 62 1050 / 1050	725	70% free water 19% fat as MCT oil multiple flavors available kosher, lactose and gluten free, low residue

Vital HN (Abbott)	1.0	$\frac{42}{17}$ partially hydrolyzed protein blend (soy, collagen), whey protein concentrate, whey protein hydrolsate,	$\frac{11}{9}$ safflower oil, MCT oil	$\frac{185}{74}$ corn maltodextrin, sucrose	$\frac{25}{36}$ $\frac{667}{667}$	500	hydrolyzed protein, peptide based, elelmental, high carbohydrate, low-fat formula 45% fat as MCT oil gluten free, low residue
Vivonex TEN (Nestle)	1.0	$\frac{38}{15}$ free amino acids	$\frac{3}{3}$ safflower oil	$\frac{210}{82}$ maltodextrin, modified corn starch	$\frac{26}{24}$ $\frac{500}{500}$	630	83% free water free amino acids high carbohydrate, low-fat formula high-protein version available

(*Continued*)

Table 14–6 **Enteral Product References: NONINFANT (1000 mL) (*Continued*)**

Product (Manufacturer)	Kcal/ mL	Protein g % kcals Source	Fat Gms %kcals Source	Carbohydrate g % kcals Source	mEq mg/1000 mL Na Ca K P	mOsm/ kg Water	General Com- ments
							flavor packets available lactose free
Vivonex Pediatric (Nestle)	0.8	24 / 12 free amino acids	24 / 25 MCT oil, soybean oil	130 / 63 altodex- trin, modified corn starch	17 970 / 31 800	360	89% free water 70% fat as MCT oil flavor packets available

Abbreviations: MCT, medium chain triglycerides; FOS, fructooligosaccharides.

At the time of publication, every effort was made to ensure that all product information was accurate. The most current information can always be obtained by referring to the package label. Some values may change with different flavors or companies.

Table 14–7 Animal Milk and Milk Alternatives

Product	1 cup/8 oz Calories	Fat (g)	Protein (g)	Ca (mg)	Vitamin D	Source	General Comments
2% milk	121	4.7	8	297	100	lactose, butterfat, cow's milk	used to reduce calories and fat not recommended for children < 2 y of age
Almond milk	40	3	1	200	100		
Coconut milk	80	5	1				coconut milk, cane syrup
Evaporated whole milk	338	19	17	658	222	lactose, butterfat, cow's milk	
Goat milk	168	10	8.6	326	29	lactose, butterfat, casein, and whey	not appropriate for use in infancy, as it is inadequate in folate and other essential nutrients

(*Continued*)

Table 14–7 **Animal Milk and Milk Alternatives (*Continued*)**

Product	1 cup/8 oz Calories	Fat (g)	Protein (g)	Ca (mg)	Vitamin D	Source	General Comments
							fat more easily digested than fat in cow's milk not used for cow's milk intolerance
Rice milk	120	2	1	20		rice, safflower oil	
Skim milk	86	0.4	8	302	100	lactose, trace butterfat, cow's milk	deficient in essential fatty acids not recommended for children < 2 y of age
Soy milk	79	4.6	6.6	40–300	120	soy protein	
Whole milk	150	8	8	295	100	lactose, butterfat, cow's milk (whey:casein 18:82)	not recommended for infants < 1 y of age 91% free water

Table 14–8 **Milk-Based Oral Supplements**

Product	Manufacturer	Form	Serving Size	Kcals/ Serving	Protein (g/ Serving)	Carbohydrate (g/Serving)	Fat (g/Serving)
Boost High Protein powder[a]	Mead Johnson	Powder	8 oz	350	21	48	9
Carnation Instant Breakfast	Nestle	Powder	9 oz	280	13	39	8.5
Carnation Instant Breakfast[a]	Nestle	Powder	8 oz	210	13	24	8.5
Health Shake	Novartis	Liquid	6 oz	300	9	53	6
Health Shake Aspartame Sweetened	Novartis	Liquid	6 oz	300	12	33 (3 g soluble fiber)	13
Resource Standard	Novartis	Liquid	8 oz	250	9	40	6

[a]Prepared with 8 oz whole milk.

(*Continued*)

Table 14–8 **Milk-Based Oral Supplements (*Continued*)**

Product	Manufacturer	Form	Serving Size	Kcals/ Serving	Protein (g/ Serving)	Carbohydrate (g/Serving)	Fat (g/Serving)
Resource Plus	Novartis	Liquid	8 oz	360	13	52	11
Scandi-Shake	Scandi-Pharm	Powder	9 oz	600	13	69	29
Scandi-Shake Sugar Free	Scandi-Pharm	Powder	9 oz	600	15	67	29
Scandi-Shake Lactose Free[b]	Scandi-Pharm	Powder	9 oz	520	17	59	25

[b]Prepared with 8 oz soymilk.

CONCENTRATION AND MODULAR COMPONENTS

Formulas may be modified to enhance energy density by concentration of the formula base and/or by the addition of carbohydrate, protein, or fat modular components (Tables 14–9 and 14–10). Children with increased energy requirements and/or volume restriction may benefit from a concentrated formula. Table 14–11 lists the suggested calorie distribution of feedings that should be considered when formulating recipes containing modular components. Concentration of a base infant formula, by adding less water or more concentrate, is generally recommended up to 24 to 26 calories per ounce. When higher energy densities are required, use of modular components should be considered for further caloric enhancement. The selection of modular type depends on the clinical situation. Table 14–12 lists situations in which particular types of macronutrient modulation may be indicated.

Table 14-9 Modular Additives

Product	Kcal/g or cc	G/Tbsp Cc/Tbsp	Energy Source	Comments
Corn oil	8.3	15	corn	nonemulsified
Cornstarch	3.81	8		30.5 kcal/tbsp
Corn syrup (Karo)	3.8	15		62 kcal/tbsp
Duocal (Nutricia)	4.92	8.5	Hydrolyzed cornstarch, blend of refined veg-etable oils	59% carbohydrate 41% fat (35% MCT, 65% LCT) Osmolality—310 mOsm/kg water

(*Continued*)

Table 14-9 Modular Additives (*Continued*)

Product	Kcal/g or cc	G/Tbsp Cc/Tbsp	Energy Source	Comments
				carbohydrate and fat source used to increase caloric density of formula/ foods 42 kcal/tbsp
MCT oil (Nestle)	7.7	15	Lipid fraction of coconut oil	Bile salts and lipase not necessary for digestion and absorption does not contain essential fatty acids nonemulsified 116 kcal/tbsp, 14 g fat/tbsp
Microlipid (Nestle)	4.5	15	Safflower oil	High in linoleic acid 50% fat emulsion that mixes easily and stays mixed with enteral formulas, beverages, and table food
Polycose (powder) (Abbott)	3.8	5.6 g carbohydrate /tbsp	Glucose polymers from hydrolyzed cornstarch	carbohydrate powder used to increase caloric density of formulas/foods/ beverages kosher, lactose and gluten free, low residue 23 kcal/tbsp
Promod (liquid) (Abbott)	100 kcal/1 ounce 3.3 kcal/mL	10 g protein/ 1 oz	Glycerine, hydrolyzed beef collagen	fruit punch flavored protein liquid that increases protein in formulas/foods/ beverages

				60% carbohydrate 40% protein
Resource Benecalorie liquid (Nestle)	7	330 kcal/1.5 oz serving	Calcium caseinate, high-oleic sunflower oil, mono and diglycerides	9% protein (7g/1.5 oz serving) 91% fat (33 g/1.5 oz serving) gluten and lactose free cholesterol free low residue low sodium
Resource Benefiber powder (Nestle)	4	4 g/tbsp or packet, 3 g fiber/tbsp or packet	Partially hydrolyzed guar gum	100% carbohydrate 16 kcal/tbsp gluten and lactose free
Resource Beneprotein (Nestle)	3.5	1 scoop = 1 ½ tbsp = 7 g, 6 g pro/scoop	Whey protein isolates, lecithin	25 kcal/scoop protein powder used to increase protein in formulas/foods
Safflower oil	8.4	15	safflower	nonemulsified
Scandical (Aptalis Pharma)	5.4	6.5	Nonfat milk, corn syrup solids, maltodextrin, vegetable oil, MCT, coconut oil, soy oil	tasteless powder used to increase calories in hot or cold foods

Abbreviation: MCT, medium chain triglycerides.

Table 14–10 Modular Additives-Human Milk Fortifiers

Product	g/Four Packets			mg (mEq) /Four Packets			Source	Osmolality (mOsm/kg of Water) General Comments
	CHO	Fat	Pro	Na / K	Ca / P	Fe		
Enfamil HMF (Mead Johnson) 14 kcal/ four packets	< 0.3	1.0	1.2	16 (0.7) / 29 (0.7)	92 (4.6) / 50	1.44	CHO-corn syrup solids FAT-MCT and soy oil PRO-milk protein isolate, whey protein isolate hydrolysate	Added to human milk to increase calories, protein, Ca, P, Na, vitamins, other minerals and trace elements Adds only 35 mOsm/kg H_2O when four packets added to 100 mL of breast milk Initiate two packet/100 mL EBM = 22 cal/oz Advance to four packet/100 mL EBM = 24 cal/oz
Similac HMF (Abbott) 14 kcal/ four packets	1.8	0.4	1.0	15 (0.7) / 63 (1.6)	117 (5.8) / 67 (2.2)	0.4	CHO-corn syrup solids FAT-MCT oil PRO-whey protein concentrate, nonfat dry milk	Added to human milk to increase calories, protein, Ca, P, Na, vitamins, other minerals and trace elements Initiate two packet/100 mL EBM = 22 cal/oz Advance to four packet/100 mL EBM = 24 cal/oz

Table 14–11 Recommended Calorie Distribution

	Carbohydrate	Protein	Fat
1–3 years old	45–65%	5–20%	30–40%
4–18	45–65%	10–30%	25–35%
Over 18	45–65%	10–35%	20–35%

Source: Adapted from Institute of Medicine, Food and Nutrition Board.[13]

Table 14–12 Indications for Calorie Enhancement by Commonly Used Modulars

Carbohydrate	Long Chain Fats	Medium Chain Triglycerides
Congenital heart disease	Bronchopulmonary dysplasia	Chylothorax
Delayed gastric emptying	Carbohydrate mal-absorption	Fat malabsorption
Failure to thrive	Diarrhea	Lymphangiectasia
Gastroesophageal reflux	Failure to thrive	Prematurity
Glycogen storage disease	Hypermetabolic states	Thoracic duct trauma
Hypermetabolic states		

Source: Reproduced with permission from Davis.[7]

Excessively concentrated formula may have a high renal solute load, which may require additional fluids to meet estimated fluid needs that will increase potential renal solute load (PRSL). When infants are fed a concentrated formula urine solute concentration should be monitored and maintained < 400 mOsm/kg of water. Practicing proper mixing of

Table 14–13 **Potential Renal Solute Load of Human Milk and Infant Formulas**

Formula	Protein (g/L)	PRSL (mOsm/L)
Human milk	10.0	36
Milk-based formula	15.0	49
Soy-based formula	18.0	62
Evaporated milk formula	27.6	102
Cow's milk (whole)	32.9	120

Abbreviation: PRSL = Potential Renal Solute Load.
Source: Reproduced with permission from Fomon and Ziegler.[14]

infant formulas is important to review with patient families to avoid accidental increase in renal solute load. Providing formulas that have high PRSL could provide more rapid dehydration than a low PRSL formula. The PRSL can be calculated by the following equation: PSLR= Na + Cl+ K + P + (protein/175). The PRSL of various milks and infant formulas can be reviewed in Table 14–13.[5]

The osmolality of the final formula feeding must also be considered. Isotonic formulations have an osmolality of approximately 300 mOsm/L, similar to blood and other bodily fluids. Hyperosmolar formulas may not be well tolerated by some infants and children.[6]

RECOMMENDATIONS FOR CONCENTRATION OF INFANT FORMULAS

Energy density should be advanced by two to four calories per ounce every 12 to 24 hours. To calculate a recipe, determine the volume of total formula needed, multiply it by the calories per volume desired from each component, and divide by the caloric density of the component. Water is the final ingredient added to achieve the total volume desired in each recipe

using a concentrated base. This step avoids dilution of the nutrient-containing components due to fluid displacement (Table 14–14). Children receiving enhanced energy formulas should be closely monitored for signs of intolerance as well as adequacy of fluid and nutrient intake. Nutrition assessment, growth, and laboratory monitoring should occur periodically, particularly with changes in clinical status.[6,7]

Table 14–14 Formula Recipes

Calculation of a Concentrated Formula
1. Determine volume of total formula needed Example 1: 600 cc or 20 oz Example 2: 960 cc or 32 oz
2. Multiply it by the calories per volume desired by each component Example 1: 20 oz × 24 calories/oz from standard infant formula = 480 calories Example 2: 32 oz × 24 calories/oz from standard infant formula = 768 calories 32 oz × 4 calories/oz from Polycose powder = 128 calories
3. Divide by the caloric density of the component (Table 14–18) Example 1: 480 calories/40 calories in 1 tablespoon of standard infant formula = 12 tbsp or ¾ cup Example 2: 768 calories/40 calories in 1 tbsp of standard infant formula = 19.2 tbsp or 1 cup plus 3 tbsp plus 1 tsp 128 calories/23 calories in 1 tbsp of Polycose powder = 5.6 tbsp or ¼ cup plus 1 tbsp plus 2 tsp
4. Add water to make final volume desired Example 1: Recipe ¾ cup standard infant formula powder Add water to make a total volume of 20 oz Example 2: Recipe 1 cup plus 3 tbsp plus 1 tsp standard infant formula powder ¼ cup plus 1 tbsp plus 2 tsp Polycose powder Add water to make a total volume of 32 oz

Initiation and Advancement of Feedings

Enteral feedings should be given in a manner appropriate to the child's condition and quality of life. Supplemental tube feedings can be given at night to allow oral intake during daytime hours; total EN may be provided as a combination of bolus and/or continuous drip feedings. Bolus feedings can allow gravity to dictate the rate of infusion or a pump can be used to deliver formula at a constant rate.[8] Continuous feedings are given over 8 to 24 hour periods at a slower rate. Table 14–15 outlines the advantages and disadvantages of each feeding method.

Feedings can be initiated using either of the above methods of administration. Progression of feedings is dictated by tolerance to the previous step in advancement. The final goal is a predetermined formula volume based on the child's nutritional requirements. Rates of infusion and concentration should not be advanced simultaneously. Adjustments to the goal volume may be required when a

Table 14–15 Administration of Enteral Feeding

	Advantages	Disadvantages
Bolus	Can mimic or supplement meals. May not require a pump. Freedom of movement between feedings.	Increased risk of aspiration. Not recommended for children with conditions associated with poor volume tolerance (e. g., gastroesophageal reflux, delayed gastric emptying).
Continuous	Preferred method for small bowel feedings. Slow infusion may improve tolerance. Can be given nocturnally to avoid disruption of daytime schedule and oral intake.	Requires pump. Child is attached to equipment for duration of feeding. Overnight feedings may result in morning fullness.

Table 14–16 **Guidelines for Initiation and Advancement of Continuous and Intermittent Tube Feedings**

Age	Initial Infusion	Advances	Goal
Continuous Feeds			
Preterm	1–2 mL/kg/h	10–20 mL/kg/d	120–175 mL/kg/d
0–12 mo	1 mL/kg/h	1 mL/kg q 2–8 h	1–5 mL/kg/h
1–6 y	1–2 mL/kg/h	1–2 mL/kg/q 2–8 h	6 mL/kg/h
> 7 y	25 mL/h	25ml q 2–8 h	100–150 mL/h
Bolus/Intermittent feeds			
Preterm (>1200 g)	2–4 mL/kg/feed	2–4 mL/feed	120–175 mL/kg/d
0–12 mo	5–10 ml/kg q 2–3 h	10–30 mL/feed	20–30 mL/kg q 4–5 h
1–6 y	10–15 ml/kg q 2–3 h	30–45 mL/feed	15–20 mL/kg q 4–5 h
> 7 y	90–120 mL q 3–4 h	60–90 mL/feed	330–480 mL q 4–5 h

Source: Reproduced with permission from Davis.[8]

child "outgrows" the calories provided by the formula volume or with changes in clinical condition. Recommendations for initiating tube feedings and attaining the desired goals are outlined in Table 14–16.

MONITORING AND EVALUATION OF TUBE FEEDING

When a NG tube is placed, it is important to confirm the placement of the tube. First, confirm the placement with a pH measurement of gastric aspirate for weighted or nonweighted NG tubes. A pH value of 0–5 suggests intragastric location.

Radiographic confirmation must be done when pH is > 5, an aspirate cannot be obtained, or a patient's condition changes during the insertion procedure. Reconfirmation of the NG tube placement is required if the tube migrates, the patient vomits, or the patient is transferred from an outside facility. In the early stages of tube feeding, monitoring is focused on assessing the patient's tolerance to the feeding plan. Once a feeding regimen has been established, monitoring involves ensuring that the goals of nutritional therapy are being met and that tube-feeding support is still required. Monitoring and evaluation of tube feedings include weight, height, biochemical and hematological indices, tube integrity, and any tube-related complications. Finally, Table 14–17 lists some common complications of tube feeding and their solutions.

Table 14–17 Complications Encountered in Tube Feeding

Complication and Possible Causes	Intervention
Gastrointestinal	
Constipation	
Low fiber intake	Use fiber-containing formula or add fiber module. Watch for clogging of the tube if fiber used.
Diarrhea	
Formula delivered too rapidly	Decrease delivery rate.
Hypertonic formula	Change to isotonic formula and gradually increase concentration as tolerated. Alter carbohydrate and electrolyte content.
Medications that change the gut flora or have cathartic effects	If possible, change the type of medication or time it is given. Note sorbitol content in drugs.

Complication and Possible Causes	Intervention
Bacterial contamination of formula	Use aseptic preparation techniques and limit the feeding time to 4–8 h. Do not add new formula to bag containing old formula.
Cold formula	Allow formula to reach room temperature before feeding.
Mucosal atrophy and malnutrition	Use isotonic or diluted formula. Start at low rate and advance rate slowly.
Malabsorption	Use elemental or semielemental formula, MCT oil.
Hypoalbuminemia	Alter the protein and fat content Dipeptide-based, low-fat formula may be beneficial.
Residuals	
Hypomotility caused by medications or hypoosmolar formula	A single gastric residual > 2 times the hourly rate should require cessation of tube feeding Check residuals every 4–6 h.
Delayed gastric emptying of medications and other fluids being added to stomach	Consider prokinetic agent, patient positioning (place in right lateral oblique position), transpyloric feeds, continuous infusion, isotonic formula).
Vomiting, nausea, bloating	
Ileus/obstruction	Stop feedings. May require parenteral nutrition if ileus is prolonged.
Improper tube placement	Check tube placement.
Infusion rate too rapid	Reduce rate and increase gradually as tolerated.
Delayed gastric emptying	Consider prokinetic agent, patient positioning, transpyloric feeds, continuous infusion, isotonic formula.
Hyperosmolar formula	Dilute formula to isotonicity then increase concentration gradually.

(*Continued*)

Table 14–17 **Complications Encountered in Tube Feeding (*Continued*)**

Complication and Possible Causes	Intervention
Hypertonic medications	Change timing or type of medication. Check for sorbitol content in drugs
High-fat formula	Change to lower-fat formula.
Unpleasant odor of formula	Use flavor packets. Use different formula.
Formula too hot or too cold	Use formula at room temperature.
Patient positioning	Elevate head of bed 30 to 45 degrees.
Swallowing excess air	Stop feeding pump once feeding is complete.
Inadequate fluid intake	Monitor fluid balance closely. Increase fluid intake by changing formula concentration or rate or through fluid boluses.
Inactivity	Avoid prolonged bed rest.
Fecal impaction	Enemas or stool softeners, digital disimpaction, increase fiber and/or fluid intake.
Mechanical	
Aspiration	
Gastric hypomotility	Infuse formula past pylorus. Consider continuous infusion. Elevate head of bed 30 to 45 degrees.
GER	
Neurologic damage	
Clogging of tube	
Improper or infrequent irrigation of the tube	Flush tubing with water every 4–8 h and after all medicines.

Complication and Possible Causes	Intervention
Administration of medications through a feeding tube	Crush medications well or use liquid form. Assess drug/formula interactions. Avoid mixing formulas with liquid medications with a pH < 5.0. Use warm water to flush or a commercially prepared formula. Replace feeding tube.
Improper size or placement of tube	Change tube size. Check placement.
Nasopharyngeal discomfort, nasal or esophageal erosions	Wet the mucous membranes or use a smaller tube.
Pressure on the nares or esophagus	Alternate nares weekly.
GI perforation secondary to malpositioning of tube, excessive manipulation, use of guide wires	Can be avoided by radiologic confirmation of tube placement, minimizing manipulation, fluoroscopic guidance of nasoenteric tube placement, choice of proper size tube.
Metabolic	
Azotemia	
High protein intake, renal immaturity or dysfunction, liver disease, metabolic dysfunction	Decrease protein content.
Congestive heart failure	Reduce fluid and/or sodium content. Provide diuretics.
Dehydration	
Inadequate fluid intake	Increase fluid intake.
Hyperosmolar or high-protein formula	Decrease formula concentration. Change to isotonic or lower-protein formula.

(*Continued*)

Table 14–17 **Complications Encountered in Tube Feeding (*Continued*)**

Complication and Possible Causes	Intervention
Essential fatty acid deficiency	Change formula, add 5 mL of safflower oil, add modular fat.
Hyperglycemia: diabetes, insulin deficiency, severe malnutrition, trauma, sepsis, or excessive carbohydrate intake	Monitor blood sugar. Initiate or adjust insulin. Reduce carbohydrate content.
Hyperkalemia: High-potassium formula or IV potassium, renal insufficiency, acidosis	Monitor laboratory values. Change formula. Stop or decrease IV potassium. Give Kayexalate, insulin, glucose.
Hypokalemia: protein-calorie malnutrition, refeeding syndrome, diarrhea, insulin administration	IV/PO potassium. Evaluate potassium intake from formula for adequacy.
Hyponatremia	
Overhydration	Restrict water. Evaluate sodium intake from formula for adequacy.
Sodium depletion	Add sodium chloride.
Hyperphosphatemia	Change formula. Use phosphate binder or calcium supplement.
Hypophosphatemia: severe malnutrition (refeeding syndrome), insulin administration	IV/PO phosphorus. Evaluate phosphorus intake from formula for adequacy.
Liver function, abnormal	May need to stop or change formula.
Overhydration	
Infusion rate too rapid	Decrease rate.
High sodium intake	Decrease sodium content.

Complication and Possible Causes	Intervention
Severe protein-calorie malnutrition	Monitor input and output.
Weight	
Rapid or excessive gain: excessive calories and/or fluid	Decrease concentration or amount of formula; evaluate electrolyte status.
Slow or no weight gain: inadequate caloric intake	Evaluate macro and micronutrient intake. Evaluate input and output.
Psychomotor development	
Child kept on tube feeding for long period of time and missed important developmental steps for learning feeding skills	Nonnutritive sucking, taking very small amounts of food from a spoon, or taking liquid from a cup to desensitize the oral area, develop an association between oral activity and satiety and learn eating and feeding skills. Consult an occupational therapist or speech pathologist.

Abbreviations: GI, gastrointestinal; MCT, medium chain triglycerides; NG, nasogastric; GER, gastroesophageal reflux.

TRANSITIONAL FEEDINGS

Enteral to Cyclic EN

Once children are able to tolerate full volume feedings at a continuous rate over 24 hours, cycling feedings should be considered to allow time off. Bolus or intermittent feeding is more physiological and therefore preferable as a standard procedure.[2] See Table 14–18 for steps in cycling enteral feedings and Table 14–19 for an example of transitional feeding to combined nighttime and bolus feedings.

Table 14–18 Recommendations for Transitioning to Cyclic Enteral Feedings

Attain goal feeding volume over 24 h.

Stop feedings for approximately 2 h then increase rate by 1–2 mL/kg or 25 mL/h (see Table 14–18) every 4–12 h, as tolerated, with a corresponding decrease in the number of hours of feedings per day. The total volume of feedings per 24 h should be constant.

When planning supplemental night tube feedings, consider running feeds only during planned feeding hours. Increase rate over these hours to the total volume desired.

Transition from continuous to bolus feedings:

- consider combination bolus and nighttime continuous feedings for exclusively tube-fed patients
- cycle to desired rate of overnight feed, then decrease number of hours, and provide remaining volume as bolus feedings; start bolus volume at 1–2 times the hourly rate

Large volume bolus feedings may not be well tolerated in patients with delayed gastric emptying; many patients will require a pump to allow volume of bolus feed to run over 1/2 to 1 h.

Table 14–19 Example of Transitional Feeding to Combination Nighttime and Bolus Feedings[a]

	Feeding Regimen	Schedule
Day 0	80 mL/h	Continuous
Day 1	100 mL/h for 19 h	4 PM to 11 AM
Day 2	115 mL/h for 16 h + 150 mL bolus	5 PM to 9 AM, bolus at 1 PM
Day 3	115 mL/h for 12 h + 250 mL bolus × 2	7 PM to 7 AM, bolus at 11 AM and 3 PM
Day 4	115 mL/h for 10 h + 250 mL bolus × 3	8 PM to 6 AM, bolus at 9:30 AM, 1 PM, and 4:30 PM

[a]For a 9-year-old, 30 kg child on continuous intact protein nasogastric feedings of 30 kcal/oz formula.

ENTERAL TO ORAL NUTRITION

The transition to oral feedings is a process rather than a single event.[9] It may prove to be long and challenging, especially in the child who has been deprived of oral stimulation during critical stages of development and has not acquired appropriate feeding skills. Common problems encountered in the transition to oral feeding include gagging, retching, and vomiting when orally stimulated and an absence of the hunger-satiety cycle.[10,11] To reduce the risk of oral hypersensitivities and feeding difficulties, early assessment and implementation of an oromotor stimulation program by a speech pathologist is recommended[2,12] (Table 14–20).

Table 14–20 Guidelines for Transition from Enteral to Oral Feedings

Assessment:

1. Assess the child's nutritional and medical status.
2. Assess the child's oral motor and swallowing skills: If the child has a history of swallowing difficulties, have the child seen by a speech and language pathologist for a swallowing evaluation. Assess for aspiration of oral feeds.
3. Assess the caretaker's readiness to begin transition: Caretakers will require education on process and reassurance that transition may be gradual.

Transition to oral feeds:

1. Gradual transition to bolus feeding: Increase the rate of feedings and lengthen the time between feedings.
2. Adjust bolus feeding to oral feeding schedule: Three meals and 2–3 snacks per day.
3. Offer oral feeds first, then bolus feed, and/or nighttime feeds to make up caloric deficit.

(*Continued*)

Table 14–20 Guidelines for Transition from Enteral to Oral Feedings (*Continued*)

4. Reduce tube feeding gradually: Tube feeding can be reduced by 25% initially to promote hunger. Continue to gradually reduce by increments of 25%, based on improvements in oral intake, feeding problems, and growth. Once the child is consuming > 75% from oral feeds, tube feeding can be stopped. Patient may need additional pedialyte or water when tube feeding is decreasing to meet fluid needs.
5. Other considerations: Consult a behavioral psychologist and/or speech therapist for feeding difficulties. Use behavior modification techniques, for example, positive reinforcement and oral stimulation exercises. Offer variety in food texture, color, taste, temperature, and smell without overwhelming the child. Do not force feed. Allow the child to play with different foods; tube feed during family mealtime to create an association between feeding and hunger.

HOME TUBE FEEDING

Home tube feeding can offer psychological benefits for the child and family and be markedly less expensive than hospitalization. Home tube feeding is indicated if the patient is medically stable and ready to be discharged from the hospital, and the child is tolerating tube feedings, and is expected to require them for longer than one week. It is important that caretakers and the patient (if old enough) be willing, able, and capable to administer tube feedings at home. Caretakers should be taught how to prepare, administer, and monitor the feedings and be able to demonstrate their skills.

It should also be confirmed that caretakers have the necessary resources for administering tube feeds, such as running water, refrigeration, and storage space (Table 14–21). A plan for insurance coverage of the cost of the formula and tube-feeding equipment should be established prior to discharge. Outpatient medical and nutrition follow-up should be in place. Nutrition follow-up will involve continued assessment

Table 14–21 Required Instructions for Home Tube Feeding

Preparation

How to use sanitary techniques, for example, proper handwashing, cleaning equipment before starting, avoiding contamination of formula.

How to place and check the feeding tube, if using a nasogastric tube.

How to prepare enteral feeding bags, program the feeding pump, and troubleshoot alarms.

Monitoring

How to distinguish signs and symptoms of intolerance, for example, vomiting, abdominal distention, and diarrhea. Excessive coughing, breathing difficulties, or skin color changes may indicate improper tube placement. The tube should be removed and replaced by either the caregiver, if a g-tube, or hospital personnel in the case of j-tubes.

Support

Names and important phone numbers to be provided: physician, nutrition support nurse, dietitian, and 24-h hotline from infusion company for technical support.

of the patient's nutritional needs and adjustments to feeding regimen as needed. A visiting nurse or social worker can provide support between clinic visits. Support groups in the area may also be available for the family.

◆ PARENTERAL TO ENTERAL NUTRITION

Adequacy of fluid and nutrient intake must be closely monitored in the transition from PN to EN. Young infants are at greatest risk due to their proportionately higher nutrient needs. Most infants and children can successfully make the transition from PN to intact formula EN once gut function has resumed and enteral access is obtained. Patients with chronic GI disease may require slower transitions, special formulas, and closer monitoring. Table 14–22 lists the steps in transitioning children from PN to EN and Table 14–23 gives an example of transitional feeding.

Table 14–22 Recommendations for Transitioning from Parenteral to Enteral Nutrition

1. Match PN caloric density with desired EN caloric density when feasible.
2. Once initial EN rate is tolerated, decrease PN rate milliliter for milliliter with further increases in EN (see initiation and advancement guidelines, Table 14–18).
3. For fluid restricted patients: continue lipid infusion until goal EN rate is tolerated, then concentrate formula as required to meet caloric requirements prior to discontinuing lipids. Calorie requirements of enterally fed patients are generally 10% higher than parenterally fed patients.

Abbreviations: PN, parenteral nutrition; EN, enteral nutrition.

Table 14–23 Example of Transitional Feeding

	Parenteral Nutrition	20% Lipids	Enteral Nutrition	Total Kcal
Day 0	15 ml/h	2 ml/h	–	88 kcal/kg/d
Step 1	11 ml/h	2 ml/h	4 ml/h	90 kcal/kg/d
Step 2	7 ml/h	2 ml/h	8 ml/h	91 kcal/kg/d
Step 3	3 ml/h	2 ml/h	12ml/h	93 kcal/kg/d
Step 4	Discontinue PN	2 ml/h	16ml/h	98 kcal/kg/d
Step 5	—	1 ml/h	Increase to 24 kcal/oz	98 kcal/kg/d
Step 6	—	Discontinue lipids	18 ml/h	96 kcal/kg/d

For a 3.6-kg infant on parenteral nutrition with 15% dextrose and 2.5% amino acids; Enteral nutrition = 20 cal/oz breastmilk; fluid limited to 120 ml/kg/d.

INTERNET RESOURCES

American Society for Enteral and Parentral Nutrition: http://clinnutr.org

Boston Children's Hospital: http://www.childrenshospital.org/nutrition

Children's Nutrition Research Center: www.bcm.tmc.edu/cnrc

Kennedy Krieger Institute: www.kennedykrieger.org

Kluge Children's Rehabilitation Center Encouragement Feeding Program: http://www.medicine.virginia.edu/clinical/departments/pediatrics/clinical-services/kcrc/rehabilitation/feeding

Company Websites:

Abbott: http://abbottnutrition.com

Mead Johnson: http://www.meadjohnson.com

Nestle Clinical Nutrition: (Infant formula) http://www.gerber.com

(Children 1–10/ adults) http://www.nestle-nutrition.com

Nutricia: http://www.nutricia-na.com

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15 Parenteral Nutrition

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INTRODUCTION

The use of total parenteral nutrition (TPN, or alternatively, PN) in the 1970s was a landmark in the history of nutrition, profoundly affecting the management of patients with gastrointestinal failure.[1,2] The application of PN to patients with nongastrointestinal disease such as malignancies, critical care, and other conditions has been adopted, although explicit evidence for its efficacy is lacking in these conditions. PN represents the most aggressive and expensive method of providing nutritional support and careful consideration is required before prescription. The literature suggests that a multidisciplinary PN consult team is a cost-effective method for patient selection, assessment, and monitoring.[3]

INDICATIONS

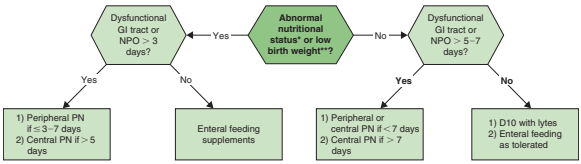
Enteral nutrition is the preferred route of nutrition support; however, there are several medical conditions for which enteral nutrition is not feasible and PN is indicated (Table 15–1). The initiation of PN is a clinical decision where the benefits of PN

Table 15–1 Conditions Commonly Requiring Parenteral Nutrition

Conditions	Examples/Comments
Surgical gastrointestinal disorders	Gastroschisis, omphalocele, tracheoesophageal fistula, intestinal atresias, meconium ileus, malrotation and volvulus, Hirschsprung's disease, diaphragmatic hernia, and prolonged postoperative ileus, gastrointestinal fistula
Short bowel syndrome	Surgical resection due to NEC, malrotation with volvulus, other congenital causes
Congenital heart disease	If blood supply to mesentery is compromised or dependent on patent ductus arteriosus
Acute alimentary disease	Pseudomembranous colitis, NEC, peritonitis, severe inflammatory bowel disease (including fistulas due to Crohn's disease), chronic or secretory diarrhea (microvillus inclusion disease, tufting enteropathy)
Motility disorders	Chronic intestinal pseudo obstruction; total colonic Hirschsprung's disease; mitochondrial and metabolic disorders
Prematurity	
Bone marrow transplantation	Anorexia, feeding intolerance, and mucositis
Hypermetabolic states	Burns, multiple trauma, sepsis

Abbreviation: NEC, necrotizing enterocolitis.

need to be weighed against the risks of PN therapy versus intravenous fluid provision alone. Pediatric patients have increased metabolic requirements and limited fuel storage in the forms of fat and protein and thus are more susceptible to the effects of starvation than are adults. An estimate of three to five days is often used as the length of time for which the provision of 10% dextrose is a reasonable alternative for nutrition support (see Figure 15–1). If the period of time of minimal to no enteral



* < 5th percentile weight for age or weight for height
** < 2500 g

Figure 15–1: Decision tree used for the selection of method of nutrition support. GI = gastrointestinal; NPO = nothing by mouth; PN = parenteral nutrition.

nutrition is anticipated to be longer than 5 days, then most pediatric patients would benefit from PN. In cases of severe malnutrition, low birth weight, hypermetabolism, or selected other conditions, the provision of PN for fewer than 5 days may be justified. If the period of minimal to no enteral nutrition is anticipated to be longer than seven days, full PN with central venous access is indicated. Peripheral access and the infusion of a more dilute solution may be adequate for periods of less than seven days, although the limitation of solution osmolarity can make it difficult to meet the patient's energy needs.

VENOUS ACCESS

Efforts to reduce technical and infectious complications of venous catheter placement and use are important in the safe delivery of the PN solution. The location of the catheter tip in the central venous circulation is crucial for the infusion of hypertonic PN solutions.[4] Central location reduces the risk of thrombus and vascular intimal damage. A central catheter tip location allows for instantaneous dilution of hypertonic PN solution (> 900 mOsm/L) into the blood stream. In children, the superior vena cava (SVC), the junction of the SVC and the right atrium, brachiocephalic/SVC junction, and the inferior vena cava (IVC) above the bifurcation of

the iliac veins all are considered central locations for the catheter tip placement and offers the largest caliber lumen and high blood flows.[4] Peripheral catheter locations preclude hyperosmolar solutions and therefore PN solutions should be limited to 900 mOsm/L or less to help reduce the risk of phlebitis, infiltration, and infection.[3] Documentation of catheter tip location by radiographic confirmation is required for PN administration, because malpositioned catheters can have serious and even fatal consequences.

FLUIDS AND ELECTROLYTES

Fluid requirements for the patient should be based on weight and clinical condition. Typically maintenance fluid is provided with the PN solution. Maintenance fluid requirements can be assessed using the Holliday-Segar method (Table 15–2).[2] Fluid requirements can be higher when there are increased insensible losses (fever or tachypnea) or sensible losses (diarrhea, vomiting, nasogastric output, ostomy, or urinary losses). In certain clinical situations, such as liver or kidney

Table 15–2 Daily Parenteral Fluid Requirements According to the Holliday-Segar Method

Body Weight	Maintenance Parenteral Fluid Requirements
0 to 10 kg	100 mL/kg
10–20 kg	1000 mL + 50 mL/kg over 10
Over 20 kg	1500 mL + 20 mL/kg over 20
For example in an 18 kg child:	
1000 mL for the first 10 kg	1000 mL
50 mL × 8 kg	400 mL
Total maintenance fluid	1400 mL per 24 h

dysfunction, fluids may need to be restricted. Therefore, routine clinical monitoring of hydration status, including electrolytes and intakes and outputs, is essential in the patient receiving PN.

If a patient's fluid requirement is being met, but his/her energy needs are not, it is generally recommended to increase the volume of PN administered rather than to increase the concentration of nutrients in the PN. This minimizes the need to infuse hypertonic solutions, which are more damaging to the intima of blood vessels. This approach assumes that the patient's cardiovascular and renal systems can tolerate the increased volume of parenteral fluids. Basal electrolyte requirements for children and adults are shown in Table 15–3. Clinical needs may vary if exogenous losses are high (e.g., diarrheal disease and diuretic use) or renal function is altered. Table 15–4 lists the estimated electrolyte losses and typical replacement fluids used in various gastrointestinal losses; however, precise quantification is possible by sending a specimen to the chemistry laboratory for measurement of electrolyte concentrations.

Table 15–3 Basal Electrolyte Requirements for Children and Adults

Element	Daily Amount (Children) (mEq/kg)	Daily Amount (Adults) (mEq/d)
Sodium	2–4	130
Potassium	2–3	60
Calcium	0.5–2.5	5
Magnesium	0.25–0.5	16
Phosphorus	1–2	20
Chloride	2–3	120

Table 15–4 Gastrointestinal Electrolyte Losses and Suggested Replacement Regimen

Source of Body Fluid Loss	Sodium (mEq/L)	Potassium (mEq/L)	Chloride (mEq/L)	Bicarbonate (mEq/L)	Typical Replacement Fluid
Gastric	20–80	5–20	100–150	–	½ NS with 10 mEq K/L[a]: mL replacement for mL losses as tolerated by patient hydration status
Ileostomy	45–135	3–15	20–115	50–70	½ to ¾ NS: mL replacement for mL losses as tolerated by patient hydration status If CO_2 is low could use Lactated Ringer's solution or may need 50% of sodium as NaCl and 50% of sodium as Na acetate salts
Colostomy	50–120	30–40	90–95	20–30	½ to ¾ NS with 20 mEq K/La: mL replacement for mL losses as tolerated by patient fluid status

[a]Any replacement solution with potassium needs to be infused over several hours depending on the total amount of potassium and total volume of replacement fluid required.

Source: Adapted from Aune GJ.[49]

COMPONENTS OF PARENTERAL NUTRITION

In pediatric PN solutions, dextrose, amino acids, electrolytes, and micronutrients are typically provided in a single solution. Due to stability limitations with small lipid provisions, lipid emulsions are usually infused separately from the dextrose-protein solution. However, in most adult and some pediatric facilities, total nutrient admixtures (TNA), in which the lipids are mixed directly with the PN solution, are used. In circumstances where severe fluid restriction is necessary, the fluid from the fat emulsion is considered in the total fluid allotment. In most cases, however, fluid provision from fat emulsion is calculated in addition to the PN volume.

Of the macronutrients, dextrose provides the primary source of energy of the PN solution. In the intravenous form, dextrose monohydrate has a caloric density of 3.4 kcal/g. This is slightly less than the 4 kcal/g caloric density attributed to all other carbohydrate (CHO) sources. (Table 15–5) In PN, dextrose infusions are typically initiated at a glucose infusion rate (GIR) of 5 mg CHO/kg/min, which approximates endogenous glucose production of premature infants and neonates[5] (Table 15–5). The increase in GIR will vary depending on the age, size, and tolerance to the dextrose infusion although in most cases, dextrose advancement is performed in daily increments of 2–5 mg/kg/min. The recommended maximum GIR for infants is 12–14 mg/kg/min.[5] There may be clinical situations where the rate needs to be greater; however, there is a potential risk of overfeeding and a high dextrose intake may contribute to the development of steatosis, cholestasis, hyperglycemia, or glucosuria.[6] Monitoring tolerance to the dextrose infusion is performed by blood glucose checks as well as urine dipsticks to assess for glucosuria as the GIR is increased. Urine glucose checks are advantageous as they are noninvasive and

Table 15–5 Macronutrients in Parenteral Nutrition

Macronutrient	Energy Density	Examples
Dextrose[a]	3.4 kcal/g	10% = 10 g/dL × 3.4 = 34 kcal/dL = 0.34 kcal/mL
Amino acids[b]	4 kcal/g	2% = 2 g/dL × 4 = 8 kcal/dL = 0.08 kcal/mL
Fats[c]	9 kcal/g	10% = 10 g/dL × 9 = 90 kcal/dL = 1.1 kcal/mL 20% = 20 g/dL × 9 = 180 kcal/dL = 2 kcal/mL 30% = 30 g/dL × 9 = 270 kcal/dL = 3 kcal/mL

[a]To convert from percentage dextrose to mg/kg/min: percentage dextrose × (1 dL/100 mL) × (1000 mg/1 g) × hourly infusion rate (ml/h) × (1 h/60 min) × (1/weight in kg). For example, 10% dextrose infusing at 10 mL/h in a 3 kg infant: 10 × 1/100 mL × (1000 mg/1 g) × 10 ml/h × (1 h/60 min) × (1/3 kg) = 5.6 mg/kg/min.

[b]A normal nonprotein energy (kcal) to nitrogen (g) ratio is between 150 and 250:1. The ratio is calculated as follows: nonprotein energy (kcal): nitrogen (g) = (Carbohydrate calories + fat calories): protein intake (g)/6.25.

[c]Additional calories are provided by phospholipid emulsifiers and glycerol.

can be checked regularly. Routine monitoring of urine for glucose can be helpful as a positive result may be the first sign of sepsis in a situation of stable GIR. If hyperglycemia and positive urine glucose occurs, the GIR may need to be reduced, even if temporarily.

If hyperglycemia persists with inadequate total energy intake, insulin therapy needs to be considered. Insulin therapy can be initiated at doses as low as 0.01 units/kg/h in a separate infusion from the PN solution and titrated as needed to help maintain euglycemia. Insulin is one of the few anabolic hormones in common use in patients receiving PN, and its combination with PN has been associated with better accretion of lean body mass.[7] Although studies in adults in the surgical intensive care unit (ICU) suggest a benefit to tight

glycemic control,[8] tight glycemic control in pediatric patients can potentially reduce morbidity and mortality in the ICU, but increases the risk of hypoglycemia requiring frequent blood glucose monitoring.[9] Randomized trials of tight glycemic control in pediatric critical care patients are ongoing.

Crystalline amino acids provide the protein source in PN solutions. Amino acid solutions commonly used in the United States in the pediatric population are Trophamine® (B.Braun Medical), Premasol® (Baxter), or Aminosyn PF® (Hospira). Due to the nutritional requirements in infants, amino acid solutions designed for infants have markedly different amino acid compositions than those used for older children and adults. Pediatric amino acid solutions have higher amounts of aspartic and glutamic acid and taurine with lower quantities of methionine, glycine, and phenyalanine (Table 15–6). In premature infants < 1000 g who have a reduced ability to metabolize methionine to cysteine and taurine, the conditionally essential amino acid cysteine (hydrochloride) is routinely added. Taurine plays an important role in solubilizing bile salts and is necessary for adequate biliary secretion and reabsorption from the ileum.[10] It supports the formation of a more water-soluble conjugated bile acid that protects against lithocholate toxicity.

In most infants, the protein provision is initiated at 1–2 g protein/kg/d and advanced by 1 g/kg/d increments to 3–4 g/kg/d. The higher dose is typical for the premature infant < 1000 g, for whom data suggest that prompt initiation of parenteral protein (e.g., 2 g/kg within the first 24–48 hours of life) is associated with optimal metabolic profiles and growth.[11] For older children (i.e., < 12 years of age), a goal 2 g/kg/d of protein is usually adequate.[3] Monitoring the safety of protein intake includes blood urea nitrogen (BUN) monitoring and in the rare instance of liver failure, serum ammonia levels. If the patient is not

Table 15–6 **Brand Specific Composition of Common Pediatric Parenteral Amino Acid Solutions**

	Solutions Designed for Infants		Standard Solutions Suitable for Ages 1 y and Above					
Product (Manufacturer)	**Aminosyn PF (Hospira)**	**TrophAmine (B.Braun) Premasol (Baxter)**	**Aminosyn (Hospira)**	**Aminosyn II (Hospira)**	**FreAmine III (B Braun)**	**Novamine (Hospira)**	**Travasol (Baxter)**	**Prosol (Baxter)**
Nitrogen mg per 100 mL of 1% solution	152	155	157	153	153	158	165	161
Amino acids (essential) mg per 100 mL of a 1% solution								
Isoleucine	76	82	72	66	69	50	60	54
Leucine	120	140	94	100	91	69	73	54
Lysine	68	82	72	105	73	79	58	68
Methionine	18	34	40	17	53	50	40	38
Phenylalanine	43	48	44	30	56	69	56	50
Threonine	51	42	52	40	40	50	42	49
Tryptophan	18	20	16	20	15	17	18	16
Valine	67	78	80	50	66	64	58	72

Amino acids (nonessential) mg per 100 mL of a 1% solution								
Alanine	70	54	128	99	71	145	207	138
Arginine	123	120	98	102	95	98	115	98
Histidine	31	48	30	30	28	60	48	59
Proline	81	68	86	72	112	60	68	67
Serine	50	38	42	53	59	39	50	51
Taurine	7	2.5						
Tyrosine	4	4.4	4.4	27		2.6	4	2.5
Glycine	39	36	128	50	140	69	103	103
Glutamic Acid	62	50		74		50		51
Aspartic acid	53	32		70		29		30
Cysteine		< 1.6			< 2.4			
N-ac-L-tyrosine	0	24	0		0	0	0	

in a catabolic state, prealbumin and C-reactive protein levels can be monitored for adequacy of protein and energy intake. Reduced protein intake occurs in chronic renal failure before dialysis is initiated or in severe liver failure; otherwise, provision of protein according to standard Dietary Reference Intakes (DRI) is a typical practice.

Ideally, the protein provided in PN is used not as a primary fuel source (as are carbohydrates and fats), but as substrate for enzyme synthesis and lean body accretion. Therefore, some centers do not include protein intake in their calculation of energy provided by the PN. Instead, energy intake is often expressed as "nonprotein" energy and is from carbohydrate and fat provision. The ratio of nonprotein calories to protein provided in PN is also a useful measure of macronutrient balance (Table 15–5). When expressed as the ratio of nonprotein energy (kcal) to nitrogen (g), metabolism is generally optimal when this ratio is between 150 and 250:1. Burn patients, and others with a very high protein requirement, may be optimally fed with a ratio of 100:1.

Intravenous fat emulsions (IFEs) provide a rich source of energy, essential fatty acids, and a balance of macronutrients. IFEs available in the United States are soy bean oil based oil in water emulsions with egg phosphatides and glycerin. Therefore, IFEs have been described to cause anaphylaxis reactions in patients with severe soy or egg allergy. Current practice is to initiate lipid infusions at 1 g fat/kg/d and advance to 3 g fat/kg/d for neonates and 1–2 g/kg/d for older children and adults.[3] IFE should not exceed 50% of the total calories because higher percentages may cause ketosis. Tolerance to intravenous fats is performed by monitoring serum triglyceride (TG) concentrations, which ideally should remain at < 250 mg/dL. Adverse metabolic effects of hypertriglyceridemia are noted at far higher concentrations, thus higher TG levels are often tolerated. Although some cases

of hypertriglyceridemia are attributable solely to excessive amounts of IFE, many patients receiving PN will have other reasons to have high serum TG levels, including acute phase stress response, sepsis, or hepatic and/or renal dysfunction.[12] Multiple medications are also associated with hypertriglyceridemia (Table 15–7). If persistent hypertriglyceridemia is

Table 15–7 Medications Associated With Hypertriglyceridemia

Abacavir	Dexrazoxane	Mirtazapine
Acitretin	Didanosine	Mitotane
Adalimumab	Efavirenz	Nafarelin
Amiodarone	Eplerenone	Olanzapine
Amprenavir	Eprosartan	Olmesartan
Aripiprazole	Estrogen	Paclitaxel
Atevirdine	Estropipate	Propofol
Bazedoxifene	Febuxostat	Raloxifene
Beta-blockers	Fluconazole	Retinoids/vitamin A
Calcitriol	Fluoxetine	Risperidone
Candesartan	Fomepizole	Ritonavir
Capecitabine	Glucocorticoids	Sertraline
Cholestyramine	Indinavir	Sirolimus
Carevedilol	Interferons	Somatropin
Clomiphene	Isotretinoin	Tacrolimus
Clozapine	Itraconazole	Tamoxifen
Cyclosporine	Ketoconazole	Thiazide diuretics
Darunavir	L-Asparaginase	Thyrotropin
Delavirdine	Leflunomide	Tipranavir
		Vitamin E

Source: Adapted from Henkin et al.[50] and the Online Formulary, Boston Children's Hospital.

noted, options include reducing the infusion time to 20 or fewer hours (and monitoring TG concentrations after a 4 h "fast") or infusing lipids on alternating days during the week.

Recent research has linked excessive IFE intake with a higher incidence of PN-associated liver disease[12] and the practice of lipid minimization (i.e., limiting IFE to 1 g fat/kg/d) is emerging in some centers. At Boston Children's Hospital, infants and children who are likely to require PN for at least three weeks are limited to 1 g/kg/d of IFE. Fat restriction potentially increases the risks of essential fatty acid deficiency (EFAD), inadequate energy intake for growth, or excessive carbohydrate intake. Three to five percent of total calories as fat are recommended to prevent EFAD, and in infants this can be met with 0.5 g/kg/d of standard soy-based IFE. In cases of limited fat intake, monitoring for EFAD with a total fatty acid profile monthly is prudent (Table 15–18). The biochemical hallmark of EFAD is an elevated ratio (> 0.2) of triene to tetraene fatty acids. Conversely, a "fat overload" syndrome has been described with excessive administration of lipids, characterized by focal seizures, fever, hepatosplenomegaly, and thrombocytopenia.[13] This typically occurs when infusion rates exceed 0.17 g/kg/h.

More recently, the use of an alternate IFE that is fish oil based has been found to be efficacious in reducing serum bilirubin levels commonly seen in patients who have been on long-term PN support. The mechanism for its effectiveness remains unclear but could be due to the high amount of the ω-3 fatty acid docosohexanoic acid (DHA) along with reduced amounts of the ω-6 fatty acid arachidonic acid (AA) resulting in less production of inflammatory thromboxanes, prostaglandins, and leukotrienes.[14] Another proposed mechanism for the hepatoprotection of fish oil–based lipid is the absence of phytosterols as compared to the high phytosterol content present in soybean oil–based IFE. Randomized trials of these newer fat emulsions are needed.

PERIPHERAL PARENTERAL NUTRITION

Peripheral parenteral nutrition (PPN) is often used in situations where central venous access is not possible. In some cases of central venous catheter (CVC) sepsis, PPN is used until the blood stream infection has resolved and/or a new catheter can be placed. PPN is not suitable for fluid-restricted pediatric patients due to the provision of inadequate energy. Because PPN solutions have low caloric concentrations, large volumes of fluid are necessary to deliver adequate calories.

Due to risks of phlebitis and sclerosis, the maximum osmolarity of PN for peripheral vein administration is 900 mOsm/L.[3] This corresponds to a solution of 10% dextrose and 2% amino acid with standard amounts of electrolytes (30 mEq/L Na, 20 mEq/L K, 15 mEq/L Ca, 10 mEq/L Mg, and 10 mM/L phosphorus) and standard vitamins and minerals. Table 15–8 lists the osmolarity and estimated

Table 15–8 Osmolarity and Energy Density of Selected Parenteral Nutrition Solutions

Solution	Osmolarity (mOsm/L)	Energy Density (kcal/mL)
5% dextrose	300	0.17
10% dextrose	600	0.34
20% dextrose	1200	0.68
10% dextrose + 2% amino acids	900	0.42
20% dextrose + 2% amino acids	1500	0.75
25% dextrose + 3% amino acids	1800	0.95
30% dextrose + 3% amino acids	2200	1.12
10% intravenous fat emulsion	276	1.1
20% intravenous fat emulsion	258	2
30% intravenous fat emulsion	310	3

Abbreviation: PN, parenteral nutrition.

caloric density of several common PN solutions. 20% IFEs provide an isotonic source of calories and can be infused through either a peripheral or central vein.

MICRONUTRIENTS IN PARENTERAL NUTRITION

The importance of vitamins in patients receiving PN has been underscored in the United States by several widespread shortages of parenteral multivitamins and reports of symptomatic thiamine deficiency.[15] Fatal vitamin deficiencies have been reported in patients receiving PN without vitamins in as short a time as a few weeks. Table 15–9 lists the current parenteral vitamin products available in the United States. The pediatric versions of multivitamins are notable for higher amounts of vitamins K and D, and lower amounts of the B vitamins, as compared to adult formulations. Certain patient conditions may require adjustments to their parenteral vitamin intake. For example, patients with high gastrointestinal fistula output may require a double dose of multivitamins due to increased losses.[16] Patients with prolonged prothrombin times may benefit from short courses of supplemental vitamin K.

In the event of a parenteral multivitamin shortage, it is imperative that practitioners provide adequate thiamine with dextrose infusions so as to avoid metabolic lactic acidosis. Adult parenteral multivitamins should never be used in the neonate because of the propylene glycol and polysorbates contained in many of these products that could be toxic to a neonate.[17] Adult multivitamin products contain less vitamin D and K and may increase the risk of metabolic bone disease in pediatric patients on long-term PN therapy. Neonates who must receive PN without conventional pediatric parenteral multivitamins should always receive parenteral thiamine in the PN at a dose of

Table 15–9 Comparison of Parenteral Multivitamin Preparations

Product	Supplier	A (int. units)	B_1 (mg)	B_2 (mg)	B_6 (mg)	B_{12} (mcg)	Biotin (mcg)	C (mg)	Folic Acid (mcg)	D (int. units)	E (int. units)	K (mcg)	Niacinamide (mg)	Dexpanthenol (mg)
Pediatric (<11 y of age)														
Infuvite® Pediatric (per 5 mL)	Baxter	2300	1.2	1.4	1	1	20	80	140	400	7	200	17	5
M.V.I.® Pediatric (per 5 mL)	Hospira	2300	1.2	1.4	1	1	20	80	140	400	7	200	17	5
Adolescents and adults (≥11 y of age)														
Infuvite® Adult (per 10 mL)	Baxter	3300	6	3.6	6	5	60	200	600	200	10	150	40	15
M.V.I.®-12 (per 10 mL)	Hospira	3300	3	3.6	4	12.5	60	100	400	200	10	–	40	15
M.V.I®. Adult (per 10 mL)	Hospira	3300	6	3.6	6	5	60	200	600	200	10	150	40	15

0.03 mg/ kg/d.[18] There is currently no parenteral vitamin preparation designed especially for premature infants, and there is some controversy concerning vitamin requirements for these patients.[19] Recommendations for pediatric parenteral vitamin doses for full-term and preterm infants are shown in Table 15–10.

Table 15–10 Recommended Levels of Intake for Intravenous Multivitamins for Term and Preterm Infants

		Preterm Infants (dose/kg)[a]	
Vitamin	**Term Infants (dose/d)[b]**	**Current Suggestion[c]**	**Best New Estimate[d]**
A (IU)	2300	920	1643
D (IU)	400	160	160
E (mg)	7	2.8	2.8
K (μg)	200	80	80
Ascorbic acid (mg)	80	32	25
Thiamine (mg)	1.2	0.48	0.35
Riboflavin (mg)	1.4	0.56	0.15
Niacin (mg)	17	6.8	6.8
Pantothenate (mg)	5	2.0	2.0
Pyridoxine (mg)	1.0	0.4	0.18
Vitamin B12 (μg)	1.0	0.4	0.3
Biotin (μg)	20	8.0	6.0
Folate (μg)	140	56	56

[a]Maximum dose not to exceed term infant dose.

[b]These are all met by currently available pediatric parenteral multivitamins.

[c]These are met by 40% of the single dose (0.4 × 5 mL = 2 mL) of a pediatric multivitamin per kg per day.

[d]Based on data suggesting a reduced need for water-soluble vitamins and increased need for vitamin A in preterm infants.

Trace elements commonly added to PN solutions include zinc, copper, manganese, and chromium. Table 15–11 lists recommendations for trace elements in PN. Due to biliary excretion of copper and manganese, these should be reduced in patients with cholestasis. Copper should not be eliminated without monitoring levels periodically as individuals on long-term PN with cholestatic jaundice can develop hypocupremia. This can result in anemia, thrombocytopenia,

Table 15–11 Suggested Intake of Trace Nutrients (Concentration/1000 mL PN)

Element	Weight < 2 kg	Weight > 2 kg	Comments
Zinc	3 mg	1 mg	Increase dose with increased intestinal losses
Manganese	50 mcg	60 mcg	Decrease dose with cholestatic liver disease
Copper	200 mcg	200 mcg	Decrease dose with cholestatic liver disease
Chromium	1.7 mcg	2 mcg	Increase dose with intestinal losses and decrease with renal dysfunction
Iron	1 mg/d, see text		Monitor for anaphylaxis with initial infusion
Selenium[a]	1–3 mcg/kg/d max dose 30–40 mcg/d		Reduce dose with renal disease; may have increased requirements with increased intestinal losses
Carnitine	8–16 mg/kg/d		Patients with primary carnitine deficiency will require higher doses

Abbreviation: PN, parenteral nutrition.

[a]May be added after 30 days of nil per os (NPO) status and/or minimal enteral intake.

osteopenia, and neutropenia.[19] Levels of serum copper and ceruloplasmin are necessary to help guide copper dosing. If manganese toxicity is suspected, erythrocyte manganese levels and a 24-hour urine manganese level should be requested and manganese should be removed from PN solution.[20] There are reports of abnormal cranial magnetic resonance imaging (MRI) findings consistent with manganese deposition, a concern for pediatric patients on long-term PN who may be already at a risk of neurocognitive dysfunction due to prematurity and other medical problems.[20] Parenteral intake of selenium, chromium, and molybdenum should be reduced or held in cases of renal dysfunction. Addition of selenium and carnitine may be necessary after 30 days of PN and no or minimal enteral intake. For patients with intestinal failure and who have greater zinc and selenium losses due to diarrhea/ostomy losses, it is a common practice to add additional zinc to help replace those losses.[21] If a multiingredient trace element cocktail is used, practitioners should take the amount provided by the product into consideration when determining the added amount to supplement.

Intravenous iron infusion is recommended in patients with iron deficiency anemia if the enteral route is ineffective or contraindicated. The use of parenteral iron dextran to treat iron deficiency anemia has been controversial due to the risk of anaphylaxis. New formulations including ferric gluconate and iron sucrose are safer with less concern with anaphylaxis, but still need monitoring for adverse reactions. Patients who receive blood transfusions may not require repletion doses of iron because blood transfusions provide a moderate amount of iron.[22] The total amount of parenteral iron (as iron dextran) needed for repletion to normalize hemoglobin level can be estimated according to the following formula:

$$\text{mg Fe} = \text{weight (kg)} \times 4.5 \times (13.5 - \text{patient's Hgb (g/dL)})$$

An initial test dose of iron dextran of 0.5 mL (25 mg Fe) (0.25 mL/12.5 mg Fe in infants) should be given on the first day at a rate of < 1 mL/h to monitor for an anaphylactic response. Medical monitoring with emergency epinephrine and diphenhydramine should be available for symptoms of anaphylaxis. If well tolerated, subsequent doses can be administered in the home setting. Daily doses of 25–100 mg may be given IV separate from PN as needed to replenish stores. Long-term, maintenance doses from 0.3 mg/kg/d to 1 mg/kg/d may be indicated in some patients and may be added directly to lipid-free PN solutions. Currently, iron dextran is the only form of parenteral iron that can be added to PN solutions. Separate infusions of iron sucrose or ferric gluconate have been used although the optimal dosing in the parenterally fed pediatric patient has yet to be established. Monitoring of laboratories initially and monthly with complete blood count (CBC), reitculocyte count, serum iron, total iron binding capacity (TIBC), and ferritin are helpful to determine adequate repletion and maintenance dosing of intravenous iron. A C-reactive protein (CRP) can help to identify possible inflammation that may affect results.

Iodine is a required trace element for the synthesis of thyroid hormones and, until recently, was not routinely added to PN solutions. PN-dependent infants and children are likely to be at risk of iodine deficiency, but limited data do not support this as an important occurrence.[23] Although lower circulating levels of thyroid hormones in preterm infants have been associated with increased rates of mortality and morbidity, at least one randomized trial of higher iodine intake was not associated with reduced morbidity.[24] Given that topical absorption has been postulated as one potential reason why parenterally fed patients have been able to maintain normal iodine status, reduced use of iodine containing topical sterilization solutions (e.g., povidone iodine) suggests the patients prolonged courses of PN may be at risk

for developing iodine deficiency. Although there are limited data in this regard, the European Society for Parenteral and Enteral Nutrition (ESPGHAN) and the American Society for Clinical Nutrition (ASCN) suggest parenteral iodine supplementation of 1 mcg/kg/d occur in infants and children receiving PN for > 30 days.[18]

CALCIUM, PHOSPHORUS, MAGNESIUM, SODIUM, POTASSIUM, CHLORIDE, AND ACETATE

Electrolyte disturbances may be corrected by increasing or decreasing the concentration of components in the volume of PN infused in the daily prescription. However, acute changes in serum electrolytes should not be treated with abrupt changes in PN infusion rate as changes in PN infusion rate will adversely affect macronutrient metabolism (e.g., increase blood glucose and potential excess protein intake) as well as alter the delivery of any medications added to PN.

Calcium, phosphorus, and magnesium balance are interrelated. Inadequate intakes of each may result in rickets, fractures, failure of appropriate bone mineralization, and reduced linear growth. In the PN dependent child, relatively high concentrations of calcium and phosphorus are needed. The provision of these nutrients in PN is particularly challenging due to the physicochemical limitations of current PN additives. When compounding a solution with high amounts of calcium and phosphorus, it is imperative that the pH is low enough to optimize solubility and that the additions of calcium and phosphorus salts are done in the correct order. According to the Food and Drug Administration (FDA), calcium should always be the last ingredient added to the PN solution.[25] Phosphorus salts should be one of the first additives, so that it is well diluted prior to the addition of the calcium. Currently, calcium gluconate is the preferred salt for use in PN solutions because

it dissociates less than chloride salts and thereby remains in solution more readily. Other factors favoring the formation of calcium–phosphorus precipitates include low amino acid content, low dextrose content, high temperature, and high pH. Because pH is primarily determined by amino acid concentration, increasing amino acid intake, the use of more acidic brands of amino acid solutions, and/or the addition of cysteine hydrochloride are common strategies used to prevent precipitation. It is also recommended that if a PN solution contains less than 1% amino acids, then only calcium or phosphorus (not both) be added. Published nomograms are useful for specific compatibility information. A conservative estimate may be obtained by adding the sum of calcium and phosphorus concentrations (mmol/L); if the sum of these numbers exceeds 40, the risk of precipitation is high. It should be noted that these recommendations do not apply to TNA because calcium and phosphorus solubility is lower in these solutions.

Like calcium, approximately 60% of magnesium is found in bone, with the remainder being intracellular.[26] Serum magnesium levels do not accurately reflect total body magnesium stores because of the slow rate of magnesium exchange. It is imperative that baseline magnesium levels are obtained prior to initiation of PN in infants born to mothers treated for hypertension or preeclampsia as these infants tend to have elevated serum magnesium levels due to poor renal elimination of magnesium. Moreover, because 25% to 30% of serum magnesium is bound to albumin, measuring total serum magnesium may provide a falsely low value in hypoalbuminemic states. One method to correct serum magnesium levels in the presence of hypoalbuminemia has been proposed as follows[27]:

corrected serum magnesium (mmol/L)
= measured total serum magnesium (mmol/L)
+ 0.005 (40 - albumin g/L)

Conversely, patients receiving drugs that increase magnesium wasting (i.e., amphotericin) may require additional supplementation. Although not as well described as calcium–phosphorus incompatibility, PN solutions high in magnesium and phosphorus are also prone to precipitation.

Sodium and potassium are typically included in amounts to provide standard electrolyte requirements. Premature infants will have increased sodium needs due to their inability to conserve sodium. Similarly, in patients with intestinal failure, sodium requirements are greater due to intestinal losses through nasogastric or gastrostomy tube drainage and/or high ostomy output (Table 15–4). Potassium requirements could also be greater in these situations of higher losses. Chloride and acetate are both important electrolytes that are included in PN solutions. The total amount varies depending on the amino acid concentration and total sodium and potassium content. Acetate salt concentrations may need to be higher in cases where there are high ostomy losses. Due to the risk of metabolic alkalosis, the use of chloride-free PN solutions should be avoided.

MEDICATION AND PARENTERAL NUTRITION

Patients requiring PN are often on multiple medications and questions frequently arise concerning whether these medications can be safely coadministrated with PN. Because of the risks of precipitation and/or infection, coadministration of medications and PN should be avoided whenever possible. Moreover, medications should not be added directly to the PN bag itself except by pharmacy staff, although in home PN patients, it may be necessary to do so immediately prior to administration due to stability issues. Medications not

directly added to PN should be coinfused through a "y" connection with the intravenous setup proximal to a filter. Whenever the PN formula changes, coadministered medications and potential compatibility problems should be reviewed. This also includes whenever there are changes in the brands of amino acids or lipid emulsions.

Tables 15–12 and 15–13 list medications generally considered safe for coadministration with PN and intralipid emulsions, respectively. Tables 15–14 and 15–15 list medications that are considered incompatible with PN and lipids. In all cases, consultation with the pharmacy is recommended. In the event no information is available, the medication should be considerable incompatible with both PN and lipid emulsion.

Table 15–12 Medications Compatible With PN Solutions

Albumin[a]	Enalaprilat	Mezlocillin
Aldesleukin	Epinephrine[b]	Miconazole
Amikacin[c]	Erythromycin	Morphine
Aminophylline[d]	Famotidine	Nafcillin
Atracurium	Fentanyl	Norepinephrine
Atropine	Fluconazole	Ondansetron
Aztreonam	Gentamicin[c]	Oxacillin
Bumetanide	Glycopyrrolate	Pancuronium
Cefepime	Granisetron	Penicillin G+ (aqueous)
Cefotaxime	Heparin	Phenobarbital
Cefoxitin	Hydralazine	Phytonidione
Ceftazidime	Hydrocortisone	Piperacillin
Ceftriaxone	HydromorphoneInsu-	Piperacillin/tazobactam
Cefuroxime	lin (U-100 regular)	Promethazine
Chloramphenicol	Iron dextran	Pyridoxine
Chlorpromazine	Isoproterenol	

(*Continued*)

Table 15–12 Medications Compatible With PN Solutions *(Continued)*

Cimetidine	Leucovorin	Ranitidine
Clindamycin	Levocarnitine	Tacrolimus
Dexamethasone	Lorazepam	Ticarcillin
Digoxin	Magnesium sulfate	Ticarcillin/clavulanic acid
Diphenhydramine	Meperidine	Tobramycin[c]
Dobutamine[c]	Mesna	Tolazoline
Doxycycline	Methylprednisolone[e]	Vancomycin[c]
		Vecuronium
		Zidovudine

[a]Will clog filter if albumin concentration > 25 g/L.

[b]Incompatible with iron containing PN.

[c]Incompatible with heparin containing PN solutions.

[d]Do not exceed 3 mg/mL for piggyback administration.

[e]Contains phosphate buffers that may precipitate in solutions high in calcium or phosphorous.

Source: Adapted from the 2012 Online Formulary, Boston Children's Hospital.

Table 15–13 Medications Compatible With Intravenous Fat Emulsions

Aldesleukin	Erythromycin
Aztreonam	Famotidine
Bumetanide	Gentamicin
Cefotaxime	Hydrocortisone
Cefoxitin	Hydromorphone
Ceftazidime	Insulin, regular
Ceftriaxone	Interlukin-2
Chloramphenicol	Isoproterenol
Cimetidine	Lidocaine
Clindamycin	Norepinephrine
Cyclosporine	Oxacillin
Digoxin	Penicillin
Diphenhydramine	Ranitidine
Dobutamine	Ticarcillin
Dopamine	Tobramycin
	Vancomycin

Source: Adapted from the 2012 Online Formulary, Boston Children's Hospital.

Table 15–14 Medications Incompatible With PN Solutions

Acetazolamide	Furosemide
Acyclovir	Ganciclovir
Amphotericin	Imipenem
Amphotericin b lipid complex	Indomethacin
Ampicillin	Mannitol
Ampicillin/sulbactam	Methotrexate
Calcium salts	Metoclopramide
Cefazolin	Metronidazole
Ciprofloxacin	Midazolam
Cis-platinum	Nitroglycerin
Cyclosporine	Nitroprusside
Cytarabine	Octreotide
Diazepam	Phenytoin
Doxorubicin	Piperacillin
Filgrastim	Promethazine
Foscarnet	Trimethoprim/sulfamethoxazole
Flurouracil	Tromethamine

Abbreviation: PN, parenteral nutrition.

Source: Adapted from the 2012 Online Formulary, Boston Children's Hospital.

Table 15–15 Medications Incompatible With Intravenous Fat Emulsions

Acetazolamide	Furosemide
Acyclovir	Ganciclovir
Amikacin	Gentamcin
Aminophylline	Heparin
Amphotericin	Imipenem
Amphotericin b lipid complex	Indomethacin
Ampicillin	Iron dextran
Ampicillin/sulbactam	Magnesium salts
Calcium salts	Metronidazole
Ciprofloxacin	Midazolam
Cyclosporine	Morphine
Diazepam	Nitroglycerin
Doxorubicin	Nitroprusside
Filgrastim	Penicillin
Flurouracil	Phenytoin
Foscarnet	Trimethoprim/sulfamethoxazole
	Tromethamine

Source: Adapted from the 2012 Online Formulary, Boston Children's Hospital.

In PN patients with limited venous access, it may be a challenge to administer parenteral medications if the medication is incompatible with PN. If possible, a compatible medication should be considered. If that is not an option, the PN infusion will need to be interrupted so that the incompatible medication may be infused. Prior to infusing the medication, the PN infusion must be stopped, the line should be flushed with a neutral fluid compatible with the medication (i.e., saline or dextrose), and the medication then infused, followed by another flush with a compatible fluid before the PN infusion is resumed. Children receiving PN with high dextrose concentrations may need to have the PN rate gradually reduced prior to the start of the drug infusion. In cases where the children cannot have their PN infusion interrupted because of an inability to maintain adequate blood glucose levels, the medication should be infused in a carrier fluid with a similar dextrose concentration as the PN. If a lipid infusion needs to be interrupted for the administration of an incompatible medication, no rate reduction before lipid discontinuation is necessary.

OTHER COMPOUNDING CONSIDERATIONS

In addition to the calcium phosphorus compatibility, other factors have received attention regarding the prevention of PN-related complications, minimizing aluminum exposure, protecting the solutions from light, and avoidance of Di(2-ethylhexyl)phthalate (DEHP) materials. Premature infants and children with intestinal failure have diminished antioxidant defenses that render them more susceptible to oxidant stress. Moreover, as children with intestinal failure receive prolonged courses of PN, they are especially prone to these complications.

Aluminum

Aluminum exposure is a risk in patients receiving prolonged courses on PN. This metal is found in raw materials, incorporated into products during the manufacturing process, and leached from glass containers during autoclaving for sterilization.[28] When aluminum is administered parenterally, it bypasses the protective barrier of the gastrointestinal tract. Specific findings of this toxicity include encephalopathy, impaired neurodevelopment, bone pain with development of osteopenia or osteomalacia, microcytic anemia, and cholestasis. In 2004, the US FDA issued a mandate that required manufacturers to include the aluminum content on the label of additives commonly used in the compounding of PN solutions.[29] The amount of aluminum provided by PN should be less than 5 mCg/kg/d, the threshold deemed "safe" by the FDA.

Calcium gluconate salts are a major source of aluminum contamination in PN patients. Because calcium gluconate salts are a large source of contamination, infants and children are at risk for developing toxicity due to their high calcium requirements coupled with renal immaturity. In response to the findings of potential adverse neurodevelopment associated with aluminum exposure,[30] the use of calcium chloride in PN solutions has been reevaluated. Calcium chloride salts are inherently less contaminated and in theory could be used as an alternative to calcium gluconate salts. This could predispose patients, especially children, however, to a potentially greater risk of developing metabolic acidosis due to the increased chloride load. Koo et al. suggest that using a 50% calcium gluconate/50% calcium chloride mix in conjunction with the use of potassium and sodium acetate salts in place of sodium and potassium chloride could minimize this risk.[31] Calcium/phosphorus solubility would still be a concern as

calcium chloride salts have a higher degree of dissociation and thus less than optimal calcium and phosphate intake would still be problematic. This risk can be minimized if calcium chloride salts are used with an *organic* phosphate salt; however, these organic phosphate salts are expensive and not available in many countries.

The implementation of the FDA mandate has been difficult to incorporate into clinical practice due to limitations in current product formulations. At present, there are few options available to reduce the aluminum load in PN solutions. One is to replace potassium phosphate with sodium phosphate salts that have considerably less aluminum. Furthermore, not all ingredients (i.e., heparin, albumin, and insulin) that are often added to PN solutions are required to list their aluminum on their label, which makes it even more difficult to accurately calculate potential aluminum exposure secondary to PN use.[32]

Ambient Light

When PN is exposed to ambient light, lipid peroxides and hydrogen peroxide are generated.[33] There is an approximate 50% reduction in the amount of hydrogen peroxide infused with PN when the entire solution and delivery system is protected from ambient light (i.e., amino acid dextrose bag, lipid syringe, and tubing).[34] This phenomenon was first reported in the early 1980s when it was observed that light exposure might cause vitamin instability, but most practitioners still choose not to cover solutions, especially if the multivitamins are added immediately prior to infusing. Multivitamins, however, are not the only component of PN that may be affected by light. The amino acids tryptophan and tyrosine undergo photooxidation to form free radicals with hepatotoxic properties.[35] Other amino acids such as methionine,

histidine, and cysteine are also susceptible to photooxidation. Riboflavin appears to facilitate the photooxidation process by serving as a photosensitizing agent.[35]

In addition to its impact on vitamins and amino acids, phototherapy might cause significant peroxidation in IFEs, resulting in the formation of cytotoxic TG hydroperoxides.[36] Lipid hydroperoxides could theoretically cause pulmonary vasoconstriction through an interference with endogenous prostaglandin synthesis.[37] It has been recommended by some that fat emulsion containers be covered with aluminum foil or that fat emulsion be supplemented with sodium ascorbate prior to light exposure.[38] However, results from a study on a large cohort of premature infants demonstrated no beneficial effect of partial light protection of PN on clinically relevant outcomes.[33] This study did not provide complete protection against ambient light; therefore, further investigation is warranted.

DEHP Toxicity

DEHP is an industrial additive plasticizer found in polyvinylchloride (PVC). PN infusion systems have been shown to be the most important source of DEHP load. Although DEHP has a rapid turnover (half-life less than 24 hours), this phthalate and its metabolites are consistently detected in human body fluids such as plasma, urine, amniotic fluid, or breast milk. In preterm neonates and infants who receive intensive care, DEHP has shown to increase oxidative stress and toxicity.[39] PN infusion sets and containers containing DEHP have been implicated as contributing to this risk. Retrospective data showed that by changing to PVC-free infusion systems, a reduction in the incidence of cholestatic liver disease was noted.[40] Moreover, the use of PVC infusion sets correlated strongly with the development of PN-associated liver disease

(p = .0004). DEHP-free containers and infusion sets should be used whenever possible so as to minimize this risk.

Supply Issues

In recent years, many of the ingredients used to formulate PN solutions have gone into short supply. A variety of reasons have been cited, including discontinuation by a manufacturer, shortages of raw materials, and failure to meet FDA standards. Organizations such as the American Society for Parenteral and Enteral Nutrition (ASPEN) have developed guidelines to help practitioners during these periods of supply shortages (Table 15–16). In addition to reminding practitioners not to stockpile materials, these guidelines include recommendations for using alternative products or different dosing strategies until a stable supply stream is reestablished. In some instances, the need for PN should be reassessed and the provision of nutrition and/or supplements through the oral or enteral route should be considered. Due to their unique needs, special guidelines for neonates are typically included. All recommendations suggest compounding PN in a single, central locations (either in a centralized pharmacy or as an outsourced preparation) to decrease inventory waste. Practitioners are also advised to consider a supply outreach to other facilities within the same geographic area. Severe drug product shortages information should be reported to the FDA Drug Shortage Program (DSP). See http://www.fda.gove/Drugs/DrugSafety/DrugShortages/ucm142398.htm. Any patient-related issues related to shortages should be reported to ISMP Medications Errors Reporting Program (MERP). During shortages, laboratory monitoring schedules may need to be altered to ensure alternative therapies are meeting the requirements and not leading to potentially life-threatening deficiencies or toxicities.

Table 15–16 **American Society for Parenteral and Enteral Nutrition (ASPEN) Parenteral Nutrition Additive Shortage Recommendations**

Product	Recommendations
Amino acids	1. Use neonatal/pediatric specific amino acids (or specialty amino acids) ONLY for their indicated patient population. 2. Consider reviewing the entire portfolio of amino acids products nationally. There may be a shortage in one concentration but availability in another. 3. Use high concentration amino acid products (>10%) sparingly (i.e., use in fluid-restricted patients only). 4. Different brands of amino acids products are not always directly substitutable (especially for 3-in-1). There may be different pH, different calcium–phosphate solubility, different amounts of inherent phosphorus. 5. Consider changing your PN formulary and system to ensure that system safeguards are still maintained despite product changes. 6. Assess your PN population to determine whether standardized, premixed commercial PN products might be an appropriate option for your patients.
Chromium	1. No need to supplement (during shortage) unless signs and symptoms of clinical deficiency present (e.g., glucose intolerance, hyperlipidemia, peripheral neuropathy, and encephalopathy).
Copper	1. Use oral/enteral supplementation if possible. Monitor for microcytic anemia.

(*Continued*)

Table 15–16 American Society for Parenteral and Enteral Nutrition (ASPEN) Parenteral Nutrition Additive Shortage Recommendations (*Continued*)

Product	Recommendations
Electrolyte/ mineral products	1. Use oral/enteral supplementation if possible. 2. Prioritize patients, saving supply for those most vulnerable (neonates, pediatric patients, short bowel/malabsorption syndrome). 3. Eliminate the use of parenteral electrolyte/ mineral injections as a supplemental additive in enteral nutrition products. 4. Minimize the use of electrolyte/mineral additives in IV fluids. 5. Reconsider the use of serum electrolyte algorithms/protocols as "automatic" IV electrolyte replacement therapies in otherwise asymptomatic patients.
Fat emulsion	1. Neonatal and pediatric hospitalized or home care patients should continue the same lipid emulsion therapy as before the shortage. 2. Adult, mild to moderately malnourished hospitalized patients on PN less than 2 wk should not receive lipid emulsion during a shortage unless its use is essential in the judgment of the health care professional. 3. Adult, hospitalized patients on PN greater than 2 wk should receive a total of 100 g fat weekly, which may be given by whatever method is safe and efficient (i.e., so as to minimize waste) to prevent EFAD with the remainder of nonprotein calories provided by glucose. Patients should be monitored for EFAD. For some specific adult hospitalized patients (e.g., patients with glucose intolerance, severely malnourished patients, patients at risk for refeeding syndrome, and during pregnancy), fat emulsion should be provided as a component of daily calories based on current practice prior to the shortage.

Product	Recommendations
	4. Adult, hospitalized, critically ill patients on propofol should not receive additional lipid emulsion as propofol contains lipid emulsion and will supply needed essential fatty acids. 5. Home or long-term care adult patients should continue same lipid regimen as before shortage; however, its use should be minimized when clinically feasible.
L-cysteine	1. Restrict to neonates < 1 kg or those neonates > 1 kg who are at risk for L-cysteine deficiency such as postsurgical or those with sepsis. 2. Reduce the dose of L-cysteine to 20 mg/g protein; studies have shown this dose to be adequate. 3. If using an automated compounding device to prepare the PN, add the L-cysteine as a separate additive rather than adding it directly to the amino acid solution. Consult the manufacturer of the device for proper placement so as to minimize the risk of calcium–phosphorus precipitation. 4. When removing or reducing the dose of L-cysteine, reevaluate the calcium–phosphorus solubility charts or software to insure that a precipitation will not develop due to the increase in pH; consider using calcium–phosphorus solubility data that do not include the presence of L-cysteine in the PN formulation.
Manganese	No need to supplement (during shortage) unless signs and symptoms of clinical deficiency present (e.g., weight loss, transient dermatitis, and occasionally nausea and vomiting).
Multivitamins	1. If unable to obtain an adult 13-vitamin product, may use an adult 12-vitamin product and supplement vitamin K. The dose of vitamin K in the 13-vitamin products is 150 mcg. Alternative vitamin K dosing is 0.5–1 mg/d or 5–10 mg/wk.

(*Continued*)

Table 15–16 **American Society for Parenteral and Enteral Nutrition (ASPEN) Parenteral Nutrition Additive Shortage Recommendations *(Continued)***

Product	Recommendations
	2. If unable to obtain a 12-vitamin product (without vitamin K), may use a 13-vitamin product (with vitamin K). The coagulation activity of the patient must be monitored and concurrent warfarin adjusted accordingly. 3. Use oral or enterally administered multivitamin preparations whenever possible, especially liquid multivitamins of defined content. Liquid oral multivitamins do not contain vitamin E, vitamin K, folic acid or biotin and these should be supplemented, if available. Patients with malabsorption syndromes should be excluded. 4. Reserve intravenous multivitamins for those patients receiving PN or those with a therapeutic medical need for intravenous multivitamins. 5. When all options to obtain intravenous multivitamins have been exhausted, ration intravenous multivitamins in parenteral nutrition, such as reducing the daily dose by 50% or giving one multivitamin infusion dose three times a week. 6. If IV multivitamins are no longer available, administer individual parenteral vitamin entities. Thiamine, ascorbic acid, pyridoxine, and folic acid should be given daily. Administer cyanocobalamin (B12) at least once per month. [a]Several deaths from cardiac failure due to thiamine deficiency when long-term PN patients did not receive vitamins for 3–4 weeks. Megaloblastic anemia secondary to folate deficiency has been reported in PN patients who did not receive folate for 4–5 weeks. Suggested daily intravenous doses of thiamine 6 mg, folate 0.6 mg, ascorbic acid 200 mg, and pyridoxine 6 mg unless otherwise clinically indicated.

Product	Recommendations
Phytonidione	1. Use oral/enteral supplementation if possible. 2. If INR is < 5, with no significant bleeding, no vitamin K is required. Reduce or skip warfarin dose and monitor INR frequently. 3. If INR is > 5 or < 9, with no significant bleeding, low doses of vitamin K of 1 to 2.5 mg given orally may be needed. For more rapid reversal give vitamin K up to 5 mg orally. Repeat a low dose of vitamin K if INR is still high the next day. Reduce or skip warfarin dose and monitor INR frequently. The INR is expected to decrease to desired level within 24 h. 4. If INR is > 9, with no significant bleeding, give higher doses of vitamin of 2.5 to 5 mg. The INR is expected to decrease within 24–48 h. 5. Patients with serious bleeds, regardless of extent of INR elevation, should receive vitamin K 10 mg intravenously supplemented by FFP, PCC, or recombinant factor VIIa. Repeat as necessary. 6. Patients with life-threatening bleeds regardless of extent of INR elevation should receive FFP, PCC, or recombinant factor VIIa supplemented by vitamin K 10 mg intravenous. Repeat as necessary. 7. Reserve any remaining supply of vitamin K10 mg ampules for severe or life-threatening bleeds. Reserve supplies of the 1 mg injection for use in newborn patients.
Selenium	Use oral/enteral supplementation if possible.
Trace elements (IV multitrace)	1. Consider prioritizing patients, saving supplies for those most vulnerable populations such as neonates, pediatric, short bowel, or malabsorption PN groups.

(*Continued*)

Table 15–16 **American Society for Parenteral and Enteral Nutrition (ASPEN) Parenteral Nutrition Additive Shortage Recommendations *(Continued)***

Product	Recommendations
	2. The use of pediatric/neonatal IV multitrace element products for adults is not recommended. Such practices may contribute to a shortage for pediatric patients. A shortage of pediatric/neonatal IV trace elements could create a potential risk of trace element deficiencies in that population who have an even greater need for trace elements. Moreover, the doses of trace elements in these products are not suitable for adults.
	3. The use of adult multitrace element products in neonatal and pediatric patients is not recommended. 4. Use oral or enteral multivitamin/multimineral products as much as possible for replacement therapy. Not all products may contain the full spectrum of trace elements nor contain daily enteral maintenance dose.
	5. Consider decreasing or eliminating the daily amount of trace elements added to PN. 6. When all options to obtain adequate supplies of IV multitrace element products have been exhausted, ration IV multitrace element products in PN by reducing the dose by 50% or administering one dose three times a week. 7. Withhold IV multitrace element products from patients receiving partial enteral/parenteral nutrition and administer oral/enteral supplements. 8. Consider withholding multitrace elements for the first month of therapy to newly initiated adolescent and adult PN patients who are NOT critically ill nor have preexisting deficits.

Product	Recommendations
	9. If IV multitrace element products are no longer available, administer individual parenteral trace elements.
Zinc	Use oral/enteral supplementation if possible.

Abbreviations: PN, parenteral nutrition; EFAD, essential fatty acid deficiency; FFP, fresh frozen plasma; PCC, prothrombin complex concentrate.

Source: Adapted from http://www.nutritioncare.org. Accessed November 24, 2012.

CYCLING PARENTERAL NUTRITION INFUSIONS

The provision of one day's worth of PN over fewer than 24 hours has been termed "cycling." Advantages of cycling include allowing the patient to be disconnected from intravenous tubing and pumps, avoiding chronic hyperinsulinemia,

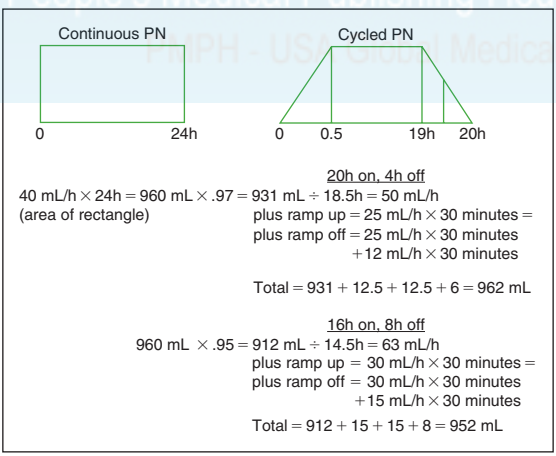


Figure 15–2: Cyclic administration of parenteral nutrition (PN).

and, perhaps, an improved visceral protein status.[41] Cyclic PN may also help reduce the chances of developing PN-associated liver disease. The suitable candidates for cyclic PN are those patients for whom long-term (> 1 month) PN is anticipated and whose endocrine, renal, and cardiac function can tolerate shifts in glucose and fluid delivery. Two to three days of metabolic stability on the solution providing the desired amount of fluid and energy are also required before cycling can begin.

Generally, urine is monitored for glucosuria to ascertain tolerance to increased dextrose infusion over shorter period of time. Blood glucose is checked while off PN infusion to monitor for rebound hypoglycemia and for appropriate gluconeogenesis. Once blood glucose levels are stable, blood glucose monitoring may be changed to an as-needed schedule.

MONITORING AND POTENTIAL COMPLICATIONS OF PARENTERAL NUTRITION

Monitoring patients' clinical and biochemical response to the initiation and continuation of PN is a vital part of patient management. In the pediatric patient, an especially important parameter with which to assess the effectiveness of PN is weight gain. In neonates and young children, weight and height gain along standard reference curves should be the goal for nutritional therapy, including PN. Serial measurements of head circumference and arm anthropometrics are also useful to monitor.

Biochemical monitoring helps insure tolerance to the individual components of PN and helps avoid the myriad metabolic complications of this therapy. Perhaps the most dangerous complication of PN is hyperkalemia, due to errors in PN ordering, transcription, and/or compounding. In order to reduce the risk of symptoms due to excessive potassium administration, our current policy is to limit parenteral potassium infusion rates

to < 0.5 mEq/kg/h in a non-ICU setting, provided continuous electrocardiogram (ECG) monitoring is used. In addition, all PN orders both at the administration as well as compounding level should be double checked to reduce the risk of error. Table 15–17 summarizes the current potassium guidelines in use at Boston Children's Hospital.

Table 15–17 Guidelines for the Infusion of Potassium

Continuous Potassium Infusion Rate, Administration, and Required Monitoring			
Maximum Total I.V. Potassium Intake	**Maximum Total Potassium/d**	**Required Monitoring**	**Administration Concentration**
≤ 0.25 mEq/kg/h (or 7.5 mEq/h)	6 mEq/kg/d (or 180 mEq/d)	Plasma potassium Vital sign monitoring every 4 h	PIV maximum 80 mEq/L (not to exceed 900 mOsm/L) CVL maximum 200 mEq/L
0.26–0.5 mEq/kg/h (7.6–15 mEq/h)	6.1–12 mEq/kg/d (181–360 mEq/d)	Plasma potassium every 12 to 24 h Continuous ECG monitoring Vital sign monitoring every 2 h	
>0.5 mEq/kg/h (>15 mEq/h)	>12.1 mEq/kg/d (>361 mEq/d)	ICU, oncology unit, or emergency department Frequent plasma potassium Continuous ECG monitoring Vital sign monitoring every 1 h	

Abbreviation: ECG, electrocardiogram.

Source: Adapted from Boston Children's Hospital Patient Care Manual: Administration of Supplemental Potassium, 2011.

Recommended monitoring parameters for inpatients are listed in Table 15–18. Table 15–19 lists multiple metabolic conditions commonly seen among patients receiving PN, as well as suggested therapeutic steps. Table 15–20 lists common technical or catheter-related complications and recommended approaches for their prevention and treatment.[42]

Table 15–18 Suggested Monitoring Schedule for Inpatients Receiving Parenteral Nutrition

Parameter	Daily	Weekly[a]	Periodically[a]
Weight	X		
Height (>24 months)			X
Length (<24 months)		X	
Head circumference (<24 months)		X	
Fluid balance	X		
Vital signs	X		
Urine glucose/ketones	X		
Catheter site/function	X		
Laboratory test:			
Sodium		X	
Potassium		X	
Chloride		X	
CO_2		X	
Glucose		X	
BUN		X	
Creatinine		X	
Triglycerides		X	

Parameter	Daily	Weekly[a]	Periodically[a]
Calcium		X	
Magnesium		X	
Phosphorus		X	
Prealbumin		X	
Albumin		X	
Total protein		X	
alanine aminotransferase (ALT)		X	
Alkaline phosphatase		X	
Bilirubin (total and direct)		X	
Gamma-glutamyltransferase (GGTP)		X	
Selenium			X
Copper			X
Zinc			X
Iron			X
Carnitine			X
C-reactive protein			X
Vitamins A, D, E, INR			X
Manganese			X
Aluminum			X
Iron studies			X
Essential fatty acid profile			X

Abbreviation: BUN, blood urea nitrogen.

More often as necessitated by clinical indication course.

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving Parenteral Nutrition

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
Macronutrient substrate complications				
Hyperglycemiat	• Diabetes mellitus • Excessive dextrose infusion • Metabolic stress/sepsis • Corticosteroids • Peritoneal dialysis or CAVH-D • Obesity • Chromium deficiency	• Elevated blood glucose (> 200 mg/dL) • Glucosuria > 2%	• Limit dextrose infusion to approximately 10%–15% • Limit increments in dextrose to 2.5–5 mg glucose/kg/min • Monitor serum glucose • Monitor urine glucose	• Decrease dextrose intake • Add regular insulin to PN or give IV insulin (starting dose 0.01 u/kg/h)
Hyperglycemic, hyperosmolar, nonketotic dehydration/coma	• Sustained, uncontrolled hyperglycemia	• Very high blood glucose levels • Elevated serum osmolarity	• Goal—200 mg/dL • Monitor: ◆ —blood and urine glucose closely ◆ —serum Osm ◆ —fluid status	• Immediate discontinuation of PN • IV hydration, insulin • Correction of metabolic acidosis

		• Osmotic diuresis • Metabolic acidosis • Lethargy and confusion • Coma		
Hypoglycemia	• Sudden discontinuation of PN • Exogenous insulin administration • Sepsis	• Blood glucose < 50 mg/dL • Diaphoresis • Lethargy or palpitations • Agitation/ irritability • Faintness • Confusion • Coma	• Avoid abrupt cessation of PN • Check blood glucose 1 h after PN discontinued in cycled patients	• IV dextrose bolus

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
Hypercapnia (elevated pCO_2)	• Excessive dextrose or total caloric intake in patients with chronic lung disease • Respiratory failure	• Increased pCO_2 • Respiratory distress	• Avoid excessive caloric or dextrose infusion • Obtain indirect calorimetry measurement; adjust PN regimen to meet needs	• Decrease total caloric intake and/or increase calories as fat
Azotemia	• Dehydration • Renal insufficiency • Excessive amino acid infusion • Lean tissue catabolism • Immature liver • Liver disease • Inborn errors of protein metabolism	• Elevated BUN • Lethargy • Coma	• Adequate hydration prior to PN initiation • Avoid excessive amino acid infusion • Provide adequate nutrition to minimize lean tissue catabolism • Monitor BUN and NH_3	• Free water administration • Decrease amino acid infusion

Abnormal amino acid profile	• Inborn error of metabolism • Liver disease • Composition of PN solution	• Serum amino acid profile out of normal range	• Monitor serum amino acid levels • Avoid excess protein intake in liver disease	• Consider use of special amino acid solution
Hypertriglyceridemia	• Excessive lipid infusion • Decreased clearance (stress/sepsis, liver failure) • Sustained hyperglycemia • Congenital hyperlipidemia • Excessive caloric intake, especially glucose • Medications (see Table 15–9)	• Lipemia • Serum TG > 250 mg/dL	• Avoid excessive lipid infusion • Monitor serum triglycerides weekly • Infuse lipids over 18–20 h	• Decrease lipid infusion • If sustained, provide only enough lipid to prevent EFAD (0.5–1.0 g/kg/d)
Fluid and electrolyte disturbances				

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
Fluid overload	• Excessive fluid administration • Renal dysfunction, congestive heart failure, liver disease, trauma	• Rapid weight gain • Fluid intake > output • Increased blood pressure • Decreased serum sodium and hematocrit Edema	• Avoid excessive fluid administration • Close monitoring of: ◆ —weights ◆ —intake/output ◆ —physical examination ◆ —electrolytes	• Concentrate PN solution • Fluid restriction • Sodium restriction and/or diuretics, if appropriate
Dehydration	• Inadequate fluid intake • Excessive diuresis • Increased gastrointestinal (GI) losses • Vomiting • Diarrhea • Fever	• Decreased urine output • Orthostasis • Increased serum sodium, BUN, hematocrit	• Provide adequate fluid • Replace insensible and GI losses • Monitor fluid status	• Fluid replacement with separate IV from PN

		• Poor skin turgor • Thirst • Rapid weight loss		
Hypokalemia	• Inadequate potassium supplementation during anabolism/refeeding • Increased GI losses (vomiting, diarrhea, and furosemide) • Medications (e.g., furosemide, amphotericin B, cisplatin, etc.)	• Metabolic alkalosis • Cardiac arrhythmias • Muscle weakness • Ileus	• Adequate potassium in PN • Measure and replace losses • Monitor serum levels daily until stable; biweekly thereafter	• Increase potassium in PN if mildly to moderately depleted • Additional IV supplementation if severely depleted
Hyper-kalemia	• Renal insufficiency • Excessive potassium administration	• Weakness • Paresthesias	• Avoid excessive potassium administration • Monitor serum levels daily until stable; biweekly thereafter	• Decrease potassium in PN

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
	• Medications (e.g., spironolactone) • Catabolism	• Hyporeflexia • Cardiac arrhythmias	• Monitor serum potassium daily in patients with renal insufficiency/restrict as appropriate	
Hyponatremia	• Fluid overload • syndrome of inappropriate anti diuretic hormone (SIADH) • Excessive losses (urinary, GI, or through skin)	• Irritability • Confusion • Lethargy • Seizures	• Adequate sodium in PN • Avoid excessive fluid administration • Monitor serum sodium daily until stable; biweekly thereafter	• Fluid restriction • Increase sodium in PN if sodium depleted • Replace with separate IV if increased losses
Hypernatremia	• Dehydration • Excessive sodium administration • Osmotic diuresis secondary to hyperglycemia	• Thirst • Restlessness • Muscle tremor and rigidity	• Provide adequate fluid • Avoid excessive sodium administration	• Fluid replacement if dehydrated

	• Pituitary tumors • Diabetes insipidus	• Coma • Convulsions	• Monitor intake/ output, urine sodium, osmolarity	• Decrease sodium in PN if appropriate
Metabolic acidosis	• Increased intestinal losses of bicarbonate (diarrhea, fistulas) • Renal bicarbonate losses • Ketoacidosis (diabetes, starvation) • Lactic acidosis (shock, cardiac arrest) • Chronic renal failure or renal tubular acidosis • Excessive chloride in PN (rare)	• Headache • Nausea/ vomiting • Diarrhea • Convulsions	• Measure and replace intestinal losses • Avoid excessive chloride in PN	• Increase acetate and decrease chloride in PN
Metabolic alkalosis	• Gastric acid losses (increased nasogastric (NG) output) • Excess base administration	• Nausea/ vomiting • Diarrhea	• Measure and replace NG output	• Treat underlying cause

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
		• Sensory changes • Tremoring • Convulsions		• Increase chloride and decrease acetate in PN • If severe, may need IV hydrochloric acid
Mineral imbalances				
Hypocalcemia	• Hypoalbuminemia • Hypomagnesemia • Hyperphosphatemia • Hypoparathyroidism • Malabsorption • Inadequate calcium in PN	• Muscular/abdominal cramping • Irritability • Confusion • Tetany • Seizures • Prolonged QT interval	• Adequate calcium in PN • Monitor serum calcium biweekly: check ionized calcium if total calcium decreased • Monitor parathyroid hormone (PTH) and vitamin D levels	• Correct magnesium deficiency • Increase calcium in PN if ionized calcium is low

Hypercalcemia	• Neoplasm • Renal insufficiency • Excessive vitamin D administration • Bone resorption caused by prolonged immobilization/stress	• Confusion • Lethargy • Dehydration • Muscle weakness • Abdominal pain • Nausea and vomiting • Constipation • Arrhythmias • Extra skeletal calcification	• Monitor serum levels daily until stable; biweekly thereafter • Restrict as appropriate	• Decrease calcium in PN • Hydrate with isotonic saline • May need to remove vitamin D from PN
Hypomagnesemia	• Increased GI losses (vomiting, diarrhea, and fistula) • Increased urinary losses secondary to drugs (e.g., cisplatin, amphotericin B, and aminoglycoside)	• Weakness • Muscle tremors • Ataxia • Tetany • Paresthesias	• Adequate magnesium in PN • Monitor serum levels daily until stable; biweekly thereafter	• Increase magnesium in PN if mildly to moderately depleted

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
	• Inadequate magnesium supplementation during anabolism/refeeding	• Dizziness • Disorientation/irritability • Seizures • Cardiac arrhythmias		• Additional IV supplementation if severely depleted
Hypermagnesemia	• Renal insufficiency • Excessive magnesium administration	• Nausea/vomiting • Lethargy/weakness • Cardiac arrhythmias • Hypotension • Respiratory depression	• Monitor serum levels daily until stable; biweekly thereafter • Monitor serum levels daily in patients with renal insufficiency; restrict as appropriate • Avoid excessive magnesium administration	• Decrease magnesium in PN

Hypophosphatemia	• Inadequate phosphorous supplementation during anabolism/refeeding • Exogenous insulin administration • Chronic use of phosphate-binding antacids • Alcoholism • Diabetic ketoacidosis	• Serum level < 2 mg/dL • Paresthesias • Confusion • Altered speech • Lethargy • Respiratory failure • Decreased red blood cell function • Coma	• Supplement in PN above standard amounts in patients at risk (diabetes, alcoholism, protein-energy malnutrition) • Monitor serum levels daily until stable; biweekly thereafter	• Increase phosphorous in PN if mildly to moderately depleted • Additional IV supplementation if severely depleted
Hyperphosphatemia	• Renal insufficiency • Excessive phosphorus administration • PTH deficiency	• Prolonged elevations may lead to tissue calcification	• Monitor serum levels daily until stable; biweekly thereafter • Monitor serum levels daily in patients with renal insufficiency / restrict as appropriate	• Decrease phosphorus in PN

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Compli-cation	Possible Causes	Clinical Findings	Prevention/Monitor-ing	Treatment
			• Avoid excessive phosphorus administration	
Other				
Refeeding syndrome	• Rapid or excessive dextrose infusion (especially in malnourished patients)	• Hyperglycemia • Hypophosphatemia • Hypokalemia • Hypomagnesemia • Edema • Pulmonary edema/ congestive heart failure (CHF)	• Identification of patients at risk (chronically malnourished, nutritionally depleted patients) • Replete serum electrolyte deficiencies prior to PN initiation • Limit initial caloric intake to basal requirements	• Decrease infusion rate • Replete serum electrolyte, phosphorus, magnesium deficiencies; monitor closely • Limit fluid in presence of edema

			• Supplement phosphorus in PN • Advance PN cautiously • Monitor serum glucose, electrolytes, phosphorus, and magnesium daily until stable; biweekly thereafter	
EFAD (essential fatty acid deficiency)	• Prolonged insufficient lipid infusion	• Dry, scaly skin • Hair loss • Thrombocytopenia • Elevated triene: tetraene ratio	• Provide at least 0.5–1.0 g fat/kg/d (can be given 2–3 x/wk)	• Daily lipid infusion • Cutaneous application of linoleic acid rich oils if IV lipid contraindicated
Hepatic dysfunction	• Cholestasis	• Elevated liver function test (LFTs) and direct bilirubin	• Avoid excess energy intake	• Reduce copper and manganese intake

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
			• Avoid excess protein intake • Rule out infectious, metabolic, or anatomic causes of cholestasis	• Reduce energy and protein to meet requirements • Cycle PN • Advance enteral nutrition
Trace mineral deficiencies	• Inadequate supplementation during long-term PN • Excessive losses via GI tract (diarrhea, fistula output)	• Varies depending upon specific deficiency	• Adequate supplementation	• Supplement deficient nutrient
Trace nutrient deficiencies				
Iron	• Long-term NPO status without Fe supplementation	• Decreased ferritin • Microcytosis	• Monitor serum Fe levels	• Maintenance dose 1 mg/d in PN

	• Increased blood loss	• Decreased transferrin saturation • Decreased hemoglobin • Tachypnea/tachycardia • Poor weight gain • Poor feeding		• Do not give Fe if being transfused • Watch for anaphylaxis with initial infusion
Zinc	• Increased GI losses • Acrodermatitis enteropathica	• Growth failure • Perineal and perioral lesions • Impaired wound healing	• Increase Zn if chronic GI losses • Monitor serum Zn • Monitor growth • Wound healing	• Increase Zn in PN if increased GI losses
Selenium	• Increased GI losses • Inadequate supplementation • Long-term NPO status without supplementation	• Cardiomyopathy • Muscle weakness • Reduced glutathione peroxidase activity • Hypopigmentation of hair and nails • Hemolytic anemia	• Provide Se supplementation with long-term NPO status • Monitor serum Se levels	• Supplement as necessary

(*Continued*)

Table 15–19 Common Metabolic Conditions Seen in Patients Receiving PN *(Continued)*

Complication	Possible Causes	Clinical Findings	Prevention/Monitoring	Treatment
			• Monitor serum or RBC glutathione peroxidase levels	
Carnitine	• Long-term NPO status without supplementation	• Liver dysfunction • Steatosis • Progressive myopathy • Growth failure • Hypertriglyceridemia • Hypoglycemia	• Monitor serum carnitine levels	• Supplement for long-term NPO, if low serum levels
Metabolic bone disease	• Etiology unclear/possibly multifactorial	• Demineralization • Hypercalciuria • Pathologic fractures • Back pain • Bone pain	• Moderate nutrient provision • Monitor minerals and other PN solutions for presence of aluminum	• Adequate Ca, PO_4, vitamin D • Weight-bearing exercise • Change diuretic therapy, if feasible

	• Possible etiologies include: —altered vitamin D metabolism —aluminum toxicity —protein induced calcium loss —drug therapy (e.g., diuretics) —inactivity —inadequate Ca or PO_4 or vitamin D			

Abbreviations: PN, parenteral nutrition; EFAD, essential fatty acid deficiency.

Table 15–20 Common Mechanical and Central Line-Related Complications in Patients Receiving PN

Complication	Clinical Signs and Symptoms	Management	Preventive Measure
Obstruction in the infusion system	• PN does not flow to gravity • Occlusion alarm sounds	• Check that all clamps in the system are open • Check the IV tubing and catheter for kinks If the catheter has clotted, one may attempt to dislodge the clot by careful flushing with 1 mL of normal saline directly attached to catheter hub, using sterile technique. If unsuccessful, a fibrinolytic agent may be necessary (see Table 15–22)	• Use a pump that detects obstruction immediately • Careful taping of catheter and dressing to prevent kinking of tubing
Dislodgment of the catheter with subcutaneous collection of PN solution	• Swelling at the insertion site of the catheter	• Removal of the catheter	• Careful handling of catheter • Securing line with tape and/or safety pin to clothing

Venous thrombosis	• Venous distention or edema of the part of the body drained by that vein	• Instillation of a fibrinolytic agent may dissolve a small thrombus • Attempt to aspirate blood to verify whether catheter is patent and intact • Evaluate need for removal	• Use a pump that detects obstructions
Fracture of silastic catheter	• Leaking of PN fluid or blood	• Clamp catheter immediately • Obtain proper size repair kit • Repair the catheter	• Careful handling of the catheter • Clamping only where indicated on CVC • Avoid forceful flushing
Accidental uncoupling of joints in the infusion system	• Leakage of PN solution or spontaneous blood return • May cause hypoglycemic reaction or infection	• Clamp off system • Clean joints with alcohol • Reconnect new sterile IV tubing or positive pressure cap.	• Use of Luer lock connectors

(*Continued*)

Table 15–20 Common Mechanical and Central Line-Related Complications in Patients Receiving PN *(Continued)*

Complication	Clinical Signs and Symptoms	Management	Preventive Measure
Air embolus	• Sudden onset of respiratory distress • Cyanosis	• Immediately clamp catheter • Place patient in Trendelenburg position with right side up	• Use a pump that detects air in the system • Clamping catheter when system is opened
Transient arrhythmias	• Irregular heart beat usually occurring during insertion	• May require repositioning of catheter	• Careful monitoring of heart beat immediately after insertion
Skin sloughing due to infiltration of PN solution	• Swelling at peripheral IV site with discoloration of surrounding skin	• Immediately remove IV • Cover skin slough with sterile dressing and warm soaks • Consider use of hyaluronidase 15 u/mL inject 0. 5 mL × 5 doses SQ around site or apply nitroglycerin ointment 2% 4 mM per Kg q 8 hours	• Hourly observation of IV site for infiltration • Changing peripheral IV sites as needed

Abbreviations: PN, parenteral nutrition; CVC, central venous catheter.

NURSING CARE IN PN ADMINISTRATION

Meticulous nursing care is essential to successful PN administration to avoid potentially life-threatening complications. Several important nursing procedures are listed in Table 15–21.

Table 15–21 Nursing Care in PN Administration

Action	Rationale
I. PN administration	
1. Change PN administration sets every 96 h (every 24 h if lipid is used), using strict aseptic technique. Solution is to be changed every 24 h. Administration sets should be changed if not used for greater than 4 h.	Administration sets, solutions, or filters may be a source of contamination.
a) Any connections in the PN system must be Luer locked.	a) Luer lock connectors reduce the incidence of accidental uncoupling of joints.
b) Scrub every connector and entry site with alcohol for at least 15 s.	b) Alcohol is a disinfectant and will also remove any traces of solution that might accumulate on connectors during set up.
c) Stopcocks are not to be used; avoid the use of added extension tubing or T-connectors.	c) Extra tubing may be a source of contamination.
d) Keep a smooth edged clamp or Kelly clamps at the bedside.	d) If the PN system should become disconnected or break, immediate clamping of the catheter above the break will prevent air embolism or blood loss.
2. A volumetric infusion pump must be used.	A volumetric pump will accurately deliver desired volume as well as signal air and/or obstruction in the system.

(*Continued*)

Table 15–21 Nursing Care in PN Administration

Action	Rationale
3. Cover solution with UV resistant light sensitive bag.	Decrease potential risk of nutrient oxidation.
II. Prevention of infection	
1. A single lumen CVC placed for nutrition is not intended to serve any other purpose (i.e., to measure central venous pressures, administer blood products, "piggyback" medications or obtain blood samples).	Frequent manipulation of the PN system increases the risk of infectious and mechanical complications.
2. The following precautions must be taken before entering the line:	
a) All entry points are to be scrubbed with alcohol for at least 15 seconds	a) Alcohol is a disinfectant.
b) No medications may be added to the PN solution outside the pharmacy.	b) Medication may precipitate in PN solution. The addition of a medication is also a potential source of contamination.
c) If blood must be withdrawn from any catheter, it must be done by a physician or nurse specifically trained in this procedure.	c) If done improperly, blood withdrawal may cause clotting or infectious complications.
3. Cover the CVC exit site with a sterile dressing and change at least every 7 d or as needed.	
III. Lipid administration	
1. Lipid may be administered with PN solution provided the following:	
a) A separate pump is used.	a) Use of a pump ensures accurate infusion and prevents backflow of PN into the lipid circuit.

Action	Rationale
b) A 1.2 μ filter is used in the system, closest to the patient.	
2. Lipid volumes < 60 mL are administered through a syringe pump.	Lipid must be administered at a steady rate to prevent fat overload.
a) Change tubing every 24 h. Solution is to be changed every 12 h.	a) Administration sets, solutions, or filters may be a source of contamination.
b) Coordinate lipid administration setup change with the change in solution to minimize manipulation of the line.	b) This decreases the risk of infection.
IV. Cyclic PN	
1. A positive pressure cap is placed on the CVC and changed twice weekly.	A Luer lock cap closes off the infusion system and prevents disconnection of the cap. It also provides a site for heparin instillation. For prevention of infection Heparin will prevent blood from clotting
a) After PN administration complete, disconnect PN line.	
b) Scrub CVC with alcohol for 15 s and flush with 3–10 mL normal saline.	
c) Scrub connection site with alcohol for 15 s and flush CVC with 3ml heparin 10 units/mL.	

Abbreviations: PN, parenteral nutrition; CVC, central venous catheter.

Source: Adapted from Canada.[45]

MANAGEMENT OF CATHETER OCCLUSIONS

Obstruction of the intravenous infusion system is one of the most common complications of PN use. There is little evidence investigating the efficacy and safety of chemical interventions for catheter precipitates and low-quality evidence

of thrombolytic drugs (e.g., Alteplase).[43] Initial management consists of repositioning the patient and insuring that there are no clamps or kinks present (mechanical obstruction). Using sterile technique, a 3–10 ml flush with normal saline should be attempted. A positive pressure cap change should be performed to rule out equipment malfunction. If occlusion is sudden, consideration for infusate composition and intracatheter precipitate should be considered. Depending on the nature of an intracatheter precipitate, Table 15–22 lists commonly used agents and doses for treatment. Persistent obstructions are often treated with thrombolytic agents. Diagnostic imaging (ultrasound, Xray, or venogram) can be helpful in distinguishing between malpositioned catheters, a fibrin sheath at the CVC tip, and mural thrombi. Complete occlusions, however, cannot be evaluated by contrast studies. Figure 15–3 describes the algorithm used at Boston Children's Hospital for the evaluation and treatment of CVC occlusions.

Table 15–22 Treatment of CVC Occlusion

Precipitate Suspected	Clinical Scenario	Pharmacologic Agent	Dose
Particulate (e.g., Ca-P) with drugs that are soluble in acidic solution	PN, Ca, and/or P; use of etoposide or Aminoglycosides + heparin	0.1 N hydrochloric acid	1–2 mL or catheter volume in 30–60 min dwell time
Particulate with drugs that are soluble in basic solutions	Phenytoin, imipenem, oxacillin, ticarcillin	1 mEq/mL sodium bicarbonate	1–2 ml or catheter volume in 30–60 min dwell time
Lipids	PN/ intralipid (IL), propofol	Ethanol 70% in water	1–2 ml or catheter volume in 30–60 min dwell time

Precipitate Suspected	Clinical Scenario	Pharmacologic Agent	Dose
None (i.e., thrombus suspected)	No precipitate suspected, line sluggish, difficulty drawing blood from catheter	Alteplase 1 mg/mL	2 mg for > 30 kg child Use CVC prime volume if < 30 kg child 120 min dwell time May repeat 1 time if unsuccessful

Abbreviations: CVC, central venous catheter; PN, parenteral nutrition.

Source: Adapted from Boston Children's Hospital CVC occlusion algorithm 2012 and van Miert.[43]

For catheter occlusions refractory to tPA (Alteplase), refer to Table 15–22 for suspected precipitate trouble shooting.

Catheter Infection Prophylaxis

At Boston Children's Hospital, we have instituted the use of 70% ethanol locks for patients who are at risk for frequent CVC-associated blood stream infections. Ethanol is bactericidal and fungicidal and there is no known microbial resistance to ethanol. Data show the use of ethanol locks is an effective mechanism in preventing central line associated blood stream infections (CLABSI).[44] The Boston Children's Hospital inclusion criteria for the use of 70% ethanol lock therapy includes silicone vascular access device, weight ≥ 5 kg, a history of confirmed CVC-related blood stream infection, and PN cycled at least four hours each day. The priming volume of the catheter is measured by the prescriber to decrease the risk for ethanol exposure. A test dose is administered and the patient is observed for adverse reactions to the therapy.

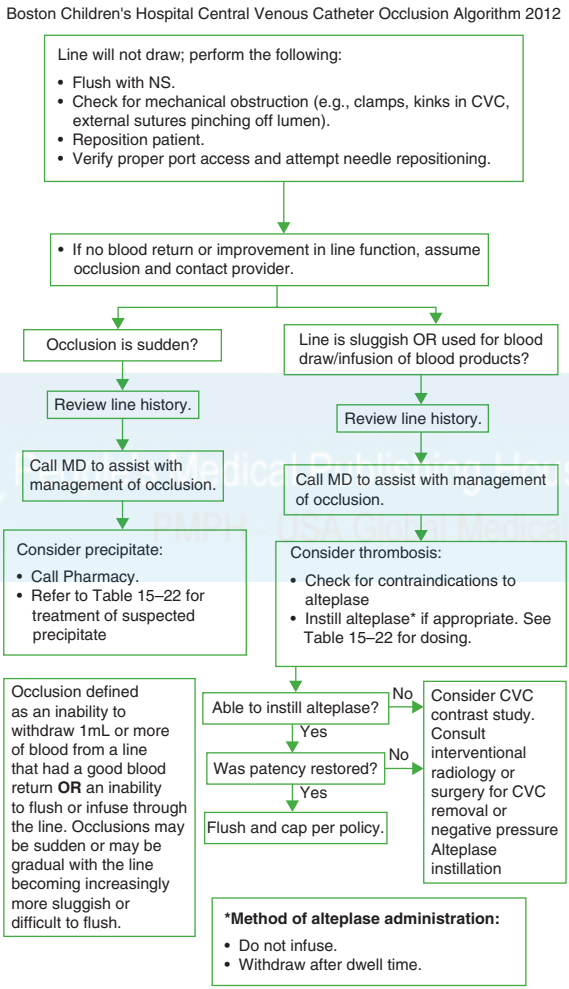


Figure 15–3: Central venous catheter occlusion algorithm.

During use, ethanol is instilled into the catheter and allowed to dwell for at least 4 hours and up to 12 hours. The ethanol is then removed from the catheter and the catheter is flushed with normal saline prior to use. Ethanol locks are used three days per week. Ethanol and heparin are incompatible and will cause a precipitate in the catheter. Because of this, heparin is not used in the catheter the days the patient is receiving ethanol locks.

WEANING FROM PARENTERAL NUTRITION

The transition from PN enteral nutrition can be highly variable. Factors affecting how quickly a patient can be weaned from PN include age, tolerance to enteral advancement, length of time NPO, psychological factors, and previous medical interventions (e.g., prolonged intubation or nasogastric tube placement). For example, a well-nourished, school-aged child taking at least 50% of calories by mouth and having tolerated advancement from clears to full liquids may wean off PN rapidly. The volume of PN could be decreased in half, lipids discontinued, and subsequent discontinuation of PN in one to two days. Younger patients, those with questionable tolerance to enteral feedings, and those with a history of feeding difficulties may take weeks to months to wean off PN. One method of weaning in this situation may be to decrease the hours of infusion during the day to encourage increased oral intake. Another method is to decrease the hourly rate of infusion. Particular detail to monitoring blood glucose and fluid status is important during the weaning process.

HOME PARENTERAL NUTRITION

Home parenteral nutrition (HPN) may be an option for children who require long-term PN support for a variety of

underlying diagnosis including but not limited to short bowel syndrome, primary motility disorders, oncology diagnoses, inflammatory bowel disease, and congenital enteropathy. Medical, social, psychological, and financial factors must all be considered in the decision to use HPN. HPN is generally delivered in a cyclic schedule allowing the patient to perform normal, daily functions while off PN. The duration of infusion time may vary from 10 to 20 hours, depending on the age, nutritional requirements, medications, and enteral intake of the patient. Barriers to cycling HPN include fluid and electrolyte imbalances and patient's age and weight precluding the patient's ability to maintain normal blood glucose levels. Use of uncycled PN should be done with caution in the out patient setting.

Continual primary caretaker education is important for the duration of HPN therapy with the goal to reduce complications related to HPN such as infusion errors and CLABSI that can be life threatening.[45] HPN monitoring is similar to in-hospital monitoring (see Table 15–18) but is usually less frequent for outpatients. We generally recommend the following parameters to be monitored every four to eight weeks: (1) height or length, weight, head circumference (if applicable), and triceps skinfold measurements; (2) a record of enteral intake, if any, should be reviewed; (3) assessment of catheter function and care; and (4) biochemical monitoring (see Table 15–18). Periodic monitoring includes vitamin D[46] trace elements (aluminum, zinc, copper, manganese, and selenium) and iron status (serum iron, ferritin total iron binding capacity, percentage transferrin saturation, CRP, reticulocyte count).[47] Long-term HPN patients are at risk for metabolic bone disease. Bone mineral density correlates well with future fracture risk; thus, evaluation by Dual-energy X-ray absorptiometry (DXA) scan should start at age 5 years and be repeated as clinically indicated.[48] Monitoring the

biochemical and trace element parameters help to determine necessary changes in PN solution composition. Assessing growth and enteral intake helps determine necessary changes in the amount and composition of the solution.

The length of therapy for HPN depends on medical indication for initiating nutrition support and can be as short as 1 month to as long as several years. Because of the high rate of infectious and noninfectious complications of prolonged PN in pediatric patients, it is imperative that every effort be made to wean patients from prolonged PN dependence. Tolerance to enteral nutrition in this setting must be managed through a transition that is carefully monitored by all caretakers.

CONCLUSION

Since its introduction in 1968, PN has become a life-sustaining therapy in the management of children unable to meet their nutritional needs exclusively by the enteral route. Although numerous advancements have been made to provide more balanced solutions, PN continues to be an artificial high-risk therapy. By working collaboratively with a multidisciplinary team utilizing nutrition and catheter guidelines, and caretaker education, these risks may be decreased. Given the inherent risks of PN therapy, continued advocacy for innovation and research is needed to improve this approach.

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16 Pediatric Human Immunodeficiency Virus

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DEFINITION AND EPIDEMIOLOGY OF PEDIATRIC HUMAN IMMUNODEFICIENCY VIRUS

Human immunodeficiency virus (HIV) is a retrovirus that replicates quickly and lyses $CD4^+$ T cells. Individuals infected with HIV may exhibit a range of symptoms, which worsen over time without therapy as $CD4^+$ T cell counts decline, resulting ultimately in severe immunodeficiency and opportunistic infections.[1]

Children can acquire HIV infection from their HIV-infected mother *in utero*, at the time of delivery, or postnatally through breastfeeding. Later childhood acquisition via sexual contact, injection drug use, and via transfused blood products are less common routes. The incidence of pediatric HIV is low in developed countries. In the United States (US) approximately 10,000 children are currently living with HIV, with only 13 new diagnoses reported in 2009.[2] The decline in HIV incidence is a result of antiretroviral therapies (ARTs), which control viral load, immune dysfunction, and improve survival. Although

the incidence has decreased dramatically in developed settings, the prevalence of HIV infection has been increasing worldwide, with 29 million HIV-infected people in 2001 and 33.4 million by 2008.[3] In pregnant mothers, the vertical transmission rate is <1% for those who receive ART and have undetectable viral loads.[4] When children are infected perinatally with HIV in developed settings, they are often diagnosed at an early age and antiretroviral therapy is initiated promptly, leading to improved survival.

ANTIRETROVIRAL THERAPY

ART for HIV infection now includes the three major drug categories of nucleoside reverse transcriptase inhibitors (NRTIs), protease inhibitors (PIs), and non-nucleoside reverse transcriptase inhibitors (NNRTIs), as well as newer classes including fusion inhibitors, entry inhibitors, and integrase inhibitors.[1] Typical ART regimens consist of at least three drugs from two different drug categories, although a number of different treatment combinations may be used.[1] Medication names, side effects and recommendations for patients on various therapies are included in Appendix 2. In addition, other medications are often used for the prophylaxis or treatment of secondary infections. These intensive drug therapies may induce side effects such as nausea, vomiting, and diarrhea that can have an impact on dietary intake and nutritional status.

Historically, nutritional complications in children with HIV have included growth failure, weight loss, feeding problems, and multiple nutrient deficiencies. However, with successful treatment, issues of chronic illness, obesity, and medication-related side effects have become more important. Body composition changes, including lipohypertrophy and lipoatrophy, metabolic complications including

insulin resistance and lipid abnormalities, and cardiovascular complications including atherosclerosis and coronary artery abnormalities, have become prevalent.[5,6] These complications have both clinical and biochemical manifestations that are multifactorial and outlined in Table 16–1. Both PIs and NRTIs are associated with body composition changes, and inflammatory cytokines have been implicated as a cause of dyslipidemia.[6,7] Insulin resistance is thought to be associated with changes in fat mass and adipocyte function leading to alterations in glucose transport that may occur with PI use, but in addition, mitochondrial toxicity associated with NRTIs is also being implicated as a mechanism.[8]

Body composition changes, particularly truncal/abdominal (central) fat accumulation, as well as dyslipidemia and insulin resistance, are all known risk factors for cardiovascular disease in otherwise healthy individuals. HIV infection itself is associated with systemic inflammation and elevation of inflammatory biomarkers (Table 16–1), which can lead to cardiac dysfunction and increased risk of myocardial infarction in HIV-infected individuals.[5] The long term effects of body fat redistribution and metabolic abnormalities in HIV-infected children are not entirely known, but cardiovascular disease risk is of particular concern in these patients when combined with the baseline inflammatory changes from HIV infection and lifelong treatment with ART.

Physical inactivity, poor diet, and other behaviors such as smoking are prevalent among adolescents and young adults in the United States, including those with HIV infection and contribute further to cardiovascular disease risk.[5] Large studies in HIV-infected adults have demonstrated that those individuals with high serum cholesterol, triglycerides, and presence of diabetes have a significantly greater risk of myocardial infarction.[5] Lipid lowering agents have been used

Table 16–1 Clinical and Biochemical Abnormalities Characteristic of Metabolic Complications in HIV-Infected Children

Clinical Features	
Lipohypertrophy (central gain)	*Lipoatrophy (peripheral loss)*
Increased abdominal (visceral) fat	Wasting of extremities and buttocks
Dorsocervical fat accumulation	Loss or thinning of facial fat (Buffalo hump)
Increased body weight/BMI	
Other Clinical Features	
Cardiovascular dysfunction	
Diastolic dysfunction	
Increased left ventricular mass	
Increased carotid intima-media thickness	
Atherosclerosis	
Biochemical features	
Dyslipidemia	*Insulin resistance*
Elevated triglycerides	Normal to elevated glucose
Elevated total cholesterol	Elevated insulin
Increased LDL	Elevated C-peptide
Decreased HDL	Decreased glucose tolerance
Biomarkers of coagulation/endothelial dysfunction	
Elevated VCAM	Elevated IL-6
Elevated ICAM	Elevated MCP-1
Elevated d-dimer	Elevated hsCRP

Abbreviations: hsCRP, high sensitivity C-reactive protein; ICAM, intercellular adhesion molecule; IL-6, interleukin 6; MCP-1, monocyte chemotactic protein 1; VCAM, vascular cell adhesion molecule.

in adults, but require careful consideration of interactions with ART. One study demonstrated that adults with HIV infection have a less effective response to lipid-lowering agents when compared to HIV-negative controls, which may further limit the use of these agents.[5] The role of lipid-lowering therapies in the pediatric population is even less clear.[5] Therefore, a focus on cardiac risk reduction through modification of diet, weight loss, increase in physical activity, and smoking cessation is critical.

Although HIV wasting is generally less of a concern in the United States, some children will still become wasted due to poor ART-adherence or drug resistance, a critical scenario to recognize since protein–energy malnutrition and HIV infection cause multiple and synergistic

Table 16–2 Etiology of Malnutrition in Pediatric HIV

Decreased Nutrient Intake	Malabsorption	Increased Requirements
Altered taste	Diarrhea/ enteropathy	Fever
Difficulty chewing/ swallowing	Opportunistic GI infections	Infection
Oral ulcerations	Bacterial over-growth	Catch up growth
Medication side effects	Steatorrhea	Metabolic abnormalities
Anorexia/depression	Pancreatic insuf-ficiency	
Encephalopathy	Hepatobiliary disease	
Abdominal pain		

immunodeficiencies. Maintaining adequate nutritional status of the HIV-infected child is, therefore, crucial for optimal immune function. Table 16–2 lists common causes of malnutrition in pediatric HIV.

NUTRITIONAL ASSESSMENT

Nutritional assessment of the HIV-infected child should be initiated at diagnosis and repeated at least every six months with more frequent evaluations for growth failure or change in clinical status. Nutritional assessment guidelines are outlined in Table 16–3. Given changes in body composition that may occur with ART, assessment of body composition

Table 16–3 Nutritional Assessment of the HIV-Infected Child[10,11]

Nutrition history
Caregiver relationship, health, and support system
Feeding history, including feeding skills
Dietary intake and analysis by 24 h or 3 d recall
Current medications, including supplements
Food security, availability of nutritious food and of preparation facilities
Safe food handling practices
Physical activity
Medical history
Transmission route
Duration of HIV infection
Drug therapies and adherence to treatment
Use of complementary therapies, medicines, or supplements
Smoking in adolescents
Current symptoms
Nausea/vomiting/anorexia
Diarrhea
Steatorrhea

- Lactose intolerance
- HIV-associated complications
- Dental or oral complications

Physical assessment

- Height, weight, and head circumference
- Z-scores for serial growth assessment (weight for length or BMI Z score) Body composition measurements, e.g., skinfold measurements or DXA (bone density)
- Obesity-related signs—blood pressure, skin examination for acanthosis and xanthomas
- Wasting-related signs (protein–energy malnutrition)—muscle bulk, skin examination, edema,
- alopecia, brittle hair

Laboratory

- Albumin, fasting glucose, insulin studies, and lipid profile
- Micronutrient levels including iron status

using anthropometric techniques such as mid-upper arm circumference (MUAC) or midarm muscle area (see Chapter 2, "Nutritional Assessment: Anthropometrics and Growth"), or, when available, dual energy x-ray absorptiometry (DXA) scanning, can help to quantify lean body mass. Normative data on non-invasive bioelectric impedance analysis (BIA) has also been developed for HIV-infected children[9] and can help calculate total percent body fat.

Since complications of obesity (hyperlipidemia, insulin resistance, and hepatitis) may overlap significantly with complications of HIV and its treatment, biochemical testing and obesity-related lifestyle assessment is required in the comprehensive nutritional assessment of HIV-infected children. Important physical examination findings in obesity, insulin resistance, and hypercortisolism include fat distribution (central vs. general), buffalo hump, acanthosis, and striae. Screening for hyperlipidemia should occur at least yearly for

all patients, and after new or second line, ART regimens are initiated. Assessment of symptoms that impact nutritional status (see Table 16–3), and communication with other medical providers to treat identified comorbid conditions are both essential. Lifestyle interventions and metabolic effects of medical therapies should be assessed at follow up visits, including repeat anthropometric measurements and biochemical testing.

NUTRITIONAL MANAGEMENT

Nutrient requirements for preserving lean body mass and supporting appropriate growth and development in the HIV-infected child are not well defined. Energy requirements can be calculated according to the general guidelines in Chapter 5, "Nutritional Requirements: DRIs, Dietary Guidelines, and Food Pyramids" with the goal of achieving normal growth velocity and age appropriate weight and height. Preserving and restoring lean body mass is a challenge. Oral supplements and tube feedings[12] improve weight gain; however, control of the viral load and inflammatory response through ART may be singularly responsible for growth improvement.[13]

Nutritional intervention should be based on the patient's growth, laboratory values, gastrointestinal function, and social environment. Diet adjustments in this population include high calorie/high protein diets with supplements as needed for weight gain. A structured exercise program that includes resistance training can improve lean body mass in children[14] and may help with insulin sensitivity and dyslipidemia.[15] Multivitamin and multimineral supplementation is recommended at RDA/DRI doses[13] or higher when micronutrient deficiencies are established or suspected. Supplementation with multivitamins has been effective in reducing disease progression among HIV-infected women,

and clinical improvements have been observed in children with supplemental vitamin A and zinc.[14] Calcium and vitamin D should be assessed and supplemented to achieve at least the DRI. Strategies for nutritional management of the symptomatic HIV-infected child are summarized in Table 16–4. In addition, to provide comprehensive care, we strongly recommend that providers identify useful programs

Table 16–4 Nutritional Management in Pediatric HIV Infection

Problem	Intervention
Anorexia	Increase nutrient density of foods
	Small frequent feedings
	Nutritional supplements
	Appetite stimulants
	Vitamin/mineral supplements
	Tube feedings
	Parenteral feedings
Oral/esophageal lesions	Soft, nonirritating foods served cold or room temperature
	Topical medications prior to feeding
	Good oral hygiene
Early satiety	Small frequent feedings
	Gastrointestinal motility-enhancing agents
Diarrhea/ malabsorption	Small frequent feedings
	Identify and manage lactose intolerance
	Evaluate and remedy food safety issues
	Semi-elemental/elemental formula
	Slow continuous drip tube feeding

(*Continued*)

Table 16–4 Nutritional Management in Pediatric HIV Infection (*Continued*)

Problem	Intervention
	Parenteral feedings
Infection/ pneumonia	Increase calories and protein
Dyslipidemia/ obesity	Minimize simple sugar intake
	Low fat diet
	Structured physical activity
	Refer to appropriate pediatric obesity programs
	Smoking cessation

for their patients that may be outside of an HIV-specific clinic. These include parallel programs focused on obesity, diabetes or diabetes prevention, adolescents, or exercise in the prevention of cardiovascular risk and treatment of obesity and hyperlipidemia in children.

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17 Burns, Trauma, and Critical Care

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INTRODUCTION

Pediatric trauma and injury continue to be the leading cause of death for children between the ages of 1 and 17 years.[1] Due to this alarming statistic, a majority of these critically ill patients, often with multiorgan involvement, are admitted to the pediatric intensive care unit (PICU).

Provision of optimal nutrition support remains a key component of the care of critically ill children.[2] Malnutrition is prevalent in children with severe injury, burns, or other critical illnesses admitted to the PICU. The stress response that follows a variety of injuries, such as sepsis, surgery, trauma, and burns is characterized by protein catabolism and increased metabolic demands. To prevent further loss of lean body mass during this catabolic phase, it is crucial to provide adequate macronutrients and micronutrients. Detailed knowledge of the metabolic stress response following injury is essential, so as to allow appropriate, individualized energy prescriptions.

In addition, a variety of barriers impede the delivery of nutrients in the PICU population. These factors may lead to

deterioration of nutritional status, subsequently affecting the ability to recover and increasing the risk of morbidity and mortality.[3]

METABOLISM

The body's response to injury, stress, surgery, or inflammation is difficult to predict and is characterized by dynamic metabolic alterations during the hospital course of illness.[4] Both a period of hypermetabolism and hypometabolism are thought to occur during the hospital course; however, the transition and timing of these dynamic metabolic states remains unclear. Children have significantly less metabolic stores when compared with adults, specifically protein and fat stores. Therefore, following critical illness, children are at much greater risk of deleterious effects, such as acute malnutrition with loss of lean body mass if nutrition support is not initiated following adequate fluid resuscitation. Prior to establishing nutritional goals, adequate fluid resuscitation following injury or critical illness is the primary focus, to maintain organ perfusion.[5]

NUTRITION REQUIREMENTS

The primary goal of nutrition therapy is to meet both macronutrient and micronutrient requirements, as well as to preserve lean body mass during the catabolic stress response following injury and critical illness. Failure to accurately estimate energy and protein needs and barriers to deliver the prescribed macronutrients results in both overfeeding and underfeeding, which can lead to nutritional deterioration during illness.[3,6]

Estimated energy prescriptions obtained from predicted energy equations are often inaccurate in the critically ill child; however, they continue to be routinely used. The most

accurate clinical measure of resting energy expenditure is obtained through indirect calorimetry.[7] (Chapter 13, "Nutritional Assessment in Sick or Hospitalized Children" explains IC in more detail.) Difficulties with wound healing, lean body mass loss, and a depressed immune system can result from underfeeding. On the other hand, overfeeding increases ventilator load with carbon dioxide production, which may be poorly tolerated by patients with an existing respiratory insufficiency. Sole reliance on equations used for estimating energy requirements has been shown to result in cumulative energy imbalance during critical illness.[7] Hence, the use of indirect calorimetry (IC) to guide energy prescriptions during critical illness is recommended whenever possible.[4]

Once goal energy needs are established, it is important to be aware of the macronutrient composition that is being provided, either enterally or parenterally, as substrate utilization may be altered during critical illness.

PROTEIN

Critical illness is characterized by increased protein turnover, with ongoing protein degradation and synthesis.[8] This adaptive response allows for amino acids to be available in the free amino acid pool, which are then redistributed away from skeletal muscle for tissue repair, wound healing, and participation in a variety of inflammatory response pathways. This contribution to the amino acid pool, as well as overall protein breakdown during critical illness, exceeds actual dietary protein intake, creating a net negative nitrogen balance. A minimum of 1.5 g/kg of protein intake may be necessary to maintain a positive balance during critical illness.[9] However, recent studies have shown that actual protein delivery in the PICU is far lower than this amount.[10] Ongoing protein

turnover that is not matched by simultaneous adequate protein intake can result in eventual loss of lean body mass.[11] Provision of optimal protein intake during critical illness to prevent unintended loss of lean body mass is one of the goals of nutrition therapy in this population. Current protein recommendations for injured children with the aim to achieve protein balance are based on limited data and consensus, which supports the need for further research.[9]

CARBOHYDRATES

The metabolism of carbohydrates during critical illness is characterized by an increase in glucose production. Gluconeogenesis ensures a steady energy source for glucose-dependent organs, such as the brain, erythrocytes, and renal medulla. Recent reports have shown an association between high serum glucose levels and poor outcomes during critical illness.[12,13,14] This relationship has prompted studies examining the role of tight glucose control, using insulin, in the intensive care unit.[15] The role of tight glycemic control strategies in critically ill children has not yet been proven and continues to be investigated.

LIPIDS

Similar to protein and carbohydrates, lipids have increased turnover rates during critical illness, with free fatty acids acting as the primary source of energy for patients under physiologic stress.[5] It is important to ensure adequate delivery of essential fatty acids during critical illness to prevent deficiency. This is usually achieved by providing 30%–40% of the total calories from fat, which is the recommended upper limit to maintain a mixed fuel system of macronutrients, while preventing associated complications, such as hypertriglyceridemia. The role of omega-3 fatty acids

as an anti-inflammatory agent in critical illness is an area of current research.

ELECTROLYTES, VITAMINS, MINERALS

Routine monitoring of electrolytes in critically ill patients is recommended to detect alterations. The body relies on a complex system of enzymes, cofactors (zinc, iron, selenium, and manganese), and vitamins (C and E) to act as a defense system against oxidant stress that exists in acute phase of injury or illness. Vitamins and minerals are redistributed from central circulation to tissues, and fluid losses from wounds and third spacing may alter micronutrient balance that results in possible deficiencies during the early phase of illness.[16,17] These abnormal levels may take weeks to return to normal. Micronutrients and their role in critically ill children continue to be researched.[18] Chapter 13, "Nutritional Assessment in Sick or Hospitalized Children" discusses the electrolyte alterations commonly seen with refeeding syndrome.

ROUTE AND BARRIERS TO NUTRITION SUPPORT

Once the individualized nutrition prescription is determined for the critically ill child, the next decision is to select the appropriate route to deliver the nutrients. The enteral route is preferred in patients with a functional gastrointestinal tract, due to its established benefits, such as preservation of intestinal mucosa integrity, enhanced mucosal immunity, safety, and cost-effectiveness, compared with parenteral nutrition (PN). PN may be used in patients with altered gastrointestinal function, hemodynamic instability, increased risk of bowel ischemia or when attempts at EN have been unsuccessful. PN may have a role as a supplement to enteral nutrition (EN), when nutrition goals cannot be met with EN alone.[4]

Many barriers exist when attempting to provide adequate nutrition via EN in the PICU, such as delays in initiating EN and frequent interruptions to feeds (due to procedures or subjective opinions related to enteral feeding intolerance). Many of these barriers are avoidable and can be reassessed by a uniform, evidence-based approach to enteral nutrition in the PICU. Recent studies have demonstrated that the use of feeding protocols in PICUs facilitate early initiation of EN, prevents unnecessary interruptions, increases the likelihood of reaching nutrition goals, and increases the overall use and success of enteral nutrition.[4] Chapter 14, "Enteral Nutrition" and Chapter 15, "Parenteral Nutrition" provides additional details on these modes of nutrition support.

IMMUNONUTRITION

As discussed in Chapter 13, "Nutritional Assessment in Sick or Hospitalized Children," immune-enhancing diets (IEDs) as well as individual nutrients, such as glutamine, arginine, fish oils, and antioxidants have been studied for their anti-inflammatory effects during critical illness. To date, there is not enough evidenced-based research available in the pediatric critical care population, to recommend either enteral or parenteral supplementation with IEDs.[4]

BURN MANAGEMENT

Severe thermal injury significantly alters a patient's metabolism, and these metabolic changes may persist for over 24 months after the initial event. This significant period of hypermetabolism and catabolism that occurs in response to a burn injury results in impaired immune function, loss of lean body mass (LBM), decreased wound healing, and delays in rehabilitative therapy. Maintaining LBM in burn injury patients is a crucial goal in current burn treatment.[19] Burn patients are at increased risk

of receiving suboptimal nutritional prescriptions due to the inability of most standard, predicted energy equations to accurately determine energy needs. Therefore, indirect calorimetry in this patient population is of great value. Current research supports the practice of early EN in burn patients, noting the benefits of early EN in relation to improved gastrointestinal and immunological function.[20] Burn patients require ongoing monitoring of their electrolyte, fluid, and overall nutritional status due to the increased risk of dynamic metabolic changes that may occur during their hospital course.

CONCLUSION

Nutrition therapy is an essential component in the treatment and recovery of critically ill children. Due to the dynamic metabolic response to stress and barriers to nutrient delivery, critically ill children are at risk of nutritional deterioration during their illness course. Hence, close monitoring of the nutritional status, individualized nutritional prescription, careful attention to maintaining nutritional intake, and continued reassessment of nutritional needs are crucial. A multidisciplinary, evidence-based approach to optimize the provision of macronutrients and micronutrients during critical illness should improve clinical outcomes in critically ill children.

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18 Cardiac Disease

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The term congenital heart disease (CHD) refers to a heterogeneous group of congenital anomalies in the structure of the heart or central vessels present at birth. Altogether, they are common congenital anomalies, affecting 8 out of every 1000 newborns. Each year in the United States, more than 35,000 infants are born with heart disease.[1] CHD lesions can be classified as either cyanotic (right-to-left shunting of blood) or acyanotic (left-to-right shunting of blood). Table 18–1 classifies CHD lesions based on the presence or absence of cyanosis; such a classification is beneficial in determining a patient's expected nutrient needs and growth patterns, as described in this chapter.

Table 18–1 Common Congenital Heart Disease Lesions

Acyanotic	Cyanotic
Atrial septal defect (ASD)	Transposition of the great arteries (TGA)
Ventricular septal defect (VSD)	Tetralogy of Fallot (TOF)

Acyanotic	Cyanotic
Patent ductus arteriosus (PDA)	Pulmonary stenosis/aortic stenosis
Common A-V canal (CAVC)	Truncus arteriosus
Pulmonary stenosis/ aortic stenosis	Total anomalous pulmonary venous return (TAPVR)
Cardiomyopathies	Pulmonary atresia/tricuspid atresia
Coarctation of the aorta	Ebstein's anomaly
HLHS	
	Single ventricle
	Double-outlet left ventricle
	Interrupted aortic arch

Abbreviations: CHD, congenital heart disease; HLHS, hypoplastic left heart syndrome.

NUTRITION RISK FACTORS IN CHD

The most common nutrition problem in patients with CHD is growth failure. Malnutrition among these patients is thought to be multifactorial; common etiologies are outlined in Table 18–2.[2–5] Growth patterns in children with CHD can vary according to the type of cardiac lesion and its hemodynamic effects. Children with cyanotic lesions generally show reduced growth in both weight and length, whereas those with acyanotic lesions often have their weight affected more than length.[6] At birth, infants with CHD usually have appropriate weight for their gestational age. However, growth problems often appear after birth, especially in infants with congestive heart failure and pulmonary hypertension.[7] Prenatal pathologies such as intrauterine growth retardation and genetic anomalies are

common in this population. Additionally, conditions such as prematurity, Down syndrome, and Turner's syndrome that may accompany CHD often affect growth. Awareness of the patient's potential growth pattern is important in assessing the child's growth and also in counseling families.

Table 18–2 Factors Contributing to Growth Failure in Patients with Congenital Heart Disease

Increased energy requirements:
Increased basal metabolic rate (tachypnea and tachycardia increase energy needs)
Increased total energy expenditure
Increased demand of cardiac/respiratory muscle
Infections
Prematurity
Decreased energy intake:
Anorexia/early satiety
Dysphasia
Gastroesophageal reflux
Swallowing abnormalities
Fluid restriction
Frequent interruptions in enteral nutrition
Increased nutrient losses:
GI malabsorption
Hyperosmolar formulas
Hepatic venous congestion (especially with right heart failure)
PLE (especially after Fontan procedure)
Renal electrolyte losses (frequently seen with diuretic use)
Inefficient utilization of nutrients:
Acidosis
Hypoxia
Increased pulmonary pressures

Congestive heart failure:
Decrease in cardiac output and renal blood flow
Stress response
Decrease in gastric capacity/inability to tolerate increased volumes of feeds

Abbreviation: CHD, congenital heart disease.

Corrective or palliative surgery is available for many CHD lesions. Correction of the hemodynamic abnormality typically results in the acceleration of growth rate with growth parameters returning to normal. Ordinarily, weight gain will start to accelerate weeks to months after surgery, whereas head circumference and height may require months to years to catch up. Children requiring surgical palliations or repairs with multiple stages (e.g., those with hypoplastic left heart syndrome [HLHS]) will require more time to achieve catch-up growth than infants with simple defects.[8] This is attributed to the persistence of an anatomical defect affecting energy intake and caloric energy needs.[5] HLHS or other single-ventricle patients often have to undergo multiple stage palliations to reconstruct systemic blood flow so that the correctly formed side of the heart can be the primary pumping chamber (which is usually the right side). The revised circulation can impose a significant volume on the heart, causing early congestive heart failure and low cardiac output. The potential for low cardiac output and decreased splanchnic blood flow increases the risk of feeding intolerance. This can potentially cause failure to thrive, malabsorption, and early fatigue during feeding.[8]

Patients who undergo the Fontan procedure are at risk for developing protein-losing enteropathy (PLE), the loss of protein and other nutrients from the gastrointestinal

tract (GI). The etiology is thought to be due to chronically elevated systemic venous pressure, which causes lymphangiectasia leading to loss of albumin, protein, lymphocytes, and immunoglobulin into the GI tract.[9] Recent research speculates that PLE may often occur as a result of mildly elevated venous pressure and low cardiac output, causing decreased intestinal perfusion with limited end organ flow.[10] Typical symptoms include generalized edema, pleural effusions, ascites, and/or chronic diarrhea with low serum albumin, protein, and lymphocyte counts.[11] PLE can occur at any point in time from weeks to years after surgery. Laboratory tests show low total protein <5.5 g/dL and albumin <3.5 g/dL. The gold standard for the diagnosis of PLE is elevated stool alpha-1-antitrypsin.[10]

Nutritional management of PLE includes providing a diet high in protein and low in long-chain fats. Supplementing the diet with a medium-chain triglyceride (MCT) oil–containing formula or MCT oil is also helpful. The rationale for these changes is as follows: Long-chain fats are absorbed via the lymphatic system as chylomicrons and transported to general circulation through lymphatics and into the thoracic duct. In contrast, medium-chain fats are hydrolyzed in the intestinal lumen to free fatty acids and are transported in portal venous blood bound to serum albumin. By limiting the amount of long-chain fatty acids in the diet, lymph flow can be reduced and protein loss in the GI tract minimized.[12] MCTs, being absorbed directly via the portal vein, may be better tolerated than long-chain fats. Patients may require additional calcium and fat-soluble vitamin supplementation when malabsorption is present.[4]

Chylothorax is a rare complication following cardiothoracic surgery in children with an estimated incidence ranging from 0.85%–3.8%.[13] It is defined as the presence of chyle (i.e., lymphatic fluid) in the pleural space secondary

to leakage from the thoracic duct, which is either damaged during cardiac surgery or malformed with the heart and great vessels.[14] Patients with chylothorax have nutritional depletion secondary to protein losses in chylous fluid, hypovolemia, and electrolyte losses. Immunodeficiency also occurs, secondary to the depletion of lymphocytes and immunoglubulins.[13] The options for nutritional management include a low-fat or fat-free oral diet, total parenteral nutrition, or a high–MCT oil formula. Parenteral lipids can be used in hospitalized patients with chylothorax to provide fat calories and essential fatty acids as these are delivered directly into the blood stream and do not have to pass through the lymphatic system.[14] Breast milk contains high levels of long-chain fatty acids and needs to be modified to be used in infants with chylous effusions.[14] Many medical centers have started to process breast milk by using a centrifuge to remove fat from breast milk. The processed breast milk requires fortification with a nutrient module to make up for what was lost through the centrifuge because fat provides half of the calories in breast milk.[14] The long-term use of a diet low in long-chain fatty acids may result in essential fatty acid deficiency; signs include decreased growth, poor wound healing, and dry scaly rash, which may manifest within 3–4 weeks.[14]

SPECIAL ASPECTS OF NUTRITIONAL ASSESSMENT

Many factors need to be considered for a thorough assessment of patients with CHD. Table 18–3 outlines the key features of this assessment. Since many patients with cardiac diseases are on multiple medications, a medication history should be taken (Table 18–4). Accurate nutrition assessment remains challenging in this population because of their

ongoing growth and varying body composition and energy needs. Postoperatively, monitoring growth becomes more complicated because of weight shifts that are caused by the shifting of fluid from the intravascular to the extravascular space (third spacing). It is crucial to use multiple modalities to assess growth such as length, head circumference, mid-upper arm circumference, and skinfold thickness when tracking growth parameters.

Table 18–3 Nutritional Assessment in CHD

History:
Type of lesion (cyanotic vs. acyanotic)
Ability to feed by mouth
Surgical history
Recent dietary recall (to assess actual caloric/protein intake)
Age at diagnosis
Current medications (see Table 18–4)
Length of time spent feeding
Weight history
Diaphoresis/fatigue during feedings
Socioeconomic factors
GI function (nausea, vomiting, diarrhea)
Supplements (multivitamin and/or iron)
Physical examination:
Height/weight/head circumference and other anthropometric measures
Clubbing
Cyanosis/pallor of skin
Fluid status/edema
Skin (dermatitis, poor wound healing)
Ability to coordinate suck, swallow, and breath

Laboratory values to evaluate:

Serum electrolytes, calcium, ionized calcium, magnesium, phosphorus, albumin, prealbumin, CRP, hemoglobin, hematocrit, oxygen saturation

Abbreviation: CHD, congenital heart disease.
Source: Adapted from Therrien and Webb.[11]

Table 18–4 Common Medications Used in CHD

Medication:	Drug–Nutrient Interaction:
Furosemide	Anorexia; nausea; decreased K, Na, Cl, Mg, Ca
Captopril	Anorexia, increased K, decreased Na
Digoxin	Nausea, vomiting, diarrhea, decrease in Mg, increase/decrease in K
Chlorothiazide	Anorexia; decreased K, Zn, Mg
Propranolol	Nausea, vomiting, hypoglycemia
Spironolactone	Anorexia; increased K, Mg, BUN/creatinine; decreased Na
Bumetanide	Nausea, vomiting
Dopamine	Nausea, vomiting
Epinephrine	Nausea, hyperglycemia
Prostaglandin (E1) alprostadil	Diarrhea

Abbreviation: CHD, congenital heart disease.

As evidenced by the frequent finding of growth failure, children with cardiac disease require additional calories beyond their recommended dietary allowance (RDA) to establish growth. Energy needs vary throughout the population, which is why indirect calorimetry (IC) is the gold standard for evaluating energy needs. Table 18–5 outlines how to determine estimated nutrition needs. Many children

are unable to tolerate the volume required to consume adequate calories with a standard dilution of formula, necessitating the use of calorically dense breast milk or formula. There are certain scenarios when starting enteral feedings should be avoided in CHD patients (Table 18–6). Parenteral nutrition may be indicated, depending on the length of time these factors are anticipated to be active.

Table 18–5 Determination of Estimated Nutrition Needs for the Infant with Congenital Heart Disease

	Critical Care	Step-Down/ Acute Care
Energy requirements	Determine by indirect calorimetry (if available) Provide REE x 1.3–1.5 (REE usually 55–60 kcal/kg) In the first 3–5 d of surgery If fluid is limited postoperatively, aim for minimum of REE	Catch-up growth (can range from 140–160 kcal/kg)
Protein	3–3.5 g pro/kg (term infant) 3–4 g pro/kg (preterm infant)	
Macronutrient percentages (from total calories)	Carbohydrate: 35%–65% Protein: 8%–10% Fat: 35%–50% If fat restriction due to chylothorax, 4% of total calories should come from essential fatty acids	
Fluid	Per ICU team fluid restriction (generally 60%–80% maintenance fluid requirements postoperatively).	100–130 mL/kg d May need to increase by 10%–15% to compensate for increased losses associated with diarrhea, emesis, or diuresis.

	Critical Care	Step-Down/ Acute Care
Micronutrients Sodium: 2–3 mEq/kg Potassium: 2–5 mEq/kg Supplement with vitamin D in breast-fed infants and those with total formula intakes less than 1 L/d		

Abbreviations: CHD, congenital heart disease; REE, resting energy expenditure.
Source: Adapted from Roman.[5]

Table 18–6 Contraindications to Enteral Feedings in Cardiac Patients

Hemodynamic instability with low cardiac output, requiring high doses of vasoactive drugs
A PDA-dependent lesion with compromised mesenteric perfusion from ongoing left-sided or right-sided outflow obstruction (i.e., interrupted aortic arch, HLHS, some coarctations of the aorta, some single-ventricle physiology lesions)
Low systemic output for large left-to-right shunt without obstruction
Recent (<24 h) cardiac arrest requiring significant resuscitation
Endotracheal intubation or extubation within 4 h
Functional or mechanical bowel obstruction
Active upper GI bleeding
Junctional ectopic tachycardia

Abbreviations: PDA, patent ductus arteriosus; HLHS, hypoplastic left heart syndrome.

The ultimate goal for patients with cardiac disease is achieving normal growth and development. Since these patients are provided lower total enteral volumes, both macronutrient and micronutrient intakes need to be evaluated. Infants and children with CHD often are in negative protein balance due to inadequate intake, dilution of protein in formula from adding additional caloric modular, or increased

protein energy losses.[12] Individual mineral supplements may be needed in addition to multivitamins. Infants presenting with congestive heart failure and a median shortening fraction of 10% have been shown to have abnormally low levels of vitamin D, serum calcium, with corresponding elevations of parathyroid hormone.[15] Close attention should be paid to potassium chloride, magnesium, and zinc as their depletion can lead to growth retardation. Patients undergoing cardiac surgery on cardiopulmonary bypass have a high incidence of hypomagnesemia. Therefore, maintaining higher levels of total magnesium (>2 mg/dL) especially in patients at risk for postoperative arrhythmias may be beneficial.[15] Successful growth can be achieved by monitoring intake and total daily volumes required to meet the patient's changing needs.

FEEDING APPROACHES

Infancy is a critical time in the development of feeding skills. Many infants with CHD often miss important milestones that greatly impact feeding skills due to prolonged hospitalization. After cardiac surgery, patients may be at significant risk of aspiration due to vocal cord dysfunction attributed to prolonged intubation, neurodevelopmental delay, or poor sucking/swallowing coordination. Therefore, the use of nasogastric tube feedings or gastrostomy tube feedings may be required to ensure adequate nutrient intakes in children with an inability to exclusively orally feed. Enteral nutrition delivery should mimic age-appropriate feeding patterns. Among young infants for whom two to three hours of feeding intervals are appropriate, an acceptable oral strategy is to allow oral trials for 20–30 minutes and then deliver the remaining volume through the feeding tube.[9] For older infants and children who exhibit adequate intake during the day, nocturnal continuous drip feeds can be used

to supplement 50% of estimated needs over 10–12 hours.[9] Infants between 4 and 6 months should start to be offered appropriate staged baby foods from a spoon as long as their oral motor skills are appropriate.

TRANSPLANTATION

Heart transplantation is an option for patients with end-stage heart failure or inoperable defects. Important factors that affect growth after heart transplantation include age at transplantation, etiology of cardiac failure, presence or absence of chronic renal dysfunction, and corticosteroid use. Posttransplant growth for infants and children younger than 6 years of age has been reported to be within low-normal range. Children on steroid therapy used to avoid rejection are at high risk of delayed growth.[16] Close monitoring of blood glucose, encouraging a balanced diet high in calcium-rich foods, and reinforcing sanitary food practices are basic nutrition guidelines to be followed for transplant patients. Frequent outpatient follow-up is strongly recommended to monitor long-term growth.

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19 Cystic Fibrosis

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Cystic fibrosis (CF) is an autosomal recessive genetic disorder. It is caused by mutations in the gene that encodes for the CF transmembrane conductance regulator protein (CFTR). The CFTR protein is responsible for chloride ion exchange across cells; a defect in this protein results in the production of abnormally thick secretions from epithelial cells throughout the body. These secretions can clog tubules and airways (e.g., bronchioles and pancreatic ducts) as well as function as a medium for bacterial growth, leading to infections and inflammation primarily in the respiratory tract.

Major clinical manifestations of CF include the following:

- Malnutrition
- Chronic pulmonary infections resulting in progressive lung failure
- Exocrine pancreatic insufficiency
- CF-related diabetes mellitus
- Meconium ileus

This chapter was based in part on Corrales K, *Cystic Fibrosis in Manual of Pediatric Nutrition*, Fourth Edition, 2005.

- Cholestatic liver disease
- Distal intestinal obstruction syndrome (DIOS)

EPIDEMIOLOGY

CF occurs in approximately 1 in every 3500 live births in the United States each year. CF affects people of all races and ethnic groups but is most common in Caucasians. There are about 30,000 people in the United States with CF. The predicted survival age for a person with CF is about 38 years. Approximately 47.5% of patients in the CF Foundation Patient Registry are over 18 years of age.[1]

NUTRITIONAL ASSESSMENT

Malnutrition is a common clinical manifestation in CF. Several factors are involved in the development of malnutrition in a patient with CF (Table 19–1). There is

Table 19–1 Nutritional Risk Factors in Cystic Fibrosis

Increased REE
Chronic cough
Pulmonary infections
Poor and deteriorating lung function
Possibly a genotype-dependent, energy-requiring cellular defect
Increased nutrient losses
Pancreatic insufficiency
Reduced bile acid and bile salt pool
Cough–emesis cycle
Poorly controlled blood sugars in CF-related diabetes mellitus
Poor energy intake
Fatigue
Anorexia
Esophagitis from gastroesophageal reflux
Depression, anxiety

good evidence that normal anthropometrics, particularly body mass index (BMI) for age, are associated with better pulmonary function and survival in patients with CF.[2] Therefore, maintaining optimal BMI or weight-for-length (infants through children 2 years of age) status is crucial for extending life expectancy and reducing disease severity. Furthermore, early diagnosis coupled with aggressive nutritional intervention can enhance long-term nutritional status.[2] The nutritional assessment of the patient with CF involves a thorough review of medical history, nutrient intake, medications, laboratory values, and psychosocial and behavioral factors (Table 19–2).

NUTRITIONAL MANAGEMENT

Nutritional counseling and education should occur at the time of diagnosis and regularly thereafter. Special attention on growth and nutrition should be placed during (1) the first 12 months after diagnosis; (2) from birth to 12 months of age, if a child was diagnosed prenatally or at birth; and (3) during the peripubertal growth period (girls 9–16 years, boys 12–18 years).[3] Children under 2 years of age presenting with growth failure should be evaluated every two to four weeks and children over 2 years of age every four to six weeks, until normal weight gain is achieved, and then every 3 months.[3] All patients should be seen at least once a year by a registered dietitian who can make accurate anthropometric measurements, analyze dietary intake, help evaluate the adequacy of pancreatic enzyme therapy, and make dietary recommendations. Guidelines for nutritional management in CF are detailed in Table 19–3.

ASSESSING MALNUTRITION

The primary goals of nutrition management in pediatric patients with CF are to promote normal growth and

Table 19–2 Special Aspects of Nutritional Assessment in Cystic Fibrosis

Medical History
Pulmonary
Number of pulmonary exacerbations
Change in pulmonary function tests
Gastrointestinal
History of gastrointestinal disease, meconium ileus, DIOS, intussusception, or gastrointestinal surgery
Symptoms of malabsorption, for example, gas and bloating; frequent, bulky, loose stools; floating, fatty, foul-smelling, frothy stools
Abdominal pain, vomiting, gastroesophageal reflux
Endocrine
Polyuria, polydipsia, unexplained weight loss, poor growth, steroid use, history abnormal blood sugars
Liver disease
History of biliary cirrhosis, ascites, or esophageal varices
Growth and Development[6]
Biological parents heights—note on growth chart (determine mid-parental height; see Chapter 2)
Measure every 3 months for children <2 years of age, then annually
Weight, height/length, head circumference,
Measure annually
Pubertal status (Tanner stage): girls starting at 9 years, boys starting at 10 years

Diet History (at diagnosis and annually) Total calorie and protein intake Percentage of total calories from fat and grams of fat per meal Grams of carbohydrate at meals and snacks if on insulin Food allergies or intolerances Appetite changes with illness Use of nutritional supplements or tube feeding Types and amounts of vitamin supplements Use of complementary/alternative medicines
Medications Enzymes Timing and method of pancreatic enzyme administration Number of enzymes with meals, snacks, and tube feeding Units of lipase per kilogram of body weight per day, units per gram of fat (if latter method used) Other medications Antibiotics, acid blockers (H2 antagonists), steroids, alternative/complimentary medicines

(*Continued*)

Table 19–2 Special Aspects of Nutritional Assessment in CF (*Continued*)

Biochemical (at diagnosis[a] and annually, unless otherwise indicated)[3]
Albumin and prealbumin
Fasting and 2-h postprandial blood glucose or OGTT
Hemoglobin A1c
Bone status evaluation if >8 years of age and has risk factors (see Table 19–9)
Electrolytes
Essential fatty acids (via triene:tetrane ratio) in infants and those with growth failure
Iron studies
Vitamin A (retinol)
Vitamin D (25(OH) D)
Vitamin E (α-tocopherol)
Vitamin K (via PIVKA II or PT)
Zinc (consider 6 mo supplementation if growth failure)
Psychosocial
Socioeconomic status, medical insurance, employment, history of depression, anxiety, substance abuse, social supports
Behavioral
Behaviors around eating/mealtime, positive/negative reinforcement to behavior, stage or readiness for change, history of eating disorder or disordered eating patterns.

Abbreviations: DIOS, distal intestinal obstruction syndrome; PIVKA, Protein induced by vitamin K absence or antagonism; PT, prothrombin time.
[a]If diagnosed by neonatal screen, measure vitamin levels at 1 month of age.

Table 19–3 Special Aspects of Nutritional Management in CF

Diet	High Calorie, Higher Fat
Calories	1.2–2 × DRI for age
Protein	1.5–2 × DRI for age
Fat	35%–40% total calories
Essential fatty acids	3%–5% of total calories
Vitamin A	
0–12 mo	1500 IU/d
1–3 y	5000 IU/d
4–8 y	5,000–10,000 IU/d
>8 y	10,000 IU/d
Vitamin D—cholecalciferol	
0–12 mo	400–500 IU/d
12 mo–10 y	800–1000 IU/d
> 10 y–18 y	800–2000 IU/d
Vitamin E	
0–12 mo	40–50 IU/d
1–3 y	80–150 IU/d
4–8 y	100–200 IU/d
>8 y	200–400 IU/d
Vitamin K	At least 0.3–0.5 mg/d
Calcium	DRI
0–6 mo	200 mg[a]
7–12 mo	260 mg[a]
1–3 y	700 mg
4–8 y	1000 mg
9–13 y	1300 mg
14–18 y	1300 mg
Iron	DRI unless deficient
Sodium	Minimum amounts noted here. Increased needs at times of sweating and during hot weather.
Infants	2–4 mEq/kg/d
Children/adolescents	5.2–21.7 mEq/kg/d (DRI)

(*Continued*)

Table 19–3 Special Aspects of Nutritional Management in CF (*Continued*)

Diet	High Calorie, Higher Fat
Water-soluble vitamins	At least the DRI
Zinc	DRI unless deficient Consider 6-mo trial of zinc supplementation if poor growth or stunting.

Abbreviation: DRI, dietary reference intake (see Chapter 5).
[a]Adequate intake rather than recommended dietary allowance. Calcium is an AI for 0-6 and 7-12 months.

Source: Adapted in part from Borowitz et al.[4]

development through the provision of adequate nutrients.[3] The Cystic Fibrosis Foundation (CFF) now recommends using BMI percentile to assess nutritional status in CF rather than the percent ideal body weight (IBW) method previously recommended.[2] Weight, length (measured lying down) or height (measured standing), and head circumference (for infants) should be measured quarterly and plotted on 2000 National Center for Health Statistics/Centers for Disease Control growth charts.[2] Additionally, weight for length should be plotted for children under the age of 2 years, and BMI should be plotted for children aged 2–20. In order to maintain optimal health, CFF recommends that children maintain a BMI status that is at or greater than the 50th percentile.[2] Mid-arm circumference and triceps skinfold measurements may be obtained and provide information regarding lean body mass and adipose tissue reserves.[2] However, it is no longer recommended by CFF that arm anthropometrics be measured annually.[3] Annually, patients with CF should have their diets analyzed to make sure that they are meeting their nutritional needs.[2]

Although CFF no longer has classifications for malnutrition since new BMI goals were established, many CF

centers have adopted methods for classifying the degree of malnutrition when a patient's BMI is below the goal of the 50th percentile. One study found that using a standardized classification of BMI status and a personalized nutritional treatment intervention significantly improved BMI percentile over 15 months.[4] The classifications used were "failure" for BMI < 10th percentile, "at risk" for BMI 10th–24th percentile, "acceptable" for BMI 25th–49th percentile, and "optimal" for >50th percentile.[4] It is important to note that malnutrition classification systems may vary among CF centers when a patient's BMI is below the 50th percentile.

ENERGY INTAKE

Patients with CF have increased energy needs due to malabsorption, chronic infection/inflammation, and increased work of breathing. For this reason, the recommended energy intake for patients with CF is 110%–200% of the energy needs of the healthy population.[2] This goal can be achieved by increasing both the amount of food and the energy density of foods consumed.[2]

ENERGY EXPENDITURE

Studies evaluating resting energy expenditure (REE) in CF have found levels in the range of 4%–20% above those of healthy controls or predicted values.[5–7] REE in CF may be influenced by pancreatic insufficiency, type of genetic mutation, stage of pulmonary infection, severity of lung disease, degree of malabsorption, and gender, as well as other factors including CF liver disease and cystic fibrosis–related diabetes (CFRD).[6,7] In presymptomatic CF, energy expenditure may be closer to normal.[8] However, with poorer lung function greater levels of REE may be seen.[6,9] The hypermetabolism seen during an acute pulmonary exacerbation

may also be dependent on the extent of lung disease, with mild-to-moderate lung disease (forced expiratory volume in 1 second [FEV_1] > 60%) less likely to be associated with an increased REE than is the case with more severe lung disease.[9] REE appears to be higher during the early stages of intravenous treatment for an acute pulmonary exacerbation and decrease with treatment.[9] Studies on total energy expenditure (TEE) in infants and children with CF have been inconsistent, with some finding elevations in the range of 12%–25% in TEE in children with CF[5,10] and others finding no differences.[8] The inconsistent results may be related to differences in clinical status, genotype, and activity level in the children as well as the methods used to determine TEE (heart rate, doubly labeled water, activity records).[8]

There is no perfect method for estimating calorie needs. The goal is sustained growth and weight gain in children and weight gain and maintenance in adult patients with CF. A good general guideline for estimating calorie needs is 1.2–2 times the dietary reference intake (DRI) for age. However, a recent study found that 1.2 times the DRI for age can often overestimate energy requirements in preadolescent children with mild-to-moderate CF lung disease.[11]

FAT

In an effort to control abdominal pain and other symptoms of steatorrhea, patients with CF were historically prescribed a low-fat diet. Later, the implementation of a high-fat diet with adjustments in exogenous pancreatic enzymes to control malabsorption was associated with better growth and survival among CF patients.[12] Current recommendations are to provide 35%–40% of calories in the form of long-chain fats (LCFs).[2] Medium-chain triglycerides (MCTs) have been used to supplement energy intake in fat malabsorption since they can be absorbed in the absence of pancreatic lipase and

bile salts. However, MCTs are not a source of essential fatty acids and can be both expensive and unpalatable.

Essential Fatty Acids

Low plasma levels of essential fatty acids are often seen in patients with CF, although symptoms of essential fatty acid deficiency are rare.[2] It has been proposed that essential fatty acid deficiency (EFAD) is due to impaired fatty acid metabolism in CF rather than malabsorption of fat caused by pancreatic insufficiency; however, the root cause of EFAD observed in CF remains unclear.[2] The Consensus Report on Nutrition for Pediatric Patients with CF suggests the use of linolenic acid–rich foods and supplements as a source of energy, in addition to the promotion of breast milk, which is rich in docosahexaenoic acid (DHA).[2] Studies have found that supplementation with omega-3 fatty acids may provide benefits to patients with CF including improved pulmonary function, increased serum phospholipid levels of essential fatty acids, and a higher level of essential fatty acids in neutrophil membranes.[13] Despite these findings, there is not enough conclusive research to make recommendations for supplementation with essential fatty acids in CF.[13] If patients are taking omega-3 or fish oil supplements, it is important to increase the dosage of pancreatic enzymes to compensate for the fat content of these supplements.[13]

◆ PROTEIN

Due to some loss of nitrogen in the presence of pancreatic insufficiency, children with CF are estimated to need at least 1.5–2 times the DRI for protein for age. These estimations are usually easily met if energy goals are being met.[14] Excessive protein intakes may reduce renal function already compromised by aminoglycoside antibiotic use and other factors.

CARBOHYDRATE AND CFRD

As life expectancy has increased in patients with CF, so has the incidence of CFRD. It is the most common complication in patients with CF with an overall prevalence of 17.5% in all people with CF and 30.5% in adults with CF.[1] Although the prevalence is higher in adulthood, CFRD occurs in pediatric patients and affects approximately 20% of adolescents with CF.[15] However, these figures may underestimate the true prevalence since many patients may not be screened for CFRD. CFRD shares the features of both type 1 and type 2 diabetes, but it is recognized as a distinct diagnosis. The cause of CFRD primarily is insulin deficiency, although insulin resistance associated with chronic illness is also thought to play a role.[15] Diabetes in CF is often asymptomatic and therefore often underdiagnosed. For this reason, CFF recommends that all children with CF be screened for CFRD beginning at 10 years of age.[15] CFRD may present similarly to type 1 or type 2 diabetes (polydipsia, polyuria, weight loss/poor growth, fatigue) but without ketoacidosis or hyperinsulinemia.

The oral glucose tolerance test (OGTT) remains the most reliable method of screening for CFRD, although casual blood glucose and 2-hour postprandial glucose checks can also be used. Hemoglobin A1c and fasting plasma glucose levels have not been found to be reliable screening tools for CFRD as they may be normal even in the presence of glucose intolerance.[16] Diagnostic criteria for CFRD can be found in Table 19–4.

The American Diabetes Association and CFF recommend the use of insulin to treat CFRD. Patients started on insulin should check their blood glucose at least three times a day and hemoglobin A1C quarterly with a goal of <7%.[15] Patients should continue on a high-calorie diet without carbohydrate restriction. Calorie needs are 1.2–1.5 times the DRI

Table 19–4 Diagnostic Criteria for CFRD

Any of the Following Can Be Diagnostic for CFRD	
Fasting blood glucose (FBG)	FBG > 126 mg/dL (7.0 mM) on two or more occasions FBG > 126 mg/dL + casual glucose ≥ 200 mg/dL (11.1 mM)
2-h postprandial plasma glucose	>200 mg/dL that persists for more than 48 h in the setting of acute illness
Casual glucose	Casual glucose ≥2 00 mg/dL (11.1 mM) on two or more occasions with the presence of classic symptoms (polyuria, polydipsia, etc.). Must be verified by a certified laboratory.
OGTT (1.75 g glucose/kg. max 75 g)	2 h glucose ≥ 200 mg/dL (11.1 mmol/L)
Hemoglobin A1C	>6.5%[a]
Enteral feedings	>200 mg/dL
Symptoms	Poor growth, delayed progression of puberty, a failure to gain weight despite nutritional intervention, or an unexplained decline in pulmonary function should warrant an evaluation for CFRD.

[a]It should be noted that an Hgb A1C < 6.5% does not rule out the diagnosis of CFRD as A1C may be falsely low in CF.

Source: Adapted from Moran et al.[16] and Moran et al.[17]

for age and should be adjusted based on weight gain and growth patterns. Protein needs in CFRD range from 1.5 to 2 times the DRI for age and are not reduced in the setting of nephropathy.[15] Patients with CFRD should be advised to consume consistent amounts of carbohydrate-rich foods at meals and snacks and be taught carbohydrate counting if started on insulin (see Chapter 21). It is recommended by

CFF and the American Diabetes Association that patients with CFRD consume calorically dense beverages and limit artificial sweeteners, as these products are low in calories.[15]

Vitamins and Minerals

Supplementation of fat-soluble vitamins is recommended for all patients with CF who have pancreatic insufficiency (see Table 19–3). Table 19–5 lists vitamin supplements typically used in fat malabsorption. Table 19–6 offers suggestions for dosing these supplements. Serum vitamins A, E, and 25-hydroxyvitamin D, should be measured at diagnosis and annually.[2] If serum levels indicate deficiency (Table 19–7), compliance should be reviewed before initiating additional supplementation. Once treatment is initiated, the serum levels should be repeated one to two months later. The patient's financial ability to obtain vitamins should also be assessed. Many insurance policies do not cover the expenses for vitamins, and patients are often faced with out-of-pocket expenses for these supplements. Depending on state laws and the patient's insurance, the patient may be eligible to receive assistance in obtaining vitamins and nutritional supplements from enzyme companies.

In addition to vitamin deficiencies, toxicity can occur with high-dose supplement use. Since vitamin A toxicity is more likely to occur with increasing plasma levels of retinyl esters, laboratory measurements of these esters are the most direct way to assess overdosage of retinol supplements. Excess free retinol may also be diagnosed by measuring the molar ratio of retinol to retinol-binding protein (Table 19–7). A serum vitamin A level should not be measured if the patient is acutely ill as vitamin A is an acute phase reactant.[2] If a patient has night blindness or difficulty seeing at night, then there is a possibility of deficiency and the level should be checked.

Table 19–5 Vitamin Supplements Available in the United States for Fat Malabsorption

	Drops			Tablets				
	AquADEK™ Pediatric (1 mL)	**VITAMAX™ Pediatric (1 mL)**	**SOURCECF™ Pediatric (1 mL)**	**AquADEK (1 Tablet)**	**AquADEK (1 Softgel)**	**VITAMAX (1 Tablet)**	**SOURCECF (1 Tablet)**	**SOURCECF (1 Softgel)**
Vitamin A	748 IU (palmitate)	3170 IU (palmitate)	~1155 IU (palmitate)	727 IU (palmitate)	~1450 IU (palmitate)	2500 IU (acetate)	1920 IU (palmitate)	1920 IU (palmitate)
β-Carotene	~5003 IU vitamin A if fully converted	—	~3470 IU vitamin A if fully converted	8357 IU vitamin A if fully converted	~16,715 IU vitamin A if fully converted	~2500 IU	14,080 IU	14,080 IU
Vitamin D	400 IU (cholecalciferol)	400 IU (cholecalciferol)	500 IU (cholecalciferol)	400 IU (cholecalciferol)	800 IU (cholecalciferol)	400 IU (cholecalciferol)	1000 IU (cholecalciferol)	1000 IU (cholecalciferol)
Vitamin E	50 IU (*d*-α-tocopheryl)	50 IU (*d*-α-tocopheryl acetate)	50 IU (*d*-α-tocopheryl acetate	50 IU (*d*-α-tocopheryl)	150 IU (succinate)	200 IU (D-α tocopherol succinate)	200 IU (*d*-α tocopherol)	200 IU (*d*-α tocopherol acetate)
Vitamin K	400 mcg (phytonadione)	300 mcg (phytonadione)	400 mcg (phyotonadione)	350 mcg (phytonadione)	700 mcg (phytonadione)	200 mcg (phytonadione)	800 mcg (phytomenadione)	800 mcg (phytomenadione)
Vitamin C	45 mg (sodium ascorbate and ascorbic acid)	45 mg (ascorbic acid)	45 mg (sodium ascorbate)	35 mg (sodium ascorbate)	75 mg (ascorbic acid)	60 mg (ascorbic acid)	100 mg (ascorbic acid and zinc ascorbate)	100 mg (ascorbic acid and zinc ascorbate)

(*Continued*)

Table 19–5 Vitamin Supplements Available in the United States for Fat Malabsorption (*Continued*)

	Drops			Tablets				
	AquADEK™ Pediatric (1 mL)	**VITAMAX™ Pediatric (1 mL)**	**SOURCECF™ Pediatric (1 mL)**	**AquADEK (1 Tablet)**	**AquADEK (1 Softgel)**	**VITAMAX (1 Tablet)**	**SOURCECF (1 Tablet)**	**SOURCECF (1 Softgel)**
Vitamin B1 (thiamin)	0.6 mg	0.5 mg (thiamine HCl)	0.5 mg (thiamine HCl)	0.75 mg (thiamine mononitrate)	1.5 mg	1.5 mg (thiamin)	1.5 mg	1.5 mg
Vitamin B2 (riboflavin)	0.6 mg (thiamin hydrochloride)	0.6 mg (phosphate)	0.6 mg (5 phosphate)	0.85 mg (5 phosphate)	1.7 mg	1.7 mg (riboflavin)	1.7 mg (cyanocobalamin)	1.7 mg
Niacin	6 mg (niacinamide)	6 mg (niacinamide)	6 mg (niacinamide)	5 mg (niacinamide)	10 mg (niacinamide)	20 mg (niacinamide)	10 mg (niacinamide)	20 mg (niacinamide)
Vitamin B6	0.6 mg (pyridoxine HCl)	0.6 mg (pyridoxine HCl)	0.6 mg (pyridoxine HCl)	0.95 mg (pyridoxine HCl)	1.9 mg (pyridoxine)	2 mg (pyridoxine HCl)	1.9 mg (pyridoxine HCl)	1.9 mg (pyridoxine HCl)
Vitamin B12	—	4 mcg (cyanocobalamin)	4 mcg (cyanocobalamin)	6 mcg (cyanocobalamin)	12 mcg (cyanocobalamin)	6 mcg (cyanocobalamin)	6 mcg	6 mcg (cyanocobalamin)
Biotin	15 mcg	15 mcg	15 mcg	50 mcg	100 mcg	300 mcg (D-biotin)	100 mcg	100 mcg
Folic acid	—	—	—	100 mcg	100 mcg	200 mcg	200 mcg	200 mcg
Pantothenic acid	3 mg (calcium *d*-pantothenate)	3 mg (*d*-Calpantothenate)	3 mg (*d*-pantothenol)	6 mg (calcium *d*-pantothenate)	12 mg	10 mg (*d*-calcium pantothenate)	12 mg (calcium pantothenate)	12 mg

Zinc	5 mg (gluconate)	7.5 mg (sulfate)	5 mg (gluconate)	5 mg (zinc amino acid chelate)	10 mg (oxide)	–7.5 mg (oxide)	10 mg (ascorbate and zinc oxide)	10 mg (ascorbate and oxide)
Selenium	10 mcg (selenomethionine)	—	—	37.5 mcg (selenomethionine)	75 mcg (selenomethionine)			
Sodium	10 mg	—	—	5 mg	10 mg			
Vitamin E (as other mixed tocopherols)	15 mg	—	—	15 mg	80 mg			
Coenzyme Q10	2 mg	—	—	5 mg	10 mg			
Ingredients	Water, *d*-α-tocopheryl polyethylene glycol 1000 succinate, modified food starch, cornstarch, mannitol, corn	Glycerin, deionized water, polysorbate 80, fructose, fructose flavor, sucralose,	Purified water, glycerine, sucrose, polysorbate 80, natural flavors, citric acid, sucralose, sodium	Dextrose, sorbitol, dicalcium phosphate, cellulose, fructose, *d*-α-tocopheryl polyethylene glycol 1000 succinate,	Caprylic/capric triglycerides, gelatin, *d*-α-tocopheryl polyethylene glycol 1000 succinate,	Sorbitol crystalline powder, citric acid, carrageenan, silicon dioxide, stearic	Sucrose, mono- and diglycerides, natural and artificial flavors, magnesium stearate,	Gelatin, glycerin, soybean oil, polysorbate 80, caramel, natural flavors, hydrogenated

(*Continued*)

Table 19–5 Vitamin Supplements Available in the United States for Fat Malabsorption (*Continued*)

	Drops			Tablets				
	AquADEK™ Pediatric (1 mL)	**VITAMAX™ Pediatric (1 mL)**	**SOURCECF™ Pediatric (1 mL)**	**AquADEK (1 Tablet)**	**AquADEK (1 Softgel)**	**VITAMAX (1 Tablet)**	**SOURCECF (1 Tablet)**	**SOURCECF (1 Softgel)**
	oil, sodium benzoate, potassium sorbate, dicalcium phosphate, sucralose, natural flavors, pectin, *dl*-α-tocopherol, disodium EDTA, vitamin B12, BHT, BHA	potassium sorbate, sodium benzoate	benzoate, potassium sorbate, EDTA, BHA, BHT	stearic acid, silicon dioxide, erythritol, oligofructose, mono- and diglycerides, magnesium stearate, modified food starch, gelatin, ascorbic acid, natural and artificial flavors, acacia, cornstarch, sucrose, soybean oil, citric acid, water, maltodextrin, sucralose, acesulfame	glycerin, water, dicalcium phosphate, corn oil, sorbitol, sorbitan, mannitol, titanium dioxide, modified food starch, FD&C yellow no. 6, FD&C red no 40, *dl*-α-tocopherol, FD&C blue no 1, fatty acids and esters, sodium citrate,	acid (veg.), magnesium stearate (veg.), FD&C Red #40 Lake + [Grape flavor: grape-citrus flavor, FD&C Blue #2 Lake, aspartame,] [Orange flavor: Natural banana flavor, FD&C	silicon dioxide, hydroxypropyl methylcellulose, locust bean gum, malic acid, sucralose, Red #40 Lake	vegetable oil, yellow beeswax, lecithin, sucralose

				potassium, mannitol, pectin, MCT, neohesperdine, coconut oil, BHT, vegetable protein isolate, sodium benzoate, *dl*-α-tocopherol, sorbic acid	citric acid, silicon dioxide, sodium benzoate, sorbic acid	Yellow #6 Lake, natural orange flavor]		
Other	Only vitamin E is water soluble; 1 g carbohydrate	All water-soluble; 1 g carbohydrate	100 mg sugar and 225 mg glycerin	100 mg sugar and 225 mg glycerin	All water soluble; 1 g carbohydrate	All water soluble; 1 g carbohydrate	All water soluble	775 mg sugar
Manufacturer	Aptalis Pharma http://www.aptalispharma.com	Shear/Kershman Labs, http://www.cfservicespharmacy.com/	SourceCF Inc., http://www.sourcecf.com	Aptalis Pharma http://www.aptalispharma.com	Aptalis Pharma http://www.aptalispharma.com	Shear/Kershman Labs http://www.cfservicespharmacy.com/	SourceCF Inc. http://www.sourcecf.com	SourceCF Inc. http://www.sourcecf.com

Table 19–6 Vitamin Dosing Suggestions for Treating Malabsorption

Age	Recommended Supplements	Alternative Option[a]
0–12 mo	• 1 mL AquADEK or 1 mL VITAMAX or 1 mL SourceCF drops daily • If ADEK or VITAMAX drops: 2.5 mg/wk vitamin K or 2.5 mg 2×/wk if on antibiotics	• 40–50 IU/d vitamin E • 1 mL Poly-vi-sol® • 2.5 mg/wk vitamin K or 2.5 mg 2×/wk if on antibiotics
1–3 y (Until able to take tablets)	• 2 mL AquADEK[a]or 2 mL VITAMAX or 2 mL SourceCF drops daily • If ADEK or VITAMAX drops: 5 mg vitamin K per week or 5 mg 2×/wk if on antibiotics • If SourceCF drops: 2.5 mg/wk vitamin K or 2.5 mg 2×/wk if on antibiotics	• 80–150 IU/d vitamin E • 2 mL Poly-vi-sol • 5 mg vitamin K per week or 5 mg 2×/wk if on antibiotics
4–10 y	• 2 AquADEK or 1 VITAMAX or 1 SourceCF chewable tablet or 1 AquADEK softgel 1 SourceCF softgel daily • 400 IU vitamin D (not necessary with SourceCF chewable)	2–3 y: • 80–150 IU vitamin E gel cap • 2 Children's multivitamin with minerals • 5 mg Vitamin K per week or 5 mg 2×/wk if on antibiotics

Age	Recommended Supplements	Alternative Option[a]
	• If ADEK or VITAMAX: 5 mg vitamin K per week or 5 mg 2×/wk if on antibiotics	4–10 y: • 100–200 IU vitamin E gel cap • 2 Children's multivitamin with minerals • 5 mg Vitamin K per week or 5 mg 2×/wk if on antibiotics
>10 y	• 2 AquADEK or 2 SourceCF softgels daily or 2 VITAMAX chewable tablets daily • If ADEK or VITAMAX: 5 mg vitamin K per week or 5 mg 2×/wk if on antibiotics	• 200–400 IU vitamin E gel cap • 2 Standard multivitamin (MVI) with minerals • 5 mg Vitamin K per week or 5 mg 2×/wk if on antibiotics

[a]Alternative options do not provide the same amount of vitamins as the CF-specific vitamins.

Table 19–7 Assessment and Treatment of Fat-Soluble Vitamin Deficiencies

	Vitamin Assessment	Therapy if Deficiency	Considerations
A	Normal: >20 µg/dL Marginal stores: 10–19 Deficient: <10	Severe deficiency with xerophthalmia <6 mo old: 50,000 IU PO QD × 2 d, then again at 2 wk 6–12 mo: 100,000 IU PO QD × 2 d, then again at 2 wk	Serum level is not a good indicator of liver stores. Low in chronic infection, liver disease, or during an acute phase response.

(*Continued*)

Table 19–7 Assessment and Treatment of Fat-Soluble Vitamin Deficiencies (*Continued*)

	Vitamin Assessment	Therapy if Deficiency	Considerations
		>12 mo: 200,000 IU PO QD × 2 d, then again at 2 wk >8 y and adults: 200,000 IU PO every 4–6 mo or 100,000 IU IM QD × 3 d, then 50,000 units/d × 14 d, then 10,000–20,000 units/d × 2 mo Continue vitamin A supplementation guidelines for CF (Table 19–3) after treatment of deficiency.	Check retinol-binding protein (RBP) circulation in plasma. Assess toxicity by using molar ratio of retinol to RBP: retinol (μg/dL) × 0.0349 = μmol/L RBP (mg/dL) × 0.476 = μmol/L Molar ratio should be between 0.8 and 1.0. Ratios >1.0 suggest increased levels of free retinol and possible toxicity.
D	25-OHD: Normal: 9–75 ng/mL (in CF prefer >30 ng/mL)	See Table 19–8 for therapy if <30 ng/mL	Low in die-tary deficiency, decreased absorption, UV light deficiency, prematurity, liver disease, and with certain drugs (anticon-vulsants). Higher in summer. Watch for hyper-calcemia and hypercalciuria and other signs of toxicity.

	Vitamin Assessment	Therapy if Deficiency	Considerations
E	Deficiency if plasma level <6 mg/L Vitamin E:total lipid ratio <0.6–0.8 mg/g in adults than serum levels Vitamin E:chol + triglyceride (TG) <1.59 μmol/mmol Do not give with medications that interfere Erythrocyte hemolysis >10%	1 unit/kg/d of water-miscible form plus usual vitamin E supplementation until normal blood levels. 1 unit = 1 mg *dl*-α-tocopherol acetate. Continue vitamin E supplementation guidelines for CF (Table X–3) after treatment of deficiency.	Carried exclusively on plasma lipoproteins thus vitamin E:total lipid ratio or vitamin E:chol + TG is a better indicator of stores than serum levels. Total lipids = cholesterol + TG + phospholipids. Conversions: Chol (mg/dL) × 0.0259 = chol (mmol/L) TG (mg/dL) × 0.0113 = TG (mmol/L) Vitamin E (mg/L) × 2.32 = vitamin E (μmol/L). Do not give with medications that interfere with vitamin E absorption (vitamin A, cholestyramine, and antacids)
K	Prothrombin time (PT) deficiency if >13.5 s	Infants and children: 1–2 mg single I.M., S.C., or I.V. dose 2.5–5 mg PO/24 h	Deficiency in malabsorption, long-term antibiotic therapy

(*Continued*)

Table 19–7 Assessment and Treatment of Fat-Soluble Vitamin Deficiencies (*Continued*)

	Vitamin Assessment	Therapy if Deficiency	Considerations
	PIVKA-II: deficiency if <3.0 ng/mL	Adults: 10 mg single I.M., S.C., or I.V. dose 2.5–25 mg PO/24 h Continue vitamin E supplementation guidelines for CF (Table X–3) after treatment of deficiency.	Deficiency in malabsorption, long-term antibiotic therapy

Source: Adapted from *Lexi-Comp Online™*[45] and Thurnham et al.[46]

Vitamin K is important for both blood clotting and bone formation. Since serum vitamin K levels do not reflect vitamin K stores, vitamin K has traditionally been evaluated indirectly via plasma prothrombin concentrations (PT). If PT is prolonged, then supplementation would be recommended. The protein induced by vitamin K absence/antagonist-II (PIVKA-II) is a more sensitive indicator of vitamin K status and is considered the gold standard for assessing vitamin K status.[2] There are no specific guidelines currently, but supplementation usually ranges from 2.5 to 10 mg given twice weekly to daily. Additional vitamin K may be required with CF liver disease and/or prolonged antibiotic use.[14]

Vitamin D status has become a topic of interest in the CF population due to the mounting literature indicating that 50%–70% of adults with CF have low bone mineral density.[17] Development of bone disease in CF is multifactorial; however, vitamin D malabsorption is postulated to play a large role in the development of low bone mineral density. Serum 25(OH) D remains the optimal form of measurement of vitamin D status. Vitamin D deficiency is defined as a serum 25(OH) D level

<20 ng/mL. Concentrations between 20 and 29 ng/mL indicate vitamin D insufficiency, and optimal concentrations are between 30 and 60 ng/mL.[18] Concentrations higher than 150 ng/mL may induce symptoms of vitamin D toxicity, which include hypercalcemia, nausea, vomiting, fatigue, and weakness.[19] New recommendations set forth by CFF recommend cholecalciferol over egrocalciferol for the treatment of vitamin D insufficiency/deficiency in CF.[20] Additional new recommendations include measuring 25(OH) D annually during the winter months, and rechecking 25(OH)D 3 months after increasing dosage in order to treat levels lower than 30 ng/mL.[20] Updated recommendations for vitamin D supplementation and stepwise treatment of low vitamin D status are summarized in Table 19–8.

Water-soluble vitamin requirements can be met through diet and through supplementation with one or two daily multivitamins. A high-sodium diet is recommended for patients with CF.[2] Additional salt supplementation is required during hot weather or during periods of increased sweating (see Table 19–3). Given the relatively low amounts of sodium in breast milk and infant formulas and foods, infants with CF should receive 2–4 mEq/kg of sodium/d added to formulas or to the applesauce used to give enzymes. From birth to 6 months of age ⅛ tsp (13 mEq) of salt should be given daily,

Table 19–8 Stepwise Therapy for Vitamin D Deficiency

Age	Routine Supplementation in Combination with CF-Specific Vitamins	Step 1 if 25(OH)D <30 ng/mL Recheck 3 mo After Dose Increase	Step 2 if Still <30 ng/mL Recheck 3 mo After Dose Increase	Step 3 if Still <30 ng/mL
0–12 mo	400–500 IU/d	800–1000 IU/d	Not >2000 IU/d	Refer to endocrinologist
>12 mo to 10 y	800–1000 IU/d	1600–3000 IU/d	Not >4000 IU/d	Refer to endocrinologist
>10–18 y	800–2000 IU/d	1600–6000 IU/d	Not >10,000 IU/d	Refer to endocrinologist

Source: Adapted from Tangpricha et al.[21]

and ¼ tsp (26 mEq) of salt should be given daily to infants over 6 months of age (as long as the infant is on the growth curve for a 6-month-old infant).[21]

ANTIOXIDANTS

Individuals with CF often have low blood levels of antioxidants including vitamin E and beta carotene. In addition, airway infections lead to progressive damage of the lungs, in part due to oxidative stress. Studies have evaluated the impact of additional supplementation of vitamins E and C, selenium, and beta carotene on CF lung disease and found evidence both for and against this practice. Serum levels of antioxidants improved with supplementation; however, there was no improvement in lung function. Currently, antioxidant supplementation is not recommended in CF beyond routine care.[22]

BONE HEALTH

Patients with CF have an increased risk of developing osteoporosis in adulthood and after lung transplantation.[23] The increase in life span of patients with CF has also brought about new consequences for those patients who survive into adulthood. One of the most common complications is low bone mineral density, which occurs in 50%–70% of adults with CF.[24] Recent evidence from pediatric studies in patients with CF suggests that low bone mineral density may begin in childhood. In the pediatric population, osteopenia is defined as bone mineral density that falls one standard deviation below normal. Osteoporosis is defined as bone mineral density that falls two or more standard deviations below normal. Osteopenia is found in 28% and osteoporosis is found in 10%–34% of children with CF.[25] Bone disease in CF is multifactorial and may be due to a range of issues including altered sex hormone production, inflammation, physical inactivity, glucocorticoid therapy, malnutrition, low calcium intake, and malabsorption of vitamin D.[26]

Recommendations for the management of CF-related bone disease include increased weight-bearing exercise and supplementation with calcium, vitamin D, and vitamin K. More research is needed to determine the best method of treatment for CF-related bone disease.[24] Table 19–9 provides guidelines on the diagnosis and treatment of bone disease in CF.

Table 19–9 Nutritional Recommendations for Prevention and Treatment of Bone Disease in Cystic Fibrosis

- Screen children >8 y old with risk factors and adults for bone disease by DXA. If bone mineral density (BMD) is normal, rescreen every 5 y or sooner if change in risk factors: IDW <90% or BMI <25th percentile, FEV1 <50%, glucocorticoids >5 mg/d for >90 d out of the year, delayed puberty, or a history of fractures.

Normal: Children: Z score = 0 ± 1 SD

Adults: T score = 0 ± 1 SD

Moderate demineralization = T score or Z score between −1.0 and −2.0; repeat DXA every 2–4 y

Severe demineralization = T score or Z score <−2.0; repeat DXA yearly

- Weight: Maintain at ≥90% IBW or ≥25th percentile BMI
- Calcium: At least the DRI/age
- Vitamin D: Monitor annually in all age groups (at the end of the winter months). Supplement to achieve a serum 25-OHD >30 ng/mL.
- Vitamin K: 0.3–0.5 mg vitamin K per day
- Other minerals: At least the DRI for magnesium, zinc, and copper
- Exercise: Foster weight-bearing exercise
- Medications: pamidronate and IV bisphosphonate under study in adults with CF. No data in children.

Abbreviation: DXA = dual-energy x-ray absorptiometry.

[a]Use of Z scores is recommended in children 18 years and under.

Source: Adapted from Sermet-Gaudelus et al.[24] Joseph, Patrick. Screening for CF Bone Disease. Pediatric Pulmonology Supplement 24, 2002 p 178–179.

Appetite Stimulants

Inadequate energy intake can lead to malnutrition in CF. Evidence has shown that an individual's nutritional status is a predictor of survival, and lung function is closely associated with nutritional status in CF. Even with this knowledge, a large portion of individuals with CF are unable to achieve this goal. When other causes of poor appetite have been ruled out and treated, appetite stimulants may be used to help an individual achieve better nutritional status. Other causes of poor appetite include, but are not limited to, pulmonary exacerbation, pain from malabsorption, constipation, distal intestinal obstructive syndrome (DIOS), zinc deficiency, hyponatremia, depression, eating disorders, CFRD, sinusitis/nasal polyps, delayed gastric emptying, and gastroesophageal reflux disease.

A number of agents that increase appetite have been used in CF, including megestrol acetate (MA), cyproheptadine hydrochloride (CH or Periactin®), Dronabinol (Marinol®), Remeron®, and oxandrolone. Remeron and oxandrolone are not typically used in the pediatric population. CH is an antihistamine with a secondary side effect of appetite stimulation, but some individuals have reported experiencing fatigue and irritability. This medication is commonly used cycled (i.e., 3 weeks on and 1 week off) and is normally well tolerated. MA is an endocrine/metabolic agent that is used as a treatment for cachexia, but it is not used as often as it once was due to the side effects of adrenal suppression. Finally, Dronabinol is an antiemetic and Cannabinoid that has the side effects of fatigue, euphoria, anxiety, and decreased mental alertness. It is dosed at 2.5–5 mg twice daily and is thought to be safe and effective without concerns over dependence.[27]

BEHAVIORAL/FEEDING EVALUATION

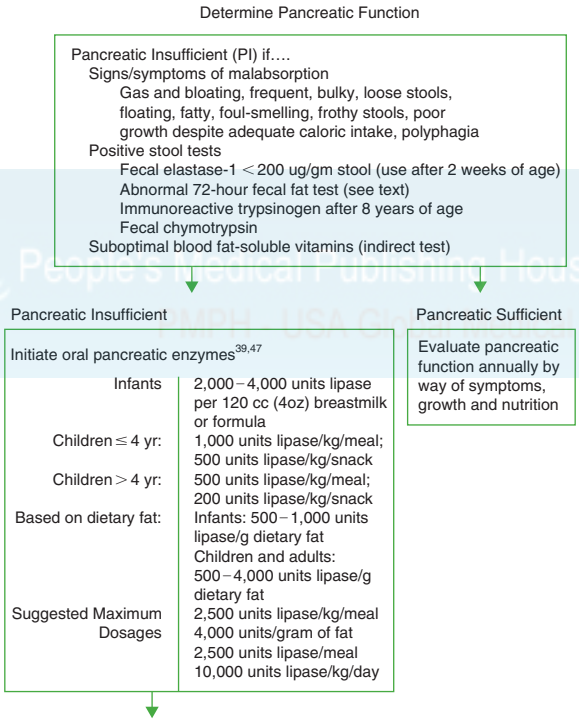
Problematic child mealtime behaviors and inappropriate parental reactions and feeding strategies occur with a higher frequency in families with CF than in children without chronic health issues.[28] Caregivers of children with CF report more disruptive child feeding behaviors and inappropriate parental responses to these behaviors than normal controls, even well into late childhood and adolescence.[29] A randomized, controlled trial in children with CF compared the effect of behavioral intervention with nutrition education to nutrition education alone and found that although both groups had improvement in caloric intake and BMI z-score, the group that received both behavioral intervention and nutrition education had a significantly greater increase in both calorie intake and BMI z-score. Interestingly, after 24 months both groups were able to maintain the increased caloric intake of 120% of the DRI for age.[30] Another trial compared an intensive behavioral nutrition intervention to the standard of care and found that the intervention group had significantly less decline in BMI z-score than the group receiving the standard of care.[31] Therefore, for children with poor growth CFF recommends intensive behavioral intervention in combination with nutrition counseling in order to facilitate weight gain (see Chapter 26 for guidelines on conducting a behavioral evaluation).

PANCREATIC INSUFFICIENCY AND PANCREATIC ENZYMES

Diagnosis

According to the 2010 CF patient registry, about 86% of the CF population receives exogenous pancreatic enzyme

therapy.[1] Guidelines for diagnosing and treating pancreatic insufficiency in CF and administering enzymes are offered in Figure 19–1. The fecal elastase-1 test is considered a highly sensitive and specific way to indirectly measure severe



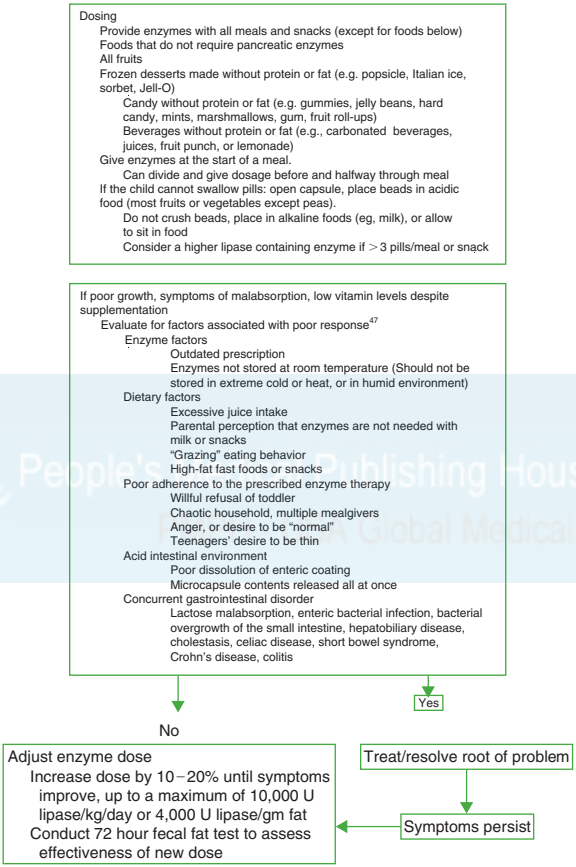


Figure 19–1: Dosing and adjusting pancreatic enzyme treatment in cystic fibrosis.[47]

exocrine pancreatic insufficiency (PI) in CF but may not be as useful in mild PI or in cases of intestinal disease.[32] It should be used in consideration of these factors.

Pancreatic Enzyme Dosing

Individuals with pancreatic insufficiency take oral pancreatic enzymes to aid in absorption and digestion. Enzyme dosages usually are prescribed in units of lipase per kilogram of body weight per meal or snack. Alternatively, the enzyme dosage can be titrated based on units of lipase per gram of fat consumed (Figure 19–1). The dosage is thereafter titrated based on symptoms of steatorrhea and/or coefficient of absorption (see below). Enzymes available in the United States are listed in Table 19–10. Generic enzymes may not be equivalent to brand enzymes and, therefore, should not be used.[33] Prescription pancreatic enzymes predated the 1938 Food, Drug, and Cosmetic Act and were previously exempt from the obligation of obtaining Food and Drug Administration (FDA) approval; however, FDA now requires that all pancreatic enzyme manufacturers obtain FDA approval for their products. Since even brand name enzymes were found to have variable potencies, the aim of this action is to ensure accurate labeling and more standardization of enzyme potency and perhaps more effective management of pancreatic insufficiency. Currently, six brands of enzymes have obtained FDA approval: Creon® manufactured by Abbott, Zenpep®, Ultresa®, and Viokace® manufactured by Aptalis, Pancreaze® manufactured by Janssen Pharmaceuticals, Inc., and Pertzye® manufactured by Digestive Care, Inc.[34–36]

Fibrosing colonopathy is an inflammatory condition of the large intestine of unclear etiology; it has, however, been associated with the ingestion of high dosages of pancreatic enzymes. In one study the median daily dosage of patients with fibrosing colonopathy was 50,000 units of lipase/kg/d,

Table 19–10 Enteric-Coated Pancreatic Enzymes

Enzyme	Company	Bead Size (mm)	Optimal Dissolution pH	Lipase USP Units	Protease USP Units	Amylase USP Units
Creon 3	Abbott	<1.7	<5.5	3,000	9,500	15,000
Creon 6	Abbott	<1.7	<5.5	6,000	19,000	30,000
Creon 12	Abbott	<1.7	<5.5	12,000	38,000	60,000
Creon 24	Abbott	<1.7	<5.5	24,000	76,000	120,000
Pancreaze MT4	Janssen Pharmaceuticals, Inc.	<3	<5.5	4,200	10,000	17,500
Pancreaze MT10	Janssen Pharmaceuticals, Inc.	<3	<5.5	10,500	25,000	43,750
Pancreaze MT16	Janssen Pharmaceuticals, Inc.	<3	<5.5	16,800	40,000	70,000
Pancreaze MT 21	Janssen Pharmaceuticals, Inc.	<3	<5.5	21,000	37,000	61,000
Zenpep (3)	Aptalis	1.8–1.9	<5.5	3.000	10,000	16,000
Zenpep (5)	Aptalis	1.8–1.9	<5.5	5,000	17,000	27,000

(*Continued*)

Table 19–10 Enteric-Coated Pancreatic Enzymes (*Continued*)

Enzyme	Company	Bead Size (mm)	Optimal Dissolution pH	Lipase USP Units	Protease USP Units	Amylase USP Units
Zenpep (10)	Aptalis	2.2–2.5	<5.5	10,000	34,000	55,000
Zenpep (15)	Aptalis	2.2–2.5	<5.5	15,000	51,000	82,000
Zenpep (20)	Aptalis	2.2–2.5	<5.5	20,000	68,000	109,000
Zenpep (25)	Aptalis	2.2–2.5	<5.5	25,000	85,000	136,000
Ultresa 13,800	Aptalis	2–2.4	<5.5	13,800	27,600	27,600
Ultresa 20,700	Aptalis	2–2.4	<5.5	20,700	41,400	41,400
Ultresa 23,000	Aptalis	2–2.4	<5.5	23,000	46,000	46,000
Viokace 10,440	Aptalis	Tablet	<5.5	10,440	39,150	39,150
Viokace 22,880	Aptalis	Tablet	<5.5	22,880	78,300	78,300
Pertzye 8,000[a]	Digestive Care, Inc.	0.8–2.2	<5.5	8,000	28,750	30,250
Pertzye 16,000[a]	Digestive Care, Inc.	0.8–2.2	<5.5	16,000	57,500	60,500

[a]Bicarbonate-buffered enteric-coated microspheres.

but dosages as low as 4900 U/kg/d were also associated with this condition.[36] Maximum dosages of 2500 units of lipase/kg/meal and 10,000 units of lipase/kg/d are now recommended, although it is recognized that some CF patients will require higher dosages to adequately treat signs and symptoms of malabsorption.[38] See Figure 19–1 for specific dosage guidelines.

Administration

Pancreatic enzyme products contain enteric-coated microencapsulated enzymes. The enteric coating prevents the inactivation of enzymes in the acidic environment of the stomach. Once in the higher pH of the upper small intestine, the enteric coating breaks down and the enzymes are released. Bicarbonate production may be poor in CF and lead to an abnormally acidic pH in the duodenum, reducing enzyme effectiveness. Acid blockers may be prescribed to reduce stomach acid production in the upper small intestine.

Enzymes should be taken at the beginning of each meal and snack. In infants and children who cannot swallow capsules, beads may be placed in applesauce or another acidic food and given with a spoon.[39] It is important to sweep the infant's mouth and chin for enzyme beads, as they can cause skin and mouth irritation. Foods that do not require pancreatic enzymes include popsicles, fruit snacks, and fruit juice. However, these foods are typically low in energy and nutritional value and should be discouraged.

ASSESSING ABSORPTION

Stool energy loss can be significant in CF. Malabsorption can be in the range of 5%–20% of gross energy intake, even in the presence of pancreatic enzyme replacement (compared to <5% among healthy children). The 72-hour fecal fat test is

considered the gold standard for assessing fat malabsorption and is conducted as follows:

1. Collect stools for 72 hours. Freeze stool.
2. Collect concomitant 3-day food record. Calculate average fat intake (in grams). Goal intake is 2–3 g fat/kg/d.
3. Calculate coefficient of fat absorption (COA):

$$\frac{\text{Grams of fat consumed} - \text{grams of fat excreted}}{\text{Grams of fat consumed}} \times 100 = \text{COA}$$

4. Normal COA: premature infants: 60%–75%; newborns: 80%–85%; 10 months to 3 years: 85%–95%; >3 years: 95%.
5. Considerations: notify the lab if the patient is using MCT. Discontinue mineral oil before starting the test.

BREAST-FEEDING AND INFANT FORMULAS

Human breast milk with appropriate enzyme replacement therapy is optimal for infants with CF[40]; otherwise, commercial formulas can be used. The choice of infant formula will depend on the child's nutritional and medical status. Infants who undergo gastrointestinal surgery may require temporary use of a semi-elemental or elemental formula if intolerance to conventional formula develops. Elemental formulas, however, are neither necessary nor recommended for routine nutritional care of an infant with CF.[41] All formulas, including semi-elemental ones, require pancreatic enzymes. The amount of pancreatic enzymes to administer will vary with the fat type and content in the formula

ORAL NUTRITION SUPPLEMENTS

Due to increased energy needs, it can be difficult for people with CF to consume enough calories to promote weight

gain and optimal growth. Typically, the first step in nutrition intervention is to add calorically dense foods to the diet.[2] Additionally, a variety of commercially available oral nutrition supplements may be utilized to help meet calorie needs; however, few oral supplements are specifically designed for the needs of patients with CF.[2] Patients with CF using oral supplements should be monitored to make sure that the supplements complement the intake of regular food rather than replacing it.[2] Pancreatic enzymes are required for oral nutrition supplements (see Chapter 14 for supplement selection).

TUBE FEEDING

When oral intake fails to achieve weight gain, enteral feedings should be initiated as a therapy to support weight gain.[3] However, the concept of tube feeding should be introduced to patients and families early, even when the child may not require tube feeding. Enteral feeding should be presented in a positive manner, as a realistic option for meeting the child's nutritional needs. There are no standard guidelines for when to initiate enteral nutrition support in CF. The decision to initiate enteral feeds should be individualized based on patients' nutritional status, their ability to meet nutrient needs by mouth, and their willingness to initiate or accept more aggressive nutritional support. Overnight tube feedings are recommended in order to promote oral intake during the day. Tube feedings should provide between 30% and 50% of a patient's estimated energy needs[2] (see Chapter 14 for guidelines on formula selection and administration).

ENZYME ADMINISTRATION WITH TUBE FEEDING

Pancreatic enzymes are required for all formulas. Elemental and semi-elemental formulas may require a smaller dose

of pancreatic enzymes. No consensus exists on enzyme administration with tube feeding. Empirically, the general recommendation is to give a meal dose of enzymes at the beginning of the feed and a meal dose at the end of the feeding. It is ideal to give a dose midway through the tube feeding; however, this often proves to be an impractical option for patients and families. Enzymes may also be dosed based on the fat content of the formula (Figure 19–1). It is preferable to take enzymes by mouth with tube feedings. There are several suggested methods for administering enzymes with tube feedings if a patient is unable to take the capsules orally, although most methods have not been well studied.

For duodenal or jejunal feeds, pancreatic enzymes may be administered by using an activated enzyme solution, and mixed directly with formula prior to infusion. To make the activated enzyme solution, enteric coated enzymes beads should first be crushed to remove the enteric coating. Next, the crushed enzymes should be mixed with sodium bicarbonate. For every 10,000 units of lipase, about 10 mL of an 8.4% sodium bicarbonate is needed to make the solution. Of note, if the enzyme beads are not crushed prior to mixing with sodium bicarbonate, it will take approximately 20 minutes for the enteric coating to spontaneously dissolve.[44]

For gastric tube feeds, one method of providing pancreatic enzymes with tube feedings involves opening the capsules, placing beads in baby food with pH < 4.5, allowing the mixture to sit for 35–45 minutes, and drawing the mixture up with a syringe and pushing through the g-tube. In order to determine whether this method caused tube clogging and if lipase activity was affected, an in vitro study was carried out using CREON enzymes (all dosages). Results showed that when using baby foods with a pH less than 4.5, lipase activity remained >90%, indicating that there was no loss of

lipase activity. There was no damage to tubes, clogging, or damage to enzyme pellets when using Kimberly Clark MIC bolus size 18 French and larger, Kimberly Clark MIC-KEY 16 French and larger, Bard Tri-Funnel 18 French and larger, and Bard Button 18 French and larger.[43] Another method that is proposed to reduce tube clogging is to suspend the enzyme beads in a nectar-thickened fruit juice and push that mixture through the tube.[44]

CONCLUSION

The relationship between nutrition and CF is well defined. Individuals with CF benefit from early and aggressive nutritional intervention to prevent malnutrition and to ensure longer and healthier lives.

EDUCATIONAL MATERIALS

CFF offers a number of educational materials for patients and families on their website: http://www.cff.org/LivingWithCF/StayingHealthy/

- Nutrition fact sheets addressing various stages of life from infant to toddler, child, teenager, and adult have been endorsed by the CF Foundation Education Committee
- *Managing Cystic Fibrosis-Related Diabetes (CFRD). An Instruction Guide For Patients and Families*. Cystic Fibrosis Foundation; 5th edition.

Cystic Fibrosis Foundation website: www.cff.org

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20 Developmental Disabilities

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Developmental disabilities (DD) are conditions characterized by physical, cognitive, psychological, sensory, adaptive, and/or communication impairments manifested during development.[1] Children with chronic diseases and/or developmental disorders, also referred to as children with special health care needs (CSHCN), require sound nutrition for growth and development, but have more frequent nutritional risk factors, which may pose challenges (Table 20–1). Oral motor and feeding difficulties are common in children with DD and will be addressed in Chapter 22, Dysphagia and Feeding/Swallowing Difficulties.[2,3]

SPECIAL ASPECTS OF NUTRITIONAL ASSESSMENT AND MANAGEMENT

History

There should be a complete review of birth, medical, and feeding history to determine the potential effects of long-term hospitalizations, surgeries, and medical procedures (i.e., intubation and supplemental tube feedings) on overall development as well as on oral feeding and feeding skill development. Early

Table 20–1 Nutritional Risk Factors for Children with Developmental Disabilities

Altered Growth
Obesity (Prader–Willi, Laurence–Moon–Biedl, Carpenter, Down syndromes)
Failure to thrive (Rett syndrome, athetoid CP)
Short stature (Down, Hurler, Russell–Silver, Cornelia de Lange syndromes)
Gastrointestinal Symptoms
Diarrhea
Constipation
Vomiting/gastroesophageal reflux
Oral Motor Difficulties
Discoordination of suck/swallow
Structural abnormalities (cleft lip/palate; dentition)
Poor oral containment (food/fluid loss)
Tone abnormalities (hypo/hypertonic)
Altered oral sensory response (hypo/hyperresponsive)
Delayed oral motor skill development
Aspiration
Altered Nutrient Needs/Nutrient Deficiencies
Drug–nutrient interactions (anticonvulsants, diuretics, laxatives, tranquilizers)
Restricted intake (metabolic disease, food allergies, food texture aversion)
Inadequate intake (poor appetite, poor oral motor control, malabsorption)
Increased calorie requirement (athetoid CP, spasticity)
Inadequate fluid intake
Behavior
Oral aversion
Pica
Rumination
Hyperactivity

Distractibility
Perseverative behaviors
Binge eating/overeating
Positioning for Feeding
Adaptive seating devices
Feeding Skill Development
Self-feeder versus dependent feeder
Adaptive feeding equipment

Abbreviation: CP = cerebral palsy.

medical/feeding history can provide information regarding development of feeding problems such as oral aversion.

Growth Assessment

Obtaining accurate weight, length/height, and head circumference measurements and plotting serial points over time can provide critical information on adequacy of growth. Growth should be plotted on the Centers for Disease Control and Prevention (CDC) and/or World Health Organization (WHO) growth charts as well as specialized syndrome-specific growth charts if available. Specialized growth charts are currently available for achondroplasia, cerebral palsy (CP) (quadriplegia), Down syndrome, Marfan syndrome, myelomeningocele, Noonan syndrome, Turner syndrome, Prader–Willi syndrome, Williams syndrome, and sickle cell disease (see Appendix 3).[1,2] The specialized charts do have some limitations because of the small sample size they were based on. Therefore, it is best to use the specialized charts as an additional tool for growth assessment along with the CDC/WHO growth charts. Accurate measurement of linear growth in children with DD may be compromised by the presence of contractures, scoliosis, kyphosis, or the inability to stand. Alternative methods of linear measurement include

crown-rump length or sitting height, arm span, tibial length, or segmented body length.[4,5] However, use of these methods may also be compromised by contractures and/or scoliosis.

It is not uncommon for children with DD to be small for their age, with growth parameters below the 5th percentile on standard growth charts.[2] Assessment of weight-for-length/height is especially important in this population, as it indicates individual proportionality, which is often a more appropriate way to evaluate adequacy of growth in children with DD. It is also important to note that alterations in head circumference (micro/macrocephaly) can skew the weight-for-age and weight-for-length parameters. Alterations in body composition with regard to muscle mass and body fat stores also impact the growth assessment. Children with DD may differ from typically developing children in body composition. Because lean muscle mass is a major determinant of resting energy expenditure, the use of measurements such as tricep skinfolds and subscapular skinfolds can aid in nutrition assessment and the development of care planning.[6]

Alterations in activity level will also have an impact on weight goals. For nonambulatory individuals, weight-for-length of 10th–25th percentile is generally an acceptable goal. In nonmobile individuals, additional weight is often accumulated as increased fat stores rather than muscle mass. Excessive weight can compromise care in terms of cardiorespiratory health as well as ease of transfers (bed, bath, and wheelchair) and progression with gross motor skills. Given all of these considerations, a visual clinical assessment, in conjunction with growth history, is essential when assessing adequacy of growth in children with DD.

Nutrient Requirements

Energy. Calorie requirements may be assessed in several ways: (1) calories per centimeter of body height/length

(Table 20–2); (2) catch-up growth equations using height age instead of weight age; or (3) standardized equations using Estimated Energy Requirements (EER) or WHO equations.[1] The WHO equation can be helpful in situations where a linear measurement is difficult to obtain, since height is not a component of the calculation. It is important to note, however, that these methods are merely *guidelines* and that individual calorie requirements should be assessed based on changes in weight over time and/or measurement of basal metabolic rate, if possible. Therefore, regular

Table 20–2 Guidelines for Estimating Caloric Requirements in Children with Developmental Disabilities

Condition	Caloric Recommendation
Ambulatory, ages 5–12 years	13.9 kcal/cm height
Nonambulatory, ages 5–12 years	11.1 kcal/cm height
Cerebral palsy with severely restricted activity	10 kcal/cm height
Cerebral palsy with mild to moderate activity	15 kcal/cm height
Athetoid cerebral palsy, adolescence	Up to 6000 kcal/d
Down syndrome, boys ages 5–12 years	16.1 kcal/cm height
Down syndrome, girls ages 5–12 years	14.3 kcal/cm height
Myelomenigocele	Approximately 50% of RDA for age after infancy; may need as little as 7 kcal/cm height
Prader–Willi syndrome	10–11 kcal/cm height for weight maintenance; 8–9 kcal/cm height for weight loss

Abbreviation: RDA = recommended dietary allowance.

weight monitoring is an essential component in managing children with DD. Calorie requirements may be as low as 5 kcal/cm of height in children with severe central nervous system impairment.[5]

Catch-up growth equations using height age (Height age is defined as the age which corresponds to the child's height when plotted at the 50th percentile on the growth chart):

$$\text{Energy (kcal/kg/day)} = \frac{\text{IBW (kg)} \times \text{RDA for Height Age (kcal/kg/day)}}{\text{Actual Weight (kg)}}$$

$$\text{Protein (g/kg/day)} = \frac{\text{IBW (kg)} \times \text{RDA for Height Age}}{\text{Actual Weight (kg)}}$$

Ideal Weight for Height = 50th percentile weight for measured height on appropriate growth chart.

Protein. Protein requirements are estimated using recommended dietary allowance (RDA) for chronological age or height age if growth parameters are significantly below chronological age.[1]

Vitamins/Minerals. The most common nutrient deficiencies seen in children with DD are vitamins A, C, and D and folate as well as iron and calcium.[4]

Fluid. Fluid requirements may be higher than normal in some children with DD due to constipation, increased fluid losses (drooling and excessive sweating), and/or increased requirements. Standard guidelines for fluid based on body weight should be followed, with adjustment for special considerations as noted above (see Table 15–2, "Fluid Requirements").

Drug–Nutrient Interactions. Some children with DD are on multiple medications that can interfere with nutrient absorption, appetite, elimination patterns, and level of alertness for feeding. For example, children with seizures

who are on multiple anticonvulsant medications should be monitored for adequate vitamin D and folic acid intake as requirements for these nutrients are increased with some seizure medications (e.g., phenytoin [Dilantin]). Also, some medications can contribute to constipation, which often inhibits appetite. Due to the potential for inadequate diet intake, drug–nutrient interactions and possible decreased mobility, and laboratory values that reflect iron, protein, vitamin D, calcium, and phosphorus status should be monitored on a regular basis (see Appendix 2).

Developmental Disabilities with Nutrition and Feeding Concerns

Down syndrome, CP, attention deficit hyperactivity disorder (ADHD), and autism are four common forms of DD with distinct nutrition and feeding concerns.

DOWN SYNDROME

Down syndrome is a chromosomal anomaly resulting from trisomy of chromosome 21 and is associated with a number of medical concerns (Table 20–3). The incidence

Table 20–3 Medical Diagnoses Associated with Down Syndrome

Cardiac anomalies
Intestinal malformations (e.g., duodenal atresia, Hirschsprung's disease)
Celiac disease
Increased incidence of infections (ear, respiratory)
Endocrine (diabetes, hypothyroidism)
Orthopedic (atlantoaxial instability, hip dislocation)
Dental (delayed/missing dentition)
Increased risk of leukemia
Hearing loss

is reported to be 1 in 700 live births, with increasing incidence with increased maternal age. Approximately 40%–60% of children with Down syndrome are born with congenital heart defects, and 8–12% are born with gastrointestinal malformations. In addition, they are at risk for other medical complications that can have an effect on their nutritional status as well as their overall development.[7]

SPECIAL ASPECTS OF NUTRITIONAL ASSESSMENT

History

A medical and feeding history should be obtained to identify issues that may impact growth and feeding (Tables 20–4 and 20–5).

Growth

Down syndrome growth charts should be used to plot growth (Appendix 2) in conjunction with the CDC growth

Table 20–4 Nutritional Risk Factors Associated with Down Syndrome

Poor weight gain (cardiac anomalies, recurrent infections, hypothyroidism)
Short stature
Obesity
Constipation (hypotonia, hypothyroid, fluid loss)
Delayed oral motor skill development
Delayed feeding skill development
Selective intake
Reduced activity (hypotonia, orthopedic concerns)
Behavior difficulties

Table 20–5 Common Oral Motor Feeding Difficulties Associated with Down Syndrome

Weak lip seal on nipple (fluid loss)
Tongue protrusion/thrust
Delayed chewing (secondary to delayed dentition and/or prolonged tongue thrust)
Difficulty with texture transition
Difficulty with thin liquids (increased fluid loss and coughing/sputtering)

charts. Body mass index should be plotted on the CDC chart as this parameter is not available on the Down syndrome growth chart.

Nutrient Requirements

Energy. Given the short stature inherent to Down syndrome, calorie requirements for children with Down syndrome aged 5–12 years should be based on body height rather than body weight to avoid overestimating calorie requirement (Table 20–2).[8] It is important to note that obesity is a significant nutritional risk factor for children with Down syndrome, with approximately 25% being affected.[7] Prevention should therefore be the focus by promoting healthy eating habits early on and avoiding use of food as a reward for good behavior.

Protein. Protein requirements for children with Down syndrome should be assessed using the RDA based on sex and age.

Vitamins/Minerals. There is much controversy surrounding variations in vitamin and mineral requirements for children with Down syndrome. Studies to date have not

shown consistent or rigorous proof that any form of nutritional supplementation improves the outcome in Down syndrome. Some children with Down syndrome may consume a limited dietary variety due to a number of issues, including oral motor difficulty. One study showed that 80% of the children in the study had problems related to food intake or feeding, including excessive calorie intake and low intakes of iron, calcium, vitamin C, and fluid.[7] If dietary intake is limited due to selective food intake, a multivitamin with iron may be indicated. Supplementation with additional nutrients beyond a standard multivitamin is not recommended at this time. Children who receive supplementation at levels well above the RDA should be monitored for signs of nutrient excess (Table 3.1, "Clinical Examination in Nutritional Deficiencies and Excesses").

Fluid. Extra fluid may be indicated for children with Down syndrome who have constipation.

CEREBRAL PALSY

CP is a group of chronic, nonprogressive disorders of the nervous system that produce abnormalities of posture, muscle tone, and motor coordination. It is classified according to the specific abnormality in muscle tone (hypertonia and hypotonia) and extrapyramidal signs (choreoathetosis, ataxia, and dystonia). The estimated incidence is 2 per 1000 live births.[9] Due to their motor involvement, children with CP may have many of the feeding problems listed in Table 20–1, including poor growth and oral motor feeding difficulties due to poor oral motor control. In addition, medications commonly used to help treat spasticity, seizures, constipation, and/or gastroesophageal reflux can impact nutrient intake and feeding skills as well as behavioral state

(lethargy, distraction, and drowsiness) at mealtime. Regular monitoring of growth, diet intake, and oral motor feeding skills by a multidisciplinary team is essential to maximize growth, intake, oral motor skills, and feeding skills. Feeding evaluations should also include assessment for adaptive seating and adaptive feeding utensils to facilitate intake.

ATTENTION DEFICIT HYPERACTIVITY DISORDER

ADHD is one of the most common neurobehavioral problems exhibited in children today. An estimated 3%–7% of school-aged children have ADHD, although surveys of parents have indicated that 9.5% of children aged 4–17 years have been diagnosed with ADHD as of 2007.[10,11] Children with ADHD present with inappropriate degrees of impulsiveness, hyperactivity, and inattentiveness. Diagnosis of ADHD often occurs in the early grade school years, when rapid growth and development are still occurring. Treatment of ADHD involves medication, behavioral management, and modifying the environment at home and at school to optimize the child's potential for success.[12] Although there have been a variety of proposed alternative treatment modes for ADHD such as nutritional supplementation, dietary modifications, and homeopathy, there is no clear evidence that supports these alternative methods as effective treatment.[13] There is some evidence to support that artificial food colors and additives may exacerbate ADHD-like symptoms, not only in children with ADHD but also in normal controls.[14] Therefore, a balanced diet that includes minimal highly processed foods is encouraged. Children who are treated with stimulant medications may exhibit decreased appetite and weight loss as a side effect. Nutritional supplements and a calorically dense diet may be helpful to prevent excessive

weight loss. Timing of meals can also be altered to coincide with when stimulant medication wears off, so that optimal nutritional intake can be achieved.

AUTISM

Autism spectrum disorder is a neurodevelopmental disorder characterized by deficits in social/communication, restricted interests, and repetitive behaviors.[14] Although symptoms and severity vary, all autism disorders affect a child's ability to communicate and interact with others. Many individuals with autism also have an intellectual disability (IQ < 70), while others may have normal or above average intelligence. The etiology of autism is unclear; it is very complex and may be related to genetic and environmental problems. Children with certain medical conditions, such as fragile X syndrome, tuberous sclerosis, Tourette syndrome, and seizure disorders, have a higher than normal risk of having autism.[15] The number of children diagnosed with autism seems to be rising; it is unclear if this is due to better detection and screening, actual increases, or both.[16] In 2008, the estimated prevalence of autism spectrum disorders in the United States was found to be 11.3 per 1000 (1 in 88) children aged 8 years, of which approximately 1 in 54 boys and 1 in 252 girls were identified as having autism spectrum disorder.[17]

The primary nutrition and feeding concern in children with autism is selective intake (Table 20–6). Children with autism spectrum disorders have increased occurrences of food refusals and more limited food repertoires and could be at risk for suboptimal nutrition. The reasons for restrictive food acceptance may be due to sensory processing, ritualistic patterns of behaviors, or excessive resistance to

Table 20–6 Common Feeding Concerns for Children with Autism Spectrum Disorder

Difficulty with texture transition
Heightened sensory responses
Restricted intake due to color/brand name/presentation style/ shape or texture
Decreased selection of foods over time
Difficulty accepting new foods
Difficulty with administration of multivitamin/mineral supplement
Difficulty with changes in mealtime environment—may eat at school but not at home
Disruptive mealtime behaviors

change (insistence on same foods with extreme distress/anxiety at small changes). For some children, intake may be limited to as few as—two to three foods or beverages. Foods may be refused due to color, temperature, texture, smell, or simply because they are new.[18] Supplementation with a multivitamin with minerals in a form that the child will accept may be difficult, possibly requiring multiple trials with various forms (liquid, powder, and tablet). It is important to note that sometimes an accepted food or beverage may subsequently be refused if alterations in the taste, smell, or texture are detected when the supplement is added. Despite selective intake, adequate growth is generally seen; with the exception of late infancy/early toddlerhood when there is sometimes poor growth as a result of the transition from baby foods to table foods. Specific energy requirements for children with autism have not been established, but the RDA for age is generally used, with modifications made based on activity level. Some children with autism are quite sedentary while others are constantly active, often with self-stimulatory behavior

(e.g., spinning, hand flapping, and rocking). Many medications used to treat behavioral and anxiety symptoms of autism such as selective serotonin reuptake inhibitors (SSRIs) and antipsychotics often cause weight gain. An autistic child consuming a selective diet of mostly refined carbohydrates that limits fruit and vegetable intake is at risk for obesity and other related consequences (Table 20-7).

Table 20–7 Helpful Mealtime Strategies for Children with Autism Spectrum Disorder

Patterns of Likeable Foods

- Try to find patterns in what foods the child will eat—texture, taste, temperature, color, etc. Some children with autism avoid especially aromatic foods or foods of a certain color
- Introduce new foods that are most similar to foods that your child already enjoys
- Food chaining is a technique used to increase food acceptance and begins with a therapist analyzing the child's current feeding habits to determine which tastes, textures, temperatures are most acceptable to him or her. Those foods that the child currently tolerates remain the base of the diet, while gradually offering other foods that have similarities but are slightly different as possibly acceptable. The child is not overwhelmed with change, as this is a very gradual process, with the introduction of only one or two foods at a time[18]

Too Many Choices

- Do not offer too many types of foods in the hopes that your child will find one that is liked. Children with autism are likely to become overwhelmed by too many choices and will refuse to eat everything

New Foods

- Desensitization is a behavioral technique that can help with introducing new foods. Introduce a new food by repeatedly placing it near your child's plate at mealtime, but without encouraging your child to eat it
- Eventually have him lick it but not eat it, taste it but not eat it, then finally swallow the food. This may take several weeks

Table 20–7 Helpful Mealtime Strategies for Children With Autism Spectrum Disorder (*Continued*)

- Exposure of the new food item one or two times a day for 2–3 weeks, especially when paired with a parent or another child enjoying the new food item, sometimes will prompt a child with autism to try it

Mealtime

- Some children with autism seem unable to sit at a table during mealtimes. Some parents find that these tips help:
  - Use a visual schedule for the day that defines meals and activities (adapted for appropriate levels of functioning that uses pictures or words)
  - Planned exercise before mealtime
  - Set a timer—the expectation is that your child only needs to remain sitting for a few minutes until a timer goes off
  - Allow your child to do a quiet activity while eating or while waiting for others to finish their meals
  - Maintain a positive attitude and do not force feed

Between Meals

- Eliminate access to preferred foods throughout the day
- Not allowing grazing on foods and beverages between meals often increases intake at mealtimes and willingness to try novel food items

Different Foods

- Alternate preferred foods with less preferred foods and encourage your child to try less preferred foods by mentioning a desirable activity. Example: "First try your favorite food, A, and try a bite of B. Then you can play with your train"

Time Limit

- Plan for a specified amount of time for meals. If your child still is refusing to eat at the end of the allotted time period, end the meal without showing that you are frustrated or upset. Simply say "dinner is done" and begin to clear the table
- Do not offer any more food until the next planned mealtime

(*Continued*)

Table 20–7 Helpful Mealtime Strategies for Children With Autism Spectrum Disorder (*Continued*)

Expectations
• Children with autism often benefit from defining task expectations. An example of this is a number board to show how many bites your child should take or how many times your child should chew a food before swallowing. The numbers are then crossed off as the meal progresses, allowing your child to see a clear beginning and ending time

Due to the special feeding challenges presented by the child with autism, the nutrition and feeding assessment should be addressed by a team that includes a registered dietitian, an occupational therapist or speech therapist with training in feeding disorders, and a psychologist/psychiatrist specializing in behavioral medicine.

Perhaps because there is no cure for autism, parents are often drawn to investigate alternative therapies. Some of the current therapies parents may try include a gluten-free/casein-free diet; however, further research regarding the efficacy of these therapies is needed. It should be noted that restrictive diets can be harmful in young children. In addition, because children with autism spectrum disorders tend to be more selective eaters, further dietary restrictions may pose significant nutrition concerns.

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21 Diabetes Mellitus and Other Disorders of Carbohydrate Metabolism

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Diabetes mellitus is a chronic disease resulting from insulin deficiency or inadequate insulin utilization that occurs in both children and adults. In the United States, there are approximately 215,000 children and adolescents with diabetes. The prevalence of diabetes is about 1 in every 400 youth under the age of 20, making it one of the most common chronic childhood illnesses.[1] Diabetes occurs either when insulin is absent or insufficient or when the target tissues do not respond normally to insulin. When insulin is unavailable to allow glucose to enter the cells of the insulin-sensitive tissues, glucose accumulates in the bloodstream. High levels of glucose in the bloodstream can cause both acute and chronic complications in the body, which are discussed further in this chapter.

Type 1 diabetes is an autoimmune disease that results in the destruction of the insulin secreting beta cells of the pancreas. Symptoms of the disease do not typically present until late in the process of beta-cell destruction when a majority of the beta cells have been destroyed. Common symptoms at time

of diagnosis include polyuria, polydipsia, and weight loss. Type 1 diabetes often has its onset in children and young adults, with peak incidence occurring during early adolescence and puberty between the ages of 10 and 13.[1] Initial therapy involves medical management to correct the hyperglycemia, glycosuria, and ketonuria, which are responsible for the symptoms occurring at diagnosis. Basic management of type 1 diabetes requires exogenous insulin, most commonly provided through daily insulin injections.

Type 2 diabetes is a disease that results from the inability to produce enough and/or properly respond to insulin. The increasing number of obese children, adolescents, and adults has resulted in a corresponding increase in the prevalence of type 2 diabetes. Recent reports indicate that 8%–45% of children with newly diagnosed diabetes have type 2 diabetes and up to 85% of these children are overweight or obese at diagnosis.[2] Most cases of type 2 diabetes in youth occur in children older than 10 years of age who are in middle to late puberty, but cases in prepubertal children have been seen. Type 2 diabetes in children is seen most often in those with a family history of type 2 diabetes and those of non-European ancestry (African American, Hispanic, Asian, and Native American descent).[2] This form of diabetes can go undiagnosed for long periods of time, as the classic symptoms are typically less dramatic than in type 1 diabetes mellitus. The insulin resistance associated with obesity and characteristic of type 2 diabetes can often be ameliorated by weight loss, improved nutrition, and exercise. If lifestyle modification fails, oral hypoglycemic medications and/or insulin are needed to control hyperglycemia.

BLOOD GLUCOSE CONTROL

Prospective, randomized trials, such as the Diabetes Control and Complications Trial (DCCT) in type 1

diabetes mellitus and the United Kingdom Prospective Diabetes Study (UKPDS) in type 2 diabetes mellitus, have shown that improved glycemic control decreases the risks of developing retinopathy, nephropathy, and neuropathy. Intensive treatment regimens reduced the average hemoglobin A1c to approximately 7% in the DCCT.[3] Complications of tighter glycemic control include more frequent hypoglycemia and weight gain. Glycemic goals are usually modified to be higher for younger children under 6 or 7 years of age who may not be able to reliably recognize and respond to hypoglycemia.

ACUTE AND CHRONIC COMPLICATIONS OF DIABETES

The major acute complications of diabetes that occur in children are hypoglycemia, hyperglycemia, and diabetic ketoacidosis. Common nutrition factors that may contribute to hypoglycemia include delayed or missed meals and snacks, excessive insulin (either from consuming inadequate carbohydrate or inaccurate estimation of carbohydrate at mealtime/snacktime), increased exercise without compensation with food/insulin adjustment, or alcohol consumption without food. Hyperglycemia may occur due to inadequate insulin (either from consuming excessive carbohydrates or inaccurate estimation of carbohydrate at mealtime/snacktime) or a decrease in usual exercise. Diabetic ketoacidosis occurs when the body is unable to use glucose as fuel because there is an absolute or relative insulin deficiency in the body. When this happens, the body burns fat for fuel instead. By-products of fat breakdown are called ketones and at high levels can become toxic and lead to ketoacidosis.

The chronic complications of diabetes are microvascular disease (neuropathy, nephropathy, and retinopathy),

macrovascular disease (ischemic heart disease, cerebrovascular disease, and peripheral vascular disease), and poor growth and development. The chronic complications can be prevented or delayed with near to normal blood glucose control, management of dyslipidemia and hypertension, proper weight management, and avoidance of smoking.

Table 21–1 provides approximations of the onset, peak, and duration of the commonly used insulin preparations. The actual action time of insulin will vary among patients and is affected by a number of factors including the size of the dose, site and depth of injection, and exercise.

Table 21–1 Insulin Action

Insulin	Class	Onset	Peak (h)	Duration (h)
Lispro (Humalog), aspart (NovoLog), and glulisine (Apidra)	Rapid acting	<15 min	1–2	3–4
Regular	Fast acting	30 min–1 h	2–3	3–6
Detemir (Levemir)	Long acting	1–2 h	Relatively flat	Up to 24
Glargine (Lantus)	Long acting	1–2 h	No pronounced peak	24
NPH	Intermediate acting	2–4 h	4–10	10–16
70/30	Mixture of 70% NPH, 30% regular			
75/25	Mixture of 75% NPH, 25% lispro			

Abbreviation: NPH, neutral protamine Hagedorn.

GOALS OF MEDICAL NUTRITION THERAPY FOR ALL PERSONS WITH DIABETES

The American Diabetes Association established the following goals for all people with diabetes[4]:

1. Achieve and maintain
   - Blood glucose levels in the normal range or as close to normal as is safely possible
   - Blood lipid and lipoprotein profile that reduces the risk for cardiovascular and peripheral vascular disease
   - Blood pressure levels in the normal range or as close to normal as is safely possible
2. To prevent (or at least slow) the rate of development of the chronic complications of diabetes by modifying nutrient intake and lifestyle
3. To address individual nutrition needs, taking into account personal and cultural preferences and willingness to change
4. To maintain the pleasure of eating by only limiting food choices when indicated by scientific evidence

NUTRITION THERAPY GOALS FOR TYPE 1 DIABETES

On top of the goals set above for all people with diabetes, additional goals have been established for nutrition interventions for type 1 diabetes. Primarily, insulin therapy should be integrated into an individual's dietary and physical activity pattern.[4] With the availability of many different insulin options, it is essential to match a regimen that will work with the lifestyle of the patient and the family. For children on a

fixed insulin regimen, consistency with the timing and composition of meals and snacks is necessary to minimize fluctuations of the blood glucose level. For those looking for more flexibility in the timing and consistency of eating habits, a basal-bolus insulin regimen may be used. With this regimen, a relatively peakless long-acting insulin (glargine or levemir) can be used to provide basal insulin need alongside a short or rapid-acting insulin injected before each meal. The premeal dose is adjusted based on the total carbohydrate content of meals and snacks.[4] Finally, for planned exercises, the preference is to adjust the insulin dose to prevent excessive consumption of carbohydrate and calories. If the exercise is unplanned, additional carbohydrate may be needed.[4]

NUTRITION THERAPY GOALS FOR TYPE 2 DIABETES

The goal for management of type 2 diabetes is to achieve and maintain optimal blood glucose and lipid control by making nutrition and lifestyle changes. Recommendations are to reduce intakes of energy, saturated and *trans* fatty acids, cholesterol and sodium, and to increase physical activity.[4] Attention must also be paid to decreasing the amount of sedentary activity such as television watching, video games, and computer use. Insulin sensitivity improves with even a modest amount of weight loss. The long-term goal for growing children and adolescents is to attain and maintain the healthiest weight possible by halting the excessive weight gain, while supporting normal linear growth. At Boston Children's Hospital, the principles of the glycemic index (GI) are employed as a strategy for type 2 diabetes management. Patients are encouraged to decrease portions of high GI carbohydrate foods, such as white bread, and substitute controlled portions of lower glycemic foods, such as whole grain breads and beans. Lean protein and heart healthy fat

are distributed throughout the day, along with fresh fruit, cooked and raw vegetables, and low fat milk to promote satiety and reduce postprandial blood glucose levels.

Table 21–2 summarizes nutrition assessment using the Nutrition Care Process for pediatric patients with diabetes.

Table 21–2 Special Aspects of Nutritional Assessment for Children and Adolescents with Diabetes[5]

Client history	Medical history (celiac disease, nephropathy, hyperlipidemia, eating disorder, high blood pressure, asthma, attention deficit disorder, hypothyroidism, and other autoimmune diseases), duration of disease, medication (insulin regimen and oral glucose-lowering medications), and supplement history, family history, and social history
Food/nutrition-related history	Food intake (composition, carbohydrate, adequacy, meal/snack patterns, environmental cues to eating, tolerance, current diets, or food modifications); nutrition health awareness and management (knowledge and beliefs about nutrition recommendations, self-monitoring/management practices, and prior education); physical activity and exercise (functional status, activity patterns, sedentary time, exercise intensity, frequency, and duration); and food availability (food planning, purchasing, preparation abilities and limitations, food safety, food program utilization, and food insecurity)
Biochemical data/medical tests	HbA1c, lipid profile, urine ketones/protein, microalbuminuria, blood pressure, fasting/non-fasting blood glucose, and screening for autoimmune diseases (thyroid and gluten enteropathy)
Anthropometric measurements	Height, weight, body mass index (BMI), growth rate, and rate of weight change
Nutrition-focused physical findings	General physical appearance, body language, polyuria, polydipsia, polyphagia, and acanthosis nigricans

There is no current consensus regarding the optimal mix of macronutrients for individuals with diabetes. It is thus recommended that children and adolescents with diabetes follow the Dietary Reference Intakes for healthy eating. To promote good health, consumption of carbohydrate from fruits, vegetables, whole grains, legumes, and low-fat milk is encouraged. A variety of fiber-containing foods is also promoted, but studies have not suggested intake different from that of the general public. Protein intake should focus on good quality protein sources such as lean meat, poultry, fish, eggs, milk, cheese, and soy. In regard to fat intake, it is recommended to limit the amount of saturated and *trans* fatty acids and dietary cholesterol to help reduce the risk of cardiovascular disease.[4]

SWEETENERS

Historically, sucrose had been restricted in the diets of people with diabetes, based on the belief that sucrose is more rapidly digested and absorbed than starches. However, research comparing the effects of dietary sucrose and an isocaloric amount of starch has shown no difference in glycemic response. It has since been accepted that sucrose and sucrose-containing foods can be substituted gram for gram for other carbohydrates within the context of a healthy meal plan.[4] Sugar alcohols (mannitol, sorbitol, xylitol, and hydrogenated starch hydrolysates) have a lower glycemic effect than sucrose, but should be limited due to their laxative effect if consumed in large amounts.[6] One must also consider that sugar alcohols are incompletely absorbed and considered to have an average of 2 calories/g compared to 4 calories/g for sucrose. To calculate the amount of carbohydrate in a food product sweetened with a sugar alcohol, subtract half of the sugar alcohol grams from the total carbohydrate grams of the food item. For example, a no-sugar added chocolate bar that

contains 40 g of total carbohydrate and 20 g of sugar alcohols should be counted as containing 30 g of carbohydrate.

There are now six FDA-approved nonnutritive sweeteners—acesulfame potassium, aspartame, neotame, saccharin, sucralose, and rebaudioside A (stevia)—which can all be safely used by people with diabetes.[5] Adequate daily intakes (ADIs) have been established for each nonnutritive sweetener and are defined as the level of each sweetener that can be eaten for a lifetime without an adverse effect on health. The usual daily intake of these sweeteners by children with diabetes is typically far less than the ADI. For example, the ADI for aspartame is 50 mg/kg/day, which is equivalent to 7–12-oz cans of diet soda each day for a 23-kg child.[5]

ALCOHOL

The use of alcohol must be addressed in adolescents. For adults with diabetes, alcohol consumption should be limited to no more than two drinks two to three times per week. One drink is equal to 12 oz of beer, 5 oz of wine, or 1 ½ oz of distilled alcohol.[4] Alcohol inhibits gluconeogenesis and interferes with the counter-regulatory response to insulin-induced hypoglycemia. It is thus recommended that alcohol should be consumed with food. Alcohol should never be substituted for food in the meal plan, and extra insulin for the grams of carbohydrate in alcohol should not be taken due to the hypoglycemic effect.

MEAL PLAN

Meal plans should be created based on the usual intake and meal pattern of the child with diabetes, ensuring adequate nutrition to promote normal growth and development. Additionally, there is often weight loss at time of diagnosis and appetite is increased with the initiation of insulin

therapy. It is important to recognize this and adjust the meal plan if necessary to accommodate the increase in appetite to restore and maintain appropriate body weight.[7]

Most young children need to eat three meals and two to three snacks each day, spaced 2.5–3 hours apart. Older children in middle or high school often choose to eliminate the morning snack to fit in with their peers and their morning insulin regimen may need to be modified to accommodate this change. While daytime snacks can contain exclusively carbohydrate, children who are on a fixed insulin regimen that includes intermediate-acting insulin at dinner or bedtime should include protein and fat in the bedtime snack to minimize the risk for nocturnal hypoglycemia.

Meal plan approaches must match the child's insulin regimen. Children on a fixed insulin regimen using rapid-acting insulin combined with intermediate-acting insulin (neutral protamine Hagedorn (NPH)] must have a meal plan that sets consistent quantity and timing for carbohydrate intake. Historically, these meal plans have been based on the exchange system created by the American Diabetes Association and The American Dietetic Association. The exchange lists group specific servings of foods together because they have a similar amount of carbohydrate, protein, fat, and calories (see Table 21–3). One food can be substituted, or exchanged, for another within each exchange list. This type of meal plan approach can encourage healthy, well-balanced meals and snacks by including the portions of fruits, vegetables, and dairy products as well as starches, protein, and fat the child should consume daily.

The difficulty with the exchange system is that it allows limited flexibility with food choices, as well as the growing number of food options available do not always fit the uniform composition considered in each exchange category. There are many diet products now available that offer reduced

Table 21–3 The American Diabetes Association/The American Dietetic Association Exchange Lists for Meal Planning

Food List	Carbohydrate (g)	Protein (g)	Fat (g)	Calories
Carbohydrates				
Starch: breads, cereals and grains, starchy vegetables, crackers, snacks, beans, peas, and lentils	15	0–3	0–1	80
Fruits	15	—	—	60
Milk				
Fat-free, low-fat, 1%	12	8	0–3	100
Reduced-fat, 2%	12	8	5	120
Whole	12	8	8	160
Sweets, desserts, and other carbohydrates	15	Varies	Varies	Varies
Nonstarchy vegetables	5	2	—	25
Meat and Meat Substitutes				
Lean	—	7	0–3	45
Medium-fat	—	7	4–7	75
High-fat	—	7	8+	100
Plant-based proteins	Varies	7	Varies	Varies
Fats	—	—	5	45
Alcohol	Varies	—	—	100

Source: Adapted from The American Diabetes Association/The American Dietetic Association Exchange Lists for Meal Planning, 2008.

carbohydrate quantities and it is confusing to understand how to count them as part of an exchange meal plan.

CARBOHYDRATE COUNTING

The majority of children with type 1 diabetes use carbohydrate counting principles in conjunction with their meal plan. Carbohydrate is the main nutrient in starches, fruits, milk, yogurt, and other foods that contain sugar and has the greatest effect on blood glucose levels. About 90% of carbohydrate converts to glucose within one to two hours after eating. In the carbohydrate counting method, the starch, milk, fruit, other carbohydrate, and nonstarchy vegetable exchange groups have been merged to be counted as 15 g of carbohydrate, or one carbohydrate choice. Carbohydrate counting allows added flexibility with food choices and works well for the way children like to eat. Parents and children are also taught to read food labels to determine how many grams of carbohydrate or carbohydrate choices they are consuming taking into consideration the portion size. Goal number of carbohydrate choices or grams of carbohydrate are provided for each meal and snack. It is important to note that with this meal planning method, proteins, fats, and nonstarchy vegetables are not incorporated, nor are the types of carbohydrates to be consumed differentiated. Therefore, it is essential for the educator to discuss the carbohydrate goals in context of a healthful diet.

Table 21–4 reviews how a sample meal would compare using the different meal planning methods.

The meal plan should be reviewed every 3–6 months[8] to adjust for changes in growth and development, changes in school routines, seasonal sports, or changes in child-care arrangements.

Table 21–4 Comparison of Different Meal Planning Methods

Foods	Exchanges	Carbohydrate Choices	Carbohydrate (g)
2 slices of bread	3½ starches	5½ carbohydrate choices	30
1 oz pretzels	1 fruit		
1 medium orange	1 milk		23
1 cup of milk	3 proteins		16
2 slices of turkey	2 fats		12
2 teaspoons mayo			
			Total = 81

ADVANCED CARBOHYDRATE COUNTING

For children with type 1 diabetes who are on an intensive insulin regimen, either using a basal-bolus insulin plan or on insulin pump therapy, it is necessary to used advanced carbohydrate counting to match the insulin dose with the amount of anticipated or consumed grams of carbohydrate. With this method, there is added flexibility in the timing of meals and the amount of carbohydrate consumed. Snacks, including at bedtime, are not necessary, but are often still desired. Each carbohydrate-containing meal and snack needs to be covered with rapid-acting insulin based on a calculated insulin-to-carbohydrate ratio. For example, a child whose insulin regimen includes an insulin-to-carbohydrate ratio of 1:10 (1 unit of rapid-acting insulin for every 10 g of carbohydrate consumed) would inject or "bolus" 6 units of rapid-acting insulin for a 60-g carbohydrate breakfast. A breakfast consisting of only 30 g of carbohydrate would require 3 units of rapid-acting insulin. These regimens offer flexible mealtimes and schedules and make it possible to accommodate varying appetites and activity levels.[9]

FIBER

Dietary fiber is not completely digested and absorbed like other carbohydrates. Because fiber does not cause the blood glucose to rise in the same way as other carbohydrates, the American Diabetes Association established the rule that if a food product has more than 5 g of fiber per serving, one should subtract half of the fiber from the total carbohydrate. Many families may find this rule complicated or difficult to remember. For those families, it may be best to simplify recommendations and have them subtract the entire quantity of fiber listed on a Nutrition Facts Panel. One can then monitor blood glucose trends to assess if modifications are needed.[7]

GLYCEMIC INDEX

GI has been considered as a method of meal planning for patients with both type 1 and type 2 diabetes. As previously discussed in this chapter, at Children's Hospital Boston, low-GI recommendations are regularly incorporated into the diet therapy for type 2 diabetes patients. The literature is mixed in regard to whether following a low-GI diet provides benefit for blood glucose control. The limitations of existing studies include differing definitions of high- versus low-GI and possible confounding dietary factors.[10] The American Diabetes Association has updated their consensus guidelines to include the following statement on GI: For individuals with diabetes, the use of the GI and glycemic load may provide a modest additional benefit for glycemic control over that observed when total carbohydrate is considered alone.

SPECIAL CONSIDERATIONS

Illness

Infection, illness, and surgery all make blood glucose control more difficult due to multiple factors, including increased counter-regulatory hormone levels, anorexia and

altered meals, and snacks. In general, sick children should be given their usual insulin dose and insulin should never be skipped. It is also common to require additional insulin as acute illness may cause insulin resistance with resultant hyperglycemia. The blood glucose level should be checked every three to four hours and urine or blood concentrations of ketones should be checked each time the child urinates or each time blood glucose is checked. If the child is able to eat their usual meal plan and/or blood glucose is greater than 200 mg/dL, he or she should be given 4–6 oz of sugar-free fluid each hour. If the child is not able to eat usual meals and snacks or blood glucose is less than 200 mg/dL, sugar-free drinks should be alternated with sugar-containing drinks. The carbohydrate grams or servings allotted in the meal plan should be replaced with sugar-containing sodas, popsicles, juices, and gelatin.

Exercise

Exercise, whether gym class, a soccer game, or a bike ride, can lower the blood glucose level both during and for up to 6–24 hours after the exercise. To evaluate the effect of physical activity, the blood glucose level should be checked both before and after the exercise, and for prolonged activity, it is often helpful to check blood glucose during the exercise as well. Exercise is not recommended if the blood glucose level is >250 mg/dL with ketones or >300 mg/dL without ketones in the urine. To prevent hypoglycemia during physical activity, one could either adjust insulin or add additional carbohydrate to the meal plan. If adding carbohydrate, basic guidelines are to add 15 g of carbohydrate for every 30–60 minutes of physical activity. For type 2 diabetes, the importance of regular physical activity on a daily basis must be emphasized as a vital component to lifestyle changes to promote weight management and improved glycemic control.

Table 21-5 American Diabetes Association's Recommended Blood Glucose Goals for Children with Diabetes

Age	Before Meals (mg/dL)	Bedtime/Overnight (mg/dL)
Toddlers and preschoolers (<6 y)	100–180	110–200[a]
School age (6–12 y)	90–180	100–180
Adolescents and young adults (13–19 y)	90–130	90–150

[a]It is very important to avoid hypoglycemia as much as possible in children less than 6 y. Frequent or severe hypoglycemia may have harmful effects on brain development.

Table 21–5 provides age-stratified blood glucose targets for pediatric patients with diabetes.

Providers are encouraged to modify glycemic goals as appropriate for each patient. Lower goals may be reasonable if they can be achieved without excessive hypoglycemia. Additionally, for patients that may have frequent hypoglycemia or hypoglycemia unawareness, higher goals may be needed.[11]

STAGES OF LIFE

Infants and Toddlers

Since young children usually do not have consistent eating habits and cannot recognize symptoms of hypoglycemia, strict blood glucose control is not usually attainable. Generally, higher blood glucose goals are accepted (see Table 21–5), and the main goal is to avoid hypoglycemia. Infants with diabetes can certainly continue to breast-feed. Toddlers are more independent in their eating habits, their appetites are decreasing, and often they are more selective in their food choices. Toddlers should be allowed to eat in a calm, relaxed manner without distractions and should never be force-fed. A meal plan encouraging consistent meals and

snacks should be taught at this age, but the variability in a toddler's eating habits must be acknowledged and accepted. Ultimately, parents are responsible for providing appropriate meals and snacks, and the child will decide how much and what to eat. Rapid-acting insulin (e.g., insulin lispro or insulin aspart) can be given after meals for young children who are especially unpredictable in their eating habits, with the dose based on the amount of food the child actually eats.

Preschool and School Age

More structured mealtime and snacktime should be established at this time. Limit snacks to regularly scheduled times as much as possible. School, sports, and physical education schedule should be reviewed. Most school lunches fit into a child's meal plan and the menus should be reviewed for the child's preferences and for acceptability within the meal plan. The child with diabetes should be encouraged to help with menu planning, selecting groceries, preparing meals, and choosing snacks. Information should be provided on how to make the best food choices at parties, sleepovers, and at restaurants.

Adolescents

Diabetes management is often most challenging at this time, as the teenager is becoming more independent in managing his or her diabetes care. There are more meals away from home and less parental supervision. Appetite and growth parameters should be monitored to guide the teenager toward how to make appropriate food choices. Practical information should be provided on fitting in fast food, how to manage restaurant eating, and ways to adjust the meal plan for school sports, activities, jobs, and other times away from home. Basal-bolus insulin regimens or insulin pump therapy offer a distinct advantage in this age group since they enable the adolescent to eat meals and snacks with friends

and to easily administer appropriate amounts of rapidly absorbed insulin.

GLYCOGEN STORAGE DISEASES

Glycogen storage diseases (GSDs) are a group of rare genetic disorders in which there is a defect in glycogen metabolism. This defect is due to enzyme deficiencies along the glycogenolytic pathway and leads to abnormal tissue concentrations of glycogen or to structurally abnormal forms of glycogen. Glycogen is primarily stored in the liver or muscle, and based on where the defect is located, different symptoms may be present. In hepatic glycogenoses, hypoglycemia is the primary symptom, and in muscle glycogenoses, weakness and muscle cramps are seen. Typically forms of GSD are described by which part of the body is affected. The most common forms affect the liver only, the muscle only, or both. Examples of other systems that could be affected include heart, kidney, and blood cells.

There are many types of GSD (Table 21–6) that are classified by a number, by the name of the defective enzyme, and/or by the name of the person who first described the condition. Dietary therapies have been developed to use alternative metabolic pathways as a form of treatment for some GSDs. The most common GSD is type 1, which is further subdivided to types 1a and 1b. GSD type 1a (80% of GSD 1) occurs due to a glucose-6-phosphatase enzyme deficiency, whereas GSD type 1b occurs due to a defect of the glucose-6 phosphate transporter. Both enzyme defects lead to an inability to release glucose from glycogen stores and result in hypoglycemia. The four major symptoms of GSD 1 include hepatomegaly, hypoglycemia, growth retardation, and abnormal biochemical profile. Symptoms become most evident when the infant begins to sleep through the night and therefore undergoes longer intervals between feeds.

Table 21–6 Glycogen Storage Diseases[12–15]

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Type 0 (hepatic glycogen synthase deficiency)	Glycogen synthase	Fasting hypoglycemia and ketosis, postprandial hyperglycemia, and glucosuria	Failure to thrive, no hepatomegaly	Frequent feeding every 3–4 h during day and uncooked cornstarch (CS) before bed, ~0.5–1 g/kg mixed with low-fat milk; diet should be high in protein and lower in carbohydrates (45% carbohydrate, 25% protein, 30% fat)	None
Type Ia (Von Gierke disease, hepatorenal glycogenosis)	Glucose-6-phosphatase	Severe hypoglycemia, elevated production of lactic acid, triglycerides, and uric acid	Hepatomegaly, failure to thrive, distended abdomen, delayed motor development	Infants: Lactose-free formula every 2–3 h during day and every 3 h over night or continuously via infusion	May need a sugar-free multivitamin and calcium supplement

(*Continued*)

Table 21–6 Glycogen Storage Diseases[12–15] (*Continued*)

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
				pump; 6 mo and older: Uncooked CS every 3–5 h during the day and every 4–6 h at night, 60%–65% CHO, 15%–20% protein, 20% fat, <300 mg cholesterol, fructose, and galactose restricted	
Type Ib (Von Gierke disease, hepatorenal glycogenosis)	Glucose-6-phosphate transporter	Severe hypoglycemia, elevated production of lactic acid, triglycerides and uric acid, constant or cyclic neutropenia, inflammatory bowel disease	Hepatomegaly, failure to thrive, distended abdomen, delayed motor development	As in type 1a	May need a sugar-free multivitamin and calcium supplement

Type II (Pompe disease, acid maltase deficiency, AMD)	Acid-α-glucosidase (GAA)	Myopathy, most have elevations of creatine kinase	Infantile: hypotonia, cardiac hypertrophy; adult onset: proximal weakness and muscular atrophy	A protein-rich diet	None
Type III (Cori disease, Forbes disease, Debrancher deficiency)	Amylo-1, 6-glucosidase (AGD)	Fasting hypoglycemia with ketosis, hyperlipidemia, profound elevation of serum transaminases, elevated creatine kinase	Hepatomegaly in childhood, myopathy (usually more prominent in adulthood)	Infants and children: small, frequent feedings and avoidance of fasting; introduction of CS if hypoglycemia (infant and younger child: 1.6 g/kg q 4 h; older child: 1.7–2.5 g/kg q 6 h); bedtime snack, CS, or overnight feeds may be needed;	May need calcium and vitamin D

(*Continued*)

Table 21–6 Glycogen Storage Diseases[12–15] (*Continued*)

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
				adolescents and adults: 25% protein, low carbohydrate <50%, avoidance of simple sugars, and fasting	
Type IV (Andersen disease, amylopectinosis, Brancher deficiency)	Glycogen-branching enzyme	Hepatic presentation: elevated serum transaminase levels, hypoglycemia with advanced cirrhosis; neuromuscular presentation: increased creatine kinase	Hepatic presentation: failure to thrive, hepatosplenomegaly, cirrhosis, portal hypertension, esophageal varices and ascites; neuromuscular presentation: myopathy	Frequent meals, snacks, and CS as needed to maintain normal blood glucose levels and provide sufficient nutritional intake in order to improve liver function and muscular strength	None

Type V (McArdle disease, muscle phosphorylase deficiency)	Muscle phosphorylase	Elevated serum creatine kinase; uric acid may be elevated	Muscle weakness and cramping with exercise, myoglobinuria	Provide a high-protein diet; moderate exercise. Glucose or fructose ingestion can improve exercise tolerance	Vitamin B6 and creatine supplement
Type VI (Hers disease, liver phosphorylase deficiency)	Liver phosphorylase	Mild fasting ketotic hypoglycemia, mild hypertriglyceridemia, and elevated serum transaminase levels	Hepatomegaly, distended abdomen, growth retardation, delayed motor development; muscle involvement may occur	Avoid prolonged fasting and ensure a bedtime snack; if hypoglycemia, uncooked CS (1.5–2 g/kg) given 1–3×/d	None
Type VII (Tarui disease, muscle phosphofructokinase deficiency)	Muscle phosphofructokinase	Elevated serum creatine kinase, hemolytic anemia, myoglobinuria, and hyperuricemia (postexercise)	Muscle weakness and cramping with exercise, myoglobinuria	Diet should be high in protein (45% CHO, 25% protein, 30%, fat), moderate exercise	None

(*Continued*)

Table 21–6 Glycogen Storage Diseases[12–15] (*Continued*)

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Type IX (phosphorylase kinase deficiency)	Phosphorylase kinase	Symptomatic hypoglycemia and ketosis with prolonged fasting or strenuous exercise; mild hypertriglyceridemia, hypercholesterolemia, and elevated serum transaminases	Hepatomegaly, growth retardation, mild delayed motor development	Avoid prolonged fasting, ensure a bedtime snack; if overnight hypoglycemia, uncooked CS (2 g/kg) given at bedtime	None
Type XI (Fanconi–Bickel syndrome)	Lactate dehydrogenase	Elevated serum creatine kinase, elevated pyruvate	Myoglobinuria, myalgia, excessive fatigue	Avoid intense exercise	None

At Boston Children's Hospital, infants with GSD type 1a or 1b are treated with a lactose-free formula, with feeds every two to three hours during the day and every three hours overnight (or continuous nocturnal feeds through gastrostomy tube). To allow longer periods of fasting as the infant grows older, uncooked cornstarch (UCCS) therapy is considered because it is slowly absorbed into the circulation allowing euglycmia.[12] The UCCS should be initiated cautiously in infants because their amylase concentrations may not be mature enough for its digestion; however, this type of therapy has been successfully used in infants as young as 6 months.[12] The UCCS should be mixed with formula or water in a 1:2 starch/liquid ratio.[16] Sugar-free juice can be used for older children or adults. UCCS is measured on a gram scale to ensure proper amounts of glucose since excess cornstarch can contribute to excess calories and weight gain. Initial dosing of UCCS should be low to allow for monitoring of side effects such as bowel distension, flatulence, and loose stools. A starting dose of 0.25 g/kg body weight can be used and then slowly increased to assure euglycemia.[16] The formula to calculate the basal glucose production rate can be used as an estimate for the minimum amount of glucose required. The formula is as follows:

$$Y = 0.0014\left(wt^3\right) - 0.214\left(wt^2\right) + 10.411(wt) - 9.084$$

(y = mg glucose/min, wt = body weight in kilograms).[12]

Example: weight 5 kg

$0.0014\ (5^3) + 0.214\ (5^2) + 10.411\ (5) - 9.084$

$0.0014\ (125) - 0.214\ (25) + 10.411\ (5) - 9.084$

$0.175 - 5.35 + 52.1 - 9.084$

37.7 mg glucose/min× 60 minutes

2268 mg glucose/h

2.26 gm glucose/h

6.8 g every 3 hours or 9 g every 4 hours

Diet therapy for GSD type 1 involves following a low-fructose and low-galactose diet as the enzyme defect prevents the body from converting these sugars to glucose and results in unwanted glycogen stores and lactic acid. Up to 1 dairy serving/d is allowed, but calcium fortified soy milk is often preferred. Carbohydrates, which are mostly in the form of starches, should comprise approximately 60%–65% of the daily calories, of which 30%–45% should come from cornstarch. Dietary fat should be restricted to approximately 20% of daily calories and <300 mg of cholesterol/d. Fruit and dairy intakes are typically low given fructose and galactose intake are limited, and it is commonly recommended to use a sugar-free multivitamin and calcium supplement (refer to Table 11–1 on multivitamins). Studies have shown that once the diet is followed and hypoglycemia and hyperlacticacidemia are prevented, growth improves, the liver size decreases, and cholesterol and triglyceride levels usually return to normal ranges. In fact, patients who are treated intensely from infancy attain adult heights within one standard deviation score of their target heights, although it is common for overweight or obesity.[12,17,18]

In GSD types 0, II, III, IV, V, VI, VIII, and IX, a higher protein diet has been recommended with daily calories consisting of approximately 45% carbohydrate, 25% protein, and 30% fat. The extra protein is promoted to provide as a substrate for gluconeogenesis and/or muscle repair.[13] Once patients

with these types of GSD advance to solid foods, protein is immediately emphasized in the diet. For patients with difficulty consuming high quantities of protein through food, use of protein powders or supplements should be considered.

A new advancement in GSD management is the use of an extended release cornstarch. One study using this type of cornstarch (Glycosade, Vitaflo International Ltd, Liverpool, UK) versus traditional cornstarch therapy found it maintained blood glucose concentrations for a significantly longer period of time. It is hoped that this cornstarch may allow patients to sleep through the night without having to wake to provide additional dosing.[19] Gene therapy is also being studied at this time as a possible treatment for people with GSD.

Various types of GSDs with guidelines are presented in Table 21–6.

Professional Organizations and Internet Resources

American Diabetes Association
www.diabetes.org
The American Dietetic Association
www.eatright.org
The Juvenile Diabetes Foundation
www.jdfcure.org
American Association of Diabetes Educators
www.aadenet.org/
National Diabetes Information Clearinghouse
www.niddk.nih.gov
CDC Diabetes Public Health Resource
www.cdc.gov/diabetes
Children with Diabetes
www.childrenwithdiabetes.com

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22 Pediatric Feeding and Swallowing Difficulties

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The estimated prevalence of feeding and swallowing problems range from 25% to 45% in typically developing children and 33% to 80% in children with developmental disabilities.[1] An apparent increase in the prevalence of these conditions may be due to the higher rate of survival among children with medical conditions and preterm infants, particularly those with very low birth weight. Developmental disabilities such as cerebral palsy have been reported up to 20% in children born between 24 and 26 weeks gestation. Among infants and children assessed for feeding and swallowing problems, approximately 40% were born prematurely, nearly 80% had developmental disorders, and 90% had at least one medical diagnosis.[1]

Classification of feeding problems in the pediatric population can be difficult since feeding is a skill involving multiple organ systems, including coordination of central nervous system, gastrointestinal, respiratory, and musculoskeletal organs among others, as well as behavior and satiety. Multidisciplinary evaluation and treatment are, therefore,

essential for effective intervention. Rommel et al.[2] found that out of 700 infants and young children, 86% of the patients referred to a multidisciplinary feeding clinic had a medical diagnosis. Of the medical diagnosis, the most common problem was gastrointestinal problem (54.3%). Other conditions were neurologic (20%), genetic (9.2%), ear–nose–throat (5.7%), cardiologic (4.4%), respiratory (4.4%), and renal (3.5%). Sixty-one percent had oropharyngeal dysfunction; 18% had a behavioral problem. The majority of children were under 2 years of age.

Feeding and swallowing disorders can be divided into preoral, oral, pharyngeal, and esophageal phases.[1] In the preoral phase, the child senses hunger and communicates the desire to eat. In infancy, feeding is a reciprocal process: the child indicates hunger and the caregiver provides nourishment. Likewise, the caregiver must be able to read a child's cues appropriately.[3] When there is a negative experience with food, such as GI pain or dysphagia, a feeding aversion can develop. Children can be resistant to feeding; ongoing unsuccessful feedings can result in disrupted caretaker–child relationship and a long-term feeding disorder.

The oral phase includes the mechanical manipulation of food to prepare the bolus for swallowing. Swallow rhythm is established as early as 32 weeks gestation.[3] Swallow maturity with well-defined suck swallow ratios of 1 suck to 1 swallow occur between 35 and 40 weeks gestation.[3] The anatomy of the oral and pharyngeal structures in the first few months facilitates nippling as the tongue fills most of the oral cavity and the larynx sits high in the pharynx to allow posterior–anterior movement of the tongue. Sucking is reflexive at this stage. As the child and oral musculature

matures, the larynx elongates and descends in the pharynx, creating a 90° angle of the oral pharyngeal complex. The tongue thrust reflex is integrated around 6 months to allow for more movement of the tongue to ready the child for spoon feeding. Some children with developmental delay will have persistence of this tongue thrust reflex, making oral nutrition difficult. Dentition also plays a role in biting and chewing skills.[2–5] At or near 6 months of age, the infant is able to maintain an upright position for sitting and the hands begin to come to the mouth for oral exploration. These changes are important to ready the child for more mature foods and development of oral feeding skills. See Table 8–1 for more detailed chronological oral motor development and corresponding foods in normally developing children.

The pharyngeal phase of the swallowing is involuntary and initiates when the oral cavity propels the bolus posteriorly to the hypopharynx. During swallowing, respiration ceases to allow the bolus to move through the hypopharynx and into the esophagus. When there is a breakdown of coordination between the oral and pharyngeal phases of the swallow, or when there is weakness of the pharynx or larynx, aspiration can occur. When a pharyngeal phase dysphagia or difficulty in swallowing is suspected, instrumental assessments such as a modified barium swallow study is useful for identifying the specific areas of deficit and compensatory strategies to reduce the risk of aspiration. Children may suffer from medical sequelae of aspiration and develop a long-term feeding aversion. Please see Table 22-3 for more detailed information about instrumental assessments.

The esophageal phase of the swallowing starts when the bolus enters the upper esophageal sphincter during swallowing. Peristaltic contractions propel the bolus to the

stomach.[4] A number of esophageal and GI problems can also result in dysphagia or discomfort with feeding, leading to feeding disorders or aspiration from gastroesophageal reflux.

Table 22–1 lists some "red flags" and common reason of referral for feeding and swallowing evaluation. If a dietitian encounters red flags that indicate possible oral motor or swallowing impairments, a referral to a Speech–Language Pathologist specializing in pediatric feeding and swallowing disorders should be made. Table 22-2 gives more details regarding the clinical assessment of feeding and swallowing. If a child also has red flags from the "feeding difficulties" column, a multidisciplinary feeding team can be a more efficient way for the child to be evaluated in a myriad of domains. The multidisciplinary Growth and Nutrition program at Boston Children's Hospital includes physicians (developmental pediatrician or gastroenterologist), nurse practitioners, dietitians, speech–language pathologists, psychologists, social workers, and home health nurse.

Several treatment decisions can be generated after thorough evaluation of a child's feeding and swallowing skills. Table 22-4 gives some common treatment strategies for feeding swallowing difficulties. Often the first consideration is given to the safest textures and consistencies to consume by mouth, depending on swallow function as well as developmental functioning. See table 22-5 for details regarding thickened liquids. Other medical and feeding issues, including oral aversion, physiologic and medical stability to fully consume an oral diet, external and environmental factors that could be limiting successful feeding, are also taken into consideration when formulating a child's overall treatment plan. Extensive counseling is often needed to help families make decisions about the safest and most developmentally appropriate feeding plan.

Table 22–1 Red Flags and Common Reasons for Referral

Age Group	Chewing or Swallowing Difficulties	Feeding Difficulties
0–6 mo	Coughing, choking, or gagging while feeding	Takes longer than 30 min to feed
		Failure to gain weight
	Color changes while feeding (red or blue around the lips)	Consistently fussy with feeding
	Large amounts of liquid loss	Arching, pulling away from nipple despite hunger cues
	Difficulty latching to nipple	
	Short sucking bursts	
	Unexplained fevers or respiratory symptoms	
	Junky wet breathing sounds or voice while eating	
6–9 mo	Same as above	Gags when trying a new food
	Gags or chokes when eating	Consistently refusing whole categories of food (fruits, vegetables, meats, purees)
	Consistently refuses liquids	
	Excessive food loss while eating	Failure to gain weight
		Not interested in mouthing objects or food

9–12 mo	Same as above	Gags or chokes when eating solids
	Appears to swallow chewable solids whole	Refusing to try new foods
		Very particular about tastes or textures or brands
	Takes a long time to swallow each bite of food	Failure to progress to age appropriate foods
	Pockets food in cheeks	Stress and anxiety at mealtime
	Over-stuffing of food	"Battles" around food
	Excessive drooling while eating	
	Difficulty transitioning to sippy cup or straw without coughing and choking while drinking	

Table 22–2 Clinical Assessment of Feeding and Swallowing[5]

Given that feeding and swallowing disorders can involve multiple systems, a multidisciplinary approach to evaluation can allow focus on the whole child and caregivers. The evaluation should encompass the following dimensions.	
Review of family, medical, developmental, and feeding history to evaluate underlying factors contributing to feeding and swallowing problems	Anatomic and physiologic abnormalities of the oropharynx, larynx, trachea
	Respiratory track disorders affecting sucking, swallowing, or breathing
	Central nervous system or neuromuscular disorders
	Cardiovascular conditions
	Genetic syndromes and conditions
	Psychological or emotional tension affecting eating success
Physical examination	Child–parent interactions
	Level of alertness, attention to task, self-regulation, communication for feeding
	Oral motor
	Tone, strength, and range of motion of the jaw, tongue, lips. Saliva management and vocal quality
Feeding observation	Infant: Level of alertness. Efficient bottle or breast feeding with minimal liquid loss and well coordinated suck–swallow–breathe pattern.
	Older infant or toddler: Try to mimic naturalistic feeding environment. Varied textures and consistencies. Evaluation of the development of oral feeding skills including use of lips, tongue, and jaw to strip spoon for purees, munch or chew solids, and transport the bolus for swallowing.
	Observe sensory or behavioral responses to food.

	Swallow function
	Observe coordination of the oral and pharyngeal phases of swallowing
	Note overt signs or symptoms of aspiration (see "Red Flags" in Table 22–1)
Other considerations	Developmental profile, underlying medical diagnosis, GI function, growth and nutritional status, family structure and dynamics, etc.

Table 22–3 Instrumental Assessment of Swallowing

Modified barium swallow study	"Gold standard" for assessment of the oral and pharyngeal phases of the swallow
	Dynamic imaging of the oral, pharyngeal, and upper esophageal phases of swallowing
	Performed jointly by a speech–language pathologist and radiologist
	Primary purpose is not to simulate a meal, but to define the physiology and underlying dysphagia, not just aspiration
	"Modified" refers to the different consistencies and textures that are studied for liquids and solids
	Child is positioned in a typical feeding position, either semi-upright or upright
	Can directly observe the bolus in the oral, pharyngeal, and upper esophageal phases of the swallow, typically in the lateral view
	Can capture the moment of penetration and aspiration
	Findings should be integrated with the clinical assessment of feeding and swallowing, as well as information from the history and other diagnostic testing and factors.

(*Continued*)

Table 22–3 Instrumental Assessment of Swallowing (*Continued*)

	Different from a "Barium Swallow" as the focus of the MBS is the oral and pharyngeal phases of the swallow, whereas the barium swallow study evaluates the esophagus and stomach
Fiberoptic endoscopic evaluation of swallowing	A flexible endoscope is passed transnasally to the hypopharynx, above the vocal cords
	It allows visualization of laryngeal structures and events occurring immediately before and after the pharyngeal swallow
	Unable to asses the oral phase (i.e. chewing or sucking)
	There is a "white out" during the moment of swallowing when the view is obscured; therefore, cannot visualize the moment of aspiration or the dynamic sequence of swallowing
	Penetration and aspiration is presumed based on residue in the laryngeal vestibule, on the true vocal cords, or in the trachea below the true vocal cords
	Best carried out by a pediatric otolaryngologist and speech–language pathologist working as a team
	Advantages include no radiation exposure, patient position is flexible, and equipment is readily available in most hospitals

Table 22–4 Treatment Goals

Oral motor deficits	Frequently seen in the developmentally delayed population (i.e., cerebral palsy) or children with anatomical abnormalities of the head and neck (i.e., cleft palate)
	Treatment goals are to identify the safest and most efficient consistencies and textures to maximize oral intake and minimize gagging or choking risk based on oral motor functioning

	Identify the correct nipple/bottle or cups for liquid intake
	Crunchy foods can provide increased sensory feedback to mouth to encourage more munching and chewing
	Counseling and education of strategies and techniques to advance to more advanced textures
Swallowing deficits	Postural changes
	Body positioning, neutral head posture or slight head down more protective of airway, head turns can be effective for older children with unilateral weakness
	Change volume and speed of delivery of food
	Different nipples and sippy cup spouts
	Change food consistency and viscosity
	Thickened liquids can slow the effects of gravity, allowing child more time to coordinate swallowing (nectar-thick liquids, and honey-thick liquids)
	Is therapeutic because there is more effortful swallowing with a thicker viscosity liquid
Behavioral challenges	Joint treatment with a behavioral psychologist to help extinguish maladaptive behaviors associated with mealtimes.
	Promote good eating habits
	Set mealtimes and routines
	No grazing on juice or sugary snacks
	Family meals (socialization)
	Verbal praise and attention for desired behaviors

(*Continued*)

Table 22–4 Treatment Goals (*Continued*)

	Include all children in meal preparation and cleanup
	Talk about the physical properties of food (i.e., color, shape, texture, taste)
	Do not have "battles" over food. Do not force feed.

Table 22–5 Thickened Liquids

Thickening options	Natural methods
	Liquids such as water, juice, or milk can be thickened using yogurt, pudding, or pureed fruits
	Some commercially available liquids are naturally thickened to a nectar consistency
	Commercial thickeners
	SimplyThick® is made from xanthan gum and is effective for all liquids at all temperatures, including breast milk
	Powder-based thickeners (i.e., Thick It or Thicken-Up) are easy to use but viscosity may change with temperature and with time. Do not adequately thicken breast milk. New xanthan-gum based powder thickeners such as the Nestle Thicken-Up Clear may adequately thicken breast milk but the product is not recommended for children under 3 years of age.
	Infant rice and oatmeal cereals can be added to formula or milk but since it does not dissolve into the liquid, can cause clogging of infant bottle nipples and sippy cup spouts. Does not adequately thicken breast milk.
	Cornstarch, potato flakes, or pureed vegetables can be used to thicken soups

Avoid semi-solids that melt into a thin liquid in the mouth	Ice
	Jell-o
	Ice cream
	Popsicles
	Juicy fruits (orange, pineapple, watermelon, etc.)

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23 Eating Disorders

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Eating disorders, including anorexia nervosa (AN), bulimia nervosa (BN) and binge eating disorder (BED) are biologically based, serious mental illnesses.[1] Identification and treatment of eating disorders is determined by psychological, behavioral, and physiologic criteria from the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*). A fifth edition of the *DSM*[2] has been proposed that includes revisions to the existing diagnostic criteria (see Table 23–1).

Eating disorders are significantly heritable; influenced by brain function; significantly impair cognitive function, judgment, and emotional stability; and restrict the life activities of persons afflicted with them.[1] Eating disorders are the third most common chronic illness in adolescents, following obesity and asthma.[3] AN, BN, and BED impact 0.3%, 0.9%, and 1.6% of adolescents, respectively, and have a median onset at 12–13 years of age.[4] Eating disorders in children and adolescents occur along the continuum of weight, affecting not only those severely underweight, but also those with weights in the healthy, overweight, and obese ranges.

Table 23–1 Diagnostic Criteria

Anorexia Nervosa
Diagnostic and Statistical Manual of Mental Disorders (DSM) V • Restriction of energy intake relative to requirements leading to a significantly low body weight in the context of age, sex, developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal, or for children and adolescents, less than that minimally expected. • Intense fear of gaining weight or becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight. • Disturbance in the way in which one's body weight or shape is experienced, undue influence of body weight or shape on self-evaluation, or persistent lack of recognition of the seriousness of the current low body weight. *Specify current subtype* *Restricting type*: during the last 3 mo, the individual has not engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas). *Binge-eating/purging type*: during the last 3 mo, the individual has engaged in recurrent episodes of binge eating or purging behavior (i.e., self-induced vomiting or the misuse of laxatives, diuretics, or enemas)
Bulimia Nervosa
• Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following: – Eating, in a discrete period of time (e.g., within any 2-h period), an amount of food that is definitely larger than most people would eat during a similar period of time under similar circumstances

(*Continued*)

Table 23–1 Diagnostic Criteria (*Continued*)

Bulimia Nervosa
– A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating) • Recurrent inappropriate compensatory behaviors in order to prevent weight gain, such as self-induced vomiting; misuse of laxatives, diuretics, or other medications, fasting; or excessive exercise • The binge eating and inappropriate compensatory behaviors both occur, on average, at least once per week for 3 months • Self-evaluation is unduly influenced by body shape and weight • The disturbance does not occur exclusively during episodes of anorexia nervosa.
Binge Eating Disorder (BED)
• Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following: – Eating, in a discrete period of time (e.g., within any 2-h period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances – A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating) • The binge eating episodes are associated with 3 (or more) of the following: – Eating much more rapidly than normal – Eating until feeling uncomfortably full – Eating large amounts of food when not feeling physically hungry – Eating alone because of feeling embarrassed by how much one is eating – Feeling disgusted with oneself, depressed, or very guilty after overeating

- Marked distress regarding binge eating is present
- The binge eating occurs, on average, at least once a week for 3 months.
- The binge eating is not associated with the recurrent use of inappropriate compensatory behavior and does not occur exclusively during the course bulimia nervosa or anorexia nervosa. *Rationale* BED is one of the disorders in the *DSM-IV* appendix. It is recommended that it be formally included as a disorder in *DSM-V*.

The rationale for recommending inclusion of binge eating disorder (BED) in *DSM-5* is based on a comprehensive literature review (*Wonderlich, Gordon, Mitchell, Crosby, & Engel, 2009*). Below we address several key recommendations offered by Kendler et al. as they apply to BED.

Consistent with Kendler et al.'s recommendation for making decisions about diagnoses in the Appendix, the Eating Disorders Work Group addressed the question, "Should the BED diagnosis be (a) deleted from the appendix, (b) promoted to the main manual, or (c) retained in the appendix?

Synopsis of the Review of Validators

The following comments are organized according to the structure of the table of validators provided by Kendler et al. (2009) and based on a literature review (Wonderlich et al., 2009). BED has been compared to both other eating disorders (i.e., anorexia nervosa, bulimia nervosa) and obesity in validational studies. Overall, BED distinguishes itself from other eating disorders and obesity across a wide range of validators, including high priority validators.

In terms of *antecedent validators*, there is evidence from family history studies that BED tends to run in families and is not a simple familial variation of obesity. Furthermore, in comparison to other eating disorders, BED shows a relatively distinct demographic profile with a greater likelihood of male cases, older age, and a later age of onset.

Regarding studies of *concurrent validators*, BED is also differentiated from obesity in terms of greater concerns about shape and weight, more personality disturbance, and a higher likelihood of psychiatric comorbidity in the form of mood disorders and anxiety disorders. Also, BED is associated with lower quality of life than obesity.

(*Continued*)

Table 23–1 Diagnostic Criteria (*Continued*)

Binge Eating Disorder (BED)

Finally, in terms of *predictive validators*, BED may be differentiated from other eating disorders in terms of its lower level of diagnostic stability and greater likelihood of remission. In clinical course, BED also shows a greater likelihood of medical morbidities (e.g., self-reported weight gain and metabolic syndrome indicators) than is typically seen in other eating disorders, or in obesity. Finally, in studies of treatment response, there is evidence that individuals with BED have a more positive response to specialty treatments than to generic behavioral weight loss treatments in terms of reduction of eating disorder psychopathology. These findings suggest some evidence of clinical utility of the BED diagnosis in terms of treatment selection; for example, antidepressant medication is useful in the treatment of BED, but is not generally useful in the treatment of obesity.

Level of change: Major.

References: Literature review (*Wonderlich et al., 2009*).

Criterion D

In the *DSM-IV* appendix, it was suggested that the frequency of binge-days, as opposed to binge episodes, be assessed, and a minimum average frequency of twice/week over 6 months be required. A literature review indicated that criteria identical to those for Bulimia Nervosa would not change caseness significantly. Therefore, criterion D for BED is recommended to be similar to criterion C for Bulimia Nervosa.

Level of change: Clarification/Modest/substantial.

References: Literature review (*Wilson & Sysko, 2009*).

Literature cited

Wilson GT, Sysko R. Frequency of binge eating episodes in bulimia nervosa and binge eating disorder: diagnostic considerations. *Int J Eat Disord.* 2009;42:603–610.

Wonderlich SA, Gordon KH, Mitchell JE, et al. The validity and clinical utility of binge eating disorder. *Int J Eat Disord.* 2009;42:687–705.

Severity criteria

Frequency of binge eating (episodes per week)
See the research criteria below from *DSM-IV,* Appendix B: Criteria Sets and Axes for Further Study. The work group is proposing that this disorder be moved from the Appendix to a free-standing diagnosis in *DSM-V.*

Research criteria for binge eating disorder

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by both of the following:
   1. Eating, in a discrete period of time (e.g., within any 2-h period), an amount of food that is definitely larger than most people would eat in a similar period of time under similar circumstances
   2. A sense of lack of control over eating during the episode (e.g., a feeling that one cannot stop eating or control what or how much one is eating)

B. The binge eating episodes are associated with three (or more) of the following:
   1. Eating much more rapidly than normal
   2. Eating until feeling uncomfortably full
   3. Eating large amounts of food when not feeling physically hungry
   4. Eating alone because of being embarrassed by how much one is eating
   5. Feeling disgusted with oneself, depressed, or very guilty after overeating

(*Continued*)

Table 23–1 Diagnostic Criteria (*Continued*)

Binge Eating Disorder (BED)
C. Marked distress regarding binge eating is present D. The binge eating occurs, on average, at least 2 days a week for 6 months. *Note:* The method of determining frequency differs from that used for Bulimia Nervosa; future research should address whether the preferred method of setting a frequency threshold is counting the number of days on which binges occur or counting the number of episodes of binge eating. The binge eating is not associated with the regular use of inappropriate compensatory behaviors (e.g., purging, fasting, excessive exercise) and does not occur exclusively during the course of Anorexia Nervosa or Bulimia Nervosa.
Avoidant/Restrictive Food Intake Disorder
• Eating or feeding disturbance (not limited to apparent lack of interest in eating or food; avoidance based on the sensory characteristics of food; or concern about aversive consequences of eating) as manifested by persistent failure to meet appropriate nutritional and/or energy needs associated with one or more of the following: – Significant weight loss (or failure to gain weight or faltering growth in children) – Significant nutritional deficiency – Dependence on enteral feeding or nutritional supplements – Marked interference with psychosocial functioning • There is no evidence that lack of available food or an associated culturally sanctioned practice is sufficient to account for the disorder

- The eating disturbance does not occur exclusively during the course of anorexia nervosa or bulimia nervosa, and there is no evidence of a disturbance in the way in which one's body weight or shape is experienced

The eating disturbance is not better accounted for by a concurrent medical condition or another mental disorder. When occurring in the context of another condition or disorder, the severity of the eating disturbance exceeds that routinely associated with the condition or disorder and warrants additional clinical attention.

Feeding or Eating Disorder Not Elsewhere Classified

Atypical, mixed, or below-threshold presentations

- Atypical anorexia nervosa

All the criteria for anorexia nervosa are met, except that, despite significant weight loss, the individual's weight is within or above the normal range

- Subthreshold bulimia nervosa (low frequency or limited duration)

All the criteria for bulimia nervosa are met, except that the binge eating and inappropriate compensatory behaviors occur, on average, less than once a week and/or for less than for fewer than for 3 mo.

- Subthreshold BED (low frequency or limited duration)

All the criteria for BED are met, except that the binge eating occurs, on average, less than once a week and/or for fewer than for 3 mo

Medical complications can occur for any type of eating disorder. Table 23–2 details some of the most commonly found complications in AN and BN. The most severe complications that can result in death have been related to sudden cardiac arrest and refeeding syndrome. Refeeding syndrome refers to severe extracellular hypophosphatemia as the body moves from using catabolized muscle and fat as the energy source to carbohydrate with refeeding. Ultimately this may result in decreased adenosine triphosphate (ATP), which can lead to cardiac and respiratory failure. See Chapter 13 for a discussion of

Table 23–2 Medical Complications of Eating Disorders

Clinical Signs	Anorexia Nervosa	Bulimia Nervosa
Labs	Low potassium, magnesium, or phosphorus related to refeeding	Low potassium, magnesium and elevated CO_2
Gastrointestinal (GI)	Bloating, constipation, and delayed gastric emptying	Bloating, constipation, delayed gastric emptying, dysmotility, reflux, and GI bleeding
Cardiovascular	Hypotension and orthostasis	Cardiac arrhythmias and palpitations
Skeletal and dental	Osteopenia and osteoporosis	Dental caries and erosion
Weight	Underweight	Variable
Growth	Can delay growth	Typically not affected
Other	Cold sensitivity, fatigue, and irregular menstrual cycles	Irregular menstrual cycles and fluid retention with edema

Source: Adapted from the American Dietetic Association. Position of the American Dietetic Association: nutrition intervention in the treatment of anorexia nervosa, bulimia nervosa, and other eating disorders. *J Am Diet Assoc.* 2006;106: 2073–2082.

refeeding syndrome. Nutrition-focused physical findings could also include calluses on hands (related to purging), lanugo, or swollen salivary glands.

Successful treatment of eating disorders begins with a multidisciplinary team (medical provider, registered dietitian (RD), mental health provider, and in some cases family therapist and/or psychiatrist) evaluation of the patient's presenting medical, psychological, and nutritional symptoms. The multidisciplinary team would initiate a treatment recommendation based on the level of care appropriate for that individual patient and family. Table 23–3 includes

Table 23–3 Levels of Care for the Treatment of Patients with Eating Disorders[a]

Level 1: (Highest level of care) Inpatient hospitalization • <85% of healthy body weight, acute food refusal even if not <85% of healthy body weight, low heart rate and/or blood pressure, and abnormal electrolytes may be present • Uncooperative with outpatient treatment and needs supervision during and after meals and/or support of nasogastric feedings
Level 2: Residential treatment • <85% of healthy body weight, however does not require daily feeding tubes, labs, or intravenous fluids • Support/supervision during and after meals needed
Level 3: Partial (full day outpatient care) • Generally >80% of healthy body weight, needs some structure around meal times to support recovery • Medically stable enough to travel from home to program daily • Support/supervision during and after meals needed
Level 4: Intensive outpatient (often evening programs) • Generally >80% of healthy body weight • Some support/supervision during and after meals needed

(*Continued*)

Table 23–3 Levels of Care for the Treatment of Patients with Eating Disorders[a] (*Continued*)

Level 5: Outpatient • Generally >85% of healthy body weight • Minimal support/supervision during and after meals needed • Frequency of visits may vary over time depending on progress

[a] *Recommended levels of care may differ between institutions and may vary on a case-by-case basis.*

recommended criteria to establish an appropriate level of care. Individuals with eating disorders frequently transit through the various levels of care throughout treatment. Some require only outpatient treatment, whereas intensive outpatient, partial, residential, or inpatient hospitalization will be necessary for most. Table 23–4 provides an example

Table 23–4 Sample Inpatient Medical Protocol

Goals To stabilize heart rate, blood pressure, electrolytes, body weight, and body temperature by improving nutritional status. This will be done by having patient eat prescribed meals and limiting activity
Medical monitoring Vital signs (heart rate and blood pressure), temperature, labs (concern for refeeding syndrome), body weight, and urine specific gravity. Multivitamin with minerals and supplement providing K/Na/P (to prevent refeeding syndrome) given daily; amount of K/Na/P may be adjusted based on lab value
Nutrition therapy At Boston Children's Hospital, standard exchange-based meal plans exist starting at 1250 kcal/d and are increased by 250 kcal/d up to 2750 kcal/d. In patient meal plans typically start with 1500 kcal meal plans (see below) and increase 250 cal/d until goal meal plan is met. Lower base calorie levels may be established in more compromised patients. Patients are able to make food selections and preferences within the exchange system for meal planning

1500-Cal meal plan
Dietary exchanges supplement equivalent (250 cal) breakfast
1 grain, 1 protein, 1 fruit, 1 milk, 1 fat, 1½ supplements
Snack
8–12 oz water (based on fluids needs)
Lunch
2 grains, 2 proteins, 1 fruit, 1 vegetable, 1 milk, 2 fats, 2½ supplements
Snack
8–12 oz water (based on fluids needs)
Dinner
2 grains, 2 proteins, 1 fruit, 1 vegetable, 1 milk, 2 fats, 2½ supplements
Snack
8–12 oz water (based on fluids needs)
Supplementation
If meal is not completed within 30 minutes, the supplement equivalent is offered
If a patient is unable to drink the supplements in the allotted amount of time, the use of a nasogastric tube may be considered
Weight gain expectations
Inpatient weight gain is expected to be 0.2 kg/d, if not met may receive supplements in addition to meal plan or meal plan may simply be increased
Exercise
Not permitted during hospitalization

of the components of an inpatient medical hospitalization protocol. Frequency of visits with the outpatient team may vary as patient is in recovery. For instance, weekly visits may initially occur with each provider.[5]

Nutrition intervention, including nutrition counseling by a RD, is an essential component of the eating disorder treatment.[6] RDs in this practice area require advanced training to provide medical nutrition therapy for the

normalization of eating patterns and nutritional status. The role of the RD in the treatment of eating disorders is very complex and should be viewed case by case, depending on presenting issues. The RD should assess current weight and determine weight goals, based on weight history and estimated mean body weight. The RD should then determine estimated energy and nutrient needs and come up with nutrition plan. It is beneficial to conduct 24-hour recall to determine starting meal plan. Nutrition plan is an exchange-based meal plan; however, the RD may discuss nutrition plan in terms of core food groups and give guidelines based on balanced meals and snacks. RDs also discuss challenge foods and work on incorporating them back into the meal plan. It is important to keep in mind that eating disorder behaviors are not going to change overnight, and it is important to set 1–2 goals for patient to work on each week.

Resources

Eating Disorder Organizations

Multi-service Eating Disorders Association, Inc. (MEDA)
www.medainc.org
National Eating Disorder Association (NEDA)
www.nationaleatingdisorders.org

Eating Disorder Reference

GÜRZE Books: Eating Disorder Resource Catalogue
www.bulimia.com

Informational Websites

www.youngwomenshealth.org
www.somethingfishy.org
www.maudsleyparents.org

Note: Health educators should be cautious when advising Internet browsing, as pro eating disorder websites are very easily accessible to this vulnerable population.

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24 Food Allergies

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Food allergy or hypersensitivity is defined as a reproducible adverse immunologic reaction to food. Food allergies may be immunoglobin E (IgE) related, non IgE mediated, or a combination of both (Table 24–1). Food allergies affect up to 6% of young children and 3%–4% of adults.[1] Based on studies in the United States and the United Kingdom, the incidence of allergy to peanuts has doubled in the past decade resulting in ~1% of the population being affected.[1] Although any food can cause

Table 24–1 Adverse Immunologic Reactions to Food

IgE Mediated	IgE Mediated and Non-IgE Mediated	Non-IgE Mediated
Oral allergy syndrome	EoE	Food protein–induced enterocolitis (FPIES)
Anaphylaxis	Eosinophilic gastritis	Dietary protein proctitis/allergic colitis
Urticaria	Eosinophilic gastroenteritis	Dermatitis herpetiformis
Food-associated exercise-induced anaphylaxis	Atopic dermatitis	Celiac disease

an allergic reaction, approximately 90% of allergic reactions are caused by milk, eggs, peanuts, tree nuts, soy, wheat, fish, and shellfish. The peak age of food allergy incidence is 0–2 years, which is thought to be due to the relatively immature gastrointestinal barrier function. Sensitization results when the immune system responds to a specific food protein, most often with the development of allergen-specific IgE. Once the individual is sensitized, an adverse reaction on exposure to a particular food may (or may not) be experienced.

Clinical symptoms involved in food allergies may be gastrointestinal, respiratory, dermatologic, or systemic in nature (Table 24–2). Symptoms of IgE-mediated reactions typically occur in minutes to hours. Symptoms of non-IgE-mediated reactions are typically delayed in onset and longer lasting. Unlike food allergies, food intolerances do not involve the immune system. Food intolerance is a nonimmunologic response to an ingested food or food additive, which can lead to a physiological reaction.

Table 24–2 Food Allergy Disorders and Symptoms

Gastrointestinal
IgE mediated
Oral allergy syndrome—angioedema of the lips, tongue and palate
Gastrointestinal anaphylaxis—rapid onset of nausea, abdominal pain, cramps, vomiting, diarrhea
IgE mediated and/or cell mediated
Eosinophilic gastroenteritis—nausea, vomiting, and weight loss
Eosinophilic esophagitis—GERD, excessive spitting up or emesis
Cell mediated
Celiac disease—diarrhea or steatorrhea, abdominal distension, and weight loss
FPIES—vomiting and diarrhea, typically delayed 1–3 h after eating

(*Continued*)

Table 24–2 Food Allergy Disorders and Symptoms (*Continued*)

Dermatological
IgE mediated
Acute and chronic urticaria
Angioedema
IgE mediated and/or cell mediated
Atopic dermatitis/eczema
Cell mediated
Contact dermatitis (marked pruritus; eczematous rash)
Dermatitis herpetiformis (marked pruritus; papulovesicular rash over extensor surfaces and buttocks).
Respiratory
IgE mediated
Allergic rhinoconjunctivitis—tearing, nasal congestion, and sneezing
IgE mediated and/or cell mediated
Asthma—cough, dyspnea, and wheezing
Mechanism unknown
Heiner's syndrome—rare form of pulmonary hemosiderosis
Generalized
IgE mediated
Anaphylactic shock

Source: Adapted from Sampson.[2]

DIAGNOSIS

When diagnosing food allergies, a thorough history of symptoms associated with the ingestion of specific foods should be obtained. Currently, a double-blind placebo-controlled food challenge continues to be the "gold standard" for the diagnosis of an IgE-mediated food allergy. However, double-blind placebo-controlled challenges are difficult to administer and often open or single-blinded challenges are used in the clinical setting. There are also clinical and laboratory tests that help in the diagnosis of food allergies (Table 24–3). Two commonly

Table 24–3 Common Laboratory Tests for Food Allergies

Laboratory Test	Procedure	Comments
SPT	A small amount of the allergen is introduced to the skin; a wheal 3 mm or greater than the control is usually considered positive. There may be falsely negative tests if antihistamines are taken a few days before testing.	A rapid method to confirm sensitivity to an allergen, but it does not confirm diagnosis. A positive skin test to some foods may persist even when clinical symptoms are no longer present. The negative predictive value of this test is 95%. A positive predictive value (PPV) is 50%.
Serum food-specific IgE testing	Blood test	Quantitative measurements of food-specific IgE antibodies. Helpful in evaluating IgE-mediated food allergies; may be substituted for skin test when history of recent anaphylaxis, significant dermatitis at skin test site, or recent use of antihistamines Like the skin test, a negative result is very reliable, but a positive result has low specificity in ruling out an IgE-mediated reaction to a specific food.
Atopy patch testing	A small amount of the allergen is placed in individual aluminum chambers and is applied to the upper back with	A method for evaluating non-IgE-mediated food allergies. Patch testing is considered an unvalidated test; therefore, its use is limited to specific medical conditions, for example, eosinophilic esophagitis.

(*Continued*)

Table 24–3 Common Laboratory Tests for Food Allergies (*Continued*)

Laboratory Test	Procedure	Comments
	an adhesive tape. Patch tests are taken off after 48 h and evaluated for local reaction 24–48 h after removal.	
Biopsy	Endoscopy	Most definitive diagnosis for many gastrointestinal hypersensitivities.

Source: Adapted from Sampson HA[2].

used tests for IgE-mediated allergies are skin prick tests (SPTs) and serum immunoassays to quantify serum-specific IgE antibodies to foods (sIgE). The term RAST is an old acronym used for an assay for food-specific IgE levels that is no longer available. Higher food-specific IgE levels and large SPT wheal sizes are often associated with a higher likelihood of having an allergic reaction. However, these tests are limited and false-positive results are very common.[1] These tests do help predict the likelihood of having a food allergy reaction but do not help predict the severity of a reaction.[1] Occasionally, one may have no detectable sIgE and a negative SPT but still react to a specific food. Serum food-specific IgE tests can be followed over time (e.g., annually), and a decreasing level is associated with an increased chance of food allergy resolution.

Eosinophilic Disorders

There are various groups of eosinophilic gastroenteropathies that involve eosinophilic infiltration resulting in the inflammation of the gut. Subgroups include eosinophilic gastroenteritis (EG), eosinophilic enterocolitis, and eosinophilic esophagitis (EoE). EoE is a disease found in both children and adults

that is increasingly documented. The definition of EoE is endoscopic testing revealing ≥15 eosinophils per high-power field isolated only in the esophagus.[3] EoE is often associated with gastroesophageal reflux disease (GERD) because it has many of the same symptoms, which include dysphagia, failure to thrive, food impactions, nausea, vomiting, diarrhea, bloating, abdominal or chest pain, difficulty in sleeping, and food refusal or poor appetite. GERD, however, responds to acid suppression treatment, whereas EoE does not. EoE may be responsive to the removal of dietary food allergens.[4] EoE is sometimes treated with swallowed steroids; however, this is a short-term solution. Nutrition therapy is thought to be the most effective treatment for EE, and there are three approaches to nutrition therapy that are often recommended: an elemental diet, an empiric elimination diet based on the most common food allergies, and an elimination diet based on individual allergy testing (see Chapter 25 for a further discussion on EoE).

◆ ELIMINATION DIETS

There is currently no cure for food allergies. Once the diagnosis is made, the offending protein(s) must be removed from the diet to avoid allergic reactions. Complete elimination of food allergens requires reading the ingredient labels of all foods, beverages, medications, crafts (young children), supplements, and topical applications (lotions, sunscreens, shampoos) to determine whether a food allergen is present. If an allergen is present, or cannot be ruled out, the product must be avoided. Reading all food labels all the time is critical to avoid accidental ingestion of food allergens. Manufacturers frequently change product ingredients, so it is critical to check labels each time a product is consumed or applied to prevent accidental exposure to the allergen. The Food Allergen Labeling and Consumer Protection Act (FALCPA) went into effect on January 6, 2006. This law requires food manufacturers to

identify, in plain, common language, the presence of any of the eight major food allergens (milk, egg, peanut, tree nut, fish, shellfish, wheat, and soy) in foods. The law requires labels to indicate the presence of these allergens in spices, flavorings, additives, and colorings.[5] FALCPA does not regulate precautionary/advisory labeling statements such as "may contain peanuts" or "made in a factory with tree nuts" or "made on shared equipment with eggs". A study in 2007 examined 200 packaged foods with precautionary labeling for peanut and found that 6% of these foods had clinically significant levels of peanut protein.[6] Generally, it is recommended that products with precautionary labeling for allergens be avoided.

Those with food allergies to foods not included in the aforementioned eight must read labels and be familiar with ingredients' names that may contain the food allergen. The Food Allergy and Anaphylaxis Network (foodallergy.org) as well as the Consortium of Food Allergy Research (COFAR) (web.emmes.com/study/cofar/) have education materials regarding how to read food labels for the top eight allergens. COFAR also provides information regarding sesame-free diets.

Registered dietitians should help educate families on the elimination diet (including terminology when reading labels), appropriate substitutions for allergenic foods (Table 25–4), and nutritional adequacy of diet, as well as provide the families with additional resources (Table 24–5).

Education about food allergy management should be thought of as an ongoing learning process. Avoidance of food allergens requires families to find alternatives to common foods, adjust recipes, and make appropriate substitutions. When a child has food allergies, it is essential that the family also educate other family members, camp counselors, teachers, and child-care providers on the avoidance of food allergens. It is important to develop allergy management strategies for home, school, and dining out to prevent

Table 24–4 Food Allergy Substitutions

Wheat	Milk	Egg
Basic gluten-free flour blend 2 c. rice flour (superfine is best) and $^2/_3$ c. potato starch (or cornstarch, in some cases) $^1/_3$ c. tapioca starch 1 tsp. xanthan or guar gum (more or less, depending on what you are baking) (see Chapter 25). For bread, pasta, crackers, and cereal: look for corn-, rice-, millet-, and quinoa-based products. For lunch and snacks, think outside the sandwich and try corn chips and dip, soup with corn chips or quinoa or rice added, corn tacos, safe trail mix, baked potato, cold rice pasta salad.	Alternative beverage**:** Calcium- and vitamin D–fortified soy milk, rice milk, almond milk. For baking when milk is called for: small quantities: substitute 1:1 using soy, rice, nut, oat, or coconut milk as safe and appropriate for cow's milk. Water, juice, or even coffee may work in some cases. **Large quantities:** If substituting rice milk, water, or another thin liquid in recipes, use $^7/_8$ c. for every 1 c. called for in the recipe. For baking, when butter is called for use a safe margarine or soy substitute. Instead of adding cheese, try legumes, avocado, seeds, or bean spreads. Try soy or coconut yogurt.	In soups, sauces, and other dishes: replace each egg with 2 tbsp. pureed vegetable Baking: (replace each egg with) 1 $^1/_2$ tbsp. water, 1 $^1/_2$ tbsp. oil, 1 tsp. baking powder 1 tsp. baking powder + 1 tbsp. liquid (water) + 1 tbsp. vinegar Place in blender: one heaping tablespoon of whole flaxseeds, blend until it becomes a fine meal. Add $^1/_4$ c. cold water, blend for 2 to 3 min until it thickens and resembles the consistency of eggs. Microwave till bubbly. Each $^1/_4$ c. of flaxseed mixture will replace one egg in baking. For thickening cream dishes and sauces: add extra flour, cornstarch, or xanthan gum.

Table 24–5 Food Allergy Resources

Food Allergy and Anaphylaxis Network (FAAN)
www.foodallergy.org
FAAN is a national nonprofit organization established to help families living with food allergies. Their mission is "to raise public awareness, to provide advocacy and education, and to advance research on behalf of all those affected by food allergies and anaphylaxis." They publish several newsletters; have books, booklets, videos, and other resources designed to educate about food allergy; and have a very informative website. All resources are checked for scientific accuracy by FAAN's 12-member medical advisory board. There is a subscription fee.

Asthma and Allergy Foundation of America® (AAFA)
www.aafa.org
AAFA works to provide free information, educational programs, advocacy, and grants for research about asthma and allergies. They support a national network of 13 chapters, which provide a variety of services, educational programs, and support to people with asthma and allergies.

Consortium of Food Allergy Research
https://web.emmes.com/study/cofar/index.htm

Allergy Home
http://www.allergyhome.org/

Kids with Food Allergies
www.kidswithfoodallergies.org
Kids with Food Allergies is a national nonprofit food allergy support organization dedicated to fostering optimal health, nutrition, and well-being of children with food allergies by providing education and a caring support community for their families and caregivers. Their website offers practical resources related to managing children's food allergies and planning for school and day care, a searchable recipe database, books for parents and children, and a directory of allergy-friendly businesses. The organization also provides an online support forum where parents can use message boards to share practical allergy management strategies and emotional support. A medical advisory team reviews educational materials and links included on the website.

American Partnership for Eosinophilic Disorders (APFED)
www.apfed.org
APFED is a nonprofit advocacy organization for those living with eosinophilic esophagitis, eosinophilic gastroenteritis, eosinophilic colitis, hypereosinophilic syndrome, and other eosinophilic disorders. It is a resource for patients, their families, physicians, and the medical community.
APFED provides accurate, up-to-date information on eosinophilic disorders and related problems. Its goals are to increase awareness, educate patients and physicians, increase funding for research, and provide support for the eosinophilic community.

American Academy of Allergy Asthma and Immunology
The AAAAI website offers tips for managing allergies and asthma, including school-related resources.
www.aaaai.org

Sully's Living Without ® Magazine
www.livingwithout.com
A quarterly "lifestyle guide for people with allergies and food sensitivities." There is a subscription fee.

SPECIALTY FOODS

www.amandasown.com
www.Cherrybrookkitchen.com
www.Divvies.com
www.Ener-G.com
www.Enjoylifefoods.com
www.Turtlemountain.com
www.Peanutfreeplanet.com
www.Reallygreatfoods.com
www.Sunbutter.com

More websites and specific descriptions of foods produced can be found at www.kidswithfoodallergies.org

COOKBOOKS
Note: Although many cookbooks are available, no one allergy cookbook will meet everyone's individual diet restrictions, but each can provide helpful recipes. Follow your own list of restrictions.

(*Continued*)

Table 24–5 Food Allergy Resources (*Continued*)

If necessary, use caution with cookbook recommendations, such as "you may be able to substitute goat cheese for cow's milk cheese," which is not recommended on a cow's milk–free diet as above. It is also helpful to search the Internet for recipes.

- *Allergen-Free Baker's Handbook* by Cybele Pascal 2009
- *Allergy-Free Desserts: Gluten-Free, Dairy-Free, Egg-Free, Soy-Free and Nut-Free* by Elizabeth Gordon (2010)
- *The Food Allergy Mama's Baking Book: Great Dairy, Egg and Nut Free Treats for the Whole Family* by Kelly Rudnicki (2009)
- *Great Foods without Worry* by Cindy Moseley (2003)
- *Sophie-Safe Cooking: A Collection of Family Friendly Recipes That Are Free of Milk, Eggs, Wheat, Soy, Peanut, Tree Nut, Fish and Shellfish* by Emily Hendrix (2006)
- *Special Diet Celebrations: No Wheat, Gluten, Dairy, or Eggs* by Carol Fenster, PhD (1999)
- *What Else Is to Eat? The Dairy-Egg, and Nut-Free Cookbook* by Linda Marienhoff Coss (2008)
- *The Whole Foods Food Allergy Cookbook: Two Hundred Gourmet and Homestyle Recipes for the Food Allergic Family* by Cybele Pascal (2006)

accidental exposure to food allergens (Table 24–6). The management of food allergy adds time and anxiety to daily chores such as food shopping and preparation. Planning is often needed for the child's participation in social and family activities involving food.[7] Parental worry about issues such as leaving a child in someone else's care and ability to respond in an emergency are common concerns.[8] A 2003 study reviewed 7–12-year-old children and found that those with peanut allergy reported a poorer quality of life and more anxiety around eating than those with insulin-dependent diabetes.[9] It is important to educate families on how to manage food allergies in a way that empowers them with safe options for their children and focuses on effective routines that can help their children safely participate in normative daily activities.

Table 24–6 Managing Life With Food Allergies

At home

- Cook an allergen-free meal first.
- Designate areas in the pantry, refrigerator, and cabinets for allergen-free foods.
- Use stickers to place on "safe" or "unsafe" foods.
- Keep an extra supply of "safe" foods frozen for quick meals.
- Be aware that cooking fumes from fish during frying and steaming can result in an allergic reaction from inhalation.
- Use squeeze top condiments rather than those requiring utensils.

At school

- Provide food for a school celebration or snack time for the entire class.
- Keep favorite treats individually wrapped in the freezer for easy access on celebration days.
- Recommend nonedible treats for classroom parties (i.e., stickers, colorful pencils, or other child-friendly collectibles).
- Pack a lunch of "safe" foods.
- Encourage your child not to trade foods at lunch or snack time.
- Encourage good hand-washing practices for all students, especially after meal and snack time.

Dining out

- Speak to the manager to explain food allergies and go to restaurants at off-hours and days when the restaurants are less busy.
- Order foods "naked" without sauces or gravies.
- Bring your own safe salad dressing, margarine, or condiments.
- Fried foods may contain protein from other foods cooked in the same oil (i.e., french fries cooked in oil that was previously used to fry fish.)
- Provide a "chef card" to the manager and chef. The allergic individual personalizes the card regarding his/her food

(*Continued*)

Table 24–6 Managing Life With Food Allergies (*Continued*)

allergies (available from The Food Allergy Network—www .foodallergy.org and www.selectwisely.com).
• Ask about food preparation techniques and remind staff about possible sources of cross contamination.

Anaphylactic reactions to food are estimated to occur 53,700 times per year.[1] Deaths are primarily reported from allergic reactions to peanuts and tree nuts. These fatalities appear to be associated with delayed treatment with epinephrine and occur more often in teenagers and young adults with asthma and previously diagnosed food allergy.[1] Early recognition of symptoms and self- or parent/caregiver-injected epinephrine (such as EpiPen®) followed by emergency room visits can save lives, and each child's emergency treatment plan should be constructed by the allergist.

NUTRITIONAL ADEQUACY OF THE DIET

Since the long-term removal of multiple food allergens from the diet may result in poor growth and development, it is critical for families to meet a dietitian and an allergy physician who are experienced with food allergies.

When a food or food group is eliminated, attention must be focused on potential dietary insufficiencies resulting from these exclusions. A cross-sectional study found that children who received nutritional counseling or consumed infant/toddler hypoallergenic formula or a fortified soy beverage had a lower incidence of inadequate calcium and vitamin D intake.[10]

Most children under 2 years of age with cow's milk or soy allergy will benefit from a hypoallergenic, extensively hydrolyzed cow's milk protein, or free amino acid–based formula, which acts as a milk substitute during infancy. Low-fat, low-protein beverages such as almond milk and

Table 24–7 Most Common Allergens and the Nutrients They Provide

Allergen	Nutrients
Milk	Protein, vitamins A and D, riboflavin, pantothenic acid, vitamin B12, calcium, and phosphorus
Egg	Protein, vitamin B12, riboflavin, pantothenic acid, biotin, and selenium
Soy	Protein, thiamin, riboflavin, pyridoxine, folate, calcium, phosphorus, magnesium, iron, and zinc and B12 if the product is fortified
Wheat	Thiamin, riboflavin, niacin, iron, and magnesium and folate if the product is fortified
Peanut/tree nuts	Protein, vitamin E, niacin, magnesium, manganese, and chromium and zinc
Fish	Protein; omega-3 fatty acids; vitamins A, D, and B12

rice milk are not generally recommended for children under 2 years of age. Case reports have associated the use of these types of beverages with kwashiorkor.[11] When more than one food group is eliminated, nutritional adequacy becomes more of a concern. Specific nutrients that are provided by the common food allergens are shown in Table 24–7. Vitamin and mineral supplements (allergen free) may also play a critical role in ensuring the adequacy of a child's nutritional intake (see Chapter 11).

◆ BREAST-FEEDING

Breast-feeding mothers of allergic infants are encouraged to continue breast-feeding while avoiding their children's allergens in their diet, following the same elimination diet guidelines. The nutritional adequacy of a mother's diet should be monitored as well and may require allergen-free vitamin and mineral supplementation. If supplementary formula is needed

for the infant, a hypoallergenic, extensively hydrolyzed protein or free amino acid formula is recommended.

FOOD CHALLENGES

Based on a child's serial sIgE testing and/or clinical history, a physician may recommend a food challenge to determine whether a food can be reintroduced into the child's diet. There are three types of food challenges: open, single-blinded, and double-blinded placebo-controlled challenges (Table 24–8). The type of challenge should be determined by the physician and depends on the age of the child and the symptoms of the allergic presentation.

Table 24–8 Food Challenges

Type of Food Challenge	Description	Example
Double blind placebo controlled (DBPC)	The most objective test: The patient, parents, and medical personnel administering the challenge are blinded to the food being challenged.	Dried egg white powder mixed into a carrier (i.e., applesauce or fruit juice), placebos can be dextrose, cornstarch, baby food, dry cereal, or others.
Single blinded	The patient and parents are unaware of the food being challenged. This type of challenge eliminates the bias of the patient and family.	Milk powder mixed with a carrier (i.e., applesauce or juice) and a placebo such as cornstarch would be mixed into the carrier as well.
Open challenge	Unblinded food challenge; it means that the	If challenging an individual to a food such as milk, he

Type of Food Challenge	Description	Example
	individual knows what food will be consumed. An open challenge can help the individual to realize that a particular food is not responsible for the symptoms. An open challenge is usually performed at the end of a DBPC and a single-blinded challenge if the challenge is successful.	or she could be provided with milk, yogurt, or cheese.

During a food challenge, the food is given in gradually increasing amounts in a controlled environment so that the child can be observed closely and treated for adverse reactions if they occur. For example, a child may start with ingesting 100 mg of protein from the food allergen and serially work up to 8 g of the food protein if tolerated.

PRIMARY PREVENTION OF FOOD ALLERGY

The American Academy of Pediatrics has recommended that infants at high risk for food allergy have delayed introduction of highly allergenic foods. Some have postulated, however, that the early introduction of allergenic foods may actually protect against the development of food allergies. In the Middle East, Southeast Asia, and Africa, where peanut is consumed in high amounts during infancy, peanut allergy is rare.[1] Further research is needed, and large studies evaluating early verses late introduction of peanut and egg are in progress.

The American Academy of Pediatrics published new recommendations in 2008 regarding early nutrition intervention.[1] Maternal dietary restriction of food allergens during pregnancy and lactation for the prevention of food allergy are currently not recommended. For infants at high risk of developing allergic (atopic) disease, evidence supports exclusive breast-feeding for four to six months over the use of cow's milk–based formulas due to suggested lower rates of atopic dermatitis and cow's milk allergy in breast-fed children. In infants who are not breast-fed, there is modest evidence to support using an extensively or partially hydrolyzed formula instead of an intact cow's milk protein–based formula. Solid foods should not be introduced until 4–6 months of age, but there is no evidence supporting delaying the introduction of foods (including common allergens) beyond 4–6 months of age. ("At risk" is defined as children with a biological parent or sibling with or having a history of allergic rhinitis, asthma, atopic dermatitis, or food allergy.) Recommendations on the introduction of allergens to infants who already have food allergies were not addressed in this report.[1]

ONOGOING RESEARCH

Ongoing research includes oral immunotherapy (OIT) and sublingual immunotherapy (SLIT). Oral immunotherapy is giving small amounts of food allergens in a highly controlled clinical setting in the hopes of developing desensitization (tolerance to accidental ingestion) and perhaps long-term tolerance. Studies evaluating OIT and SLIT have been promising treatment for food allergies. However, there is a high rate of adverse reactions with OIT and more data are required to look at safety with desensitization.[2] Some studies include anti-IgE medication during the desensitization process.[15] Clinical studies have also looked

into extensively heated (baked) milk and egg consumption. In one study, 75% of milk-allergic children tolerated milk in well-baked products.[1] Additional placebo-controlled trials examining the dose of the allergen, dose of escalation, duration of therapy, additional medication, and route of administration are necessary to determine whether these forms of therapy can induce lasting oral tolerance rather than simply desensitization, which requires daily treatment.[1]

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25 Gastrointestinal Diseases

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INTRODUCTION

Most pediatric gastrointestinal diseases require nutritional assessment and therapy to augment medical therapy, and in some diseases, nutrition therapy is the primary treatment. In this chapter, we review the nutritional management of gastroesophageal reflux disease (GERD), celiac disease (CD), constipation, diarrheal diseases, lactose intolerance, inflammatory bowel disease (IBD), and eosinophilic esophagitis (EoE).

GASTROESOPHAGEAL REFLUX

GER is the effortless movement of gastric contents into the esophagus and is considered a normal physiologic process. Regurgitations occur due to transient relaxations of the lower esophageal sphincter (LES) and are characterized as postprandial, lasting a few minutes, and not associated with other symptoms. As many as 50% of healthy infants have several physiologic regurgitations daily as a newborn and in early infancy despite being fed breast milk or formula milk. Infant regurgitations resolve over the first few months of life without treatment.[1]

GASTROESOPHAGEAL REFLUX DISEASE

A diagnosis of GERD is made when the presence of troublesome symptoms or complications of multiple reflux episodes occur.[1] Endoscopy can reveal erosions (mucosal breaks) or Barrett esophagus in the distal esophagus suggestive of GERD or evaluate for other causes of esophagitis (EoE). [1] Symptom correlation (respiratory symptoms such as pneumonia, cough, or chest pain) can be further evaluated by esophageal ph monitoring combined with multiple intraluminal impedance testing (MII) if indicated.[1]

Most commonly, a diagnosis of GERD is made on history and physical exam alone. Symptoms of GERD vary by age group and regurgitation and vomiting associated with crying and food refusal may not be a specific indicator of GERD in infants and toddlers. GERD in toddlers and young children (1–6 years) tends to present with food refusal, regurgitation, vomiting, and abdominal pain. In older children (6–17 years), regurgitation or vomiting is associated with epigastric pain or heartburn or cough.[1] See Table 25–1 for signs and symptoms typically associated with GERD.

Children at higher risk for GERD include children with neurologic disorders, hypotonia, repaired esophageal atresia, repaired achalasia, congenital diaphragmatic hernia, hiatal hernia, cystic fibrosis, lung transplantation, obesity, and a family history of GERD.[1] Multiple physiologic factors are thought to be responsible for GERD, including a decreased LES tone, delayed esophageal peristalsis, and delayed gastric emptying that leads to esophageal mucosal irritation from hydrochloric acid, pepsin, and possibly bile acid exposure.

Treatment for GERD may include dietary and lifestyle and pharmacologic therapies; however, evidence for efficacy of diet and lifestyle changes is limited (Table 25–2). In infancy, milk protein allergy can present with similar symptoms

Table 25–1 Signs and Symptoms Associated With GERD in Children[1]

Symptoms	Signs
Recurrent regurgitation with/without vomiting	Erosive esophagitis
Weight loss or poor weight gain	Esophageal stricture
Irritability in infants	Barrett esophagus
Ruminative behavior	Laryngeal/pharyngeal inflammation
Heartburn or chest pain	Recurrent pneumonia
Hematemesis	Anemia
Dysphagia	Dental erosion
Odynophagia (painful swallowing)	Feeding refusal
Wheezing	Dystonic neck posturing (Sandifer syndrome)
Stridor	Apnea spells and apparent life-threatening events (rarely due to GERD)
Cough	
Hoarseness	

Abbreviation: GERD, gastroesophageal reflux disease.

of GERD including excessive crying, regurgitation, or vomiting, and a trial of an extensively hydrolyzed or free amino acid infant formula for two to four weeks is warranted.[1] Breast-fed infants with symptoms may benefit from a trial of withdrawal of cow milk and eggs from the maternal diet.[1] Thickening of formula (or use of a commercial anti-regurgitation formula) decreases the height of reflux in the esophagus, thus visible regurgitation, but may not significantly decrease the frequency of esophageal reflux episodes and may increase coughing with feeds.[1] The addition of rice cereal to thicken infant formula increases the energy density of the formula and may displace calories (see Table 25–2). In an infant with poor weight gain, a trial of concentrated calorie formula with education to caregivers on the required volume of formula needed to meet nutritional needs for growth is recommended in addition to hydrolyzed

Table 25–2 Diet/Lifestyle Interventions for Infants, Children, and Adolescents With GERD

Dietary Interventions in Infancy and Children With GERD
Formula change: 2–4-week trial of an extensively hydrolyzed or free amino acid formula (to evaluate for milk or soy protein allergy): Thicken feedings: 1 tbs rice cereal to 1 oz formula (25 cal/oz formula), 1 tsp to 2 oz formula (27 cal/oz), 1 tbs rice cereal to 1 oz formula (34 cal/oz formula) Dietary changes to consider in infancy: Change formulas: Trial of whey predominant (to assist gastric emptying) Change feeding schedule: Smaller, more frequent feeding schedule Dietary changes in infants/children with poor weight gain or enteral nutrition support: Concentrate formula: Increase caloric density per ounce and decrease total volume. NG/GT/JT fed: Lengthen continuous feeding time and lower volume rate per hour
Dietary Interventions in Children and Young Adults with GERD
Limited evidence for dietary changes in GERD Avoidance of high fat, acidic, spicy foods Avoidance of caffeinated beverages or foods(tea, coffee, cola, chocolate) Avoidance of carminatives (spearmint and peppermint) Avoidance of late night eating and large volume meal volume helpful in obese adults Weight reduction may help if obesity exists
Lifestyle Interventions in Infants with GERD
Change positioning: Supine positioning recommended from birth to 1 year (due to increased SIDS risk). After 1 year, prone positioning may reduce amount of esophageal exposure. Avoidance of cigarette smoke exposure
Lifestyle Interventions in Children and Young Adults with GERD
Elevate head of bed and sleep in left lateral decubitus position Avoidance of excessive alcohol and smoking (adult studies)

Abbreviations: GERD, gastroesophageal reflux disease; GT, gastrostomy; JT, jejunostomy; NG, nasogastric; SIDS, sudden infant death syndrome.

and thickened formula. Large volume feedings promote regurgitation, thus smaller frequent feedings may decrease regurgitation. In older children, evidence to support dietary modification for GERD is lacking; however, expert opinion suggests small frequent lower fat meals, with the avoidance of carbonation, caffeine chocolate, and spicy foods if they provoke symptoms. In adults, obesity, large meal volume, and late night eating are associated with symptoms of GERD; however, only weight loss improved symptoms and regurgitations in overweight adults.[1] In severe cases, transpyloric feeding may be trialed; however, in children with reflux, transpyloric feeding did not eliminate reflux episodes.[2] In neonates, prolongation of the feeding duration and slowing the feeding rate may decrease the frequency of reflux events.[3]

Lifestyle interventions for GERD (Table 25–2) include avoidance of exposure to cigarette smoke.[4] Positioning of the infant prone (on stomach) post feeds may reduce esophageal acid exposure; however, given the higher risk of sudden infant death syndrome (SIDS), infants from birth to 12 months of age should sleep in the supine (on back) position.[1] After 1 year of age, prone and left-sided sleeping can be considered to help decrease reflux episodes. Studies are limited in children and adolescents, but adult studies show left-sided sleep positioning with elevation of the head of bed decreases reflux episodes. Lifestyle modifications may also include alcohol cessation and smoking cessation if needed in adolescents. In adults, smoking and alcohol intake are associated with symptoms of GERD.

Pharmacologic therapy, antacids, H_2 receptor antagonists, and proton pump inhibitors (PPI), is used if dietary and lifestyle changes do not alleviate symptoms especially in school-aged children.[1] There is insufficient evidence to support the routine use of PPI in infancy, but a 2–4-week trial of PPI is recommended in adolescents with GERD

symptoms with continuation to 3 months if applicable. There is insufficient evidence to support the use of prokinetic agents—metoclopramide, erythromycin, bethanechol, and domperidone—unless benefits of reflux reduction outweigh potential side effects. Surgery is considered if severe GERD refractory to medical management if life-threatening complications of GERD exist.[1]

CELIAC DISEASE

CD is a common permanent, immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. The immunologic response to gluten causes cellular damage to the small intestinal villi leading to the malabsorption of nutrients, predisposition to intestinal lymphoma, and early mortality. The only treatment for CD is a lifelong gluten-free (GF) diet.

Gluten is the common name for the storage proteins (prolamins) in many cereal grains. The toxic prolamins that damage the small intestine in individuals with CD are gliadin (in wheat), secalin (in rye), and hordein (in barley). The prolamin, avenin, in oats has been found to be safe for CD.[5] A wheat-, barley-, rye-, and oat-free diet is recommended to patients with a new diagnosis of CD due to the cross-contamination of oats that occurs if harvested and milled with barley and wheat, as remains a concern in North America. Once individuals are tolerating a GF diet with negative serology testing, patients with CD can consider the consumption of "certified pure, uncontaminated oats" (grown, harvested, processed, stored, and manufactured under a dedicated system). Many national celiac associations are endorsing moderate consumption of pure oats (20–25 g/d or ¼ cup dry rolled oats for children) to a GF diet as they contain fiber and nutrients.[5] Individuals with

CD who include pure oats in their diet should have serial monitoring of clinical status and repeat serology to assess for intolerance to oats with consideration for endoscopy if symptoms persist.

CD is common and occurs in 0.5%–1% of the general population. CD occurs in healthy children (2.5–15 years of age) at a rate of 3–13 per 1000 children or 1:300 to 1:80 healthy children.[6] Conditions that increase the risk of CD and require routine testing for CD at repeated intervals in asymptomatic children include type 1 diabetes mellitus (3%–12%), Down syndrome (5%–12%), autoimmune thyroid disease (up to 7%), Turner syndrome (2%–5%), Williams syndrome (up to 9%), IgA deficiency (2%–8%), autoimmune liver disease (12%–13%), and first-degree relatives with CD (10–20%).[7]

Clinical manifestations of CD require exposure to dietary gluten and are highly variable (see Table 25–3). CD should

Table 25–3 Clinical Manifestations of Celiac Disease[7]

Common Signs and Symptoms	Atypical Signs and Symptoms
Abdominal distention/pain	Amenorrhea
Microcytic anemia (iron deficiency)	Arthritis/arthralgia
Macrocytic anemia (folate deficiency)	Chronic fatigue
Anorexia	Delayed puberty
Decreased bone mineralization (fracture/osteoporosis)	Dental enamel defects
Diarrhea	Dermatitis herpetiformis
Failure to thrive	Irritability
Increased liver enzymes (Alanine transaminase (ALT), aspartate transaminase (AST))	Nausea/vomiting
Short stature	Neuropathy
Weight loss	Recurrent aphthous ulcers
Constipation, chronic	

be evaluated in children with dermatitis herpetiformis, dental enamel defects, iron deficiency anemia, osteoporosis, delayed puberty, short stature, as well as some neurologic disorders. Testing for CD should be offered to children and adolescents with the common presenting symptoms for CD—diarrhea, constipation, abdominal pain, vomiting, and failure to thrive (FTT).[6]

The recommended initial test for celiac is an IgA antibody to human recombinant tissue transglutaminase (tTG IgA) with a 95% sensitivity and specificity for CD.[6] Antiendomysial antibody (EMA) IgA is just as sensitive, however, observer dependent and more costly. Due to inferior accuracy, the use of anti-gliadin antibodies (IgG and IgA) and anti-reticulin antibodies is not recommended. The occurrence of both IgA deficiency and CD in symptomatic children is 2%.[6] In individuals who are IgA deficient, anti-tissue transglutaminase antibodies (tTG IgG) should be tested with consideration for IgG anti-deamidated gliadin or IgG endomysial antibody.[6,7] In symptomatic children under 2 years of age, tTG IgA is recommended, research for the use of anti-deamidated gliadin IgG and IgA, EMA, and HLA typing before endoscopic evaluation is emerging.

Currently, it is recommended that positive serological tests should be confirmed by intestinal biopsy to diagnose CD.[6] An intestinal biopsy, with the characteristic histological features (flattened villi, crypt hyperplasia, and intraepithelial lymphocytes), is still considered the gold standard for diagnosis. The diagnosis of CD is considered definitive when there is complete symptom resolution after treatment with a gluten-free diet. The CD guideline committee recommends remeasurement of tTG IgA after 6 months of treatment with a gluten-free diet to show a decrease in antibody titer as an indicator of dietary adherence and intestinal health.

A gluten rechallenge is generally reserved for the few patients in whom the diagnosis remains in doubt after serology and intestinal biopsy and gluten restriction. For this challenge, the addition of wheat flour to the child's gluten-free diet is recommended. Providing a consistent amount of wheat protein for 3 months, or until symptoms recur, is recommended. If clinical symptoms return, serological confirmation of the diagnosis may be adequate. On the other hand, if symptoms do not return, a repeat small intestinal biopsy may be warranted.

According to the National Institutes of Health consensus statement on CD, there are six key elements in the management of individuals affected by CD[8]:

- Consultation with a skilled dietitian
- Education about the disease
- Lifelong adherence to a gluten-free diet
- Identification and treatment of nutritional deficiencies
- Access to an advocacy group
- Continuous long-term follow-up by a multidisciplinary team

TREATMENT

A GF diet that involves complete elimination of wheat, barley, and rye and its derivates is the primary treatment for individuals with CD and results in the resolution of symptoms with a few weeks, improves bone mineralization, and decreases the risk of intestinal cancer lowering mortality rate.[6,9] Persistent symptoms may be due to non-adherence to the diet or other gastrointestinal issues, such as irritable bowel syndrome or secondary lactase deficiency or constipation due to lack of dietary fiber.[10] If secondary lactose intolerance exists, a 1-month trial off lactose while initiating a GF diet may allow mucosal healing before lactose is reintroduced.

A variety of foods can be included in the GF diet including all fresh fruits and vegetables, all fresh meats, poultry, fish, and other animal meats, and a variety of grains. Avoiding obvious dietary gluten is not sufficient to manage this disease. All sources of gluten must be identified to ensure that the diet is GF as gluten is often hidden in many food additives or preservatives such as hydrolyzed vegetable protein (HVP), modified food starch, malt flavoring, broth, seasonings, and medications. Table 25–4 highlights grains to be avoided in the GF diet. Table 25–5 highlights safe grains to be included in a GF diet. Table 25–6 provides a list of additives and ingredients to question in the GF diet.

Table 25–4 Grains and Starches to Avoid in the Gluten-Free Diet

Atta	Malt (extract, flavoring, syrup, vinegar)
Barley	Matzoh
Brewer's yeast	Modified wheat starch
Brown rice syrup (if made from malt)	Oat bran
Bulgur	**Oats**[b]
Cereal binding	Orzo
Couscous	Pasta (unless from GF grains)
Dinkel	Rusks
Durum	**Rye**
Einkorn[a]	Semolina
Emmer[a]	Spelt
Farina	Triticale
Farro[a]	Udon
Gluten or gluten flour	**Wheat** (bran, flour, enriched flour, germ, starch, protein, stabilizers)
Graham flour	
Kamut[a]	
Kasha	

[a]Types of wheat.
[b]Cross-contamination of oats with wheat and or barley is a concern; therefore, oats are not recommended unless manufactured using GF practices.

Table 25–5 Grains and Starches Allowed in the Gluten-Free Diet

Amaranth	Potato flour, starch
Arrowroot	Quinoa seed, quinoa flour
Buckwheat	Rice (all forms brown, white, wild, basmati, jasmine, bran)
Corn (bran, flour, grits, hominy)	Rice flour (brown, sweet, white)
Flax	Sago
Legume/bean flours (garbanzo/chickpea, fava, lentil, pea)	Seed flours (sesame)
Millet	Soy flour
Mesquite flour	Sorghum
Montina flour (Indian rice grass)	Tapioca (manioc, cassava, yucca)
Nut flours (almond, hazelnut, pecan)	Teff grain, flour
Oats (uncontaminated with wheat, barley, rye)	

Table 25–6 Additives and Ingredients to Question in a Gluten-Free Diet

Alcohol	Groats	Modified food starch
Baking powder	Hydrolyzed plant protein (HPP)	Miso
Brown rice syrup (made from barley)	Hydrolyzed vegetable protein (HVP)	Nondairy creamer
Beer (most made with barley or wheat)	Textured vegetable protein (TVP)	Nuts, dry roasted
Bran	Malt, malt extract, malt flavoring, malt syrup	Preservatives
Brewer's yeast (if by-product of beer)	Monoglyceride and diglyceride	Seafood analogs
Caramel color/flavoring[a]		Seasoning (powder, cubes)
Clarifying agents[a]		Stabilizers
Dextrins[a]		Starch[b]
Emulsifiers		Soy sauce
Fat replacers		Tocopherols
Flavorings (natural and artificial)		Vegetable gum
		Vegetable protein

[a]Caramel color and dextrin in North American products are almost always made from corn.
[b]Starch in food products is usually from cornstarch, but medications often contain gluten-containing starch.

The Food Allergen Labeling and Consumer Protection Act of 2006 required that manufacturers identify on their food labels if the food contains any of the eight food allergens, including wheat. While this makes it easier for individuals with CD to identify wheat in a product, the absence of wheat does not necessarily indicate the absence of gluten since barley or rye may be in the product. If there is any question about ingredients on the label, the manufacturer should be contacted to assure that the ingredients are gluten free before consuming the food. In 2007, the U.S. Food and Drug Administration (FDA) proposed a rule that foods marketed as gluten free must contain less than 20 parts per million (ppm) or 20 mg/kg of gluten but the rule has yet not been formalized.[11] Limitations include inaccurate techniques for detecting gluten and the lack of solid scientific evidence for a threshold of gluten consumption below which no harm occurs.[6] Thus, parents and caretakers must keep abreast of changes in ingredients by food manufacturers and all food labels need to be checked on a regular basis.

The increasing diagnosis of CD and the subsequent awareness and use of the GF diet by the general public for "gluten intolerance" has led to the increased availability of gluten-free foods, even in restaurants. GF foods can be found in mainstream grocery stores, health food stores, Asian markets, kosher markets, or can be ordered online from various companies specializing in GF foods.

VITAMIN AND MINERALS IN CELIAC DISEASE

The nutritional status of the person with a new diagnosis CD can vary depending on the length of undiagnosed CD, the degree of villous damage, and the extent of malabsorption.[9] Iron, folate, vitamin B_{12}, calcium, magnesium, and fat-soluble vitamin (A, D, E, and K) deficiencies may be found

Table 25–7 Gluten-Free Diet

Food Item	Foods Recommended	Foods to Question[a]	Foods Not Recommended
Grains, flours	Almond, arrowroot starch, artichoke, amaranth, buckwheat, corn starch, cornmeal, corn bran, corn flour, flax, legume flours(peas, lentils, beans), millet, Montina flour, potato starch and flour, quinoa, rice bran, rice flours, sago, sorghum, soy flour, sesame, sunflower, teff, tapioca	Safe flours in bulk bins in health food stores Some buckwheat or millet flour mixes	Low-gluten flours All flours containing wheat, rye, barley, or oats such as follows: Durham wheat, all-purpose flour, white enriched flour, wheat flour, wheat germ, whole wheat flour, wheat starch, wheat bran, oat bran, bulgur, graham, kasha, kamut, spelt, triticale, matzo and matzo meal, rusks, semolina, farina, einkorn, emmer, faro
Breads	Specially prepared breads using only allowed flours (100% corn, rice, tapioca, soy, bean, nut, amaranth, buckwheat, millet, quinoa, teff, sorghum, etc.) Commercial gluten-free baking mixes	Buckwheat mixes (assure they are manufactured in a dedicated facility)	All breads, rolls, etc. made with wheat, rye, oats, barley, or unsafe flours

(*Continued*)

Table 25–7 Gluten-Free Diet (*Continued*)

Food Item	Foods Recommended	Foods to Question[a]	Foods Not Recommended
Cereals	Hot and cold Puffed amaranth, puffed corn, puffed millet, puffed rice, cornmeal, cream of buckwheat, cream of rice, hominy grits, soy grits, rice flakes, soy flakes, quinoa flakes, soy cereal	Hot and cold Rice and corn cereals (may have malt flavoring)	Hot and cold Cereals containing wheat, wheat starch, rye, barley, oats, bran, graham, wheat germ, malt, kasha, bulgur, matzo, durham wheat, rusks, triticale Cereals made with malt flavoring
Noodles, pastas, potatoes, other starches	Macaroni, spaghetti, noodles made from allowed flours Rice, wild rice, oriental rice noodles White or sweet potatoes, yams Corn tacos, corn tortillas	French fries Commercial rice or pasta mixes	Macaroni, spaghetti, noodles, pastas made from wheat, wheat starch, other gluten-containing grains Scalloped potatoes (containing wheat flour) Couscous Tabbouleh
Crackers, snack foods	Corn chips (plain) Rice cakes (plain) Popcorn (plain) Crackers made with allowed flours Potato chips (plain) Plain nuts and soy nuts	All containing malt Flavored potato chips, rice cakes, tortilla chips Rice crackers	All containing wheat, wheat starch, rye, barley, oats, bran, graham, wheat germ, bulgur, matzo, durham wheat, rusks, triticale Pretzels Rice crackers made with brown rice syrup Flour tortillas

Food Item	Foods Recommended	Foods to Question[a]	Foods Not Recommended
Milk	Plain milk products: fresh, dry, evaporated or condensed Cream Plain yogurt	Sour cream Whip cream Flavor/fruited yogurts Nondairy creamers Commercially prepared milkshakes and chocolate drinks Frozen yogurt and ice cream Soy and rice milks	All milk products containing ingredients not allowed Malted milk
Cheese	Aged cheeses Cottage cheese Cream cheese	Cheese sauces Cheese spreads Imitation cheese products Low-fat or fat-free cheese Ricotta cheese	Cheese products containing ingredients not allowed Blue cheese
Meat, meat alternatives	Fresh meat, fish, poultry, eggs Plain nuts or soy nuts Dried beans and peas Fish canned in oil, water, or brine Plain peanut butter	Soybean and other meat substitutes Luncheon meats, frankfurters, sausages, bacon without fillers Egg substitutes, dried eggs, egg whites Dry roasted nuts Imitation meat and fish Canned soups, chilies, stews	Any meat or meat product containing wheat, rye, barley and oat fillers, or stabilizers Bread containing meat products; swiss steak, meatballs, pot pies, croquettes, most vegetable burgers, meatloaf, etc. Meats or fish injected with hydrolyzed vegetable protein (HVP) or hydrolyzed plant protein (HPP) Tuna canned with HVP

(*Continued*)

Table 25–7 Gluten-Free Diet (*Continued*)

Food Item	Foods Recommended	Foods to Question[a]	Foods Not Recommended
Fruits, fruit juices	Most fresh, frozen, canned fruit	Thickened or prepared fruits and pie fillings Dried fruits	Fruit products containing ingredients not allowed
Vegetables	Most plain, fresh, frozen, or canned vegetables Dried beans, peas, lentils Tomato puree and paste	Vegetables in sauces prepared commercially Baked beans	Battered dipped vegetables
Fats	Butter, margarine Vegetable oil Lard Shortening	Salad dressing Mayonnaise	Packaged suet
Desserts	Special gluten-free cakes, cookies, baking mixes Honey, coconut, chocolate (plain), gelatin, meringues, pure cocoa, hard candies, sherbet	Ice cream, frozen yogurt Pudding/custard mixes Candy, jelly and jam, frozen desserts, icing, powdered sugar, marshmallows, molasses, ices	Most commercially prepared cakes, cookies, other baked goods Instant and bread puddings Ice cream cones Licorice
Soups	-Homemade broth and soups made with allowed ingredients -Special gluten-free commercial soups or broth	Canned soups, soup mixes, bouillon, bouillon cubes/powder	Soups or bouillon cubes containing ingredients not allowed

Food Item	Foods Recommended	Foods to Question[a]	Foods Not Recommended
Beverages	Plain tea, plain brewed coffee, hot chocolate made with pure cocoa powder, fruit juice, most carbonated drinks, cider	Some soy and rice beverages -Instant tea, coffee and hot cocoa mixes, flavored fruit drinks, root beer Distilled alcohol: wine, brandy, rum	Beer, ale, lager Malted beverages Ground coffee with added grains
Miscellaneous	Vinegar (apple cider, rice, balsamic, wine) Plain pickles, olives, relish Ketchup, mustard, salt, black or red pepper, pure herbs, pure spices, pure flavoring extracts, soy sauce (wheat-free), monosodium glutamate (MSG) Pure baking chocolate Yeast, cream of tartar, baking soda Distilled alcohol	Curry powder, distilled white vinegar, dry seasoning mixes, gravy extracts and meat sauces, yeast flakes, extracts, imitation flavoring, mustard powder, baking powder	Imitation pepper Soy sauce Worcestershire sauce Malt vinegar Communion wafers

[a]Contact manufacturers to ensure the product does not contain any gluten.

in patients with untreated CD[9] The gluten-free diet alone and subsequent healing of the intestine improving absorption may correct these deficiencies,[9] but supplementation with a gluten-free multivitamin with minerals at diagnosis should be considered. Individual dosing for severe deficiencies,

particularly of the fat-soluble vitamins, may be warranted. Given the high risk of bone disease in CD and to improve bone mineral density, strict adherence to the diet coupled with adequate consumption of calcium and vitamin D is essential. Measurements of serum calcium, alkaline phosphatase, parathyroid hormone, and a Dual energy x-ray absorptiometry (DEXA) bone scan are recommended at diagnosis by some.[9]

With careful planning, the GF diet can meet all the nutrient needs of the individual. However, since gluten-based fortified grain products (cereals, breads, and pasta) comprise a majority of children's intake of iron, fiber, zinc, folic acid, and B vitamins and most gluten-free alternatives are not fortified, these nutrients may be low in the gluten-free diet.[9] Children on the diet may also require additional calcium and vitamin D supplementation, particularly if they have a secondary lactase deficiency, given the risk for bone disease in this population. The GF diet shown in Table 25–8 provides guidelines for the GF diet recommended at Boston Children's Hospital.

Table 25–8 Dietary Reference Intakes for Fiber

Children	
1–3 years old	19 g/d
4–8 years old	25 g/d
Boys	
9–13 years old	31 g/d
14–18 years old	38 g/d
Girls	
9–13 years old	26 g/d
14–18 years old	26 g/d

CONSTIPATION

Constipation is a common medical condition in children characterized by infrequent and painful defecation, fecal incontinence, and abdominal pain.[12] The clinical presentation of constipation may include abdominal distention, anorexia, vomiting, poor appetite, and irritability.[12]

While there is insufficient research evidence to show the advantage of supplemental fluid or the use of prebiotics and probiotics in the treatment of constipation, an increase in fiber to recommended levels may be effective.[12] The new Dietary Reference Intakes (DRI) set forth by the Food and Nutrition Board of the Institute of Medicine can be much higher than a child's usual intake[13] (Table 25–8); thus, when increasing fiber in the diet, it is important to increase slowly. It is also important to provide adequate fluids (6–8 cups/d) to ensure the effectiveness of the fiber.

Not all fiber is equivalent in modifying stool size and consistency. Wheat bran is the most effective in increasing weight of the stool, followed by fruits, vegetables, oats, corn, soya, and pectin. The bulking effect of the fiber is multifactorial and may affect colonic microflora, water retention, and other mechanical factors. Fiber should be introduced to the diet slowly and adjusted based on symptoms. Table 25–9 provides a guide for high fiber diet meal planning for children. If it is difficult to increase fiber from food sources in the diet, Table 25–10 provides a list of commercially available fiber supplements helpful in the treatment of constipation.

In severe constipation, case reports series suggest a trial of a milk-free diet to be helpful in some patients in the treatment of constipation.[14] The medical workup may include laboratory testing, abdominal examination, and abdominal radiography. The mainstay of medical treatment of constipation involves the use of osmotic laxatives (glycolax aka PEG 3350,

Table 25–9 Dietary Fiber Contents of Foods

	Little (<0.5 g)	Low (1 g)	Moderate (2 g)	High (3 g)	Highest (>4 g)
Dairy	Cheese Ice cream Milk Pudding Yogurt				
Protein	Beef Chicken Eggs Fish Pork Turkey		2 tbs Peanut butter		½ cup Chickpeas (6) Kidney beans (6) Lentils (8) Lima beans (5) Navy beans (5) Northern beans (4) Pork and beans (6)
Fruit	Fruit juice Watermelon	½ cup canned Fruit cocktail Peaches Pears Pineapple ½ cup Applesauce Cherries Grapes (fresh) Mango	Fresh 3 apricots ½ grapefruite 1 peach ½ cup Blueberries strawberries	Fresh 1 apple 1 banana (6"–7") 3 dates 1 orange 3 plums ¼ cup dried Apricots, apples, prunes, raisins	Fresh ½ avocado (4) 1 pear (5) ½ cup Raspberries (4)

Vegetables		½ cup Cabbage Cauliflower Celery Cucumber Lettuce Spinach Tomato Tomato juice	½ cup cooked Green beans Peas Spinach	Broccoli Carrots Corn Potato salad	1 baked potato with skin (4) ½ cup cooked Sweet potato
Breads, cereals	**Bread** 1 slice French bread Italian bread Raisin bread White bread 1 each Pancake Doughnut ½ plain bagel **Cereals** ½ cup Cheerios	**Bread** 1 slice Cracked wheat Pumpernickel Rye 1 whole wheat pancake 1 corn tortilla **Cereals** ½ cup Oatmeal Life cereal Nutri-Grain	**Bread** 1 slice 100% whole wheat 3 oz bran muffin 2 Eggo multi-grain waffles 1 (42 g) whole wheat flour tortilla **Cereals** ½ cup Shredded wheat	**Cereals** ½ cup Bran flakes Kashi Heart to Heart Raisin bran 2 tbs wheat germ **Crackers** 1 rye crisp	**Bread** 1 slice Sprouted wheat breads (4) **Cereals** ½ cup 100% bran (14) All Bran (13) Fiber One (14) Grape nuts (7) Kashi (5) Steel-cut oats ¼ cup

(*Continued*)

Table 25–9 **Dietary Fiber Contents of Foods (*Continued*)**

	Little (<0.5 g)	Low (1 g)	Moderate (2 g)	High (3 g)	Highest (>4 g)
	Corn flakes Frosted flakes Lucky charms **Pasta** ½ cup Macaroni **Crackers** Goldfish Saltines Ritz	Wheaties Total Honey nut shredded wheat **Pasta** ½ cup Egg noodles White rice **Crackers** 2 graham 16 wheat thins 1 granola bar	Granola Crispy wheat-n raisins Wheat Chex **Pasta** ½ cup Brown rice **Crackers** 3 harvest wheat 3 triscuit 2 Kashi TLC		Unprocessed wheat bran (7) **Pasta** ½ cup Whole wheat Spelt Quinoa **Crackers** 2 Metamucil wafers
Desserts	Chocolate chip cookies	Oatmeal cookies	Fig Newtons	Fresh fruit salad	
Miscellaneous	Beverages Fats sweets	1 cup Popcorn	¼ cup Cashews Pecans	¼ cup Almonds Peanuts Walnuts	¼ cup Coconut

Table 25–10 Commercial Fiber Supplements

Product	Fiber/Serving	Considerations
Benefiber Novartis Consumer Health, Inc www.benefiber.com	3 g/2 tsp powder 3 g/3 chewable tablets or caplets 3 g/1 stick pack packet	Wheat dextrin Sugar-free, gluten-free Available in powder, chewable tablets, stick packs, caplets Available flavored and unflavored Not recommended for carbonated beverages
Citrucel with SmartFiber GSK Corp. www.citrucel.com	2 g/dose 1 g/caplet	Methylcellulose Sugar-free, clear mix, caplets available
FiberCon Wyeth www.fibercon.com	0.5 mg insoluble fiber/caplet	Calcium polycarbophil Caplets only 224 mg calcium/2 caplets
FiberChoice GSK Corp. www.fiberchoice.com	3 g/2 tablets	Inulin Available in chewables Some fortified with chromium, antioxidants, calcium
Metamucil Proctor & Gamble www.metamucil.com	3.4 g/1 tbs or packet 3 g/6 capsules 5 g/2 wafers 5 g inulin fiber/tbs Clear and natural	Psyllium fiber Clear and natural—inulin fiber Available in capsules, powder, or wafers
Vitafusion Fiber Gummies Northwest Natural Products info@nnpvitamins.com http://nnpvitamins.com	5 g/2 gummies	Polydextrose (soluble fiber) Gluten-free, peanut-free, dairy-free, soy-free Natural food colors

milk of magnesia, and lactulose) and intermittent stimulant laxatives (senna and bisacodyl) along with a behavioral stool sitting regimen. The use of suppositories (glycerin and bisacodyl) or enemas may be necessary if the patient is not tolerating oral intake and stool burden in the rectal vault is high.

◆ ACUTE DIARRHEA

Acute diarrhea is defined as three or more loose or watery bowel movements during a 24-hour period that lasts less than 7 days and no more than 14 days.[15] Any change in stool consistency may be indicative of diarrhea over the number of stools, in the first year of life and in breast-fed babies.[15] Appropriate therapy for acute diarrhea consists of rehydration with a reduced osmolarity oral rehydration solution (ORS) and continued feeding (Tables 25–11 and 25–12).[16] The immediate use of oral rehydration therapy (ORT, defined as ORS plus nutritional support) is an effective treatment for acute diarrhea. If oral rehydration is not feasible, then nasogastric tube feeding is as effective if not better than IV fluids.[15] Substantial data support the use of early feeding during diarrheal disease, as it has been shown to improve gastrointestinal function as well as anthropometric, biochemical, and clinical outcomes.[16,17] Recent guidelines recommend that feeding should not be withheld longer than four to six hours after the start of rehydration.[15] Although children with acute diarrhea commonly suffer anorexia, it is crucial to maintain adequate hydration and nutrient intake (Table 25–13).

Recommendations for diet therapy in acute diarrhea may vary by age, nutritional status, and the medical history of the patient. Breast-fed infants should continue nursing on demand. Formula-fed infants can remain on full-strength

Table 25–11 Available Oral Rehydration Solutions (ORS)

Name (Manufacturer)	Carbohydrate (g/L)	Na (mmol/L)	K (mmol/L)	Base (mEq/L)	Osmolality (mOsm/L)	Comments
ORS (WHO, 2003)	13.5	75	20	30	245	Solution recommended by the World Health Organization (WHO, 2003)
Oral rehydration salts (Jianas)[a]	20	60	20	30	311	Available in packets, efficacy in cholera, monitor for hypernatremia in viral and other causes of childhood diarrhea
Pedialyte (Abbott)	25	45	20	30	250 (unflavored) 270 (flavored)	Available in liters, single-servings (8 oz), freezer pops Available in unflavored, fruit, grape, bubble gum flavors 7.8 mg zinc/L
Enfalyte (Mead Johnson)	30	50	25	30	200	Rice-syrup solids is carbohydrate source

(*Continued*)

Table 25–11 Available Oral Rehydration Solutions (ORS) (*Continued*)

Name (Manufacturer)	Carbohydrate (g/L)	Na (mmol/L)	K (mmol/L)	Base (mEq/L)	Osmolality (mOsm/L)	Comments
CeraLyte 70 (Cera Products)[b]	40	70	20	30	<260	Whole cooked rice is carbohydrate source Packets of 50, 75, 90 mEq sodium also available
Kao Lectrolyte (Pharmacia & Upjohn Inc.)	21	50	20	30	232	One packet makes 8 oz Available in unflavored, grape, bubble gum flavors

[a]Jianas Brothers, 2533 Southwest Boulevard, Kansa City, MO 64108-2395.
[b]Cera Products: http://www.ceraproductsinc.com, Accessed March 8, 2013.

Table 25–12 Commonly Used Beverages

Name	Carbohydrate (gm/L)	Na (mmol/L)	K (mmol/L)	Base (mmol/L)	Osmolality (mOsm/L)	Comments
Apple juice	120	0.4	44	N/A	730	Not appropriate for diarrhea treatment
Coca-Cola Classic	112	1.6	N/A	13.4	650	Not appropriate for diarrhea treatment

Source: Adapted from King et al.[16]

Table 25–13 Oral Rehydration Therapy for Acute Diarrhea

Degree of Dehydration	Rehydration Therapy	Replacement of Losses	Nutrition
None	None needed	<10 kg: 60–120 mL ORS for each diarrheal stool or vomiting episode >10 kg: 120–240 mL ORS for each diarrheal stool or vomiting episode	Regular diet for age (1) Breast milk or full strength formulas for infants and (2) Complex carbohydrates, fresh fruits, vegetables, lean meats for older children
Some	ORS, 50–100 mL/kg over 3–4 hours	As above	As above
Severe	Lactated Ringer's solution 20 mL/kg IV route until perfusion and mental status improve, then 100 mL/kg of ORS over 4 hours	As above; administer via nasogastric tube if unable to drink	As above; NB: children with a history of severe dehydration may have a higher likelihood of lactose-intolerance during recovery

ORS, oral rehydration solution.

Source: Adapted from King et al.[16]

formula and do not usually need a lactose-free version. Soy infant formulas or hydrolyzed protein formulas do not provide an added benefit. Dilution of infant formula or a gradual introduction of feeding is not required. Children receiving solid foods should continue to eat their regular diet with the exception of foods high in simple sugars

(i.e., carbonated soft drinks, juice, and gelatin desserts) since the osmotic load of these foods may exacerbate diarrhea.[15] Although some fatty foods may be malabsorbed, a diet moderate in fat is recommended to maintain adequate caloric intake.[16] Undiluted cow's milk and cow's milk–based formulas can safely be given to most children with acute diarrhea. A minority of children will have clinically significant lactose intolerance and a significant increase in stool output requiring a lactose-free diet.[15] Highly restrictive diets, like the BRAT diet (bananas, rice, applesauce, and toast), do not offer any benefit and may worsen the child's nutritional status.

Supplemental zinc therapy is effective in treating and preventing diarrheal disease, particularly in the malnourished patient.[15] Recent data also suggest that zinc supplementation may reduce the severity and frequency of childhood diarrhea. UNICEF/WHO recommend zinc supplementation as standard treatment for all children with diarrhea although studies supporting the role of zinc in reducing diarrheal disease have largely been performed among children at risk of inadequate dietary zinc intake. There is no published evidence on the benefit of zinc supplementation in well-nourished children.[15] The recommended dose is 10 mg of elemental zinc in children below 6 months of age and 20 mg in older infants and children for 10–14 days.[15] The applicability of these results to children from industrialized countries where zinc deficiency may not be an issue is unclear.

Probiotics have a role in both the prevention and the treatment of acute diarrhea. The benefits include reduction in the duration of diarrhea or volume of stool and if started early in the course of diarrhea in healthy infants and young children with diarrhea secondary to viral gastroenteritis or bacterial infections. Studies have shown a benefit of using *Lactobacillus reuteri* and *Saccharomyces boulardii* strains.[18,19] Safety issues with the use of probiotics may be a concern

in children with chronic disease or immune disorders. Antiemetics, such as ondansetron and metoclopramide, may reduce the need for intravenous rehydration therapy in children with vomiting and acute diarrhea but increased diarrhea may occur.[15,20]

PERSISTENT DIARRHEA

An episode of diarrhea that lasts for 14 days or more is termed "persistent diarrhea."[21] In developing countries, the cycle of persistent diarrhea, malabsorption, anorexia, and malnutrition is one of the leading causes of death in children less than 5 years of age. Nutritional and medical management centers on treating infection, correcting acidosis and dehydration, gradually reintroducing enteral nutrition, and correcting micronutrient deficiencies. Culturally acceptable and cost-effective formulas have been employed with great success.[21]

In industrialized countries, diarrhea and malnutrition should prompt an evaluation for malabsorption or systemic illness (Table 25–14). In the cases of persistent diarrhea due to extensive gastrointestinal mucosal disease (e.g., allergic disease, CD, or other flat gut lesions), nutritional management may be undertaken with a wide range of enteral formulas. These are generally lactose-free (to avoid lactose malabsorption), protein hydrolysate or peptide-based (to treat possible protein

Table 25–14 Persistent Diarrhea in Industrialized Countries

Weight Loss Present	Normal Nutritional Status
Cystic fibrosis or other causes of pancreatic insufficiency Hepatobiliary diseases Protein-losing enteropathy Crohn's disease or ulcerative colitis AIDS or other immunodeficiencies Celiac disease or allergic disorders	Infection (e.g., giardia) Lactose intolerance Chronic nonspecific diarrhea Excessive juice intake

sensitivities), and isotonic (to prevent osmotic loads worsening diarrhea). (See Chapter 14, Enteral Nutrition). Occasionally, parenteral nutrition is indicated, although the enteral route is preferred.

CHRONIC NONSPECIFIC DIARRHEA

Chronic nonspecific diarrhea (CNSD), often called toddlers' diarrhea, is characterized by 2 or more loose, odoriferous, voluminous stools per day and generally occurs between 6 and 36 months of age. The diarrhea lasts more than four weeks and is not associated with significant abdominal pain, fever, or growth failure. The etiology of the diarrhea is unknown, although it may be initiated by an acute infection. Nutritional management of CNSD centers on normalizing the diet as much as possible to avoid iatrogenic malnutrition. The prognosis of CNSD is excellent, with the majority of children improving by the age of 4 years.

LACTOSE INTOLERANCE

Lactose intolerance refers to the inability to digest lactose, the main carbohydrate in milk. Clinical symptoms of lactose intolerance include abdominal pain, bloating, diarrhea, or flatulence. The severity of symptoms and the amount of lactose that will cause symptoms varies between individuals and depends on the degree of lactase deficiency, how much lactose is consumed, the mixture of lactose with other foods, gastric emptying rate, and colonic scavenge of malabsorbed carbohydrate.[22]

Lactose malabsorption is attributed to a relative deficiency of the disaccharidase lactase, which can be primary, secondary, congenital, or developmental. Primary lactase deficiency is a condition in which lactase activity falls after weaning and can happen at any point in childhood,

adolescence, or adulthood. Onset is subtle and gradually progressive over time. Race, ethnic origin, and age will influence the presence of lactose intolerance. Primary lactose intolerance is prevalent in African-American, Hispanic, Native American, and Asian populations (from 60% to 100% of these populations) and is less common in Northern Europeans and certain African and Indian populations.[22]

Secondary lactose intolerance is usually due to mucosal injury associated with disease (e.g., infectious diarrhea, Crohn's disease (CD), short bowel syndrome, and untreated CD). Congenital lactose deficiency is very rare. Developmental lactase deficiency is defined as lactase deficiency seen among preterm infants of less than 34 weeks' gestation.[22]

The diagnosis of lactose intolerance can be done using a good clinical history and the observation of whether symptoms develop after lactose ingestion. If suspected, improvement with a trial of a lactose-free diet for two weeks can reveal this causal relationship. If symptoms are more subtle, a hydrogen breath test can be administered. A dose of lactose (2 g/kg to a maximum of 25 g) is ingested and expired hydrogen is measured over two to three hours. An increase >20 PPM of hydrogen expiration in 60 minutes indicates lactose malabsorption. Factors that may influence the results include consumption of a high fiber diet before the test as well as use of antimicrobial agents and probiotics, lack of hydrogen-producing bacteria, bacterial overgrowth in the intestine, and disorders of intestinal motility.[22]

The treatment of lactose intolerance involves the removal of lactose from the diet. Lactose deficiency secondary to primary lactase deficiency is very rare before 2–3 years of age and any suspected lactose malabsorption before these ages should trigger an evaluation of other etiologies.[22] Lactose restriction is not usually necessary in secondary lactose intolerance since resolution of the underlying issue

will reverse the lactose intolerance.[22] However, in infants less than 3 months of age or malnourished children, lactose intolerance can influence the course of their illness and lactose restriction may need to be considered.[22]

Lactose is a common ingredient in many foods, including milk and milk products and also breads, crackers, soups, cereals, cookies, granola bars, chocolate, candy, salad dressings, luncheon meats, margarine, and baked goods. See Table 25–15 for common ingredient labeling terms, which indicate lactose.

Eliminating or reducing lactose-containing ingredients from the diet is usually adequate to relieve symptoms of lactose intolerance. Individuals with primary lactose intolerance may tolerate varying amounts of lactose; however, they may require a permanent dietary change. Individuals with secondary lactose intolerance should eliminate all lactose from their diets for a short period of time (two to six weeks). If symptoms resolve, lactose may be reintroduced slowly, as tolerated by the individual. The amount of lactose that an individual can tolerate is highly variable. In fact, including dairy products in the diet has been shown to improve tolerance to lactose for some individuals.[23] Many children can tolerate small amounts of lactose, particularly yogurt, hard cheese, or ice cream, without discomfort. Many adults who

Table 25–15 Lactose-Containing Ingredients

Butter	Ghee
Buttermilk	Lactose
Cheese	Margarine
Cream	Milk (malted, liquid, evaporated, powder, condensed)
Curds	Sweet or sour cream
Dry milk solids	Whey

consider themselves lactose-intolerant can actually tolerate moderate amounts of milk.[22]

For individuals who choose to restrict lactose in their diets, a variety of lactose-free and low-lactose food choices are available. Lactose-reduced products, containing 70%–100% less lactose than standard foods, may be purchased commercially. Individuals may also choose to consume dairy products with lactase enzyme tablets or drops.

A lactose-free diet can provide adequate amounts of all essential nutrients when a varied diet is consumed. However, children maintained on a strict lactose-free diet may not meet their recommended calcium and vitamin D requirements and may require supplementation. Table 25–16 provides a list of low-lactose foods, which are high in calcium.[22] Table 25–17 provides a list of some commercially available lactose-free calcium supplements.

Table 25–16 High-Calcium, Low-Lactose Foods

Food Item	Milligrams of Calcium/Serving
Milk/dairy products	
Lactose-free milk	300
Cheddar cheese, 1 oz	200–260
Cottage cheese (1% milk), ½ cup	70
Sherbet, 1 cup	80
Protein	
Salmon, canned w/bones, 3 oz	210
Beans, cooked, 1 cup	90
Soybeans, cooked, 1 cup	175
Tofu, firm, 1 cup	507
Vegetables	

(*Continued*)

Table 25–16 High-Calcium, Low-Lactose Foods (*Continued*)

Food Item	Milligrams of Calcium/Serving
Broccoli, cooked, 1 cup	60
Kale, cooked, 1 cup	94
Spinach, cooked, 1 cup	245
Fruits	
Orange juice (calcium fortified) 8 fl oz	~500
Miscellaneous	
Fortified soymilk, rice milk, almond milk, hemp milk, 8 fl oz	250–300
Black strap molasses, 1 tbsp	180

Table 25–17 Commercial Calcium Supplements

Product	Manufacturer	Mg Elemental Calcium	IU vitamin D/1 tablet/ gummy
Citracal + D, regular (Ca citrate)	Mission Pharmacal	250	200 D3
Citracal + D, maximum	Mission Pharmacal	315	250 D3
Citracal + D, gummies	Mission Pharmacal	250	250 D3
OsCal 500 + D3 (Ca carbonate)	Marion Lab	500	200
OsCal 500 + D3, chewable	Marion Lab	500	600
OsCal 500 + D3, ultra	Marion Lab	500	200
Tums (Ca carbonate)	SmithKline Beecham	200	0

Product	Manufacturer	Mg Elemental Calcium	IU vitamin D/1 tablet/ gummy
Calcium Milk Free (2 chews)	Nature's Plus	500	100
Cal-citrate + D	Freeda	250	100

INFLAMMATORY BOWEL DISEASE

IBD is a general name for diseases that cause chronic intestinal inflammation. The two most recognized forms of IBD are CD and ulcerative colitis (UC). It is estimated that approximately 1.1 million US citizens suffer from IBD.[24] IBD manifests during childhood or adolescence in at least 25% of patients.[25] CD is characterized by transmural granulomatous intestinal inflammation and can involve the entire gastrointestinal tract, including the colon, small intestine, stomach, esophagus, and mouth. In contrast, UC is characterized by mucosal inflammation limited to the large intestine. Both forms of IBD are manifested by exacerbations and remissions of gastrointestinal symptoms including abdominal pain, bloody diarrhea, rectal bleeding, fever, arthritis, and rashes.

The incidence of IBD has increased in the past 60 years and is attributed in part to changes in dietary habits of populations toward a more "Westernized" diet that is higher in fat, particularly in the ratio of omega-6 fatty acids to omega-3 fatty acids, as well as refined sugars. Fruits, vegetables, fiber, and breastfeeding may be protective against the development of CD.[26]

Children and adolescents with IBD often present malnourished. Poor nutrient intake and malabsorption of nutrients associated with gastrointestinal exacerbations contribute to weight loss, growth failure (decreased height velocity leading to short stature), and nutrient deficiencies seen in the IBD pediatric population. Growth failure is seen in about 30% of all children and adolescents with CD and

in about 5%–10% with UC.[27] Protein-energy malnutrition is seen in 20%–85% of patients with CD and is the third most common symptom besides abdominal pain and diarrhea.[26] Factors contributing to the nutritional complications in pediatric IBD patients include inadequate energy and nutrient intake leading to weight loss; increased nutrient requirements secondary to elevated resting energy expenditure; malabsorption with enteric leakage of protein, blood, vitamins, minerals, electrolytes, and trace elements from the bowel during periods of inflammation; and long-term corticosteroid use.[28] The etiology of decreased intake is multifactorial and may include gastritis and esophagitis, cytokine-mediated anorexia, fear of eating secondary to diarrhea, and decreased taste sensation due to micronutrient deficiencies (e.g., zinc deficiency).[28] Treatment with antibodies to tumor necrosis factor (TNF)-α may help reduce the frequency and severity of secondary malnutrition in CD.[26]

Patients with IBD, particularly those with CD, present with deficiencies of vitamins, minerals, and trace elements as a result of inadequate intake or increased losses. Deficiency of the water-soluble vitamin folic acid can occur as a result of the interference of sulfasalazine and methotrexate with folate metabolism and is relatively common.[27] Vitamin B_{12} deficiency may occur in patients with CD or ileal resection and may be suspected in the presence of macrocytic anemia or if anemia does not respond to iron supplementation.[27] Patients with IBD are at an increased risk for developing fat-soluble vitamin deficiencies likely reflective of disease activity.[28] Vitamin D deficiency is found in about 35% of children and young adults with UC and appears to be more prevalent in those with darker skin, with CD with upper gastrointestinal involvement, and in the winter months. Iron deficiency anemia is common in patients with IBD and may be caused by gastrointestinal blood loss and/or

impaired utilization of iron with chronic disease. Inflammation and corticosteroids can increase urinary excretion of vitamin C, potassium, calcium, magnesium, phosphorus, zinc, and sulfur and prolonged corticosteroid use can affect the metabolism of vitamin D. Low blood zinc levels occur in up to 50% of patients with active IBD.[28] Routine monitoring and supplementation of water- and fat-soluble vitamins and trace minerals is recommended. Table 25–18 provides guidelines on routine and therapeutic supplementation. See Table 19-7 "Assessment and Treatment of Fat Soluble Vitamin Deficiencies" in Chapter 19 Cystic Fibrosis.

Low bone mineral density is seen in approximately 25% of children IBD and may be associated with the combined effects of chronic inflammation, corticosteroid use, excessive calcium urine loss, vitamin D malabsorption, decreased calcium intake, and cytokine-mediated bone resorption.[28,29] Early identification of children at risk of osteopenia through monitoring plasma 25-OH vitamin D levels, urinary calcium excretion, and bone density scans is recommended. Adequate intake of calcium and vitamin D following the recommendations by the DRI is important for normal growth and development. CD patients who present with vitamin D deficiency may benefit from therapeutic supplementation with vitamin D_2 or D_3. See Table 25–18 for routine and therapeutic supplementation recommendations.

Management of children with IBD often requires a combination of nutritional therapy, pharmacologic agents, surgical consultations, and psychological intervention.[30] The primary nutritional therapy goals are to replace nutrient losses, to correct specific nutrient deficiencies, and to provide sufficient nutrients to promote energy and nitrogen balance for the restoration of normal growth and maturation.[27,28] Nutritional therapy may also help to achieve and maintain remission by modifying the mucosal cytokine profiles and

Table 25–18 Nutrition Recommendations and Supplementation for the Pediatric Inflammatory Bowel Disease (IBD) Patient

Routine Supplementation	Comments
Energy, protein	Schofield or WHO equation[37] multiplied by activity factor and goal weight
Vitamins, minerals	One age appropriate multiple vitamin with minerals per day
Calcium	Dietary guidelines for age for calcium 1–3 years old: 500 mg/d 4–8 years old: 800 mg/d 9–18 years old: 1100 mg/d Ca^{+} supplementation is indicated with steroid use
Vitamin D	400–1000 IU/d
Therapeutic Supplementation	
Vitamin D (ergocalciferol (D2))	Children with normal absorption: 1000–5000 IU/d × 6–16 weeks Children with malabsorption: 10,000–25,000 IU/d x 4 weeks then recheck
Iron	2–4 mg elemental Fe/kg/d
Zinc	100%–200% DRI; stool losses may be high during acute exacerbations
Vitamin B_{12}	100–1000 mcg IM monthly (if terminal ileum resected or diseased)
Folate	100%–200% DRI; sulfasalazine and methotrexate may interfere with metabolism

Abbreviations: DRI, dietary reference intakes; IM, intramuscular.

reducing inflammation in the gut.[26] While no studies have shown that nutritional intervention can induce remission in patients with UC, controlled studies have shown that the exclusive enteral nutrition (EEN) with the use of medical

nutrition supplements, whether orally or through enteral feeding tube or both, is as effective as corticosteroids in inducing remission in CD, particularly in children.[26,27] Remission rates in children with CD treated with polymeric enteral formulas is as high as 79% and in newly diagnosed children >80%.[26] EEN, whether through elemental or polymeric formula, is also associated with better growth outcomes than corticosteroids.[31] No added benefit has been found in the use of elemental versus polymeric formulas in CD,[32] and the improved taste and reduced expense of the latter may make it the better choice for EEN.

The major advantages of using EEN include the avoidance of corticosteroids, increased growth velocity, nutritional repletion, and decreased disease activity in children with IBD. However, long-term compliance of EEN remains difficult for children and their families. If successful supplementation by mouth is not achieved, providing nutritional supplementation nocturnally through nasogastric or gastrostomy feedings can be done. The length of use of EEN varies between centers, but a period of six to eight weeks to achieve remission and growth is often used.[33] Patients with IBD often make use of supplements including glutamine, fish oil, short chain fatty acids, and prebiotic and probiotic, but data are currently insufficient to allow specific recommendations regarding their use. Insufficient data exists for the benefits of adding anti-inflammatory agents, such as transforming growth factor-β (TGF-β) and prebiotic and probiotic in enteral formulas.[26] Enteral nutrition is the preferred choice in the treatment of IBD although parenteral nutrition may be necessary when there is stricture, feeding intolerance, or immediately postsurgery.

The first approach to providing nutritional supplementation is to increase caloric intake with an unrestrictive high calorie, high protein diet. Minor food sensitivities and

intolerances may occur during a flare, but generally do not persist and are of an insufficient importance to warrant elimination from the child's diet. On occasion, a low-fiber or lactose-restricted diet may be necessary when reintroducing food after active colitis if there is a stricture in the intestinal lumen or with widespread mucosal disease. However, dietary restrictions should be made on an individual basis.

When patients are unable to increase dietary calorie and protein intake through food, oral supplementation with commercially available enteral formulas is appropriate. Numerous preparations that meet individual requirements are available (See Chapter 14 "Enteral Nutrition"). However, long-term compliance of EEN remains difficult for children and their families. If successful supplementation by mouth is not achieved, providing nutritional supplementation nocturnally through nasogastric or gastrostomy feedings or total parenteral nutrition may be warranted.

Nutritional support and monitoring are essential in the pediatric patient with IBD to minimize malnutrition and maximize growth. The use of EEN versus pharmaceutical therapy continues to be widely debated, but EEN provides some added advantages, as discussed above. Currently, the combination of nutritional and drug therapy remains the standard of care.

EOSINOPHILIC ESOPHAGITIS

EoE is defined as a chronic, immune/antigen-mediated disease characterized clinically by symptoms related to esophageal dysfunction and histologically by eosinophil-predominant inflammation.[34] EoE is a disease limited to the esophagus. Both clinical symptoms and abnormal histology (e.g., greater than 15 eosinophils per high power field) determined by esophageal endoscopy with biopsies

must be present to diagnose EoE.[34] Since EoE is associated with IgE-mediated allergies, both food-related and aeroallergens, the typical management includes corticosteroid treatment coupled with elimination of both environmental and food allergens. Inhaled corticosteroids, like fluticasone or budesonide, in swallowed form have been shown to be as effective as prednisone in reducing esophageal inflammation in EoE.[35] Untreated EoE over a prolonged period of time can at the very least cause chronic inflammation and at worst result in esophageal scarring and strictures.[36]

Feeding difficulties are common clinical symptoms in infants and toddlers with EoE, whereas school-aged children are more likely to present with vomiting and adolescents with dysphagia and food impactions.[34] Other symptoms include chest pain, GERD-like symptoms that do not resolve with medical or surgical management, abdominal pain, anorexia, and early satiety. Since children may engage in behaviors to reduce symptoms, parents and clinicians should watch for compensatory behaviors that indicate esophageal discomfort such as avoiding highly textured foods, persistent cutting of food in small pieces, lubricating foods with liquid or fats before eating, extensive chewing of foods, washing food down with liquids, and prolonged mealtimes.[34]

Atopic diathesis (food allergies/anaphylaxis, asthma, eczema, chronic rhinitis, and environmental allergies) are frequent in children with EoE and are often managed with elimination of specific antigens.[34] Children with EoE should receive a thorough evaluation by an allergist to assess for both IgE-mediated food allergies through skin prick testing (SPT) and non-IgE-mediated food intolerances through atopic patch testing (APT) and help with the reintroduction of foods, particularly if immediate hypersensitive reactions are suspected.[36]

Given the presence of food allergies in EoE, nutritional management plays a key role in the treatment of this disease. In fact, dietary therapy can result in near-complete resolution of both clinical and histological symptoms.[34] There are three dietary methods (Table 25–19) that have been shown to be effective: (1) the exclusive use of an amino acid–based, elemental formula; (2) guided elimination of food allergens specific to the patient tested positive in SPT or APT; or (3) empiric elimination of the eight major food allergens (milk, soy, wheat, egg, fish, shellfish, peanuts, and tree nuts). Although the use of elemental diets has been shown to be the most effective of these three approaches, the clinician must take into account the potential psychosocial issues as well as non-adhered to this stricter method before a decision is made. Foods proven to cause EoE symptoms should be restricted indefinitely from the diet. Those foods not proven to be antigenic can be reintroduced with careful observation of recurrence of symptoms.

Repeat endoscopy is required to assess the effectiveness of both medical and dietary treatments in EoE. Since EoE is a chronic condition, recurrence of symptoms is not uncommon after discontinuation of medications or reintroduction of food allergens. Long-term application of dietary restrictions may be required in individuals with EoE.[34]

Table 25–19 Dietary Strategies to Treat Eosinophilic Esophagitis (EoE)

Exclusive use of an amino acid-based, elemental formula
Guided elimination of food allergens specific to testing positive in SPT or APT
Elimination of the 8 major food allergens (milk, soy, wheat, egg, fish, shellfish, peanuts, tree nuts)

Abbreviation: SPT, skin prick testing; APT, atopic patch testing.

A thorough nutrition assessment should be conducted in all patients with EoE looking for signs of acute or chronic malnutrition and to ensure the proper inclusion of adequate calories, vitamins, minerals, and other micronutrients. The elimination of food allergens particularly in the setting of multiple food allergies increases the risk for inadequate energy and protein intake, micronutrient deficiencies, and growth failure. Education on the elimination of food allergens and specific foods to avoid, the proper reading of food labels and ingredients lists, and the appropriate food substitutions to avoid nutrient deficiencies must be conducted to prevent nutritional deterioration and increase adherence. Regular follow-up with a registered dietitian will both offer support to the child and family and reduce the risk of prolonged inadequate nutrient intake. In cases where adequate protein or calories is not achieved through diet, the use of an elemental formula to supplement the diet can be implemented. Hypoallergenic vitamins and mineral supplements are available in instances of dietary deficiencies. Please refer to Chapter 24 "Food Allergies" for further discussion of food allergen elimination.

General Resources on Gastrointestinal Conditions

Academy of Nutrition and Dietetics
120 South Riverside Plaza, Suite 2000
Chicago, IL 60606-6995
www.eatright.org

American Society for Pediatric Parenteral and Enteral Nutrition
8630 Fenton Street, Suite 412
Silver Spring, MD 20910
http://www.nutritioncare.org/

North American Society Pediatric Gastroenterology, Hepatology and Nutrition
Resources available on Celiac disease, Eosinophilic Esophagitis, Inflammatory Bowel Disease, GERD
NASPGHAN
PO Box 6
Flourtown, PA 19031
http://www.naspghan.org/

National support groups

Celiac Disease Foundation
13251 Ventura Blvd., #1
Studio City, CA 91604
www.celiac.org/
Celiac Sprue Association
CSA/USA, Inc.
PO Box 31700
Omaha, NE 68131-0700
http://csaceliacs.info/
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www.CeliacCentral.org
Inflammatory Bowel Disease:
Crohn's and Colitis Foundation of America, Inc.
386 Park Ave. South, 17th Floor
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www.ccfa.org

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26 Growth Failure

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Growth failure, also called failure to thrive or undernutrition, describes children whose weight or length/height are not increasing at a rate consistent with a growth reference or growth standard.[1] The definition of growth failure is controversial, but commonly used definitions include[2]:

Delayed growth: Weight-for-age or weight-for-height is less than the third percentile or more than two standard deviations below the mean for age and sex, on more than one occasion.

Decreased growth velocity: Weight or height curve has crossed downward more than 2 major percentile lines (such as 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles) after having previously achieved a stable growth pattern.

Other relevant terms related to growth failure include wasting, defined as a decreased or low weight-for-height and representative of acute undernutrition. Stunting is defined as a decreased height-for-age and represents chronic undernutrition.

ASSESSMENT OF GROWTH PATTERN

The growth pattern of a child is best assessed with serial measurements plotted on a growth chart, as a single point on the growth chart will not reflect growth fluctuations or a child's growth pattern. For children with certain medical conditions (e.g., cerebral palsy) or genetic syndromes (e.g., Down syndrome), growth pattern should be assessed using the specific growth reference. For most children, the two growth charts used in the United States are the Centers for Disease Control (CDC) growth reference and the WHO growth standards (see Chapter 2 for more information on growth charts). The CDC and the American Academy of Pediatrics have recently recommended that the WHO growth charts be used for all children from birth to 2 years, with 2000 CDC growth charts used for children aged 2 years and older.[3] For children under the age of 2 years, the WHO growth charts were developed using longitudinal data from infants who were all breastfed for the first year of life, contrasting with the cross-sectional data from predominantly formula-fed infants used for the 2000 CDC growth charts. Breastfed infants show a greater growth velocity than formula-fed infants during the first few months of life but subsequently have lower rates of weight gain in infancy.[3] Data in U.S. children suggest that use of WHO charts is likely to reduce the prevalence of growth failure diagnoses in early childhood[3,4] but may increase the prevalence of growth failure diagnoses in the first six months of life.[5]

In the first two years of life, it is common for healthy children to exhibit shifting of growth percentiles. A U.S. study estimated that 39% of children between birth and 6 months, 6%–15% of children between 6 and 24 months, and 1%–5% of children between 24 and 60 months crossed

two major weight-for-age percentiles.[6] For weight-for-height, 62% of children between birth and 6 months, 20%–27% of children between 6 and 24 months, and 6%–15% of children between 24 and 60 months crossed two major percentiles.[6] The authors speculated that the shifts in growth percentile could be due to genetic predisposition and regression to the mean (e.g., a large infant born to slim parents, who crosses weight percentiles downward), measurement error, or random variation.

Growth failure should be differentiated from normal variations in growth pattern, including genetic short stature and constitutional growth delay. The classic pattern for undernutrition is a decline in weight percentile, followed by a decline in linear growth percentile. Children who cross percentiles downward because of genetic predisposition will maintain normal growth velocity once they reach their genetically appropriate height percentile, and bone age will match chronological age.[7] Children with constitutional growth delay are born with a normal birth size but begin crossing percentiles downward in the first two to three years, followed by a normal growth velocity. In children with constitutional growth delay, bone age will be delayed compared to the chronological age, and they will tend to have later puberty than their peers, resulting in a normal adult height.[7]

ETIOLOGY

Growth failure results from condition(s) that cause inadequate caloric intake, malabsorption, excessive caloric expenditure, or defective use of nutrients (Table 26–1). Most children with growth failure are not consuming or not retaining sufficient calories to meet their caloric needs. Historically, growth failure has been conceptualized as having either organic or nonorganic

Table 26–1 Pathogenesis of Growth Failure

Mechanism	Examples of Associated Conditions
Inadequate caloric intake	Reduced appetite (anorexia) Mechanical feeding problems Oromotor or swallowing dysfunction Congenital anomalies Altered mental status Chronic vomiting or gastroesophageal reflux Dietary factors Breastfeeding difficulties Improper formula mixing High intake of low calorie foods Excessive fruit juice consumption Behavioral factors Disordered feeding techniques Infantile anorexia Sensory based food aversions Inadequate access to food Neglect or abuse Poverty
Inadequate absorption	Gastrointestinal disease Pancreatic insufficiency Celiac disease Inflammatory bowel disease Cystic fibrosis Biliary atresia or liver disease Short bowel syndrome Allergic enterocolitis Micronutrient deficiencies (zinc, vitamin C)

Mechanism	Examples of Associated Conditions
Excessive caloric expenditure	Hypertonia Chronic disease Congenital or acquired heart disease Chronic pulmonary disease Hyperthyroidism Chronic renal failure Chronic infection, recurrent fevers HIV or other immunodeficiency Malignancy
Defective utilization	Genetic conditions Trisomies 21, 18, 13, progeria Metabolic disorders Storage disorders, amino acid disorders

Source: Adapted from Stephens et al.,[8] Krugman and Dubowitz,[9] and Markowitz et al.[2]

causes. Organic growth failure results from specific medical disorders, such as malabsorptive disease, genetic syndromes, endocrine disorders, or neurological dysfunction. Nonorganic growth failure results from psychosocial or behavioral factors, which may meet diagnostic criteria for specific developmental or mental health disorders (Table 26–2). The Diagnostic Classification of Mental Health and Developmental Disorders of Infancy and Early Childhood (DC:0-3R) has defined "Feeding Behavior Disorder" as difficulty in regulating feeding in response to physiological feelings of hunger or fullness, and six disorder subtypes have been defined (Table 26–2). In DSM-V, the proposed "Avoidant/restrictive food intake disorder" would replace the DSM-IV term "Feeding disorder

Table 26–2 Classification of Feeding Disorders

Diagnostic Classification of Developmental Disorders of Infancy and Early Childhood[10] (Based on Classification System Originally Developed by Chatoor[11])					DSM-V (Proposed Revision)[12]
Disorder Type	**Timing of Presentation**	**Etiologic Hypotheses**	**Clinical Presentation**	**Treatment**	**Avoidant/Restrictive Food Intake, Subtype Descriptions**
Feeding disorder of state regulation	Age 0–6 months	Disordered development of behavioral regulation	Difficulty reaching and maintaining calm alertness required for feedings, or hard to awaken for feedings	If irritable, reduce stimulation at feeding times (calm environment). If sleepy, gently stimulate before feedings (e.g., infant massage). Treat any parental exhaustion, depression, or anxiety	Not included

Feeding disorder of caregiver-reciprocity	First year of life	Lack of emotional nurture and infrequent feedings Parental risk factors include poverty, mental disorder, or substance abuse	Absence of developmentally appropriate signs of social reciprocity with caregiver during feedings Severe growth failure may be present Caregiver may be unaware of or deny feeding problems	Multidisciplinary clinic, home-based intervention, or in severe cases, hospitalization Family counseling and education regarding nurturing emotional and physical development of child Social services and child protection as appropriate	Not included

(*Continued*)

Table 26–2 Classification of Feeding Disorders (*Continued*)

Diagnostic Classification of Developmental Disorders of Infancy and Early Childhood[10] (Based on Classification System Originally Developed by Chatoor[11])					DSM-V (Proposed Revision)[12]
Disorder Type	**Timing of Presentation**	**Etiologic Hypotheses**	**Clinical Presentation**	**Treatment**	**Avoidant/Restrictive Food Intake, Subtype Descriptions**
Infantile Anorexia	Age 6 months to 3 years	Poor hunger drive and feeding refusal which may be associated with inappropriate parental response, resulting in child not learning to regulate own eating	Refuses to eat adequate amounts of food for at least 1 month Behavioral difficulties (may throw food, climb out of high chair, refuse to open mouth) Does not appear hungry or interested in food. Use of distractions or coercive feeding may be present	Parental education on separation of feeding roles Structured meal and snack times, spaced at 2- to 4-hour intervals, duration 20–30 minutes Foster self-feeding and eliminate distractions, coercive feeding Do not use food as a reward Limit setting and time-outs	Individuals who do not eat enough or show little interest in feeding

				Consider cyproheptadine	
Sensory Food Aversions ("picky eater," "food aversion," "food neophobia")	First 3 years after aversive response to introduction of specific foods	Learned association of specific food characteristics with aversive response, based on inherited traits, food availability, and feeding practices	Consistently refuses specific foods or beverages based on taste, texture, temperature, or smell for at least 1 month Sensory difficulties (gag, vomit, or grimace with food)	Continue to introduce a variety of foods, but avoid foods eliciting strong aversive reactions Model behavior (parents, peer feeding group) Provide supplemental macro- and micronutrients if required Behavioral therapy	Individuals who only accept a limited diet in relation to sensory features

(*Continued*)

Table 26–2 **Classification of Feeding Disorders (*Continued*)**

Diagnostic Classification of Developmental Disorders of Infancy and Early Childhood[10] (Based on Classification System Originally Developed by Chatoor[11])					**DSM-V (Proposed Revision)[12]**
Disorder Type	**Timing of Presentation**	**Etiologic Hypotheses**	**Clinical Presentation**	**Treatment**	**Avoidant/Restrictive Food Intake, Subtype Descriptions**
Post-traumatic feeding disorder	Any age	A traumatic event involving oropharynx or gastrointestinal tract triggers intense and anticipatory fear of feeding	Severe, consistent refusal of solids and/or beverages following the traumatic event Child becomes distressed at sight of food or food reminders (bottle, high chair, bib)	Behavioral therapy (extinction or desensitization) Enteral feeding support May require inpatient treatment	Individuals whose food refusal is related to aversive experience
Feeding disorder associated with a concurrent medical condition	Any age	Medical condition believed to cause distress (gastroesophageal reflux, celiac disease, food allergy)	Readily initiates feeding but becomes distressed or refuses to continue feeding	Treat underlying medical condition Behavioral therapy	Exclusion criterion for this diagnosis

of infancy and childhood," with three proposed disorder subtypes that would map well onto the DC:0-3R classification. Frequently, more than one physiologic and psychological factor is contributing to a child's growth failure, and a comprehensive biopsychosocial approach is useful in planning evaluation and treatment.

MANAGEMENT OF GROWTH FAILURE

Effective management of growth failure in a young child often benefits from a multidisciplinary team approach. The team can include a physician, dietitian, behavioral psychologist, feeding specialist (speech and language pathologist), and social worker.

The physician collects a detailed medical history. Collected information should include prenatal, birth, and developmental history; family history, including parental heights and onset of puberty; and psychosocial information, including the parents' education, financial status, household living conditions, and psychological and mental health status of the caregivers. A comprehensive physical examination should be conducted[9] to identify physical features consistent with a genetic syndrome or underlying medical condition contributing to growth failure; to identify signs of child abuse; and to determine the severity and complications associated with undernutrition.

Observation of a feeding at the clinic, home, or by video recording by a behavioral psychologist and/or feeding specialist is helpful in identifying any oromotor problems affecting chewing or swallowing, as well as family dynamics and environmental interactions affecting child feeding. Key details of the feeding observation can include the following[13]:

- Parental behaviors: Anxious, inattentive to child, force-feeding, bothered by food messes, does not allow child

to participate in feeding, props bottle, ignores child's feeding signals

- Child's behaviors: Cries, spits up, gags, vomits or ruminates, holds food in mouth, arches, plays with food or toys at mealtime, takes more than 30 minutes to eat, refuses to stay seated

If the history and physical examination findings suggest specific underlying etiologies or complications related to undernutrition, targeted laboratory testing can be considered. Screening tests may include a complete blood count, albumin, erythrocyte sedimentation rate, lead concentration, and urinalysis. Screening for celiac disease (tissue transglutaminase IgA along with total serum IgA) should be considered. If malabsorption is suspected, stool studies and a sweat test for cystic fibrosis may be indicated. For toddlers consuming excessive cow's milk, breast milk, or juice, iron studies are indicated. A modified barium swallow is helpful if aspiration or mechanical feeding problems are suspected (see Chapter 22 on dysphagia).

NUTRITIONAL MANAGEMENT

Nutritional Assessment

In addition to evaluating the child's growth pattern (see the section "Assessment of Growth Pattern" in this chapter), the severity of malnutrition should be evaluated. Severe, chronic malnutrition may place the child at risk for refeeding syndrome upon replenishment of calories. Specific criteria used to categorize the severity of malnutrition include the Gomez criteria, Waterlow criteria, or anthropometric *z*-scores (see Table 2–1). Wasting, defined as a low weight-for-height, reflects acute changes in energy balance, and can both develop and be reversed relatively rapidly. Stunting, defined as a low height-for-age,

signifies slowing of skeletal growth and reflects chronic undernutrition. Weight-for-height is a better index of acute risk than is weight-for-age, and is valuable in identifying children who need nutritional treatment. Anthropometric z-scores (available from the CDC or WHO websites) measure the units of standard deviation from the population mean of weight, height, or weight-for-height. The use of anthropometric z-scores (rather than percentiles) permits a quantifiable assessment of a response to intervention, when a measurement is well below the third percentile. Average daily weight or length gain is calculated and compared with expected growth velocity for age and gender (see Table 2–2). Expected gains in weight, length, and head circumference over a defined period can also be estimated using the appropriate growth chart.

Feeding history: A detailed feeding history from birth will help determine whether feeding has progressed along a normal developmental spectrum. Key features of the feeding history include the following:

- Breastfeeding: initiation and duration, latch, frequency, night time feedings
- Formula feeding: formula type(s), tolerance, mixing
- Mixed feedings: preference for bottle vs. breast, if any
- Food intake: age at which solids or table foods were introduced, types and texture of preferred or rejected foods
- Use of bottle or cup for beverages and other utensils for food
- Feeding schedule: day and night time feedings schedule, meal duration
- Feeding atmosphere: where meals or snacks are eaten and with whom, presence of distractions (TV, toys)

- Feeding-related behaviors: child expression of hunger and satiety, feeding control (self- vs. force-feeding), positive (bribing or rewards) or negative (withholding toys, punishment)

The small quantities of food consumed by young children, and the common presence of multiple caregivers, render accurate assessment of caloric intake a challenging task. For breastfed infants, estimation of the volume of breast milk intake requires the use of a scale sufficiently sensitive to detect a difference in an infant's pre- and post-feeding weights. Assessment of food intake can use the following methods:

- Food record: caregivers record the type and amount of food and beverages consumed by the child for three to seven days. Parents should be instructed to note the amount eaten and not the amount served.
- Twenty-four-hour recall: dietitian asks caregiver to recall types and amounts of food and beverages consumed by the child over a 24-hour period. Because caregivers are relying on their memory, they may under- or overestimate intake.

A computerized nutrient analysis program such as Food Processor (Esha Research, Salem, OR) can be used to estimate macro- and micronutrient intake from a food record or 24-hour recall.

Estimation of Caloric Needs for Catch-Up Growth

Daily energy needs can be calculated using prediction equations, coupled with an estimated stress and activity factor (see Chapter 13). In a study that compared predictive equations against resting energy expenditure (REE), the weight- and height-based Schofield equation was least likely to underestimate REE in children with growth failure.[14]

To promote weight gain, additional calories to allow for catch-up growth can be calculated by using the following

formula[2]:

1. Determine the child's Dietary Reference Intakes (DRI) for age
2. Determine the child's ideal weight-for-height or ideal weight-for-age (50th percentile on the sex and age-specific growth chart)
3. Multiply DRI for age by ideal weight
4. Divide by the child's actual weight

Nutrition and Feeding Interventions

For mild to moderate undernutrition, ad libitum oral feedings using calorically dense foods are appropriate (Table 26–3). For severe undernutrition, a dietitian should be consulted

Table 26–3 Strategies to Increase Caloric Density of Food and Beverages

Butter or oil	45 calories/teaspoon
Add to soups, gravies/sauces, mashed potatoes, cooked cereals, vegetables, rice, and pasta (1 teaspoon of butter/oil to ½ cup of food). Spread on crackers, breads, muffins, and sandwiches.	
Cheese	100 calories/ounce
Melt cheese on vegetables, casseroles, fish, meats, eggs, pasta and rice. Add slices of cheese to crackers and sandwiches.	
Cooked Meats	50–75 calories/ounce
Add cooked or diced meats, poultry, shrimp or tuna to soups, casseroles, cooked noodles, and sauces.	
Cream cheese	50 calories/tablespoon
Spread on toast, crackers, bagels, breads, muffins and fruits. Try it on a sandwich with jelly.	
Granola	30 calories/tablespoon

(*Continued*)

Table 26–3 Strategies to Increase Caloric Density of Food and Beverages (*Continued*)

Add to cereals, yogurt, ice cream, and salads. Mix into cookie or cake batters.	
Half and half	20 calories/tablespoon
Add to whole milk, pasta sauce, pudding, or smoothie.	
Heavy cream	50 calories/tablespoon
Add to hot chocolate, cooked cereals, mashed potatoes, desserts, eggs, cream soups, milk, and milkshakes.	
Mayonnaise	100 calories/tablespoon
Use mayonnaise instead of salad dressing for twice as many calories. Use on salads, sandwiches and dips.	
Nuts/Sunflower seeds	50–100 calories/tablespoon
Add to hot or cold cereals, vegetables, baked goods, or ice cream, or eat as a snack.	
Peanut Butter or other nut butters	100 calories/tablespoon
Spread on toast, bread, crackers, cookies, celery or fruits such as apples or bananas. Add to yogurt or ice cream.	
Avocado	80 calories per ¼ avocado
Spread on toast or sandwiches or mash to make a guacamole.	
Carnation Instant Breakfast powder	130 calories/packet
Add to whole milk or milkshakes.	
Sour cream	30 calories/tablespoon
Add to potatoes, beans, squash and carrots. Use to make a dip or add to gravies and casseroles.	
Powdered Skim Milk	15 calories/tablespoon
Stir into potatoes, cream soups, eggs, ground meats, cooked cereals, puddings, yogurt, milkshakes, and ice cream.	
Snack ideas	

- English muffin or bagel with melted cheese or cream cheese.
- Cheese, meat, poultry, or tuna sandwich with mayonnaise.
- Cereal with whole milk, 1 tablespoon of cream.
- Whole milk yogurt with granola cereal and fruit.
- Granola bar with peanut butter.
- Banana or apple spread with peanut butter.
- Milk shakes/frappes using blended ice cream, whole milk or heavy cream, Carnation Instant Breakfast, peanut butter and/or fruit.

- Muffin with butter or cream cheese.
- Slice of pizza.
- Full fat ice cream with fruit or other toppings
- Crackers with cheese, peanut butter or hummus.
- Scrambled eggs mixed with whole milk, shredded cheese and cooked in butter or olive oil.
- Eggnog, pudding custard
- Guacamole

early and caloric intake should be advanced slowly to prevent complications associated with refeeding syndrome. Treatable etiologies of the growth failure should be addressed, and treatment should be tailored to the type of feeding disorder (Table 26–2). Consultation with a physician regarding the potential use of cyproheptadine, an antihistamine appetite stimulant, can be considered. If access to food is a concern, a social worker can help identify food resources such as WIC, Food Stamps, and food pantries, as well as support systems to minimize parental stress. If oral feedings are unsuccessful in increasing the rate of weight gain, then enteral feedings may be necessary (see Chapter 14).

INFANTS

Breastfeeding should be supported as it provides many other health benefits beyond nutrients to the infant. Inadequate intake of breast milk may be due to insufficient milk production, which can result from improper latching to the breast or a weak suck. Irritability associated with breastfeeding can be related to a strong let-down reflex or a cow's milk protein allergy. Increasing the frequency of breastfeeding or breast pumping can increase a mother's milk supply. If necessary, formula powder can be added to expressed breast milk to increase the caloric density of the breast milk. Before supplementing breast milk with formula, the infant's growth failure should be verified using the WHO growth charts, and consultation with a lactation consultant should be considered to assess problems with breastfeeding technique or breast milk supply. The decision to supplement should not be made lightly as exclusive breastfeeding has many nutritional and health benefits. However, the diet of older infants should be supplemented with iron rich cereal and then progressing to other foods such as fruits, vegetables, grains, and meats.

Irritability associated with feedings, with or without reflux or vomiting, may be indicative of a milk protein allergy or gastroesophageal reflux. Such symptoms may warrant an empiric trial of a maternal and infant milk elimination diet, or administration of medications to treat the gastroesophageal reflux.

For formula-fed infants, powdered formula can be concentrated to provide more calories in the same volume. Most infant formulas are mixed to provide 20 kcal/oz or 0.67 kcal/mL. Caloric density can be advanced up to 26 kcal/oz by concentrating the formula. Commercially available modulars such as Polycose and Duocal can be used to further increase the caloric density of the formula, up to a typical maximum of 30 kcal/oz. Household ingredients such as cooking oil can also be used to

increase the caloric density of formula although the oil may adhere to bottle plastic, making it difficult to clean. Care must be taken to ensure that an infant's hydration status is monitored and fluid requirements are met.

TODDLERS AND PRESCHOOL-AGE CHILDREN

Meals and snacks should be spaced two to three hours apart to foster the child's recognition of hunger and satiety cues. Parents should be encouraged to offer nutritious, calorically dense foods, rather than "junk foods," such as candies, desserts, or fried foods, because regular consumption of nutritionally poor foods may cause other health problems. Sugar-sweetened beverages or 100% fruit juice should be avoided and replaced with milk and/or plain water. Calorie enhancers can be added to foods (Table 26–3). Commercially available nutritional supplement such as PediaSure® or Boost® may be considered. Clear liquid nutritional drinks such as Ensure Clear™ and Resource® Breeze are available for children who may not drink milk-based supplements (see Chapter 11).

Breastfeeding toddlers that are not growing well should receive supplemental food or drink calories in addition to the breast milk. A meal pattern consisting of three meals and two to three snacks between meals is recommended. Offering food before breastfeeding is recommended, and the frequency of feeding at the breast may need to be reduced if it resembles "grazing" throughout the day and night.

When addressing concerns about poor oral intake, care should be taken to avoid creating behavior problems around mealtimes (Table 26–4). As toddlers strive to become independent, mealtimes can be quite stressful for parents, especially if the child has growth concerns. The concept of division of feeding responsibilities proposed by Ellyn Satter[15] is helpful in explaining to parents how to avoid battles at mealtime.

Table 26–4 Strategies to Promote Healthy Eating Behaviors in Preschool-Age Children

- Offer a meal or snack every 3 hours in a high chair or a booster seat. Each meal or snack should last no longer than 30 minutes. Offer nothing to eat or drink in between meals/snacks except water.
- At each meal and snack, offer 2–3 foods preferably of different textures and tastes. Offer one portion fruit or vegetable, one portion of protein, and one portion of starch. A high calorie drink such as fortified milk or commercial nutritional beverage should be offered towards the end of the meal.
- Comments about the food should be kept positive and descriptive and not negative or judgmental. Allow mealtime to be social. If the child has delayed chewing, model behavior using overexaggerated eating movements and talk about the mechanics of the food and eating.
- If child tries to end the meal too early, they can be made to wait. Use phrases such as "wait until mommy's and daddy's tummies are full."
- Never force the child to eat foods. Encourage the child to explore and interact with the food on his/her own. When spoon-feeding, wait until the child opens his/her mouth before placing the spoon inside the child's mouth. Do not use physical force to restrain the child or chasing the child for feeding.
- Minimize all distractions at mealtimes. Turn off the TV and phone; do not bring toys and other distractions to the table. Make mealtimes social, by eating with the child.
- Use concrete language during mealtime when referring to food. Instead of asking the child if she/he wants another bite, use a directive, such as "take one more bite."
- To increase the variety of foods a child accepts at a meal, offer a new food that is similar to a preferred food. The new food should share at least one thing with the preferred food

such as taste (e.g., cinnamon flavored) or texture (e.g., both foods are crunchy). It may take up to 12–15 trials before a child accepts a new food. Avoid short order cooking as much as possible.

- It is best not to "sneak" food into a preferred food, especially for a child who is very picky. He or she will distrust the food when offered again.

The parent chooses food that is safe and appropriate for the child and offers it in a safe and supportive manner. The child is responsible for deciding how much and whether they eat. Parents should not force a child to drink or eat predetermined target amounts of liquid or food prescribed by the child's clinicians. Force-feeding can worsen feeding disorders or cause posttraumatic stress disorder. Parents should be encouraged to notify the child's clinician if they find that their child is not able to drink or eat the goal amount prescribed.

PROGNOSIS

The majority of children with growth failure will show improved intake and weight gain with intervention. Some children with picky eating or food refusal may continue to have feeding problems into childhood, especially if untreated,[11] and some may be diagnosed with anxiety or other psychiatric disorders.[1,11] A small percentage of children, particularly those with underlying medical conditions and neurologic disorders, may require ongoing supplemental nutrition by enteral tube feeding. In developing nations, severe childhood undernutrition is related to adverse cognitive, health, and social outcomes,[16] but whether a slow rate of weight gain among healthy term infants in developed nations adversely affects cognitive or other health outcomes remains controversial.[17,18] Iron deficiency anemia in

infancy has been shown to adversely affect long-term cognition even if the iron deficiency is treated,[19] and it is possible that other micro- or macronutrient deficiencies might negatively impact cognitive development. A multidisciplinary approach that addresses the biological, psychological, and social factors underlying a child's growth failure is important to ensure optimal long-term health outcomes.

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27 Hepatobiliary Diseases

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Nutritional issues are common in pediatric liver disease. In acute liver failure, most patients present with adequate nutritional status. They require only short-term, uncomplicated strategies to meet nutritional goals. In contrast, children with chronic liver disease often develop some degree of malnutrition. Protein energy malnutrition is present in 20% of patients with well-compensated cirrhosis and 60% of patients with severe liver dysfunction.[1] Poor nutritional status prior to liver transplant can negatively impact outcomes following transplant.[2] Table 27–1 highlights clinical manifestations and etiologies of nutritional deficiencies seen in liver disease. The primary cause of malnutrition is inadequate energy intake. The underlying mechanisms are multifactorial, including gastric dysmotility, ascites, bacterial overgrowth, hepatomegaly, and secondary effects from medications. Moreover, infants and children with chronic liver disease may have increased energy needs. For example, resting energy expenditure is increased by 30% in extrahepatic biliary atresia.[3] Contributing factors for hypermetabolism in chronic liver disease include ascites, infection, and portal hypertension.

Table 27–1 Clinical Manifestations and Etiologies of Common Nutritional Problems in Liver Disease

Nutrient Affected	Manifestation	Etiology
Protein	Stunting, muscle wasting, motor developmental delay	Protein energy malnutrition, decreased insulin-like growth factor 1 synthesis
	Ascites or peripheral edema	Decreased albumin synthesis leading to decreased oncotic pressure
	Coagulopathy	Alteration of synthesis in clotting factors
	Hepatic encephalopathy	Decreased aromatic amino acid metabolism
Fat	Steatorrhea, essential fatty acid deficiency (rash), fat-soluble vitamin deficiencies (see below)	Impaired intestinal absorption, decreased intake of essential fatty acid
	Hypercholesterolemia, hypertriglyceridemia (xanthomas)	Impaired hepatic lipid clearance
Carbohydrate	Hyperglycemia	Insulin resistance leading to impaired muscle and liver glycogen syntheses
	Fasting hypoglycemia	Decreased glycogen stores with hepatocellular dysfunction

Nutrient Affected	Manifestation	Etiology
Vitamin A	Night blindness, degeneration of retina, xerophthalmia, poor growth, hyperkeratosis	Impaired intestinal absorption
Vitamin D	Rickets, osteoporosis, cranial bossing, epiphyseal enlargement, persistently open fontanelle in infants	Impaired intestinal absorption and decreased hepatic 25-hydroxylation
Vitamin E	Peripheral neuropathy, ataxia, hemolytic anemia	Impaired intestinal absorption
Vitamin K	Coagulopathy, hemorrhagic manifestations such as bruising, bone disease	Impaired intestinal absorption
Minerals	Low iron, copper, zinc, selenium, calcium	Impaired intestinal absorption

The underlying liver dysfunction determines what nutritional issues occur. Cholestatic conditions, such as Alagille syndrome, extrahepatic biliary atresia, and intestinal failure-associated liver disease, are commonly associated with intestinal malabsorption. Decreased hepatic bile salt excretion leads to inadequate micelle formation, and impaired lipid- and fat-soluble vitamin uptake. Cholestatic conditions are also associated with impaired triglyceride clearance. Patients with cirrhosis can have impaired glucose tolerance with hyperinsulinemia and insulin resistance. On the other hand, decreased glycogen stores and decreased glucose production in all types of end-stage liver disease

result in hypoglycemia. Protein turnover is usually normal or increased.

Tables 27–2 and 27–3 highlight nutritional monitoring and assessment techniques in pediatric liver disease. Evaluation begins with careful dietary history and review of growth records. Special attention should be paid to sodium and fluid intake. Ascites and edema may lead to changes in weight over time deceptively similar to weight gain. In addition, hypoalbuminemia may reflect impaired liver synthetic function as opposed to protein–energy malnutrition. Interpretation

Table 27–2 Specific Nutritional Monitoring in Liver Disease

Nutrient	Monitoring
Energy	Diet recall, energy expenditure (indirect calorimetry), changes in growth parameters over time, total body potassium
Protein	Prothrombin time, total protein, albumin, prealbumin, clotting factor levels, ammonia, total body nitrogen, midarm muscle circumference
Fat	Triceps skin folds, body habitus, triene-tetraene ratio, triglycerides, total cholesterol
Carbohydrate	Serum glucose
Vitamin A	Vitamin A, ratio of retinol to retinol-binding protein
Vitamin D	Vitamin 25-OH D, calcium, phosphorus, parathyroid hormone, alkaline phosphatase, dual-energy x-ray absorptiometry scan for bone density
Vitamin E	Ratio of vitamin E level to total lipid
Vitamin K	International normalized ratio (especially response to vitamin K supplementation)
Iron	Iron, total iron-binding capacity, ferritin
Zinc	Serum zinc, alkaline phosphatase
Copper	Serum copper, ceruloplasmin, 24-hour urine copper excretion

Table 27–3 Special Considerations of Nutritional Assessment in Liver Disease

Diet History
Total calorie intake
Total macronutrient intake and source
Total fluid intake and fluid status
Sodium intake
Medications with potential effects on nutritional status
Stooling pattern/steatorrhea
Functional capacity and physical activity
Physical Examination and Assessment
Evidence of edema or ascites
Jaundice
Hepatosplenomegaly
Height, weight, head circumference (if < 2 years old)
Arm anthropometrics

of certain micronutrients levels requires simultaneous measurement of carrier proteins. Because calcium and magnesium are bound to albumin, serum levels may appear falsely low in setting of hypoalbuminemia. Ionized calcium may be helpful in this setting. Similarly, ratio of retinol to retinol-binding protein is a preferred method of interpreting vitamin A status. Possible toxicity is suggested by ratio greater than 1, and deficiency is suggested by ratio less than 0.8. Similarly, vitamin E status should be interpreted by ratio of vitamin E to total lipid concentration. Vitamin E deficiency is suggested by ratio <0.6 mg/g in children under 1 year and <0.8 mg/g in older children. See Chapter 19, "Cystic Fibrosis," for calculations of molar ratios of these nutrients and their carrier proteins.

Table 27–4 addresses special aspects of nutritional management in hepatobiliary disease. To compensate

Table 27–4 Special Aspects of Nutritional Management in Hepatobiliary Diseases

- Daily calorie and protein requirements
  - Energy needs: 100%–150% Dietary Reference Intakes
  - Protein needs: 2–3 g/kg/d
- Use gut if possible; tube feedings if inadequate by mouth
- Total parenteral nutrition (TPN)
  - Use cautiously, as long-term TPN can cause liver dysfunction
  - Standard amino acid solutions generally tolerated

Enteral product selection

Standard infant formulas:

Enfamil Premium Infant (Mead Johnson)

Gerber Good Start (Nestle)

Similac Advance (Abbott)

Infant formulas for fat malabsorption:

Alimentum (Abbott)

Pregestimil (Mead Johnson)

Standard pediatric formulas:

Boost Kid Essentials (Nestle)

Nutren Junior (Nestle)

PediaSure (Abbott)

Pediatric formulas for fat malabsorption (contain MCT oil):

Peptamen Junior (Nestle)

Vital Jr. (Abbott)

Vivonex (Nestle)

Modulars

MCT oil (Nestle)

- Post–liver transplantation
  - Initiation of enteral feeds (with normal liver function)
  - Diet appropriate for age with mild sodium restriction due to steroid therapy
  - Tube feeding may be necessary to ensure optimal calories and protein
  - Short-term parenteral nutrition may be necessary

for increased energy needs and anorexia, supplemental nasogastric tube feeds may be helpful. Hepatosplenomegaly, ascites, or varices may limit the feasibility of placing a permanent feeding tube. Parenteral nutrition should be reserved for those incapable or unwilling to receive enteral feeds by mouth or feeding tube. Although there is unease surrounding parenteral nutrition hepatotoxicity, it may be used safely for short intervals without problems. Standard parenteral amino acid solutions are adequate for nearly all situations. The use of branched-chain amino acids (BCAAs) in adult studies may be beneficial in uncontrolled encephalopathy. At this time, BCAA formula in children with chronic liver disease is only investigational.

In choosing enteral formulas, standard products may be adequate. Patients with intestinal malabsorption may benefit from formulas rich in medium-chain triglycerides (MCTs) or formula supplemented with MCT oil. When using specialized formulas chronically, long-chain triglycerides are also needed to prevent essential fatty acid deficiency. Restrictive diets are not necessary, and may be dangerous. Protein should be provided according to recommended daily allowances to prevent protein catabolism. It may be appropriate to temper sodium intake for ascites or edema. Table 27–5 lists recommendations for vitamin and mineral supplementation for chronic liver disease.

Successful liver transplantation is usually associated with improved growth and developmental outcomes. Following liver transplantation, enteral feeds should be started as soon as possible, but short-term parenteral nutrition may be safely used while awaiting return of bowel function. Tube feeds may be helpful for postoperative anorexia. Mild sodium restriction may be necessary to minimize edema with steroids. Table 27–6 lists common medications prescribed for patients with chronic liver disease.

Table 27–5 Maintenance Recommendations for Vitamin and Mineral Supplementation in Patients With Cholestasis

Nutrient	Product	Dose
Vitamin A[4]	Liquid vitamin A	5,000–25,000 IU/d
Vitamin D[5]	Vitamin D	200–1000 IU/d
Vitamin E[6,7]	Liquid vitamin E	15–25 IU/kg/d
Vitamin K[8]	Vitamin K_1 (Mephyton)	2.5–5 mg/d, every 2–3 d
Zinc[5]	Zinc sulfate	1 mg/kg/d
Calcium[5]	Elemental calcium	25–100 mg/kg/d
Phosphorus[5]	Elemental phosphorus	25–50 mg/kg/d

Table 27–6 Medications Commonly Used in Chronic Liver Disease

Drug	Potential Side Effects Affecting Nutritional Status	Nutrition Therapy
Cholesty-ramine	• Fat-soluble vitamin malabsorption • Fat malabsorption	• Monitor and supplement fat-soluble vitamins • Consider MCT oil
Neomycin	• Mucosal toxicity • Steatorrhea • Carbohydrate malabsorption • Vitamin B-12 deficiency	• Consider MCT oil • Supplement with vitamin B12
Ursodiol	• Diarrhea	• Ensure adequate hydration

Drug	Potential Side Effects Affecting Nutritional Status	Nutrition Therapy
Systemic steroids	• Edema • Hypertriglyceridemia • Hyperglycemia • Cushing's syndrome • Decreased bone mineral density	• Avoid overfeeding • Avoid excessive salt intake • Insulin replacement as needed
Tacrolimus (posttransplant)	• Hypomagnesemia • Hypertriglyceridemia • Hyperglycemia • Hypophosphatemia	• Magnesium supplementation
Lactulose	• Osmotic diarrhea • Hyponatremia • Hypokalemia	• Monitor and adjust diet • Supplement electrolytes

Source: Adapted from Kleinman R, Warman KY. Nutrition in liver disease. In: Baker SB, Baker RD, Davis A, eds. *Pediatric Enteral Nutrition*. New York: Chapman and Hall, Inc.; 1994:264.[9]

In summary, children with chronic liver disease have special nutritional needs. Treatment is aimed at reversing consequences of anorexia, increased energy needs, and associated intestinal malabsorption, as well as altered carbohydrate and protein metabolism.

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Web sites
www.liverfoundation.org
http://www.childliverdisease.org/
http://www.childrennetwork.org/

28 Intestinal Failure

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INTRODUCTION

Intestinal failure (IF) has been defined as a condition characterized by the "reduction of functional intestinal mass necessary for adequate digestion and absorption of nutrient, fluid, and growth requirements."[1] Three main types of IF include short bowel syndrome (because of acquired or congenital disorders of the gastrointestinal tract), intestinal motility disorders (where intestinal length is preserved but function is limited), and intestinal epithelial defects (such as microvillus inclusion disorder, tufting enteropathy, and others). These latter two classes of IF are substantially less common than IF owing to surgical treatment of congenital or acquired anomalies, and much of the pediatric literature, especially the nutrition literature, is based on clinical experience with so-called surgical short bowel syndrome. This chapter, therefore, generally refers to care of patients with this type of IF.

IF can lead to malabsorption of macronutrients and micronutrients, electrolyte abnormalities, dehydration, and ultimately malnutrition. Since no clear anatomic definition

of IF exists, the literature has commonly defined pediatric IF as dependence on parenteral nutrition (PN) for at least 90 days. Table 28–1 lists common etiologies of short bowel syndrome in children. The prognosis of IF depends on several factors, including (1) the length and portion of small and/or large bowel affected by a disease process or surgically resected, (2) the presence or absence of the ileocecal valve (ICV), (3) the adaptive and functional capacity of the remaining bowel, and (4) the health of other organs that assist with digestion and absorption.[2]

Length and Portion of Small Bowel Resected

Normal small intestine length has been approximated at 70 cm in infants 24–26 weeks gestational age and 143 cm in infants ≥35 weeks. At term, mean length is reported to be 150–240 cm and continues to increase with age, weight, and linear gains. The large intestine is 33–57 cm at birth, growing to 122 cm by 5 years of age (Figure 28–1).[3]

Table 28–1 Common Causes of Short Bowel Syndrome in Infants and Children

Necrotizing enterocolitis (NEC)
Intestinal atresia
Gastroschisis
Midgut volvulus
Crohn's disease
Tumors
Radiation enteritis
Ischemic injury
Intestinal pseudo-obstruction
Total intestinal aganglionosis

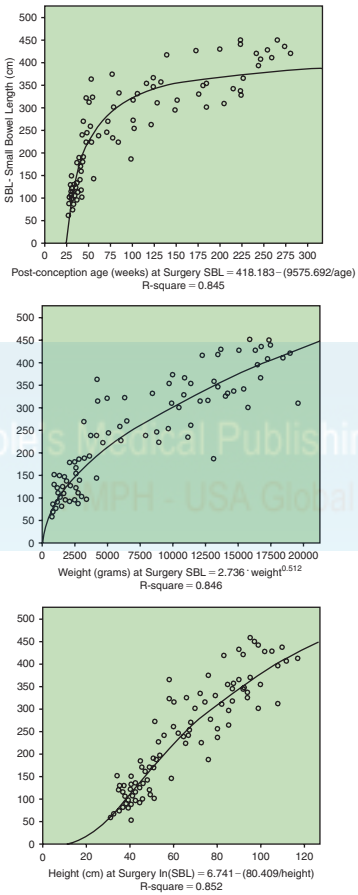

Figure 28–1: Predictors of small bowel length. (Adapted from Struijs et al.[3])

Loss of intestinal length can limit digestion by reducing exposure of nutrients to brush border hydrolytic enzymes, as well as pancreatic and biliary secretions. Many studies have examined the relationship between length of residual small intestine and successful weaning from PN. It appears that infants require approximately 10–30 cm of small intestine, with intact ICV, to avoid lifelong dependence on PN. If the ICV is not present, then 30–50 cm of small intestine is generally needed for successful weaning of PN.[4] These anatomic estimates, however, are mere "rules of thumb," and individual results can and do vary substantially.

Portion of Small Bowel Resected

The location of resected bowel has an impact on nutrient loss in IF. Duodenal resection may result in iron or folate malabsorption. Calcium absorption may be impaired with proximal small bowel resection. The jejunum has long, large villi, extensive absorptive surface area, highly concentrated digestive enzymes, and many transport carrier proteins and is the primary digestive and absorptive site for most nutrients. Loss of jejunum is also associated with reduction of cholecystokinin and secretin levels, which secondarily impairs pancreatic and biliary secretion, causing subsequent malabsorption of fat and fat-soluble vitamins.[5] Loss of the terminal ileum results in malabsorption of bile acids. Steatorrhea, fat-soluble vitamin malabsorption, and the formation of lithogenic bile may ensue. The terminal ileum is also the primary site for vitamin B12 absorption, so resection there can lead to B12 deficiency. The ileum secretes hormonal substances that slow gastrointestinal motility in response to fat malabsorption. The antimotility effect of fat in the ileum is known as the ileal brake and is important in ensuring adequate fat absorption from the small intestine.[6]

Intestinal transit time decreases following small bowel resection. Changes in transit time will vary depending upon the area of intestine removed. Normally, motility in the distal ileum is considerably slower than in the jejunum.[7] Consequently, ileal resection reduces intestinal transit time more than proximal bowel resection. Gastric emptying tends to be more rapid following ileal resection, but can be normalized if the colon is retained. In patients with ileal or colonic resection, cells that release peptide YY are missing, resulting in a loss of inhibition on gastric emptying and faster intestinal transit time. Following jejunal resection, gastric emptying is more rapid; however, intestinal transit time may remain normal due to the ileal brake.[8] In patients with residual bowel in continuity, gastric emptying is slower and similar to normal controls. Colon resection is associated with delays in bowel adaptation and loss of energy from malabsorption of short-chain fatty acids (SCFAs).[4] The colon has an important role in the control of fluids and electrolyte losses, and thus resection of the colon will decrease transit time further.

Presence or Absence of the Ileocecal Valve

The ICV serves to regulate the flow of enteric contents from the small bowel into the colon. The absence of an ICV reduces gastrointestinal transit time and increases fluid and nutrient losses. In a cohort of children with IF followed during their wean from PN, resection of the ICV was a significant risk factor for having at least one vitamin deficiency.[9] In the absence of the ICV, colonic bacteria may "overgrow" into the small intestine (termed "small intestine bacterial overgrowth (SIBO)"). SIBO may cause deconjugation of bile acids and an inflammatory response that damages small bowel mucosa. This leads to exacerbation of the malabsorptive state,[6] particularly dietary fat, fat soluble vitamins, and B12. The use of a rotating schedule of oral antibiotics is commonly used to treat SIBO (Table 28–2).

Table 28–2 Comparison of Agents Used for Treatment of Bacterial Overgrowth[a]

Medication	Pediatric Dose	Comments	% Orally Absorbed	% Renally Excreted
Amphotericin	<5 years: 100 mg bid	Injection given orally	9%	40% (2%–5% active)
	5–12 years: 250 mg bid			
Augmentin	10 mg/kg/dose bid		Complete (amoxicillin)	30%–40%
Ciprofloxacin	20–40 mg/kg/d bid		50%–80%	30%–50%
Clindamycin	10–30 mg/kg/d		90%	10%
	Divided tid/qid			
Colistin	<5 years: 25 mg 2–4 times/d	Injection given orally	Insignificant	75% in 24 h
	5–12 years: 50 mg 2–4 times/d			
Doxycycline	>8 yrs: 100 mg bid		100%	23%
Gentamicin	2 mg/kg/dose bid	Injection given orally	None	100%
	Others: 2.5 mg/kg/dose tid not to exceed 300 mg/d			

Medication	Pediatric Dose	Comments	% Orally Absorbed	% Renally Excreted
Metronidazole	10 mg/kg/dose bid		90%	10%
	Others: 5–10 mg/kg/dose bid–tid			
Neomycin	50 mg/kg/d	Available as tablets only	3%	0.9%–1.5%
	Divided every 6 h			
Tetracycline	>8 years: 25–50 mg/kg/d in divided doses every 6 h	>8 years: 25–50 mg/kg/d in divided doses every 6 h	75%	60%
Tobramycin	<5 years: 10 mg 2–4 times/d	Injection given orally	Poor	90%–95%
	5–12 years: 40 mg 2–4 times/d			
Rifaxamin	Not estalished 20–30 mg/kg/d has been used		<0.4%	<1%
Vancomycin	125 mg every 6 h (10 mg/kg/dose qid)		Poor	Oral doses primarily via feces
	Max total daily dose: 2 g/d			

[a]Typical course 7–10 d; all medicines are to be given orally.

One important, but relatively rare, consequence of SIBO is D-lactic acidosis. The inability of humans to metabolize the D-dimer (as opposed to the L-dimer) of lactic acid synthesized by intestinal bacteria leads to a variety of associated symptoms, including headache, drowsiness, stupor, confusion, behavioral disturbance, ataxia, blurred vision, opthalamoplegia, or nystagmus.[10] D-Lactic acidosis should be suspected when there is an acidosis with an unexplained anion gap accompanied with behavioral changes in the child.

Adaptive and Functional Capacity of the Remaining Small Intestine

Following extensive resection, the remaining intestine has an ability to compensate, but this depends on the area of resection and other trophic stimuli. The ileum appears to be more able to adapt and compensate for loss of proximal small intestine. Intestinal adaptation refers to the gross anatomic and histologic changes that occur after significant intestinal resection (Table 28–3). These adaptive changes begin 12–24 hours after massive intestinal resection and

Table 28–3 Adaptive Changes in the Small Bowel Following Extensive Resection

Increased bowel circumference
Increased bowel wall thickness
Increased bowel length
Increased villus height
Increased crypt depth
Increased cell proliferation and migration to villus tip

likely continue for years after resection.[11] These changes include lengthening of the villi, an increase in intestinal absorptive surface area, and gradual improvements in absorptive function. The younger infant is, therefore, at an advantage for improvements in bowel function over time when compared to adults due to the opportunity for further growth of intestinal length.

Enteral nutrition is an important stimulant of mucosal hyperplasia. This is thought to be a result of direct contact of nutrients with epithelial cells, stimulation of gastric, pancreatic, and biliary secretions, as well as stimulation of trophic hormone production.[12] Much research has been directed at examining whether specific nutrients promote adaptation more than others, but to date no rigorously designed study has defined these for children.

Health of Other Organs that Assist with Absorption and Digestion

Cholestasis and liver dysfunction can occur in patients with IF, thereby affecting the absorption and utilization of nutrients. Most case series identify so-called IF-associated liver disease as the major cause of death in this population,[13] with venous catheter-related blood stream infections a leading cause, as well. The relationship between PN use and cholestasis is likely multifactorial and includes the risk factors of sepsis, mucosal atrophy, and bacterial overgrowth. Recent data have linked the provision of soy-based intravenous fat emulsions with the development of liver disease, and open label reports suggest the efficacy of reducing lipid infusion and/or providing intravenous omega-3 fatty acids[14] as ways to reduce cholestasis. Every effort should, therefore, be made to reduce the risk of IF-associated liver disease (Table 28–4).

Table 28–4 Steps to Reduce the Risk of Intestinal Failure-Associated Liver Disease

Method	Comments
Avoid overfeeding	Provide adequate kcals for desired growth
	Infants: 90–100 kcal/kg from PN
	Children: Utilize a REE and apply an appropriate stress factor
Limit exposure to soy-based fat emulsions	Reduce risk of hepatocellular damage induced by exposure to phytosterols and inflammatory mediators
Cycle PN off at least 2–6 h/d	Promotes cyclic release of GI hormones
	Mimic age-appropriate feeding patterns when considering time free from PN
Aggressively treat and prevent infections	Meticulous CVL care
	Treat bacterial overgrowth
Push enteral nutrition	The ultimate goal of therapy

Special Aspects of Nutritional Therapy in IF

The goals of nutrition therapy in IF are to maintain normal growth, promote intestinal adaptation, and avoid complications associated with intestinal resection and PN.

◆ WHAT TO FEED

Fluid, Electrolytes, and Parenteral Nutrition

During the early postoperative phase, fluid and electrolyte balance is the goal of therapy. Large fluid losses are common and tend to be high in sodium content. Parenteral solutions with at least 80–100 mEq/L of sodium are often required to maintain sodium balance.

Meticulous attention needs to be paid to the fluid and electrolyte status of IF patients. This includes daily

weights, careful measurement of urine, stool, and ostomy losses, and laboratory monitoring of electrolytes. PN is indicated in the management of IF until small bowel growth and adaptation permit growth on enteral nutrition alone.

Because day-to-day variations in fluid loss is common, it is often advantageous to place the patient on a stable PN solution with fluid and electrolytes appropriate for age, growth requirements, and metabolic considerations, while subsequently replacing abnormal losses with a separate solution comparable in fluid and electrolyte content. For example, ostomy sodium concentration can be quantified and replacement fluids prescribed based upon the assessment of the secretions. When losses have stabilized and/or use of additional hydration becomes habitual in nature, the fluid and electrolyte content of the patient's PN should be altered to compensate for chronically elevated gastrointestinal losses.

Enteral Feedings

Once the patient's fluid and electrolyte status has stabilized and postoperative ileus has resolved, a slow introduction of enteral feedings should be started. Mothers of newborns with IF should be referred to a lactation consultant to encourage continued breast milk production. Breast milk has special immunologic and anti-infective properties that are especially advantageous to the infant having undergone intestinal resection, although the transition from parenteral to full enteral feedings may take weeks to months. Breast milk from mothers of premature infants with IF may require fortification to meet the child's unique nutritional needs (see Chapter 34, Prematurity). Breast milk also contains growth factors, nucleotides, glutamine, and other amino acids that may play an important role in assisting intestinal adaptation.

If breast milk is unavailable, the selection of enteral formula remains somewhat controversial. The choice of formula should consider age, functional anatomy of the remaining small bowel, and the capacity of digestion and absorption.[15, 16] Premature infants have special needs that must also be considered (see Chapter 34, Prematurity). Studies suggest that complex nutrients that require more work for digestion and absorption tend to stimulate intestinal adaptation more effectively.[6] However, limited mucosal surface area can lead to lactose, protein, and long-chain fatty acid (LCFA) malabsorption with the use of intact formulas. If this malabsorption is severe, fluid, electrolyte, and energy balance can be difficult to achieve. At the initial stage of feeding, it is customary to use either breast milk or, if that is unavailable, an amino acid–based formula that is lactose-free and may include medium-chain triglycerides (MCTs) to facilitate nutrient absorption.

Protein is generally tolerated well and is least affected by decreased intestinal absorptive surface area.[11] Intact protein contributes little to osmotic load. It appears that there may not be a significant absorptive advantage from the use of hydrolysate or amino acid–based formulas, particularly with older children.[17] However, infants and young children with bowel inflammation may be at risk for secondary intestinal allergic disease and, therefore, may benefit from the use of protein hydrolysate or amino acid–based formulas.[15]

MCTs are more water-soluble than long-chain triglycerides (LCTs) and are better absorbed in the presence of bile acid loss or pancreatic insufficiency. However, MCT fats have a slightly lower caloric density and exert a greater osmotic load in the small intestine. Studies suggest that LCT have a trophic effect by stimulating gut adaptation after intestinal resection.[12] Although fat tends to be poorly absorbed in IF, it is a dense calorie source relative to carbohydrate or protein. Considering the relative adverse effect of carbohydrate on

osmotic diarrhea, it is usually advantageous for patients with IF to include at least moderate amounts of fat in their diets. A mixture of both LCT and MCT may be beneficial.

Carbohydrates may be poorly tolerated as they are broken down by gastrointestinal bacteria into small, osmotically active organic acids that can exert a significant osmotic load in the distal small intestine and colon. Glucose may be absorbed without hydrolysis, but its small molecular weight increases solution osmolality. Carbohydrate may be given in the form of glucose polymers to reduce the osmotic load. Lactose may be restricted initially after intestinal resection. In general, lactose-containing foods should only be restricted when intolerance is demonstrated or when there is significant resection of proximal small intestine.[11] Fiber supplementation may be helpful in older children with IF who have an intact colon. Some fermentation of the fiber will occur, producing trophic SCFAs, which are an important fuel for the colonocyte. Because SCFAs stimulate sodium and water absorption, a decrease in stool output and sodium losses may be expected, as well.[16] Table 28-5 provides a comparison of enteral formulas commonly used in the pediatric IF patient.

HOW TO FEED

Continuous enteral feedings via a nasogastric or gastrostomy tube is advantageous in the patient with IF since they permit constant saturation of carrier transport proteins, thus taking full advantage of the absorptive surface area available. Oral feedings, however, are also important to initiate early in the child's course to avoid oral aversion, a common morbidity among infants with a history of critical illness in the neonatal period. We, therefore, commonly employ a regimen of both continuous and oral bolus feeding. Older children and adults have a better capacity to regulate gastric emptying and, therefore,

Table 28–5 Common Enteral Formulas Used in Pediatric Short Bowel Syndrome Management

Formula Type	Infant			Child		
	Product	Calories per Ounce[a] (Osmolality mOsm/kg H_2O)	Notable Characteristics	Product	Calories per Ounce[a] (Osmolality mOsm/kg H_2O)	Notable Characteristics
Amino acid–based	Elecare infant	20 (350)	33% of fat as MCT oil; Preparation consistent with standard infant formula preparation	Elecare Junior	30 (590)	Vanilla flavor available for children 1 year and older
	Neocate infant	20 (375)	95% of fat as LCT	Neocate Junior	30 (590–700)	35% of fat from MCT oil
	Neocate infant with DHA and ARA	20 (375)	33% of fat as MCT	Neocate (E028) Splash	30 (820)	Ready to feed nutritionally complete hypoallergenic fruit beverage

	Nutramigen AA	20 (350)	100% LCT fat blend	Pediatric Vivonex	24 (360)	68% of fat from MCT oil. Manufactured in the same plant as formulas that contain soy, milk, egg, and wheat
Semi-Elemental	Pregestimil Lipil[b]	20 (320)	55% of fat as MCT oil; used in cases of severe fat malabsorption	Peptamen Jr[b]	30 (260–400)	60% of fat from MCT oil; 100% whey protein
	Alimentum[b]	20 (370)	33% MCT oil; casein hydrolysate blend	Peptamen Jr 1.5[b]	45 (450)	60% of fat from MCT oil; unflavored
				Pediasure Peptide[b]	30 (390)	50% of fat from MCT oil; also available in a 1.5 calorie per mL

(*Continued*)

Table 28–5 Common Enteral Formulas Used in Pediatric Short Bowel Syndrome Management (*Continued*)

Formula Type	Infant			Child		
	Product	Calories per Ounce[a] (Osmolality mOsm/kg H_2O)	Notable Characteristics	Product	Calories per Ounce[a] (Osmolality mOsm/kg H_2O)	Notable Characteristics
				Pepdite Junior[b]	30 (250–390)	Available as unflavored or banana flavored. Not ready to feed
Isomeric	Breast milk	20 (295–300)	First choice for all infants with SBS	Pediasure[b]	30 (335)	Also comes with fiber. Available in a 1.5 calorie per mL
				Boost Kids Essential 1.5[b]	45 (390)	Useful for the patient with fluid restriction or high energy demand; also comes with fiber

[a]Based on standard preparation/dilution.

[b]These products should be used only in the patient with known mucosal adaptation and tolerance to milk protein.

Source: Adapted from Duggan et al.[25]

tolerate gastric bolus or oral bolus feedings better than infants. Enteral feedings are slowly advanced by concentration then volume, while parenteral calories are decreased by rate or number of hours to maintain nutritional status, control fluid losses, and ensure intestinal adaptation. Small quantities of oral feedings should be introduced in infants 2 or 3 times a day to stimulate sucking and swallowing and minimize the risk of feeding aversion. Solid feedings should be initiated at developmentally appropriate stages.

The rate of advancement of enteral feeds should be determined by multiple factors, including stool or ostomy output, gastric residuals, and signs of malabsorption. We have employed the scheme in Table 28–6. In general, it is acceptable for infants to have 5–10 watery stools per day, as long as reducing substances are less than 1.0% and stool pH is below 5.5, which may indicate excessive carbohydrate malabsorption. If intolerance occurs soon after an increase in rate or concentration of the formula, a return should be made to the previously tolerated rate or concentration. Once tolerance is established, advancement can be attempted again. Frequent setbacks are not unusual. Enteral feedings may eventually be transitioned to oral/bolus feedings or oral/bolus and nocturnal feedings to allow more freedom from the feeding pump. Oral feedings should consist of small, frequent meals.

Excessive fluid and electrolyte losses may continue to complicate advancement of enteral feedings, particularly in patients with high output jejunostomies. Oral rehydration solutions with a sodium concentration of 75–90 mEq/L should be used to replace losses (see Chapter 25, Gastrointestinal Diseases for a list of commercially available oral rehydration solutions).

Table 28–6 Suggested Guidelines for Enteral Feeding Advancement in the Infant With Intestinal Failure

A. Feeding Initiation

Audible bowel signs?
Functioning ostomy (if applicable)?
No contraindications?[a]
No, then continue IVF/PN/NPO.
Yes, then start feeds (NG/NJ/G-tube/J-tube)
Day 1: Breast milk (full strength) or amino acid–based formula (20 cal/oz) at 10–20 mL/kg/d continuously × 24 h
Contraindications to enteral feeding[a]:

1. Paralytic or drug-induced ileus
2. Grossly bloody stools or ostomy output and/or radiological changes of intestinal ischemia
3. Shock/poor perfusion due to cardiac or respiratory insufficiency
4. Bilious and/or persistent vomiting (defined as more than 3 episodes of emesis in 12 h)
5. Clinical suspicion of obstruction or ileus (severe abdominal distension, decreased ostomy or stool output, and/or radiologic changes of obstruction or ileus)

Bolus feeds may only be offered as follows:

1. Infant is developmentally able to feed by mouth (PO)
2. One hour's worth of continuous feeds may be offered PO QD-TID after 5 d of continuous feeds (during bolus feeds, tube feeds should be held)
3. More than one hour's worth of continuous feeds may be offered PO once the infant has reached full volume of feeds by continuous route OR at least 7 d have passed on the feeding advancement protocol

B. In-Patient Feeding Advancement:

Principle 1: Quantify feeding intolerance primarily by stool or ostomy output

Principle 2: Tolerance assessed no more than twice per 24 h; no more than one advance per 24 h period

Principle 3: Ultimate goals: 150–200 mL/kg/d
100–140 kcal/kg/d

Principle 4: If ostomy/stool output precludes advancement at 20 cal/oz for 7 d, then increasing caloric density of the formula can be performed

Principle 5: Isocaloric reductions in PN support should be undertaken simultaneous with feeding advancement

1. Stool output
If <10 g/kg/d or <10 stools/d → advance rate by 10–20 mL/kg/d
If 10–20 g/kg/d or 10–12 stools/d → no change
If >20 g/kg/d or >12 stools/d → reduce rate or hold feeds[b]
or 2. Ileostomy output
If <2 g/kg/h → advance rate by 10–20 mL/kg/d
If 2–3 g/kg/h → no change
If >3 g/kg/h → reduce rate or hold feeds[b]
3. Stool reducing substances
If <1% → advance feeds per stool or ostomy output
If =1% → no change
f >1% → reduce rate or hold feeds[b]
4. Signs of dehydration:
If absent → advance feeds per stool or ostomy output
If present → reduce rate or hold feeds[b]
5. Gastric aspirates
<four times previous hour's infusion → advance feeds
>four times previous hour's infusion → reduce rate or hold feeds[b]

[a] 1. Paralytic or drug-induced ileus
2. Grossly bloody stools or ostomy output and/or radiological changes of intestinal ischemia
3. Shock/poor perfusion due to cardiac or respiratory insufficiency
4. Bilious and/or persistent vomiting (defined as more than 3 episodes of emesis in 12 h)
5. Clinical suspicion of obstruction or ileus (severe abdominal distension, decreased ostomy or stool output, and/or radiologic changes of obstruction or ileus)

[b]Feeds should generally be held for 8 h, then restarted at 3/4 the previous rate.

Mineral Supplementation in Intestinal Failure

Mineral supplementation requires an individualized plan for each patient. For those with cholestasis who are dependent upon PN, the provision of manganese and copper should be carefully considered, given their dependence upon entero-hepatic circulation for excretion and risk of toxicity with cholestasis. Cholestatic patients are at risk of manganese

accumulation and potentially damaging effects to the developing basal ganglia. Copper toxicity may also be seen in cholestasis, although copper requirements can increase in the setting of increased gastrointestinal losses. Copper deficiency manifests as a microcytic anemia unresponsive to iron supplementation and may also negatively impact proper bone development. Similar to copper, zinc deficiency is common in the patient with high volume GI losses. The need for additional supplementation is common, and serum values should be assessed periodically, given the risk of growth failure in the presence of zinc deficiency. Selenium status should be carefully assessed in the PN patient, given historical selenium deficiencies in this population and the risk of fatal cardiomyopathies associated with deficiency.[18] Abnormal values should be carefully assessed and applied to the current clinical picture to assess if supplementation or treatment of toxicity is required. If parenteral selenium is not available, enteral supplementation should be considered, when possible (see Table 15–16, "American Society for Parenteral and Enteral Nutrition (ASPEN) Parenteral Nutrition Additive Shortage Recommendations," in Parenteral Nutrition).

For IF patients receiving both parenteral and enteral nutrition, close monitoring of electrolyte status is crucial because of the high concentration of electrolytes in gastrointestinal secretions. Many IF patients may require supplementation of sodium, potassium, and magnesium based upon routine laboratory assessment and/or clinical findings. Adequate intake of calcium, phosphorus, and magnesium should also be encouraged for adequate bone mineralization. The IF patient remains at risk of decreased bone mineral density and delayed linear growth secondary to metabolic bone disease associated with long-term PN exposure as well as malabsorption of calcium and vitamin D that accompanies fat maldigestion. Bone mineral density should be

routinely monitored.[19] Iron deficiency can result from loss of duodenal-jejunal absorptive area and has been shown to impact upwards of 30% of patients with IF.[20]

Vitamin Deficiencies

Children with IF, especially those with hepatic disease, are at risk for developing a variety of fat-soluble vitamin deficiencies related to fat malabsorption and/or inadequate dietary intake. The frequency of vitamin deficiencies in the IF population is rather marked with recent studies identifying 33%–70% of children with IF as having at least one vitamin deficiency.[20] The risk for vitamin deficiencies increased with discontinuation of PN support, loss of the ICV, or the absence of multivitamin supplementation.[20] Table 28–7 contains dosing recommendations of fat-soluble vitamins in children with malabsorption and/or cholestasis. Common deficiencies include vitamins A, D, and E. Low-serum vitamin A concentrations are present in children with cholestatic liver disease receiving routine vitamin supplementation.[9] Altered hepatic synthetic function may also decrease retinol-binding protein synthesis, suggesting that unbound vitamin A concentrations could actually be elevated in liver failure. Interestingly, vitamin E levels remain normal in this population, although unsupplemented infants and children continue to demonstrate deficiencies.[9] Vitamin K is synthesized by bacteria in the colon, and thus, deficiency may occur in patients without residual colon or those on broad-spectrum antibiotics.[11] Even with supplementation, children with mild-to-moderate cholestatic liver disease are at risk for developing vitamin K deficiency. Traditional assessment of vitamin K status (i.e., prothrombin time) may be inadequate, and it has been suggested that elevations in PIVKA-II (protein induced by vitamin K absence-II) concentrations may be a more sensitive marker of vitamin K stores.[21] Patients with ileal resection should be monitored carefully for vitamin B12 deficiency.

Table 28–7 Suggested Dosing of Fat-Soluble Vitamins for Intestinal Failure Patients

Vitamin	Deficiency	Recommended Formulations	Recommended Dose in IF	Comments
Vitamin A	Night blindness, xerophthalmia, keratomalacia, Bitot's spots	Retinol (water soluble) palmitate injection, 50,000 units/mL (15 mg retinol/mL)	Prophylaxis: children >8 years and adults, 10,000–15,000 units/d water-miscible product orally	Adjust dose according to levels, check levels regularly in prolonged therapy
				Patients receiving doses >25,000 units/kg should be closely monitored for toxicity
				Injectable form may be given orally
			Suggested dose for infants with cholestasis receiving enteral feedings is 3000 units/d (provided in 2 mL of infant multivitamin drops)	1 USP vitamin A unit = 0.3 mcg of all-trans isomer of retinol, 1 RE (retinol equivalent) = 1 mcg of all trans-retinol
Vitamin D	Rickets, osteomalacia, dental caries, hypocalcemia, hypophosphatemia,	Ergocalciferol (vitamin D2, calciferol, Drisdol)	Suggested dose for infants with cholestasis receiving enteral feedings is 1200 units/d (provided	1.25 mg ergocalciferol provides 50,000 units of vitamin D activity

	phosphaturia, aminoaciduria		by 2 mL of infant multivitamin drops plus 400 units additional)	
Vitamin E	Anemia, hemolysis, neurologic deficits (wide-based gait, decreased DTRs	α-Tocopherol polyethylene glycol succinate (water soluble)	Full-term neonates: 5 units/L of formula PO; chronic cholestasis (oral): 50 units/kg/d, and increase in 50 unit/kg/d increments to 150–300 units/d Alternative dosage for infants with cholestasis receiving enteral feedings is 50 units PO daily	1 unit vitamin E = 1 mg DL-tocopherol acetate Necrotizing enterocolitis is reported with oral administration of large dosages (>200 units/d) of hyperosmolar vitamin E preparations in low-birth weight infants Adjust dose according to blood levels
Vitamin K	Coagulopathy, prolonged PT, abnormal bone matrix synthesis	Phytonadione, vitamin K1	Suggested dose for infants with cholestasis receiving enteral feedings is 2.5 mg PO QOD or 1 mg SQ q/wk	Severe reactions resembling anaphylaxis/hypersensitivity were reported during or immediately after IV administration Chronically ill children receiving long-term antibiotics may require larger doses

The method of micronutrient supplementation in IF patients will vary based upon the patient's anatomy, degree of malabsorption, and routes of nutrition. Vitamin and mineral preparations are available for patients dependent upon PN (see Chapter 15, Parenteral Nutrition), allowing provision of multiple micronutrients in a single product. The provider should be aware of the concentrations of vitamins and minerals in these products and dose appropriately to meet the patient's needs. Although the provision of intravenous micronutrients is a valuable tool for the patient unable to fully absorb vitamins and minerals enterally, recent findings have demonstrated micronutrient deficiencies in patients receiving PN fortified with these preparations, pointing toward the need for routine monitoring of micronutrients even when provided parenterally.[20]

For the patient who continues to experience maldigestion following PN weaning and/or has a history of ileal resection, the use of a complete water miscible multivitamin with mineral supplement (i.e., AquADEK or CF Source) is warranted. By providing fat-soluble vitamins in a water soluble form, absorption of these key nutrients is enhanced. These products should be reserved for patients with known risk factors for micronutrient deficiencies and/or malabsorption, since they are costly and are rarely covered by private insurance. For the patient with minimal malabsorption and an intact terminal ileum, use of an over-the-counter complete pediatric multivitamin with mineral supplement may be sufficient (see Chapter 11, Dietary Supplements). In either case, routine monitoring of micronutrient blood concentrations is indicated, and doses of vitamin and mineral products should be modified based upon these laboratory findings and clinical presentation.

Metabolic Complications of Intestinal Failure

In patients with steatorrhea, LCFAs combine with magnesium and calcium, leaving calcium unavailable for the formation

of calcium oxalate. Unabsorbed bile salts in the colon are thought to increase mucosal permeability to oxalate. These two factors combine to increase enteric oxalate absorption, which in turn increases the risk of oxalate renal stones.[10] Dietary oxalate restriction and oral calcium supplementation may help in the prevention of calcium oxalate renal stones.[11]

An increased presence of gallstones, both among patients with ileal resection and those without an ICV, has been noted.[10] It is assumed that precipitation of cholesterol occurs due to the low concentration of bile salts following ileal resection, causing an interruption of the enterohepatic circulation.[22]

Pharmacologic Management of Intestinal Failure

Patients with IF often require unique therapies to assist in bowel adaptation. Depending on the patient, they may require prokinetic, antimotility, or antisecretory agents. Because of the complexities of IF, dosage recommendations are often quite different from established norms.

Intolerance to enteral nutrition is a hallmark of IF with nausea, vomiting, and abdominal distention presenting as common signs and symptoms. Prokinetic agents such as metoclopramide, erythromycin, and cisapride have been shown to promote gastrointestinal motility in these patients.[23] Side effects, however, have limited their usefulness.

In IF, gut motor activity is typified by a normal feeding pattern, along with more frequent interdigestive motor complexes and a marked reduction in phase 2 activity. Loperamide is often used in IF patients to reduce transit rate and enhance absorption. By slowing intestinal motility, water and sodium loss is reduced by approximately 20%–30% from an ileostomy.[22] This drug should not be used in patients with slow transit times, those with refractory small bowel bacterial overgrowth, or patients with acute

gastrointestinal infections, including *Clostridium difficile*. The liquid formulation should not be used unless confirmed to be both a sugar-free and alcohol-free formulation to avoid the side effect of osmotic diarrhea.

Immediately after extensive gastrointestinal resection, gastrin secretion is increased, resulting in excess gastric acid secretion.[5] Hyperacidic secretions impair carbohydrate and protein digestion, micelle formation, and lipolysis, resulting in malabsorption and diarrhea.[24] Acid blockers can be used to decrease gastric acid and improve absorption. H_2 antagonists and proton-pump inhibitors have both been used for this purpose, as acid blockade can reduce jejunostomy output. Parenteral administration may be preferred, especially in those patients with extremely short bowel, as the patient's capacity for enteral absorption may be insufficient to achieve a therapeutic effect.

SUMMARY

The nutritional management of IF is a multistage process that may take years. Aggressive use of enteral nutrition to stimulate intestinal adaptation, as well as recognition and treatment of possible complications, can significantly improve prognosis. Multidisciplinary care has been associated with better outcomes.[25]

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29 Ketogenic Diet

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Ketosis is the production of ketone bodies (β-hydroxybutyrate, acetoacetate, and acetone) that appear in the blood and urine during starvation or when carbohydrate is limited and fat is the primary fuel source in the diet. Ketogenic diet (KGD) is a diet prescription that is high in fat, adequate but not excessive in protein, and low in carbohydrates carefully calculated to produce ketosis. KGD is used therapeutically to manage refractory seizures and, whenever possible, to reduce the use of antiepileptic medications, which often have unacceptable side effects. In addition, KGD is the current therapy for glucose transporter 1 deficiency syndrome and is a treatment for pyruvate dehydrogenase deficiency. The diet has been prescribed successfully in infants, children, and teenagers. The diet consists of foods or formula components calculated in grams. The ratio of fat (in grams) to protein plus carbohydrate (in grams) is termed the ketogenic ratio.

Nearly a century ago, several investigators noticed that epileptic patients had fewer seizures while fasting or while on a "water diet." The original KGD was developed in the 1920s to mimic the biochemical changes associated with

starvation. The diet has been an effective therapy for seizures for nearly 90 years.[1] The use of this diet decreased in many centers in the 1940s, when newer antiepileptic medications became increasingly available. Since the early 1990s, the diet has regained popularity as an effective alternative or adjunct to antiepileptic medications. A meta-analysis of 19 retrospective and prospective studies including 1084 patients indicated that one-third of patients have >90% reduction in seizure frequency and one-half have >50% reduction.[2] The first randomized controlled study of KGD demonstrated that seizure frequency was reduced by 38% in children in the KGD group compared with controls after 4 months.[3] Five children in the KGD group had a >90% reduction in seizures. The seizure frequency increased by 37% in the control group.

KGD THERAPY

The exact mechanism of action of KGD are still unknown, although a multifactorial etiology is likely. Glucose restriction, achieving and maintaining ketosis, increased levels of glutathione, and increases in polyunsaturated fatty acids are postulated to be among the key factors involved.[4] The diet may possess neuroprotective and/or antiepileptogenic properties as some patients who have discontinued anticonvulsant medications do not have seizure recurrence when the diet is withdrawn.[5] Traditionally, ketosis has been monitored by measuring urinary acetoacetate. Although urine ketones are an inexpensive way to measure ketones on a daily basis in the home setting, periodic measurement of blood ketones (e.g., β-hydroxybutyrate) at outpatient follow-up visits is useful and may correlate with seizure control.

Strict adherence to the diet is essential since even a small variation in dietary intake can affect the maintenance of ketosis and thus seizure control. Food is usually divided into three meals per day and zero to three snacks per day. Intake other than meals and snacks is restricted to foods and liquids

providing little or no carbohydrates such as carbohydrate-free and calorie-free fruit-flavored beverages made with saccharin or sucralose; carbohydrate-free and caffeine-free diet soda and water; and measured amounts of nuts, iceberg lettuce, and olives. All foods and formula components are measured on a digital gram scale. For nutritional adequacy, the diet must be supplemented with a multivitamin and multimineral supplement, as well as with calcium and vitamin D. A magnesium supplement may be indicated when multimineral content is suboptimal. The carbohydrate content (including sugar alcohols and glycerin) of all medications must be considered and calculated as part of the total carbohydrate allotment.[6] Additionally, toothpastes, moisturizers, and sunscreens must contain minimal amounts of carbohydrate.

The cream diet (traditional diet) introduced in 1921 by Wilder, provides 87%–90% of kilocalories from long-chain triglycerides (LCTs). Both calorie and fluid restrictions were initial features of the traditional diet (in an attempt to fully mimic fasting.) Most centers no longer engage in these practices, though avoidance of overfeeding is believed to be important to maintain high ketone levels. Currently, two broad categories of KGDs are commonly used. These categories are based on the predominant fat source prescribed, either medium-chain-triglyceride (MCT) oil or long-chain dietary fats (LCT) (such as cream, butter, oil, mayonnaise, and margarine). The MCT oil diet provides 60% of kilocalories from MCT oil and 11% of kilocalories from LCT. Because MCT oil is more ketogenic than LCT, the MCT oil diet allows for inclusion of more carbohydrate and protein than the traditional diet. The use of large amounts of MCT oil may cause side effects such as bloating, cramping, diarrhea, and vomiting. These side effects prompted the development of a modified MCT diet, which provides 30% of kilocalories from MCT oil and 30% of kilocalories from LCT.

Prior to diet initiation, the patient should be evaluated by a multidisciplinary team to determine whether he or she is a candidate for the diet. Evaluation should include a comprehensive diet history; baseline laboratory values; anthropometrics; and the caregiver's ability to comprehend, comply with, and commit to the diet. Any history of food allergies, feeding, swallowing, or gastrointestinal problems should be taken into consideration. Menus can be designed for children with milk, soy, and egg allergies or intolerances. Diet initiation is best done in an inpatient setting in case hypoglycemia, dehydration, and/or acidosis occur or an undetermined metabolic disorder is unmasked. Historically, children were fasted (only carbohydrate-free and calorie-free oral beverages or dextrose-free intravenous fluids were allowed) until urinary ketones, measured as acetoacetic acid on urinary dipsticks, registered large (80–160 mg/dL). This usually occurred in 24–48 hours. Among current KGD programs, the length of time that a child is fasted (if any) varies. Ketosis can be achieved without fasting, though fasting may lead to a quicker onset of seizure reduction. Omitting fasting has been associated with lower frequency and severity of initiation-related side effects, whereas no difference has been detected in seizure control at 3 months in fasted versus unfasted groups.[7] The calorie provision is gradually advanced over 2–3 days to allow tolerance to the high fat content of the diet to develop. For orally fed patients, eggnog (composed of heavy cream, pasteurized egg whites, and artificial sweetener and flavoring) is often used for the first few feedings. On the second or third day, the full amount of calories is given in the form of ketogenic meals. An alternate method of feeding advancement involves providing full calories throughout the admission, starting with a low ketogenic ratio and advancing it daily.[7] In-depth education is provided to parents and caretakers during the hospitalization. Dextrose sticks, hydration status, serum electrolyte levels (including bicarbonate), urine

ketones, and urine and stool output need to be carefully monitored during the initial hospitalization.

Individualized meal plans are calculated by a registered dietitian to provide the determined amounts of carbohydrate, protein, and fat per meal according to the diet prescription (see the following instructions on calculating the diet prescription). If a child or infant requires tube feeding or a liquid diet, specific types of formula and modulars are used (Tables 29–1 and 29–2). A KGD will typically be prescribed as a ratio of 3:1 to 4:1. In a 4:1 diet, four times as much fat as protein plus carbohydrate is prescribed. Table 29–3 illustrates a sample meal plan for one day on KGD. Nutricia North America KetoCalculator (https://www.ketocalculator.com) is a web-based program that is used for accurate and efficient calculation of meal plans.

Table 29–1 Available Formula Components

Name	Manufacturer	Nutritional Information
RCF (Ross Carbohydrate Free): soy-based fortified formula for infants or children without added carbohydrate	Abbott Nutrition	Per 100 mL: 81 calories, 4 g protein, 7.2 g fat, 0 g carbohydrate
Microlipid: safflower oil emulsion	Nestle	4.5 calories/cc, 0.5 g fat/cc
Polycose powder: glucose polymers	Abbott Nutrition	3.8 calories/g, 2 g/tsp.
KetoCal: 4:1 ketogenic formula powder for children age ≥1 y (cow's milk based)	Nutricia North America	Per 100 g of powder: 15 g protein, 3 g carbohydrate, and 72 g fat
KetoCal: 3:1	Nutricia North America	Per 100 g of powder: 15.3 g protein, 7.2 g carbohydrate, and 67.7 g fat

Table 29–2 Formula Calculation Example

Component	Protein (g)	Fat (g)	Carbohydrate (g)	Calories (cal)	Fluid (mL)
RCF 375 g	15	27	.03	303	375
Microlipid 146 mL	0	73	0	657	146
Polycose powder 10.5 g	0	0	9.87	39	0
Water 479 mL	0	0	0	0	479
Total	**15**	**100**	**9.9**	**999**	**1000**

Sample formula recipe for a child who requires 4:1 ratio, 1000 cal, 1000 mL of fluid, and 15 g protein per day using RCF, Polycose powder, and Microlipid.

Table 29–3 Sample Menu for an 8-Year-Old Girl

Diet: 1500 kcal, 4:1 ratio, 3 meals per day, 0 snacks per day		
Per meal: 50.0 g fat, 7.4 g protein, 5.1 g carbohydrate		
Breakfast	**Lunch**	**Dinner**
50 g Egg	29 g Tuna fish	48 g Hot dog
32 g Orange	18 g Celery	38 g Broccoli
23 g Butter	23 g Apple	6 g Catsup
9 g Oil	37 g Mayonnaise	25 g Mayonnaise
45 g Heavy cream	49 g Heavy cream	44 g Heavy cream

Typically, fruit and vegetable exchange lists are provided to the caregiver (Table 29–4). Allowed fruits and vegetables are divided into the following four categories: 10% fruits, 15% fruits, group B vegetables, and group A vegetables. Foods within a group are interchangeable because they have similar carbohydrate, fat, and protein content. Fruits in the

10% fruit list are calculated into the meal plan as grams of 10% fruit; 15% fruits may be substituted as two-thirds of the amount of 10% fruit. Vegetables in the group B list are calculated into the meal plan as grams of group B vegetables. Double the amount of group A vegetables may be used in place of group B vegetables. The exchange lists used by our institution slightly differ from those published in *Ketogenic Diets: Treatments for Epilepsy and Other Disorders* (Kossoff et al., 2011), as we have subtracted fiber from the total carbohydrate content of the fruits and vegetables. Allowed margarines and mayonnaise can be substituted for butter in prescribed meal plans. Oil can be used in place of butter simply by dividing grams of butter by 1.3.

One of the benefits of KGD is that its use may allow the reduction or discontinuation of antiepileptic medications (which often have adverse side effects). Nonetheless, the diet itself may result in a number of short-term and long-term complications for which all patients should be carefully monitored.[4,8–15] Table 29–5 reviews possible side effects of KGD therapy and suggests steps for their prevention and treatment.

Increased potential for the development of kidney stones (primarily uric acid or calcium oxalate stones) on KGD is one possible side effect.[9,10] This risk exists as the diet may cause hypercalciuria, urine acidification, and hypocitraturia. As a result, patients should be monitored for elevated serum uric acid levels, hematuria, and elevated spot calcium/creatinine ratios in urine. At Boston Children's Hospital, fluids are encouraged, not restricted, to enhance urine flow. In addition, children are treated for acidosis with oral citrates such as Cytra-K crystals (Cypress Pharmaceuticals, Madison, Mississippi). Since the carbohydrate content of each generic product differs, it is important that the carbohydrate content be confirmed and minimized.

Table 29–4 Exchange Lists

	10% Fruit	15% Fruit	Group B Vegetable	Group A Vegetable
Foods	Applesauce, apricot, blackberries, cantaloupe, grapefruit, honeydew melon, nectarine, orange, papaya, peach, plum, raspberries, strawberries, watermelon	Apple, blueberries, sweet cherries, figs, green grapes, red grapes, guava, kiwi mango, pear, pineapple, pomegranate, tangerine	Beets (C), broccoli (C), brussels sprout (C), carrots (R or C), dandelion greens (C), eggplant (C), green beans (C), green pepper (C), kale (C), kohlrabi (R or C), leeks (C), mushrooms (R or C), onion (R), parsley (R), pumpkin (C), sweet red pepper, (R), rutabaga (C), scallions (R or C), winter squash (C), sweet yellow pepper, (R)	Asparagus(C), basil (R), beet greens(C), cabbage (R or C), cauliflower (C), celery (R or C), chicory greens (R), collard greens (C), cucumber (R), endive (R), green pepper (R), mustard greens (C), okra (C), dill pickles radish (R), rhubarb (R), romaine lettuce (R), sauerkraut (C), spaghetti squash (C), spinach (R or C), summer squash (C), Swiss chard (C), tomato (R or C), tomato juice, turnips (C), turnip greens (C), watercress (R), zucchini (C)
Macronutrient content of group per 100 g of food calculated into meal plans	0 g Fat, 1 g protein, 10 g carbohydrate	0 g Fat, 1.5 g protein, 15 g carbohydrate	0 g Fat, 2 g protein, 7 g carbohydrate	0 g Fat, 1 g protein, 3.5 g carbohydrate

Abbreviations: C = cooked; R = raw.

Table 29–5 Possible Acute and Chronic Complications of KGD Therapy

Complication	Prevention or Therapy
Dehydration	Encourage fluids Dextrose-free IV fluids may be necessary during initiation of the diet or during an acute illness
Hypoglycemia	On initiation of KGD, check dextrose sticks every 6 h Consider giving 10–15 cc juice if blood glucose is less than 40 mg/dL and child is symptomatic Metabolic screen prior to diet initiation May need to decrease diet ratio During acute illness, 1–2 tbsp. of juice may be indicated for signs of hypoglycemia
Acidosis	Encourage adequate fluids Monitor serum bicarbonate levels Consider oral citrate supplementation
Vomiting	Encourage carb-free beverages, diluted bouillon, and diluted eggnog as tolerated Monitor closely for dehydration Dextrose-free IV fluids may be indicated
Medication toxicity	Monitor antiepileptic medication levels with initiation of the diet
Diarrhea	Encourage carb-free fluids and diluted bouillon Increase soluble fiber intake Monitor hydration status May need dextrose-free IV fluids Note: increased amounts of MCT oil may cause diarrhea

(*Continued*)

Table 29–5 Possible Acute and Chronic Complications of KGD Therapy (*Continued*)

Complication	Prevention or Therapy
Food refusal	Adjust meals to increase variety Limit mealtimes to 20 min, avoid negative reinforcement, and encourage setting of limits at mealtimes and a positive feeding relationship Encourage mixing together the components of a meal so that if the meal is not finished at least the food is consumed in the proper ratio Try to make family meals similar to ketogenic meals Use flavorings or cocoa to turn ketogenic eggnog into ketogenic ice cream
Nephrolithiasis	Encourage allowed fluids Monitor spot urine calcium-to-creatinine ratio (<0.3 is normal) Consider oral citrate if acidotic Renal ultrasound, decrease in diet ratio, and referral to a nephrologist may be indicated
Hyperuricemia	Encourage sugar-free fluids; consider diet ratio liberalization Evaluation by a nephrologist may be indicated
Growth retardation	Ensure adequate calorie, protein, vitamin, and mineral provision
Hypoproteinemia	Monitor serum albumin and prealbumin levels Assess for protein loss in urine or stool Increase dietary protein if needed
Carnitine deficiency	Monitor blood carnitine levels May need supplementation
Constipation	Encourage fluids Increase the use of high-fiber vegetables Medical treatment may be necessary (Miralax and Phillips brand Milk of Magnesia are carbohydrate free)

Hyperlipidemia	Monitor fasting lipid profiles Decrease saturated fat in the diet and increase unsaturated fats by using more oils, avocados, soy products, and nuts Calculation of MCT oil in the diet may be of use
Vitamin and mineral deficiencies	Ensure that the child is receiving 100% of the DRI of vitamins and minerals Check serum zinc, copper, and selenium levels annually or as indicated
Osteopenia	Ensure adequate calcium, vitamin D, and phosphorus provision Encourage weight-bearing activity
Exacerbation of gastroesophageal reflux disease	Decrease size and increase frequency of meals and snacks Gastroenterology evaluation may be indicated
Lethargy or irritability	Ensure adequate calorie provision Evaluate serum and urine ketone levels A decrease in ratio may be indicated
Pancreatitis	Check serum triglyceride levels Monitor serum amylase and lipase levels Discontinuation of diet may be indicated

Abbreviations: DRI, dietary reference intake; IV, intravenous; MCT, medium-chain triglyceride.

Liquid oral citrates may be used; but they typically contain more carbohydrate in the form of sugar alcohols, which must be accounted for in the total daily carbohydrate allotment. Typical starting doses are 1–2 mEq/kg/d divided into two to three doses. Prescription of citrate salts helps to correct acidosis and alkalinize the urine. Urine alkalinization may help dissolve uric acid stones and may decrease the formation of calcium stones.[10] Children with high uric acid levels and elevated spot urine calcium in proportion to spot

urine creatinine levels may also require renal ultrasound and a referral to a nephrologist.

Hyperlipidemia is another possible side effect of KGD.[11] Hyperlipidemia can often be treated through dietary fat modification. For example, the use of saturated fats such as heavy cream and butter can be limited, and high polyunsaturated or monounsaturated oils can be used instead. Foods rich in monounsaturated and polyunsaturated fats such as fish, nuts, nut butters, seeds, olives, and avocados can be incorporated into the diet. In addition, MCT oil can be incorporated into the diet. Increases in lipids and cholesterol tend to be modest (~20%) and to decrease spontaneously with time.[1] To date, no evidence shows that treatment with KGD predisposes one to the later development of atherosclerosis.

Concerns during acute illness include dehydration, acidosis, excessive ketosis, and hypoglycemia. When children are ill at home, carbohydrate-free fluids and diluted eggnog or formula should be encouraged. Parents may give carbohydrate-free pain relievers as needed. Diluted bouillon can be offered to provide electrolytes in the setting of diarrhea. Half-strength Pedialyte® should be used only as a last resort as it contains a significant amount of carbohydrate. Parents should be educated on the signs of dehydration, excess ketosis, and hypoglycemia and when to seek medical attention. Small amounts of juice (1–2 tbsp.) can be given under medical supervision to treat hypoglycemia. If a child is hospitalized for an acute illness or planned surgery, intravenous fluid with added electrolytes should be provided without dextrose. In addition, children should be monitored for acidosis and hypoglycemia when they are not being fed.

Close outpatient follow-up by a multidisciplinary team (registered dietitian, nurse, neurologist, and social worker), as well as family commitment, is essential for the success of KGD. Typically, patients are seen as outpatients at 2 weeks, 6 weeks,

and then every 3 months after the initial hospitalization. At each outpatient visit, biochemical monitoring; anthropometrics; and appropriateness of the current calorie level, ratio, and supplementation are assessed. Frequently, the diet needs to be adjusted following initiation. There are several situations that may indicate that the diet needs to be adjusted, especially if the child has continued seizure activity. Excessive weight gain can interfere with ketosis; therefore, if weight gain velocity exceeds the average expected velocity for age, energy intake may need to be decreased. Children often have lower urine ketones in the morning; if seizure activity is occurring in the early morning, a child may benefit from a bedtime snack to provide fuel for the production of ketones overnight. Both urine ketones and serum β-hydroxybutyrate should be monitored; if these levels are suboptimal, a review of the current diet prescription is necessary. Dietary comprehension and compliance should also be evaluated. In some instances, free foods and processed foods may need to be avoided and individual fruits and vegetables should be calculated in some meals instead of using the fruit and vegetable exchange lists.

Sample Diet Calculation (Traditional Cream-Based Diet)

April is a 6-year-old ambulatory child. She weighs 19.4 kg (25th–50th percentile weight for age) and is 110 cm tall (10th–25th percentile height for age). Her weight for height is 50th–75th percentile. The ideal body weight for her height is 18.5 kg. She is on the following medications: Topamax (topiramate) 100 mg tablet twice daily, Lamictal (lamotrigine) 25 mg chewable tablet twice daily, and Banzel (rufinamide) 400 mg tablet twice daily.

1. **Energy needs:** Resting energy expenditure may be estimated using the Schofield or World Health Organization equations, with a stress/activity factor applied to

estimate daily calorie requirements. Alternatively, the Estimated Energy Requirements (EER) for Boys and Girls Ages 3–18 Years equation may be used. Determination of energy needs should be individualized and take into consideration the child's usual intake, current weight for height, and activity level. The aim of calorie and protein provision typically is linear growth and appropriate weight gain. Weight maintenance or slow weight loss is usually indicated for overweight patients. April's estimated calorie needs per the EER equation (based on low/moderate level of physical activity) = 1387–1571 kcal/d.

2. **Ketogenic ratio:** The choice of goal ketogenic ratio at diet initiation is based on several factors including but not limited to age, weight, medical conditions, and medications. It can range from 2:1 to 4:1. Very young children (<18 months), teenagers (>12 years), overweight children, and those with very low calorie needs may be started at the lower end of the range.
3. **Dietary units:** Dietary units are the building blocks of KGD. The calories for one dietary unit are calculated as follows:

Ratio	Fat	CHO + PRO	kcal/Dietary unit
3.5:1	3.5 × 9 kcal/g = 31.5	1 g × 4 kcal/g = 4	31.5 + 4 = 35.5

For example, April is prescribed a 3.5:1 ratio, so each dietary unit will be made up of 35.5 cal.

4. **Dietary unit quantity per day:** Divide the total daily calories by the number of calories per dietary unit. For example,
1400 kcal divided by 35.5 kcal/dietary unit = 39.44 dietary units/d

5. **Fat allowance**: Multiply the number of dietary units by the units of fat in the prescribed ketogenic ratio to determine the grams of fat permitted daily. For example,
   39.44 units × 3.5 g fat/dietary unit = 138.04 g fat/d
6. **Protein–carbohydrate allowance:** Multiply the number of dietary units by the number of units of protein plus carbohydrate in the prescribed ketogenic ratio, usually 1. For example,
   39.44 units × 1 g (CHO + PRO)/dietary unit = 39.44 g CHO + PRO
   where CHO = carbohydrate and PRO = protein
7. **Protein allowance:** Prescribe at least the minimal protein allowance, using the 2005 recommended dietary allowance for protein (see Chapter 5 for protein recommendations). Base the calculation on ideal weight if overweight or underweight; otherwise, use actual weight. For example,
   1.1 g/kg × 18.5 kg = 20.35 g/d
8. **Carbohydrate allowance:** Subtract the grams of protein from the grams of carbohydrate plus protein. For example:
   39.44 g (CHO + PRO) – 20.35 g PRO = 19.09 g CHO/d
9. **Additional carbohydrates:** The carbohydrate content of all required medications and supplements must be determined. This carbohydrate must be factored into the diet (usually replacing a portion of the fruit or vegetable serving). Typically, 1000 mg of carbohydrate from medications and supplements is allowed before any adjustment is made to the diet. Using Table 29–6, for example,
   CHO in medications and supplements = 330 mg (from Topamax) + 20 mg (from Lamictal) + 614 mg (from Banzel) + 340 mg (from vitamin) = 1304 mg CHO (in the following example, we have adjusted the diet by sub-

tracting all of the CHO contained in the medications and supplements. Another option would be to subtract only a portion but at least 304 mg of the CHO from medications and supplements.)

CHO allowance – CHO in meds = 19.09 g – 1.30 g = 17.79 g CHO

Alternatively, fat can be given with the medication so that the appropriate ratio of fat to carbohydrate in the medication is consistent with the child's diet ratio. The additional caloric content of fat given with medications should be considered.

Table 29–6 Carbohydrate Content of Medications

Brand Name (Generic Name)	Dose	Carbohydrate per Tablet or Capsule (mg)	Carbohydrate per Day (mg)
Lamictal (lamotrigine)	25 mg chewable tablet twice daily	10	20
Topamax (topiramate)	100 mg tablet twice daily	165	330
Banzel (rufinamide)	400 mg tablet twice daily	307	614
Sugar Free Scooby Doo Complete (multivitamin–multimineral)	1 chewable tablet daily	340	340
Calcimix® (calcium carbonate)	1 capsule 1250 mg daily (500 mg elemental calcium)	0	0

10. **Composition of meals and snacks:** Divide each daily allotment by 3.5 to get three equal meals and one snack. The snack will be equivalent to one-half of a meal. For example,
    Fat: 138.04 g/d divided by 3.5 = 39.44 g/meal and 19.72 g/snack
    PRO: 20.35 g/d divided by 3.5 = 5.81 g/meal and 2.91 g/snack
    CHO: 17.79 g/d divided by 3.5 = 5.1 g/meal and 2.6 g/snack
11. **Fluid allowance:** Although fluid restriction was historically recommended on the traditional diet, there is no scientific evidence to suggest that fluid restriction is needed. In addition, because of the possible complications of kidney stones and constipation, adequate fluids are important. Typically, maintenance fluids are recommended (please refer to Chapter 15, Table 15-2). In hot seasons or climates, additional fluids may be necessary. Therefore, April's recommended fluid goal based on her ideal body weight for height would be 1425 cc/d. Ideally, fluids should be spread evenly throughout the day.
12. **Supplements:** It is recommended that the child receive 100% of the established dietary reference intake (DRI) or adequate intake (AI) for vitamins and minerals. The vitamin and mineral content of formula, food, and supplements combined should be considered and compared with DRI or AI for age. (See Chapter 11 for a list of sugar-free supplements.)

The following supplements may be required:

- Calcium
- Vitamin D

- Multivitamin with minerals (one age-appropriate dose in sugar-free form)
- Magnesium

Exclusively formula-fed children or those eating few processed foods may require sodium and chloride supplementation.

Children who are successful on KGD typically remain on the diet for an average of approximately 2–3 years before weaning is attempted. However, children with glucose transporter type 1 deficiency and pyruvate dehydrogenase deficiency, as well as children who experience recurrent seizures when weaning is attempted, may remain on the diet longer. Other reasons for weaning include unacceptable seizure control, medical complications, or behavioral complications. No formal or scientific recommendations exist on how to wean the diet. Children who have been on the diet for a short period of time (less than 2–3 months) without apparent decrease in seizure frequency or intensity may be weaned off the diet relatively quickly. For example, the diet ratio can be decreased by 0.5–1 g of fat per gram of protein plus carbohydrate every 1–2 weeks. Children who have been responsive to the diet should be weaned off the diet more slowly. Weaning in this case may take up to 1 year. Children should be reevaluated each time the ratio is changed as some children may have improved seizure control on a lower ratio or an increase in seizures with diet weaning.

ALTERNATIVE DIETS FOR EPILEPSY

The modified Atkins diet (MAD) and low glycemic index treatment (LGIT) were developed in the early 2000s in an effort to provide more palatable and easier to implement alternatives to KGD. These diets are not intended for exclusively tube-fed patients or infants, as ketogenic formula is

easy to use and infants require especially close nutrition supervision. Regardless of the diet treatment selected, all therapeutic diets for epilepsy require medical supervision by a neurologist and dietitian involvement. The alternative diets do not require hospitalization for initiation; however, an increased amount of caregiver independence is needed for meal planning.

MAD involves carbohydrate restriction to 10–15 g/d and unrestricted protein, fat, and calorie intakes.[16] Carbohydrate-containing foods are not weighed but must be carefully measured using household measurements so that the carbohydrate restriction is maintained. A MAD approximately provides a 1:1 ratio, though this may be higher or lower depending on the amount of fat versus protein consumed. LGIT allows 40–60 g of carbohydrate/d (~10% of calories); the carbohydrates consumed must be those with a glycemic index <50.[17] One possible mechanism of action of KGD is maintenance of stable blood sugar levels. The premise of LGIT is that provision of LGI carbohydrates prevents blood sugar spikes. LGIT provides ~60%–70% of calories from fat and ~20%–30% of calories from protein. In prospective and retrospective studies, 43% of patients treated with MAD demonstrated >50% seizure reduction and 11% became seizure free.[1] A small number of uncontrolled studies describe benefit with LGIT (greater than 50% seizure reduction in approximately 50% of patients),[17,18] though additional studies are necessary.

NEW HORIZONS

In the past, KGD was viewed as a treatment of last resort. The diet is a vital treatment for glucose transporter 1 deficiency syndrome and pyruvate dehydrogenase deficiency. It is now recognized that KGD is effective in a range of seizure types and is especially useful in certain epilepsy

syndromes including Doose syndrome, West syndrome, Dravet syndrome, infantile spasms, Rett syndrome, and tuberous sclerosis.[19–24] Earlier diet initiation should be considered in a patient's medical course for one of the aforementioned syndromes or if two medications have been unsuccessful and the patient is a not a surgical candidate. Current research focuses include elucidation of the mechanisms of the diet, comparison of the efficacy of modified diets versus standard diets, optimal length of treatment, and further investigation into which patients are most likely to respond to diet treatment.

Recommended Resources
Computer Program
The SHS North America KetoCalculator. Available from SHS North America, P.O. Box 117 Gaithersburg, MD 20884-0117 1-800-365-7354 https://www.ketocalculator.com/ketocalc/
For Parents and Practitioners
Martenz, DM and Cramp, L. *The Keto Cookbook; Innovative Delicious Meals for Staying on the Ketogenic Diet.* **New York, NY: Demos Medical Publishing; 2012.**
Kossoff E, Freeman J, et al. *Ketogenic Diets; Treatments for Epilepsy and Other Disorders*. **5th ed. New York, NY: Demos Medical Publishing, Inc; 2011.**
Snyder, D. *Keto Kid; Helping Your Child Succeed on the Ketogenic Diet*. **New York, NY: Demos Medical Publishing; 2007.**
Zupec-Kania BA. *Ketogenic Diet: Parent's Guide*. **Santa Monica, CA: The Charlie Foundation; 2009.**
Keto News (monthly newsletter): www.epilepsy.com/ketonews
My KetoCal: www.myketocal.com
Atkins diet recipes: www.atkins.com/Recipes.aspx
Introductory video to the ketogenic diet.
Jim Abrahams, director. Starring Meryl Streep.
Available from The Charlie Foundation,

1223 Wilshire Boulevard #815,
Santa Monica, CA 90403; 310-395-6751
Internet Resources
Bickford Flavors
http://www.bickfordflavors.com
The Charlie Foundation
http://www.charliefoundation.org/
Matthew's Friends
http://www.matthewsfriends.org
United States Department of Agriculture, Nutrient Data Laboratory
http://ndb.nal.usda.gov/

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30 Inborn Errors of Metabolism

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Inborn errors of metabolism are inherited disorders caused by a defect in the enzymes required to metabolize protein, carbohydrate, or fat. The inheritance of most metabolic disorders is autosomal recessive. Many of the disorders result in severe clinical manifestations that often appear soon after birth. Rapid diagnosis and treatment are essential to prevent neurological damage, intellectual disability, and possible death. Newborn screening using tandem mass spectrometry makes it possible to detect over 20 metabolic disorders, often before clinical symptoms occur.

Nutrition therapy is a key component in treating metabolic disorders. The overall goal of nutrition therapy is to correct the metabolic imbalance while providing adequate energy, protein, and nutrients for normal growth and development. Frequent monitoring of growth, nutrient intake, and laboratory values is necessary to evaluate the adequacy of diet. Small, frequent changes in the diet prescription are often needed to ensure metabolic stability and optimal growth. Treatment is based on the specific

metabolic defect and is designed to correct the primary metabolic imbalance by reducing available substrate through dietary restriction, supplementing the product of the blocked pathway, supplementing cofactors in vitamin-responsive defects, and/or using medications that facilitate excretion and detoxification of toxic metabolites.

Selected metabolic disorders are discussed briefly below, with guidelines for additional disorders presented in Table 30–1. Detailed protocols on the nutritional management of specific metabolic disorders are available.[1] Resources for nutritional products used to treat these disorders are listed at the end of this chapter.

DISORDERS OF AMINO ACID METABOLISM

Disorders of amino acid metabolism and the affected amino acids associated with each include phenylketonuria (PKU) (phenylalanine), tyrosinemia (tyrosine, phenylalanine), homocystinuria (methionine), and maple syrup urine disease (MSUD) (leucine, isoleucine, and valine). Nutritional management of amino acid disorders involves restricting one or more essential amino acids to the minimum requirement through the use of medical foods (formulas), which are age and diagnosis specific. A medical food is administered enterally under the supervision of a physician and is intended for the specific dietary management of a medical condition. These formulas provide a major portion of the daily intake of protein, calories, vitamins, and minerals. Formulas are generally composed of L-amino acids. Because these amino acids are absorbed and oxidized more rapidly than amino acids derived from digestion of whole protein, recommended protein and calorie intakes for children with metabolic disorders are often higher than the dietary reference intakes (DRI).[2]

Table 30–1 Inherited Metabolic Disorders

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Amino acid disorders					
Phenylketonuria: Severe (classical), moderate (atypical), mild (hyperphenylalaninemia)	Phenylalanine hydroxylase	Increased blood phenylalanine Severe: >1200 µmol/L Moderate: 360–1200 µmol/L Mild: 120–360 µmol/L	If untreated, intellectual disability, seizures, hyperactivity, and eczema; normal development with proper treatment	Phenylalanine restriction, ±tyrosine supplementation	None
Maternal phenylketonuria	Phenylalanine hydroxylase	Same as above	Untreated PKU in the mother causes intellectual disability, congenital heart disease, low birth weight, and microcephaly in offspring	Phenylalanine restriction, ±tyrosine supplementation	None

Hyperphenylalaninemia (pterin defect)	Dihydropteridine reductase; GTP cyclohydrolase	Mild to moderate hyperphenylalaninemia (see above)	Psychomotor retardation, tonicity disorders, hyperthermia, hypersalivation, difficulty swallowing	±Phenylalanine restriction, ±tyrosine supplementation	Tetrahydropterin 2 mg/kg/d orally, ±neurotransmitter supplements
Tyrosinemia type I	Fumarylacetoacetate hydrolase	Increased blood phenylalanine and tyrosine; increased α-fetoprotein; urinary succinylacetone	Liver failure; renal tubular acidosis, failure to thrive, vomiting, diarrhea, rickets, porphyria-like crises, hepatic carcinoma	Phenylalanine and tyrosine restriction (diet used in conjunction with NTBC or until liver transplantation is possible)	None
Tyrosinemia type II	Tyrosine aminotransferase	Increased blood phenylalanine and tyrosine	Intellectual disability, photophobia, palmar keratosis	Phenylalanine and tyrosine restriction	None

(*Continued*)

Table 30–1 **Inherited Metabolic Disorders (*Continued*)**

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Homocystinuria (pyridoxine nonresponsive)	Cystathionine ß-synthase	Homocysteine in blood and urine, increased methionine and decreased cystine in blood	Dislocated lenses, Marfanoid-like skeletal changes, intravascular thromboses, intellectual disability, osteopenia	Methionine restriction; cystine, betaine, folate supplementation	Betaine 100 mg/kg/d orally
Homocystinuria (pyridoxine responsive)	Cystathionine ß-synthase	Same as above	Same as above	None	Pyridoxine 25–500 mg/d orally
Maple syrup urine disease	Branched-chain ketoacid dehydrogenase complex	Elevated blood, urine and CSF leucine, isoleucine, valine, alloisoleucine	Neonatal form: poor feeding, fluctuating tone, apnea, seizures, death, developmental delay Variant forms: milder ketoacidosis triggered by protein load or illness	Valine, isoleucine, and leucine restriction	Only in variant forms where 100–300 mg/d oral thiamin may enhance residual enzyme activity

Organic acidemias					
Glutaric acidemia type I	Glutaryl-CoA dehydrogenase	Elevated blood, urine and CSF glutaric acid and 3-OH-glutaric acid, metabolic acidosis	Acute metabolic crisis (vomiting, acidosis) and neurological deterioration triggered by illness; macrocephaly, ataxia choreoathetosis, developmental delay	Lysine and tryptophan restriction; carnitine supplementation	May have partial response to riboflavin 100–300 mg/d orally
Glutaric acidemia type II	Multiple acyl-CoA dehydrogenase	Elevated blood, urine and CSF glutaric acid and 2-OH glutaric acid, metabolic acidosis, hyperammonemia, hypoglycemia (±ketones), impaired fatty acid oxidation	Malformations in most severe form, hypotonia, hepatomegaly, developmental delay	Mild protein and fat restriction; fasting avoidance, ±carnitine supplementation	±Riboflavin 100–300 mg/d orally

(*Continued*)

Table 30–1 **Inherited Metabolic Disorders (*Continued*)**

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Isovaleric acidemia	Isovaleryl-CoA dehydrogenase	Elevated blood, urine and CSF isovaleric acid; metabolic acidosis, hyperammonemia, hypoglycemia	Poor feeding, vomiting, sweaty-feet body odor, seizures, coma, death if untreated	Leucine restriction; glycine and carnitine supplementation	None
Methylmalonic acidemia	Methylmalonyl-CoA mutase	Metabolic acidosis, ketonuria, hypoglycemia, hyperammonemia, hyperglycinemia	Lethargy, failure to thrive, vomiting, hepatomegaly, hypotonia, coma, death if untreated	Isoleucine, methionine, valine, threonine restriction; carnitine supplementation	None
Methylmalonic acidemia	Cobalamin processing defect (hydroxocobalamin or adenosylcobalamin)	Metabolic acidosis, ketonuria, ±homocysteine in urine and blood, ±folate deficiency	Lethargy, failure to thrive, vomiting, hepatomegaly, hypotonia, coma, death if untreated	Carnitine supplementation	Hydroxocobalamin 1–2 mg daily to weekly intramuscularly

Propionic acidemia	Propionyl-CoA carboxylase	Metabolic acidosis, ketonuria, hyperglycinemia, hypoglycemia, hyperammonemia	Poor feeding, vomiting, lethargy, hypotonia, seizures, coma, death if untreated, developmental delay	Isoleucine, methionine, valine, threonine restriction; carnitine supplementation	None
Urea cycle disorders					
NAGS deficiency	N-acetylglutamate synthetase	Hyperammonemia, respiratory alkalosis	Lethargy, vomiting, apnea, coma and death if untreated	Protein restriction; N-carbamylglutamate	None
Carbamyl phosphate synthetase deficiency	Carbamyl phosphate synthetase	Hyperammonemia, respiratory alkalosis	Lethargy, vomiting, apnea, coma and death if untreated	Protein restriction; essential amino acid and arginine supplementation; sodium phenylbutyrate	None

(*Continued*)

Table 30–1 **Inherited Metabolic Disorders (*Continued*)**

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Ornithine transcarbamylase deficiency	Ornithine transcarbamylase	Hyperammonemia, respiratory alkalosis	Lethargy, vomiting, apnea, coma and death if untreated; developmental delay	Protein restriction; essential amino acid and arginine supplementation; sodium phenylbutyrate	None
Citrullinemia	Argininosuccinic synthetase	Hyperammonemia, respiratory alkalosis	Lethargy, vomiting, apnea, coma and death if untreated; developmental delay	Protein restriction; essential amino acid and arginine supplementation; sodium phenylbutyrate	None
Argininosuccinic aciduria	Argininosuccinic lyase	Hyperammonemia, respiratory alkalosis	Lethargy, vomiting, apnea, coma and death if untreated; cirrhosis, developmental delay	Protein restriction; essential amino acid and arginine supplementation; sodium phenylbutyrate	None

Argininemia	Arginase	±Hyperammonemia	Spastic diplegia, intellectual disability	Restrict protein; essential amino acid supplementation; sodium phenylbutyrate	None
HHH syndrome	Defect in mitochondrial transport of ornithine	Hyperornithinemia, hyperammonemia, homocitrullinuria, hyperglutaminemia, hyperalaninemia	Ataxia, lethargy, vomiting, choreoathetosis, seizures, coma, developmental delay	Protein restriction; arginine supplementation	None
Disorders of carbohydrate metabolism					
Galactosemia	Hepatic and erythrocyte epimerase	Galactose in blood and urine	Hepatomegaly, jaundice, vomiting	Restrict galactose; calcium and vitamin D supplementation	None
Galactosemia	Galactokinase	Galactose in blood and urine	Cataracts	Restrict galactose; calcium and vitamin D supplementation	None

(*Continued*)

Table 30–1 **Inherited Metabolic Disorders (*Continued*)**

Disorder	Enzyme Affected	Biochemical Findings	Clinical Features	Nutritional Modification	Vitamin Therapy
Galactosemia	Galactose-1-phosphate uridyl transferase	Galactose in blood and urine; renal Fanconi syndrome	Cataracts, diarrhea, failure to thrive, hepatomegaly, jaundice, vomiting, *Escherichia coli* sepsis	Restrict galactose; calcium and vitamin D supplementation	None
Pyruvate dehydrogenase complex deficiency	Pyruvate dehydrogenase	Elevated blood pyruvate and lactate, elevated blood alanine	Hypotonia, failure to thrive, seizures, ±dysmorphism, developmental delay	Restrict carbohydrate, provide high-fat diet (50% of energy) or ketogenic diet	Thiamin 50–100 mg/d orally
Disorders of fatty acid oxidation					
VLCAD deficiency LCHAD deficiency	Very long chain acyl-CoA dehydrogenase; Long chain 3-hydroxyacyl-CoA dehydrogenase	Hypoketotic hypoglycemia, ±hyperammonemia	Cardiomyopathy, failure to thrive, hypotonia, hepatomegaly, lethargy, coma	Fasting avoidance; ±long-chain fat restriction (10%–25% of energy); MCT oil, ±carnitine and ±essential fatty acid supplementation	None

MCAD deficiency	Medium chain acyl-CoA dehydrogenase	Hypoketotic hypoglycemia, mild hyperammonemia and metabolic acidosis	Metabolic decompensation with fasting (lethargy, vomiting, and coma), hepatomegaly	Fasting and MCT avoidance; ±fat restriction (30% of energy); ±carnitine	None
SCAD deficiency SCHAD deficiency	Short chain acyl-CoA dehydrogenase; Short chain 3-hydroxyacyl-CoA dehydrogenase	Hypoketotic hypoglycemia, ±hyperammonemia, metabolic acidosis	Poor feeding, vomiting, failure to thrive; ±developmental delay	Fasting avoidance; ±carnitine	None

Abbreviations: CSF, cerebral spinal fluid; HHH, hyperornithinemia–hyperammonemia–homocitrullinuria; MCT, medium-chain triglyceride.
NTBC, 2-(2-nitro-4-trifluoro-methylbenzyol)-1,3 cyclohexanedione
VLCAD, Very long chain acyl-CoA dehydrogenase
LCHAD, Long chain hydroxyacyl-CoA dehydrogenase
MCAD, Medium chain acyl-CoA dehydrogenase
SCAD, Short chain acyl-CoA dehydrogenase
SCHAD, Short chain hydroxyacyl-CoA dehydrogenase

To supply only the minimum amount of restricted amino acids required for growth, dietary intake of intact protein is very limited. For infants, intact protein is supplied by breast milk or standard infant formula. In older children, table foods with low-to-moderate protein content provide intact protein. The recommended protein or amino acid restriction is individualized and is based on the specific disorder as well as age, growth rate, and degree of enzyme activity. Over restriction of protein or specific amino acids is detrimental and can result in poor growth. Close monitoring of plasma amino acids is important in assessing individual protein and amino acid needs.

Adequate energy intake from nonprotein sources is essential to provide for growth and to minimize tissue catabolism that can lead to poor metabolic control. Foods such as fruits, vegetables, and limited grain products are supplemented with concentrated sweets and fats. Special foods that have been modified to be low in protein, such as pastas, breads, and baked items, also provide energy and variety in the diet without significantly increasing protein intake. Inadequate energy intake may result from diet restrictions that severely limit food choices, unpleasant taste of medical foods containing L-amino acids, and poor appetite.

Recommended vitamin and mineral intakes follow the DRI guidelines. In low protein diets where special metabolic formulas provide the majority of protein intake, medical food is the primary source of vitamins and minerals because the variety of natural foods is very limited. Low plasma concentrations of ferritin, zinc, retinol, and vitamin B12 have been reported in patients with amino acid disorders.[2] Intake of vitamins and minerals needs to be monitored, especially when formula intake is suboptimal. Pharmacologic doses of vitamins, which function as cofactors to enzymes, are useful in some metabolic disorders. Recommendations for clinical, nutritional, and laboratory monitoring of children on amino acid and protein-restricted diets are found in Table 30–2.

Table 30–2 Monitoring of Nutritional Therapy

	Amino Acid Disorders	Organic Acidemias	Urea Cycle Disorders	Galactosemia	Fatty Acid Oxidation Disorders
Anthropometrics					
Length/height Weight Head circumference BMI	×	×	×	×	×
Nutritional intake					
Energy Protein Fat Vitamins/minerals	×	×	×	×	×
Laboratory indices					
Plasma amino acids	×	×	×		
Prealbumin Albumin Total protein	×	×	×		

(*Continued*)

Table 30–2 Monitoring of Nutritional Therapy (*Continued*)

	Amino Acid Disorders	Organic Acidemias	Urea Cycle Disorders	Galactosemia	Fatty Acid Oxidation Disorders
Hemoglobin Hematocrit	×	×	×	×	×
Serum ferritin	×	×	×		
Vitamin B12[a]	×	×	×		
RBC folate[a]	×	×	×		
Serum zinc[a]	×	×	×		
25-hydroxy vitamin D	×	×	×	×	×
Essential fatty acid profile[b]	×	×	×		×
Organic acids (urine/plasma)		×			
Acylcarnitines		×			×
Carnitine		×			×

Ammonia		×	×		
Galactose-1-phosphate Urine galactitol				×	
DXA	×	×	×	×	
Urine ketones	×[c]	×			

Abbreviation: BMI, body mass index.

[a]If metabolic formula intake is suboptimal.

[b]If dietary fat intake is low and/or metabolic formula contains no fat.

[c]Monitor urine ketones only in maple syrup urine disease.

[d]DXA, Dual-energy X-ray absorptiometry.

PHENYLKETONURIA

PKU is the most common amino acid disorder. In PKU, there is a defect in the enzyme phenylalanine hydroxylase, which converts phenylalanine to tyrosine. The recommended diet is restricted in phenylalanine and supplemented with tyrosine. Early treatment of PKU prevents severe intellectual disability. Diet should be continued for life as learning difficulties and behavioral problems have been reported in children who have discontinued the diet or have poor dietary control.[3] In adults, untreated or poorly treated PKU is characterized by emotional difficulties and problems in executive functioning.[4]

For children with PKU, formula provides the primary source of protein, calories, vitamins, and minerals. The prescribed intake of formula is based on the recommended protein intake for age. Protein and calorie content of the formula and age and taste preference of the child are considerations when choosing a formula. Formulas made from glycomacropeptide, an intact protein derived from whey that is naturally low in phenylalanine, offer an alternative to formulas made from L-amino acids. These products are more palatable for some children and adults.

A prescribed amount of phenylalanine is allowed from food. High protein foods such as meat, poultry, fish, dairy products (milk, cheese, yogurt), nuts, soy products, and legumes must be avoided. Bread and cereal products, pasta, rice, and starchy vegetables are allowed in very limited amounts. Fruits, vegetables, and special low protein foods may be eaten in larger quantities. Detailed food lists are available to assist in estimating phenylalanine intake from foods.[5] Phenylalanine intake is counted in milligrams of phenylalanine, equivalents (1 equivalent = 15 mg of phenylalanine), or grams of protein. For many children with

classical PKU, daily intake of phenylalanine is limited to approximately 300 mg (5–6 g of natural protein).

Adherence to diet is monitored by following blood phenylalanine concentrations. Blood phenylalanine concentrations of 120–360 μmol/L are recommended for neonates through 12 years of age, whereas adolescents and adults should maintain concentrations of 120–900 μmol/L, with lower concentrations (from 120 to 600 μmol/L) encouraged for adolescents.[3] The diet is very restrictive, and maintaining the recommended plasma phenylalanine concentrations is difficult. Children must develop the knowledge and skills necessary to manage their diet successfully as an adult.

In adults with poor dietary compliance, large neutral amino acid (LNAA) therapy may be of benefit. Phenylalanine and other LNAAs share a common transporter across the blood–brain barrier, so supplementation with LNAA reduces uptake of phenylalanine into the brain and may have a beneficial effect on cognitive function and mood. The diet is more relaxed than the traditional diet for PKU, with about 20% of the recommended dietary intake of protein from LNAA supplements that are taken with meals.[6] The remaining protein is provided through more liberal intake of cereals and grains and may also include limited amounts of dairy or meat products. Because LNAA therapy does not lower plasma phenylalanine concentrations, this treatment is not recommended for children or pregnant women.

In some individuals with PKU, supplementation with high doses of tetrahydrobiopterin (BH4), the cofactor to phenylalanine hydroxylase, lowers blood phenylalanine concentrations. A synthetic form of BH4 is available as sapropterin dihydrochloride (Kuvan®) and is dosed at 5–20 mg/kg. Patients with milder forms of PKU are more likely to respond to BH4 therapy. Some responders are able to liberalize phenylalanine intake, which allows increased intake of intact protein from

food and a more varied diet while still maintaining blood phenylalanine control.[7]

Pregnant women with PKU who do not follow a phenylalanine-restricted diet are at an increased risk for bearing children with low birth weight, microcephaly, cardiac anomalies, and mental retardation. These problems are believed to result from the effects of high maternal blood phenylalanine concentration on the developing fetus and are prevented by a strict phenylalanine-restricted diet implemented prior to conception. Research shows that children born to mothers with PKU who maintained blood phenylalanine concentrations of 120–360 μmol/L throughout pregnancy developed normally if the postnatal environment was sound. Developmental outcomes were fairly good even when the diet was started after conception as long as strict control of blood phenylalanine was attained by 10 weeks gestation, and no greater risk for developing heart defects was seen in offspring of women who controlled blood phenylalanine by 8 weeks gestation.[8]

MAPLE SYRUP URINE DISEASE

MSUD is caused by a deficiency of branched-chain α-ketoacid dehydrogenase, an enzyme in the metabolic pathway of the branched-chain amino acids (BCAAs). The recommended diet is restricted in leucine, isoleucine, and valine. Leucine is the toxic metabolite. In classical MSUD, infants present within the first two weeks of life with poor feeding, lethargy, dystonia, ketoacidosis, encephalopathy, and life-threatening brain edema. Immediate treatment is necessary to correct metabolic imbalances in these infants.

During acute metabolic decompensation, the treatment goals are the rapid removal of toxic metabolites, reduction of catabolism, and promotion of anabolism. Aggressive enteral nutrition using a BCAA-free formula to supply energy intake

of 120%–150% of ordinary maintenance needs decreases the elevated plasma concentrations of leucine, isoleucine, and valine. Plasma amino acid concentrations are closely monitored with isoleucine and valine falling more rapidly than leucine. Supplementation of isoleucine and valine should begin when plasma concentrations fall to the upper limit of the treatment range to promote protein synthesis and prevent deficiencies of these amino acids. Plasma leucine will not decrease if isoleucine or valine is deficient. Leucine from intact protein is introduced when the plasma concentration reaches the upper limit of the treatment range. Parenteral nutrition using specialized BCAA-free amino acids, glucose, and lipid may be used for acutely ill patients who are unable to tolerate adequate enteral feedings.

The goal of long-term nutritional management in MSUD is to maintain plasma concentrations of leucine, isoleucine, and valine as close to the normal range as possible while providing adequate nutrients for growth and development. A BCAA-free metabolic formula is supplemented with small amounts of intact protein from breast milk, standard formula, cow milk, or table foods, with the prescribed intact protein based on leucine intake. Supplemental isoleucine and valine are prescribed to maintain plasma concentrations slightly above the normal range. The recommended plasma ratio of isoleucine:leucine is approximately 0.5 mol:mol, with a plasma ratio of valine:leucine of ≥2 mol:mol.[9] Growth, nutrient intake, and plasma amino acids are monitored. At times of illness, urine is checked for ketoacids using Ketostix or 2,4-dinitrophenylhydrazine.

Experience with pregnancy and MSUD is limited. Energy, protein, vitamins, and minerals are provided in amounts generally recommended for pregnant women without MSUD. Use of a BCAA-free formula is necessary to provide adequate protein and to maintain recommended

concentrations of plasma BCAA. Women may require L-carnitine supplementation. Metabolic decompensation requires aggressive treatment, with special attention needed during labor and delivery and for at least six weeks postpartum as these are periods of significant catabolism.

Liver transplantation is a treatment option to the traditional BCAA-restricted diet for MSUD. Liver transplantation eliminates the risk of metabolic decompensation and decreases plasma BCAA concentrations, so dietary restriction is no longer needed.

ORGANIC ACIDEMIAS

Organic acidemias are inherited enzyme deficiencies that affect the catabolic pathways of amino acids, resulting in accumulation of intermediary metabolites (organic acids). The organic acidemias and the affected amino acids associated with each include glutaric acidemia (lysine and tryptophan), isovaleric acidemia (leucine), and propionic acidemia (PROP) and methylmalonic acidemia (MMA) (isoleucine, methionine, threonine, and valine). In these disorders, excessive protein intake or catabolic stress, such as infection or prolonged fasting, produces an accumulation of organic acids resulting in ketoacidosis, hypoglycemia, and hyperammonemia.

PROPIONIC ACIDEMIA AND METHYLMALONIC ACIDEMIA

The disorders PROP and MMA are caused by defects in the enzymes propionyl-CoA carboxylase and methylmalonyl-CoA mutase, respectively. The recommended diet is restricted in the amino acids isoleucine, methionine, threonine, and valine. Clinical symptoms of the neonatal form of organic acidemias include vomiting and dehydration, poor feeding,

failure to thrive, hypotonia, metabolic ketoacidosis, and hyperammonemia; severe brain damage or coma leading to death may occur without immediate treatment to correct metabolic imbalances. The late-onset form may present with metabolic decompensation during an intercurrent infection, or with failure to thrive, developmental delay, and neurological features such as seizures.

During illness, acute metabolic decompensation can occur from catabolism of amino acids stored as protein, resulting in metabolic acidosis, hyperammonemia, and ketonuria.[10] An increase in risk of basal ganglia stroke is associated with episodes of acute metabolic decompensation. The treatment goal is to reduce toxic concentrations of organic compounds and promote anabolism. Nutritional therapy consists of discontinuing protein, providing adequate energy in the form of glucose to suppress catabolism, and increasing fluid to prevent dehydration and assist in removal of abnormal metabolites in the urine. Intravenous dextrose in combination with lipid or protein-free formula is used for 24–48 hours to lower ammonia concentrations; energy intake should be maximized, with a goal of 120% of ordinary maintenance needs. Protein is gradually reintroduced. Inadequate energy intake or use of a protein-free diet for more than two days can lead to protein catabolism and rebound ketoacidosis and hyperammonemia. Parenteral nutrition may be used when enteral feedings are not tolerated, with protein supplied through specially formulated amino acid mixtures or with a standard solution providing 0.5 g of protein per kilogram.

Long-term nutritional management of PROP and MMA involves restricting the amino acids isoleucine, methionine, threonine, and valine to the minimum requirement through the use of a special metabolic formula. Approximately 50% of prescribed protein may be provided by intact protein from standard formulas and foods. The goal is to maintain

plasma concentrations of the restricted amino acids in the low normal range and to minimize toxic metabolites. Low plasma concentrations of isoleucine and/or valine may require additional supplementation of individual amino acids. Adequate nonprotein energy is essential to prevent tissue catabolism. L-Carnitine supplementation is recommended to prevent deficiency and increase excretion of toxic compounds. Extended periods of fasting should be avoided due to increased production of odd-chain fatty acids leading to increased toxic metabolites. Adequate hydration assists in excretion of toxic compounds. Home monitoring of urine ketones is used to assess metabolic stability. The intermittent use of antibiotics helps reduce gut bacteria loads, a major source of endogenous propionate production. Some patients with variant forms of MMA due to defects of vitamin B12 metabolism respond to pharmacologic doses of vitamin B12. Dietary management may be complicated by feeding problems and poor appetite, necessitating nasogastric or gastrostomy tube feedings. Growth, nutrient intake, plasma amino acids, and urine organic acids are monitored routinely to guide adjustments in the diet.

Information on long-term outcomes is limited. Children show varying degrees of growth retardation and neurological impairment.[11] Chronic renal failure is a complication in MMA and may require renal transplant. Medical complications in PROP include pancreatitis, cardiomyopathy, and diabetes. Liver transplantation may decrease the risk of severe metabolic decompensation and improve quality of life, but it does not eliminate the need for a modified diet.

GLUTARIC ACIDEMIA TYPE 1

Glutaric acidemia type 1 (GA1) is an organic acid disorder caused by the deficiency of glutaryl Co-A dehydrogenase, the enzyme involved in metabolizing the essential amino acids

lysine and tryptophan. Infants with GA1 are usually healthy at birth, although many are macrocephalic. Other symptoms usually occur between 2 months and 4 years of age and are triggered by an acute infection, prolonged fasting, or other stress factors. If untreated, metabolic acidosis ensues, and severe and permanent neurological problems may result, including dystonia, choreoathetosis, and seizure disorders. During acute crises, metabolic acidosis may lead to brain edema, coma, and death. The most critical component of care is the early and aggressive treatment of illnesses to prevent a metabolic crisis. Intravenous glucose, insulin, and L-carnitine are often recommended even if the child has a mild illness, is vomiting, or has decreased appetite.

Some individuals with GA1 have mild forms and are only found to be affected after a brother or sister is diagnosed. Others may be identified presymptomatically through newborn screening. These individuals are treated with diet to help prevent the onset of symptoms.

Chronic treatment includes the restriction of protein, use of medical foods that are low or devoid of lysine and tryptophan, and carnitine and riboflavin supplementation. Prolonged fasting must be avoided. How effective the diet is in preventing symptoms and whether to continue treatment after 6 years of age (when risk of acute metabolic crises diminishes) is not well understood. Even without metabolic crises, individuals with GA1 may exhibit mild neurological and learning problems and the prognosis for GA1 is guarded.[12]

UREA CYCLE DISORDERS

Urea cycle disorders result from a defect in one of the enzymes involved in the conversion of ammonia to urea in the liver. Hyperammonemia is common to all the disorders. The enzyme defects include carbamoyl phosphate

synthetase (CPS) deficiency, ornithine transcarbamylase (OTC) deficiency, argininosuccinic acid synthetase deficiency (citrullinemia), argininosuccinic acid lyase deficiency (argininosuccinic aciduria), and argininemia (arginase deficiency). Infants with neonatal onset present with hyperammonemia, poor feeding, vomiting, and hypotonia, which may progress rapidly to seizures, coma, and death. Plasma ammonia concentrations are often greater than 1000 μmol/L. Rapid diagnosis and treatment are essential as neurological outcome is related to duration of severe hyperammonemia and coma. Older infants and children may present with less severe hyperammonemia; these children often have a history of self-limiting protein intake.

Catabolism during illness can lead to life-threatening hyperammonemia. Nutritional therapy during acute metabolic crisis consists of discontinuing protein and providing intravenous fluids and glucose to correct dehydration, provide energy, and suppress catabolism. Intravenous dextrose in combination with lipid or protein-free formula is used for 24–48 hours to maximize energy intake and decrease ammonia concentrations; protein is then gradually reintroduced. Inadequate energy intake or use of a protein-free diet for more than 2 days can lead to protein catabolism and rebound hyperammonemia. Parenteral nutrition can be used when enteral feedings are not tolerated, with protein supplied through a standard solution providing 0.5 g of protein per kilogram.[13]

The long-term goals of nutritional therapy are to reduce ammonia concentrations to normal by restricting protein intake, provide sufficient nitrogen for optimal growth, and provide adequate calories to prevent catabolism. Protein intake depends on the severity of the disorder and the child's age and rate of growth. Dietary protein is generally limited to less than the DRI; a protein intake of 1.5 g of protein per kilogram would

be a realistic goal for a newborn. Medical foods containing essential amino acids are often used to provide 25%–50% of the total protein, reducing the load on the urea cycle by using surplus nitrogen to synthesize nonessential amino acids.

Supplementation of L-arginine is required in all of the urea cycle defects except arginase deficiency; in CPS and OTC deficiency, L-citrulline may be substituted for arginine. Sodium phenylbutyrate or sodium benzoate and sodium phenylacetate are used to provide alternate pathways for waste nitrogen excretion. These drugs, which are quite unpalatable, should optimally be taken four times each day with dosing linked to meals. Vitamin and mineral supplements are recommended because the protein restriction leads to a diet limited in many nutrients, including vitamin B12 and zinc. Special low protein foods help provide additional calories and variety in the diet. Growth, nutrient intake, plasma amino acids, and ammonia should be monitored routinely; plasma glutamine is generally considered a better marker for chronic management than ammonia. Dietary management may be complicated by poor appetite. Long-term outcome and intellectual development in urea cycle disorders are variable depending on the severity of the disorder and the number of acute metabolic episodes.

Liver transplantation is a treatment option and improves outcomes for some patients, especially those with severe phenotypes who are prone to frequent episodes of hyperammonemia. Liver transplantation corrects the metabolic defect, and no further protein restriction is needed after transplantation.

Women with urea cycle disorders have successfully borne children, but women must be monitored carefully during pregnancy and especially in the postpartum period. Additional calories and protein restriction are necessary for at least 6 weeks postpartum. Some women with milder forms of urea

cycle disorders first come to attention with hyperammonemia during the metabolically stressful postpartum period.

GALACTOSEMIA

Galactosemia is an inherited disorder of galactose metabolism resulting from a defect in one of the enzymes required to convert galactose to glucose. The most common defect is in the galactose-1-phosphate uridyltransferase enzyme. Symptoms of vomiting, diarrhea, failure to thrive, jaundice, hepatomegaly, cataracts, and *Escherichia coli* sepsis are usually seen within the first two weeks of life. Galactosemia is treated by restricting dietary galactose. Because lactose is hydrolyzed into galactose and glucose, both lactose and galactose must be eliminated from the diet. Therefore, galactosemia is one of the few true contraindications to breastfeeding. Dietary restrictions should be followed for life.

Infants with galactosemia are fed lactose-free formulas, which are often soy based. Older children must avoid milk and milk products as well as incidental sources of lactose found in prepared foods and medications. Labels on all processed foods and medications should be checked to avoid ingredients such as whey, casein, nonfat dry milk, milk solids, lactose, lactoglobulin, lactalbumin, caseinate, and hydrolyzed protein. Food ingredients that are unacceptable on this diet are listed in Table 30–3. Certain fruits, vegetables, and legumes may also contain substantial amounts of galactose. The availability of galactose from these foods is not known; whether they should be eliminated from the diet remains a matter of debate.[14] Certain aged cheeses that have been processed in a salt bath are galactose free, including Austrian Emmentaler and Gruyere cheeses. However, the galactose content of many cheeses is not known, and care must be used when including cheese in a galactose-restricted diet.

Table 30–3 Ingredients to Avoid on a Galactose-Restricted Diet

Butter	Lactoglobulin
Buttermilk	Lactose
Buttermilk solids	Margarine[b]
Casein	Milk
Cheese	Milk chocolate
Cream	Milk solids
Curds	Nonfat dry milk
Dry milk	Nonfat dry milk solids
Dry milk protein	Nonfat milk
Garbanzo beans	Organ meats (liver, heart, kidney, and brain)[c]
Ghee	Sherbet[d]
Hydrolyzed protein[a]	Sour cream
Ice cream	Whey and whey solids
Lactalbumin	Yogurt

[a]Hydrolyzed protein is unacceptable if it is made from casein or whey.

[b]A few diet margarines do not contain any milk products and are acceptable. Check labels before using any brand.

[c]Organ meats are often listed on labels as meat by-products.

[d]Sherbet contains nonfat dry milk. However, many brands of sorbet do not and are acceptable.

Source: Reproduced with permission from Gleason et al.[18]

Early treatment with a galactose-restricted diet prevents neonatal sepsis, corrects liver disease, and causes regression of cataracts; however, dietary treatment does not guarantee a normal long-term outcome. Even with good dietary control, many children have speech and visual perception problems. Growth may be stunted, and primary ovarian failure is seen in most females. Endogenous galactose production may account

for these difficulties, but the etiology remains unknown. Growth, nutrient intake, plasma galactose-1-phosphate, and urine galactitol are monitored. Reduced calcium intake from elimination of dairy products may lead to decreased bone density. Calcium and vitamin D supplements are usually required.

FATTY ACID OXIDATION DISORDERS

Fatty acid oxidation disorders (FAODs) are inborn errors in the mitochondrial beta-oxidation of fatty acids. Defects in the breakdown of fatty acids of specific carbon chain lengths lead to impaired production of ketones as an energy source for the brain and other organs. FAODs are identified by elevated fatty acid acylcarnitine profiles by newborn screening. More severe forms traditionally have presented clinically following a period of fasting, febrile illness, or increased muscle activity. Features include hypoketotic hypoglycemia, cardiomyopathy, episodic vomiting, liver dysfunction, muscle weakness, and risk of sudden death. Age of presentation varies, but severe forms of the disorders often present during early infancy.

Defects have been identified in enzymes involved in the transport of long-chain fatty acids by carnitine into the mitochondria as well as in the mitochondrial fatty acid beta-oxidation cycle. Defects in mitochondrial fatty acid oxidation and their specific treatment strategies are included in Table 30–4. The treatment goal for all FAOD is to avoid dependence on fat as an energy source. Metabolic decompensation can be triggered by the catabolic processes that occur during periods of infection or prolonged fasting because of the inability to metabolize lipid stores. During acute illness, treatment with intravenous dextrose is often necessary to correct hypoglycemia and prevent catabolism.[15]

Table 30–4 FAODs and Recommended Nutrition Intervention

FAOD	Affected Fatty Acids Species	Long-Chain Fat Restriction	Medium Chain Triglyceride Supplementation	Other supplements to consider
LCHAD, TFP deficiency	C12OH–C18OH	10% of energy	1–3 g/kg/d or 20%–30% of energy	Docosohexaenoic and essential fatty acids if intake is low; cornstarch
VLCAD deficiency	C12–C18	10% of energy (severe form), 25% of energy (mild form)	1–3 g/kg/d or 10%–30% of energy	Essential fatty acids if intake is low; cornstarch (severe form)
MCAD deficiency	C6–C12	Normal heart healthy guidelines (30% of energy)	Contraindicated	L-Carnitine
SCAD, SCHAD deficiency	C2–C6	No diet necessary	None	L-Carnitine

Abbreviations: FAOD, fatty acid oxidation defects.
LCHAD, Long chain hydroxyacyl-CoA dehydrogenase
TFP, Trifunctional protein
VLCAD, Long chain acyl-CoA dehydrogenase
MCAD, Medium chain acyl-CoA dehydrogenase
SCAD, Short chain acyl-CoA dehydrogenase
SCHAD, Short chain hydroxyacyl-CoA dehydrogenase

Long-term management involves avoiding extended periods of fasting and providing increased intake of carbohydrate calories during periods of increased energy demand (illness or exercise). Frequent meals and snacks that

Table 30–5 Essential Fatty Acid Content of Selected Oils

Oil[a]	Linoleic Acid g/100 g[b]	Linolenic Acid g/100 g[c]
Canola	20.3	9.3
Cod liver	0.9	0.9
Corn	58.0	0.7
Flaxseed	14.0	35.1
Safflower	14.4	0
Soybean	40.2	5.1
Sunflower	3.6	0.2
Walnut	52.9	10.4

[a]One teaspoonful of oil contains 4.5 g fat, 0 g carbohydrate, 0 g protein, and 40 kcal.

[b]Linoleic acid = C18:2; (n–6); recommended intake for infants >3% of energy.

[c]Linolenic acid = C18:3; (n–3); recommended intake for infants 0.3%–1% of energy.

are high in carbohydrate are used during the day. Uncooked cornstarch (1.5–2.0 g/kg) at bedtime is sometimes used in severe forms of FAOD to provide an energy source at night. Cornstarch therapy is not recommended in infants under 9 months of age because pancreatic enzyme activity may be insufficient. Either cornstarch or a high complex carbohydrate snack or beverage may be recommended prior to intense activity.

Formulas that contain a significant percentage of fat as medium-chain triglyceride oil are often used in the treatment of the long-chain fat disorders. Over restriction of fat is detrimental and can lead to poor growth and essential fatty acid deficiency. To prevent essential fatty acid deficiency, linoleic acid and alpha-linolenic acid should provide 3% and 1% of total energy, respectively. Oils that may be used to supplement essential fatty acid intake are listed in Table 30–5.

MITOCHONDRIAL DISORDERS

Mitochondrial disorders are a group of diseases that affect mitochondrial energy metabolism primarily due to defects of the respiratory chain enzymes. Mitochondrial disorders result in decreased energy production and impaired body functioning and can present at any age. They can affect any organ or tissue and are often multisystem in nature and therefore may present with a variety of symptoms including seizures, developmental delay, autonomic nervous system dysfunction (breathing problems, temperature instability, diarrhea, or pseudo obstruction), cardiomyopathy, hepatic and renal dysfunction, muscle weakness, gastrointestinal dysmotility, and endocrine abnormalities such as diabetes, vision and hearing problems, and poor growth.[16] They are progressive and usually result in significant disabilities.

Treatment is mainly supportive and is based on individual symptoms. Muscle fatigue, developmental delay, gastroesophageal reflux, and poor oropharyngeal coordination all predispose to poor intake. Undernourished states may produce symptoms that suggest an accelerated deterioration in the status of the patient. Attention to adequate nutrition is essential to maintain optimal growth, development, and level of functioning in these patients. Many of these patients require tube feedings or other forms of calorie or protein supplementation to meet nutrient needs. Therapy to improve oropharyngeal coordination may be beneficial. Cofactors for the respiratory chain enzymes have been used to increase mitochondrial energy production and to decrease the progression of clinical symptoms, with varying degrees of success. Therapies that have been reported to have a positive effect include Coenzyme Q10, ascorbic acid, vitamin E, lipoic acid, riboflavin, thiamin, niacin, vitamin K, creatine, and carnitine.[17]

Products for Nutritional Therapy
Abbott Nutrition (abbottnutrition.com)
Applied Nutrition (medicalfood.com)
BioMarin Pharmaceutical (kuvan.com)
Cambrooke Foods (cambrookefoods.com)
Coram Specialty Infusion (coramhc.com)
Dietary Specialties (dietspec.com)
Mead Johnson Nutrition (meadjohnson.com)
Nutricia North America (nutricia-na.com)
PKU Perspectives (pkuperspectives.com)
Solace Nutrition (solacenutrition.com)
Vitaflo North America (vitaflousa.com)

Other Resources
Fatty Oxidation Disorders Family Support Group (fodsupport.org)
Genetic Metabolic Dietitians International (gmdi.org)
MSUD Family Support Group (msud-support.org)
National PKU Alliance (npkua.org)
National PKU News (pkunews.org)
National Organization for Rare Diseases (rarediseases.org)
National Urea Cycle Disorders Foundation (nucdf.org)
New England Consortium of Metabolic Programs (newenglandconsortium.org)
Organic Acidemia Association (oaanews.org)
Parents of Galactosemia Children (galactosemia.org)
United Mitochondrial Disease Foundation (umdf.org)

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31 Lipid Disorders

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Much research has shown that serum cholesterol is an important contributor to cardiovascular disease (CVD). CVD is the leading cause of death and morbidity in the United States with one in every three deaths due to heart disease and stroke.[1] Research has illustrated that cholesterol during childhood contributes to vascular abnormalities in childhood.[2] In November 2011, new guidelines emerged on CVD risk assessment and reduction from the National Heart Lung and Blood Institute, which recommended that lipid disorders should be identified during childhood to allow for treatment, both nutritional and pharmacotherapeutic.[3] This chapter covers lipids and liporproteins, disorders of lipid metabolism as they present in childhood, screening in childhood, pediatric norms, nutrition assessment, nutrition treatment, and a brief overview of the indications for pharmacotherapy for lipid disorders in pediatrics.

PHYSIOLOGY OF LIPIDS AND LIPOPROTEINS

There are two major forms of lipids circulating in the body, triglycerides (TGs) and cholesterol. Cholesterol and TG are

insoluble in plasma and require lipoproteins, phospholipids, and apolipoproteins (apoproteins) for transport.[4] Physiologically, lipoproteins have an outer core of cholesterol, phospholipids, and apoproteins, and their inner core is composed of TG and cholesterol ester (CE). The five major lipoproteins are chylomicrons, very low-density lipoprotein (VLDL), intermediate-density lipoprotein (IDL), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C).[4,5] The following are useful definitions related to lipid disorders.

Chylomicrons: Large particles that carry dietary lipid, mostly TG. Chylomicrons are associated with a number of apoproteins (A-I, A-II, A-IV, B-48, C-I, C-II, C-III, and E) including Apo B 48, which is essential for the assembly, secretion, and metabolism of chylomicrons.[4,5]

Very low-density lipoproteins: Carry endogenous TGs and some cholesterol from the liver. Its major lipid composition is TG, and it is the major TG carrier. Apolipoproteins associated with VLDL are B-100, C-I, C-II, C-III, and E.[4,5] ApoB100 is a very large glycoprotein that is essential for TG transport and also plays functional roles in lipoprotein biosynthesis in liver and intestine. ApoB100 is the ligand recognized by the LDL-C receptor during receptor-mediated endocytosis.[6]

Intermediate-density lipoprotein cholesterols: Carry CE and TG; it is the intermediate between VLDL and LDL-C. IDL is associated with apolipoproteins B-100, C-III, and E.

Low-density lipoproteins cholesterols: The major cholesterol carrier; it is associated with apolipoprotein B-100. Its value on a fasting lipid panel must be calculated using the Friedewald equation: LDL-C = Total cholesterol – HDL-C – TG/5.[4,5] This equation fails if TG > 400 mg/dL. LDL-C can also be measured directly in the nonfasting state; however, treatment decisions are generally based on the fasting

calculation if at all possible because the direct measurement assays give results that differ from the calculated number.

High-density lipoprotein cholesterols: Carry cholesterol; its role is antiatherogenic. HDL-C is associated with apolipoproteins A-I, A-II, C-I, C-II, C-III, D, and E. Apolipoprotein-A1, is the primary protein component of HDL-C, produced in the liver and intestines.[4,5]

Triglycerides: The major form of fat in the body. Chemically, it is composed of three molecules of fatty acids combined with alcohol glycerol. TGs are the backbone of many types of lipids and can be found in the food we eat, as well as produced by the body. TG levels are influenced greatly by recent fat and alcohol intake. TG levels should be obtained in the fasting state for 8–12 hours prior.

Lipoprotein (a): Considered a risk factor for heart disease. Normal values are below 30 mg/dL or 75 mmol/L.[7]

Acceptable, borderline-high, and high plasma lipid, lipoprotein, and apolipoprotein concentrations for children and adolescents are shown in Table 31–1.

Table 31–1 Acceptable, Borderline-High, and High Plasma Lipid, Lipoprotein, and Apolipoprotein Concentrations (milligrams per deciliter) for Children and Adolescents[3]

Category	Acceptable	Borderline	High+
TC	<170	170–199	≥200
LDL-C	<110	110–129	≥130
Non-HDL-C	<120	120–144	≥145
ApoB	<90	90–109	≥110
TG			
0–9 y	<75	75–99	≥100
10–19 y	<90	90–129	≥130

(*Continued*)

Table 31–1 **Acceptable, Borderline-High, and High Plasma Lipid, Lipoprotein, and Apolipoprotein Concentrations (milligrams per deciliter) for Children and Adolescents[3] (*Continued*)**

Category	Acceptable	Borderline	Low+
HDL-C	>45	40–45	<40
ApoA-I	>120	115–120	<115

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; TC, total cholesterol.

DISORDERS OF LIPID METABOLISM IN PEDIATRICS

Abnormal levels of circulating lipids enhance lipid (cholesterol) accumulation in arterial walls, which contributes to plaque formation and ultimately CVD. Elevated TG levels, particularly in the form of chylomicrons, increase the risk for pancreatitis. A summary of major lipid disorders in children and adolescents is shown in Table 31–2. Primary lipid disorders are due to genetic mutations and are generally more severe than lifestyle-related abnormalities; they require more aggressive interventions earlier in life.[3] Secondary lipid disorders are related to lifestyle, medications, or medical diagnosis (Table 31–3). For some children, abnormal cholesterol is the results of an unhealthy, inactive lifestyle mediated through overweight/obesity or independently from poor dietary choices. Medical conditions (e.g., diabetes, thyroid abnormalities, polycystic ovary syndrome, renal disease, and eating disorders) can also lead to lipid disorders (Table 31–3). Exposure to cigarette smoke can lower HDL-C levels in children. Certain medicines such as oral tretinoin, immunosuppression agents, oral contraceptive pills, diuretics, β-blockers, and some antidepressants can also raise cholesterol levels.

Table 31–2 Summary of Major Lipid Disorders in Children and Adolescents

Primary Lipid Disorders	Lipid/Lipoprotein Abnormality
Familial hypercholesterolemia	Homozygous: ↑↑ LDL-C Heterozygous: ↑ LDL-C
Familial defective apolipoprotein B	↑ LDL-C
Familial combined hyperlipidemia	Type IIa: ↑ LDL-C Type IV: ↑ VLDL-C, ↑ TG Type IIb: ↑ LDL-C, ↑ VLDL-C, ↑ TG Types IIb and IV often with ↓ HDL-C
Polygenic hypercholesterolemia	↑ LDL-C
Familial hypertriglyceridemia (200–1000 mg/dL)	↑ VLDL-C, ↑ TG
Severe hypertriglyceridemia (≥1000 mg/dL)	↑ Chylomicrons, ↑ VLDL-C, ↑↑ TG
Familial hypoalphalipoproteinemia	↓ HDL-C
Dysbetalipoproteinemia (TC: 250–500 mg/dL; TG: 250–600 mg/dL)	↑ IDL-C, ↑ chylomicron remnants

Abbreviations: HDL-C, high-density lipoprotein cholesterol; IDL-C, intermediate-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; VLDL, very low-density lipoprotein.

Table 31–3 Causes of Secondary Dyslipidemia[3]

Exogenous Alcohol Drug therapy Corticosteroids Isoretinoin β-Blockers Some oral contraceptives Select chemotherapeutic agents Select antiretroviral agents Endocrine/Metabolic	Hepatic Obstructive liver disease/ cholestatic conditions Biliary cirrhosis Alagille syndrome Inflammatory Disease Systemic lupus erythematosus Juvenile rheumatoid arthritis Storage Disease Glycogen storage disease Gaucher's disease

(*Continued*)

Table 31–3 Causes of Secondary Dyslipidemia[3] (*Continued*)

Hypothyroidism/hypopituitarism	Cystine storage disease
Diabetes mellitus types 1 and 2	Juvenile Tay–Sachs disease
Pregnancy	Niemann–Pick disease
Polycystic ovary syndrome	Other
Lipodystrophy	Kawasaki disease
Acute intermittent porphyria	Anorexia nervosa
Renal	Post solid-organ transplantation
Chronic renal disease	Childhood cancer survivor
Hemolytic uremic syndrome	Progeria
Nephrotic syndrome	Idiopathic hypercalcemia
Infectious	Klinefelter syndrome
Acute viral/bacterial infection	Werner's syndrome
HIV	
Hepatitis	

Familial Lipid Disorders

Familial lipid disorders (familial hyperlipidemia [FH], combined hyperlipidemia, hypertriglyceridemia, and dysbetalipoproteinemia) begin at birth and are passed down through family members. FH presents as either heterozygous (one defective gene LDL-C 160–400 mg/dL) or homozygous (both genes are defective, LDL-C 400–1000 mg/dL; substantially higher risk). Most FH patients require lipid lowering pharmacotherapy as part of their treatment plans. In patients with homozygous FH, LDL-C apheresis is usually necessary in addition to pharmacotherapy. Liver transplantation has been used in some cases of homozygous FH. Physical findings may present in severe heterozygous FH or homozygous FH; these patients have xanthomas; fatty cholesterol skin deposits over the elbows, knees, buttocks, tendons, and/or arcus cornea; and cholesterol accumulation in the cornea. Cholesterol deposits in the eyelids are called xanthelasmas. Patients with homozygous FH develop coronary artery disease at a young age, in the first or second decade of life. Men and women with heterozygous FH are at an increased risk of early cardiac events, in their third, fourth, and fifth decades.[8]

NUTRITION ASSESSMENT

The patient history is the initial phase of the nutrition assessment, by which the dietitian can gather background knowledge about his/her patient. Food and nutrition-related history including a diet recall and/or typical day's food intake is the most relevant aspect of subjective data collection, with special attention paid to between meal snacking.[9] Assessment of the family and home situation, identifying patient's supports and elements that might sabotage success, is also valuable. See Table 31–4 for important components of nutrition assessment and Table 31–5 for frequently used nutrition diagnoses in lipid disorders.

Table 31–4 Nutrition Assessment in Lipid Disorders[10,11]

Patient History
Age, sex, and ethnicity
Diagnosis; type of lipid disorder
Medical history
History of failure to thrive, small-for-gestational age, or premature birth
Food allergies
Family history
Medications
Laboratory assessments: Total cholesterol, LDL-C, HDL-C, TG, less often Apo-B, Apo A1
Alcohol/smoking (adolescents), smoke exposure
Support system: With whom does the child live? Who prepares meals? What resources are available to purchase food (supplemental nutrition programs)? What is the access to physical activity?
Food and Nutrition-Related History
Energy intake
Sources of saturated and trans fat rich foods
Sources of carbohydrates, proteins, and fats (e.g., whole grains versus refined grain sources)
Sugar consumption (e.g., beverages, sweets)
Sodium consumption
Fiber intake (e.g., fruits, veggies, whole grains)

(*Continued*)

Table 31–4 Nutrition Assessment in Lipid Disorders[10,11] (*Continued*)

Meals outside of the home (e.g., dining out, fast food) Herbs, vitamins, minerals (e.g., MVI, omega-3) School meals Cultural food preferences Cultural response to weight Physical activity
Physical Observations Anthropometric data Overweight/obesity (waist circumference) Xanthomas (deposits of lipids in the skin) Acanthosis nigricans Biochemical data (e.g., lipid profile, lipoprotein (a), hemoglobin A1c, 25-OH vitamin D, thyroid function tests, C-reactive protein)

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride.

Table 31–5 Nutrition Diagnosis in Lipid Disorders[12]

Problems Food and nutrition-related knowledge deficit NB-1.1 Excessive carbohydrate intake NI-5.8.2 Inappropriate intake of refined carbohydrate NI-5.8.3 Excessive energy intake NI-1.5 Inadequate fiber intake NI-5.8.5 Excessive oral intake NI-2.2 Not ready for diet/lifestyle change NB-1.3 Self-monitoring deficit NB-1.4 Undesirable food choices NB-1.7 Physical inactivity NB-2.1 Limited adherence to nutrition-related recommendations NB-1.6 Undesirable food choices NB-1.7 Excessive fat intake NI-5.6.2 Inappropriate intake of saturated and/or trans fats NI-5.6.3
Etiology Hyperlipidemia (and need for heart-healthy diet) Minimal fruit and vegetable intake Undesirable food choices Inability to limit or refuse offered foods Food and nutrition compliance limitations Denial of need to change

Lack of social support for implementing changes Exposure to unhealthful foods Need for continued adherence to nutrition and physical activity–related recommendations
Signs and Symptoms Most recent lipid panel 24-hour recall and self-report Infrequent and limited duration of physical activity Excessive amount of sedentary activity (TV, computer, video game, Ipad, Ipod, and cell phone) Disinterest in selecting foods consistent with the nutrition guidelines Verbalized disinterest in learning information Increased body adiposity (weight gain of × kg × mo/wk/y)

NUTRITION INTERVENTION

Research aimed at CVD risk reduction has identified dietary and overall excess energy as major contributors to hypercholesterolemia and obesity in pediatrics.[3] Repeated dietary counseling is effective in improving serum lipids, specifically decreasing saturated fat intake and serum LDL-C levels from infancy until 19 years of age. Liberalizing of the use of fat with an emphasis on monounsaturated fat in a subset of children following an excessively fat-restricted diet on presentation seems to improve HDL-C levels.[13] TG levels have been shown in one study to decrease by a mean of 22 mg/dL following dietary counseling.[14] A diet consisting largely of low-calorie vegetables, fruits, and nuts markedly reduced lipid risk factors for CVD in a 1997 study, with vegetables specifically lowering LDL-C by 20%.[15] The mechanism of action by which fruits and vegetables lower LDL-C may be split between fiber itself, and replacing foods high in saturated fat with fruits and vegetables.

Breastfeeding

The Surgeon General's Office, the World Health Organization, and the American Academy of Pediatrics all recommend

that babies be exclusively breastfed for the first six months. Continued breastfeeding is recommended to at least 12 months of age with the addition of complementary foods. Breastfeeding may be associated with a reduced risk of atherosclerosis in later life.[16]

Dietary Fat

Total fat intake can be safely limited to 25%–30% of total calories (30% of total calories <24 months). Those <12 months should not have their fat restricted in an effort to promote adequate brain development. The remaining fat intake should be composed of mono and polyunsaturated fats. Trans fats should be limited as much as possible. When reviewing the various types of fats, label reading is beneficial.[3]

Saturated fat: The initial treatment for most is limiting saturated fat to 8%–10% of total calorie needs after 12 months of age. In children (>2 years) with identified hypercholesterolemia and elevated LDL-C, dietary recommendations with a saturated fat restriction of ≤7% of calories has been shown to be safe and moderately effective in lowering the LDL-C level.[3] Common sources of saturated fat include red meats (beef, lamb, veal, and steak), poultry skin, deep fried foods, full fat dairy, butter, shelf-stable nut butters, margarine, shortening, pastries, doughnuts, pie crusts, processed cookies, and crackers.

Trans fats: Trans fatty acids ("trans fats") should be avoided as they have been shown to both raise LDL-C cholesterol and lower HDL-C cholesterol. Trans fats are created when hydrogen is added to vegetable oil to harden it; this preserves shelf life. Common sources of trans fat include fried and processed foods, shelf-stable nut butters, margarine, shortening, pastries, doughnuts, pie crusts, processed cookies, and crackers.

Monounsaturated fats: In children with identified elevated LDL-C, 10% of fat should be from monounsaturated sources.[3] Commonly consumed sources of monounsaturated fats include vegetable oils (olive oil, canola oil, peanut oil, sunflower oil, and sesame oil) as well as avocados, natural peanut butters, and many nuts and seeds.

Polyunsaturated fats: Polyunsaturated fats should make up another 10% of daily kilo calories per Estimated energy requirements (EER) in children >12 months.[3] Foods high in polyunsaturated fat include a number of vegetable oils (soybean oil, corn oil, and safflower oil), fatty fish (salmon, mackerel, herring, and trout), and some nuts and seeds (walnuts and sunflower seeds).

Dietary cholesterol: Children >2 years with identified hypercholesterolemia and/or elevated LDL-C dietary should limit their intake of dietary cholesterol to <200 mg/d. The initial recommendation for children with dyslipidemia is <300 mg/day of cholesterol, after 12 months of age.[3] In general, research is split on the effect of dietary cholesterol on serum cholesterol. Some studies suggest that dietary cholesterol causes a modest elevation in LDL-C,[17–19] whereas others show that dietary cholesterol has little or no effect on serum lipids.[20–22]

Lean Proteins

Encouraging lean proteins as a replacement for high saturated fat options aids in lowering saturated fat content of the diet. Examples of lean protein sources include lean turkey breasts, white meat chicken, fish, pork tenderloin, tofu, beans, and legumes. If choosing red meat, choose round cut and trim meat to remove fat. Ground beef should be at least 90% lean.

Low-Fat Dairy

Between 12 and 24 months, reduced fat milk (2% or lower) can be used. More than 24 months, fat-free milk is

recommended, as it optimizes the nutrient benefit without adding saturated fat. Low-fat dairy products should be encouraged in an effort to lower overall saturated fat intake.[3]

Cooking Methods

In an effort to reduce deep or pan frying, patients should be encouraged to use heart healthy cooking options. Heart healthy preparation options include baking, braising, broiling, grilling, sautéing, poaching, roasting, steaming, and stir frying. Discourage the use of heavy sauces as they are often higher in saturated fats.

Sugar Sweetened Beverages

Reducing sugar sweetened beverage (SSB) consumption can aid in TG reduction.[23] In addition, it is thought that SSBs contribute to an increased risk of type 2 diabetes mellitus and CVD as a contributor to a high dietary glycemic load leading to inflammation, insulin resistance, and impaired β-cell function.[24] A 2011 study reported that the incident of coronary heart disease risk (CHD) associated with plasma HDL-C or TG levels was significantly increased only in the presence of insulin resistance. Dyslipidemia associated with high TGs and low HDL-C is frequently associated with metabolic syndrome and subsequent CHD. Ideally, the primary beverage should be water or fat-free unflavored milk.[3]

Fiber

The recommended total dietary fiber intake from food sources is the child's age in years plus 5 g for young children (<11 years old) and up to 14 g/1000 kcal for older children and adolescents.[3] Ideally fiber intake comes from fiber-rich fruits, veggies, beans, lentils, and whole grains. Fiber supplements are not generally advised for the purpose of lowering lipids.[3] Research has shown that fiber intake has

been associated with decreased serum cholesterol levels and improved vitamin and mineral intake in pediatrics when compared with its absence.[25]

Plant Sterols/Stanols

Many stanol-containing food products are now on the market, including as additives to some foods and also as margarines. The mechanism of sterols and stanols is to block cholesterol absorption in the gut; stanols are not absorbed and sterols are partially absorbed. Plant sterols or stanol esters (up to 2 g/d) have been studied as replacements for usual fat sources to safely enhance LDL-C in short-term studies in children with FH. However, long-term studies on the safety and efficacy of sterols and stanols have not been performed in adults or children, thus these supplements should be reserved for children who do not achieve LDL-C cholesterol goals with conventional dietary treatment alone. The health care provider may choose to monitor fat soluble vitamin levels.

Omega-3 Fatty Acids

A high intake of dietary fish intake, specifically those high in omega-3 fatty acids, has been associated with lower rates of CVD. Eating fish two to three times per week is recommended; fish high in omega-3 fatty acids include wild salmon, tuna, sardines, bluefish, herring, and trout.[3] If TGs are >200 mg/dL, some providers will recommend omega-3 supplements.[10] Research on the effects of fish oil supplementation in pediatrics is limited. Some research has shown omega-3 supplements showing a slight increase in LDL-C cholesterol while lowering TGs, whereas others have reflected a decrease in LDL-C density.

Physical Activity

At least 1 hour of moderate or vigorous activity every day of the week is recommended for children older than 5 years.[3]

Promoting physical activity in childhood may lead to an active lifestyle in adulthood. Furthermore, physical inactivity has been identified as an independent risk factor for CHD. A 2007 meta-analysis revealed that adults who exercised 40 minutes three to four times/week had an increase in their HDL-C of ~2.5 mg/dL. Cardiac risk is thought to drop by 2%–3% for each 1 mg/dL increase in HDL-C.[26]

MONITERING AND EVALUATION

Registered dietitians should council children and their families about implementing a diet low in saturated and without trans fats and high in fruits, vegetables, and fiber. RDs can monitor patient's progress ensuring weight is appropriate (without excessive loss in normal weight children, and with appropriate loss in overweight/obese children) through a variety of parameters and discussions with the patient and family. Although weight loss is not the primary goal in nutrition counseling for lipid disorders, weight loss may accompany improvements in lipid values secondary to lifestyle medications. A moderate weight reduction has been shown to decrease insulin resistance and dyslipidemia in severely obese children and adolescents.[11]

The patient's ability to recall nutrition goals covered in the previous session(s) provides the dietitian with a baseline for the patient's current knowledge. Fasting lipid panels every 3 months help to track progress. Body mass index and corresponding changes in weight and height should be noted. Tracking the patient's stage of change may help guide the RD as to how best to approach lifestyle change, allowing him/her to tailor the nutrition goal setting process.

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32 Obesity and Bariatric Surgery

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DEFINITION AND PREVALENCE

Obesity, the excessive accumulation of body fat, is one of the leading preventable causes of morbidity and mortality in the United States.[1] Body mass index (BMI), defined as the weight in kilograms divided by the height in meters squared (kg/m^2), is the standard predictor of adiposity (see Table 32–1). Currently, one-third of all US children and adolescents are either "overweight" or "obese." An overweight child plotting above the 85th percentile for BMI on the

Table 32–1 Definition and Prevalence of Overweight and Obesity Among Children in the United States[2]

Category	Definition	Prevalence
Overweight	BMI >85–95 percentile for age and sex	32%
Obesity	BMI >95th percentile for age and sex	17%
Extreme obesity	BMI >99th percentile for age and sex	4%

2000 CDC growth charts corresponds to a BMI of 25 kg/m^2 by age 18 years, the adult definition of "overweight," whereas an obese child plotting above the 95th percentile on the 2000 CDC growth chart corresponds to a BMI of 30 kg/m^2 by age 18 years, the standard of adult "obesity."[1]

Although the prevalence of obesity tripled from the 1970s to the year 2000, the prevalence of obesity in children has remained relatively stable in recent years. According to 2010 data, the overall prevalence of obesity in US children is 17% (see Table 32–1). Obesity in racial/ethnic minorities is disproportionately higher than in white children with prevalence of 23% in Hispanic children and 24% in non-Hispanic black children.[2] The prevalence of extreme obesity is 3.8%–4.0%, with the highest prevalence also seen in Hispanic children and black children.[3]

ETIOLOGY

The rapid increase in the prevalence of obesity in the past 30 years points to an obesogenic environment as a trigger among those genetically susceptible for weight gain and adiposity. Monogenic disorders (melanocortin 4 receptor deficiency and leptin receptor deficiency) and syndromic disorders (Prader Willi, Albright hereditary osteodystrophy, and Bardet–Biedl syndromes) are rare causes of childhood obesity. The genetic predisposition to obesity is usually polygenic, meaning several single genes make a contribution to the development of obesity. The heritability of BMI among adolescents raised in an obesogenic environment is estimated[4] to be 77% and, for children under the age of 10 years, parental obesity more than doubles their risk of becoming an obese adult.[5]

HEALTH CONDITIONS ASSOCIATED WITH OBESITY

Childhood obesity is associated with multiple medical conditions and poor quality of life (see Table 32–2).[6] Children with extreme obesity (BMI > 99th percentile) are at high risk for biochemical abnormalities and have a high likelihood of

Table 32–2 Health Conditions Associated With Childhood Obesity

System	Condition
Cardiovascular	Hypertension, hypercholesterolemia, hypertriglyceridemia, Increased LDL and VLDL, decreased HDL
Endocrine	Insulin resistance, acanthosis nigricans, impaired fasting glucose, type 2 diabetes mellitus, precocious puberty, polycystic ovary syndrome, Cushing's syndrome, hypothyroidism
Gastrointestinal	Nonalcoholic fatty liver disease, gastroesophageal reflux, constipation, gallstones
Pulmonary	Pickwickian syndrome, obstructive sleep apnea, hypoventilation syndrome, asthma, exercise intolerance
Musculoskeletal	Slipped capital femoral epiphysis, Blount's disease (tibia vara), osteoarthritis, back and joint pain, fractures
Neurological	Recurrent headaches, pseudotumor cerebri
Psychological	Depression, poor self-image, social isolation, poor quality of life

Source: Adapted from Barlow and the Expert Committee.[11]

developing severe adult obesity and obesity-related diseases.[3] Eighty-four percent of obese children become obese young adults and carry cardiovascular risk factors such as type 2 diabetes, hypertension, dyslipidemia, and carotid-artery disease into adulthood leading to risk of early mortality.[3,7]

NUTRITIONAL ASSESSMENT

Anthropometric Measurements

BMI percentiles and *z*-scores are the preferred measure of overweight and obesity in clinical practice and research. Although BMI is an indirect measure of body fat mass and thus cannot account for lean body mass or pubertal status, it is highly correlated with body fat at higher BMI levels. In obesity, direct measures of adiposity, such as skin fold thickness, are not thought to be as beneficial; waist circumference measurements are often impractical and are currently not recommended due to a lack of standardization of measurement techniques.

Energy Requirements

Obese children have basal metabolic rates equal to or greater than their nonobese counterparts due to increased lean body mass needed to support the extra weight. The percentage of lean body mass for each additional kilogram of body weight above ideal body weight is highly variable. For hospitalized obese patients, resting metabolic rate should be measured by indirect calorimetry as equations often overestimate energy needs.[8] For obese outpatients, a detailed dietary history will provide some insight into a child's actual intake, although children have been found to under-report caloric intake by as much as 40%.[9]

Clinical and Dietary Evaluation

Assessment of an overweight or obese child should include a thorough medical evaluation to assess heritable risk factors

(see Table 32–3) with a review of serial growth points targeting the onset of abnormal weight gains. A detailed nutrition and activity history to assess environmental and behavioral risks is necessary. A focused assessment of key modifiable behavioral risk factors that have the strongest evidence for association with energy balance is recommended. These include specific eating habits, physical activity, and sedentary behaviors. Specific recommendations should be targeted to each area and specific goals for behavior change identified (see Table 32–3). Before any behavior-based treatment can occur, it is important to identify attitudes of the patient and family, readiness for change, and health behavior beliefs or goals that will underlie the motivation for behavior health changes.

Table 32–3 Assessment of Risk and Readiness for Change

Medical risk	• Persistent obesity • Obesity-related medical conditions
Genetic risk	• Parental obesity • Type 2 diabetes • Cardiovascular disease (hypertension, high cholesterol) • Early deaths from heart disease or stroke
Environmental risk	Eating behaviors • Ounces, cup, or cans of sugar-sweetened beverages consumed each day • Ounces, cups, or cans of 100% fruit juice consumed each day • Fruit and vegetable servings consumed each day • Frequency of eating food prepared outside of the home,

	including food in restaurants, school and work cafeterias, and fast food establishments and food purchased for "take out" • Frequency of family meals • Portions that are large for age (qualitative assessment) • Frequency and quality of breakfast • Consumption of foods that are high in energy density • Number of meals and snacks eaten each day and quality of snacks Physical activity behaviors • Time spent in moderate physical activity each day (organized physical activity versus play) • Goal of 60 min of moderately vigorous activity daily • Routine activity patterns, (such as walking to school) • Sedentary behavior (TV time, television, videotape/DVD, videogame viewing, and computer use) • Goal <2 h per day Sleep behaviors • Insufficient hours of sleep for age, sleep disturbance, nighttime eating syndrome
Attitudes	• Self-perception or concern about weight • Readiness to change • Successes, barriers, and challenges

Table 32–4 Prevention of Childhood Obesity—Expert Committee Recommendations[6]

Prevention counseling

1. Eating a diet rich in calcium
2. Eating a diet high in fiber
3. Eating a diet with balanced macronutrients (energy from fat, carbohydrates, and protein in proportions for age, as recommended by Dietary Reference Intakes)
4. Encouraging exclusive breastfeeding to 6 mo of age and maintenance of breastfeeding after introduction of solid food to 12 mo of age and beyond
5. Promoting moderate to vigorous physical activity for at least 60 min each day
6. Limiting consumption of energy-dense foods

PREVENTION

Strategies to prevent obesity include promoting breastfeeding during infancy and encouraging healthy lifestyle behaviors among children with a BMI in the healthy range (Table 32–4). Pediatricians and pediatric dietitians should be aware of the increased risk of obesity in young adulthood for children with obese parents even if their current weight is normal. Children should routinely be assessed for obesity risk by calculating and plotting BMI at least annually and screened for medical risks and unhealthy eating and physical activity habits. When discussing obesity with clients, clinicians should use more neutral terms such as weight, unhealthy weight, and unhealthy BMI to reduce the risk of stigmatization, blaming, or harm to self-esteem.[10]

TREATMENT

The goal of obesity treatment is to minimize health risks and improve quality of life by preventing further abnormal weight gain, reducing adiposity, and increasing lean body

mass over a prolonged period without affecting linear growth. A reasonable goal for obese prepubertal children is to stabilize weight while linear growth continues to accelerate. When weight loss is desired, a reasonable goal is 1–2 pounds of weight loss/week. Reducing caloric intake by 200–500 calories per day may achieve gradual weight loss in younger children, whereas a 500- to 1000-calorie/day deficit may be required in older children and adolescents.

Treatment should be multidisciplinary and include counseling on diet, exercise, and behavior modification. Focusing on specific diet and behavior modifications has been shown to have the greatest efficacy. In 2007, an expert committee was formed to review all current literature regarding the treatment of childhood overweight and obesity.[11] A four-staged intervention program was recommended (see Table 32–5). These new recommendations use current, evidence-based data, and in some cases, clinical experience where evidence does not exist, to provide practitioners with practical guidelines. In general, treatment begins with Stage 1 Prevention Plus (Table 32–5) and progresses to the next stage if there has been no improvement in weight/BMI velocity after three to six months and the family is ready. The first stage can be delivered in a health care office, whereas subsequent stages require more time and resources including a dietitian. Advancement in stages should be made based on the child's age, weight or BMI classification, and risk factors. The first focus is on the reduction of consumption of sugar-sweetened beverages, as these have been associated with excess weight gain and increased rates of obesity. It is important to reduce the frequency of television and computer use, with an emphasis on also increasing physical activity that is consistent, enjoyable, and in keeping with the patient's lifestyle. Stage 2 treatment of obesity is structured with an emphasis on a planned diet and activity schedule, with further reductions in screen time and

Table 32–5 Staged Treatment of Childhood Obesity—Expert Committee Recommendations[6]

Stage 1—prevention plus 1. Limiting consumption of sugar-sweetened beverages 2. Encouraging consumption of diets with recommended quantities of fruits and vegetables 3. Limiting television and other screen time 4. Eating breakfast daily 5. Limiting eating out at restaurants, particularly fast food 6. Encouraging family meals in which parents and children eat together 7. Limiting portion size
Stage 2—structured weight management 1. A planned diet or daily eating plan with balanced macronutrients 2. Structured daily meals and planned snacks (breakfast, lunch, dinner, and 1 or 2 scheduled snacks, with no food or calorie-containing beverages at other times, may reduce excess intake) 3. Additional reduction of television and other screen time to <1 h per day 4. Planned, supervised, physical activity or active play for 60 min per day 5. Monitoring of these behaviors through use of logs (TV time, exercise time, food/beverage) 6. Planned reinforcement for achieving targeted behaviors
Stage 3—comprehensive multidisciplinary intervention 1. A structured program in behavior modification including food monitoring, short-term diet and physical activity goal setting, and contingency management 2. Negative energy balance resulting from structured dietary and physical activity changes is planned 3. Parental participation in behavior modification techniques is needed for children <12 y of age; parental involvement would be progressively less with older youths

4. Parents should be trained regarding improvement of the home environment
5. Systematic evaluation of body measurements, diet, and physical activity should be performed at baseline and at specified intervals throughout the program
6. A multidisciplinary team with experience in childhood obesity should be involved
7. Frequent office visits should be scheduled; weekly visits for a minimum of 8–12 wk seem to be most efficacious; subsequently, monthly visits can help maintain new behaviors
8. Group visits may be more cost-effective and have therapeutic benefit

Stage 4—tertiary care intervention

1. *Medications*: The Food and Drug Administration has approved Orlistat for patients ≥12 y of age
2. *Very-low-calorie diets*: Provides 400–800 calories per day in a nutritionally complete formula (Optifast™, protein sparing modified diet plus multivitamin supplements); generally not recommended due to lack of outcome data in children and risk of iatrogenic malnutrition
3. *Bariatric surgery*: Laparoscopic roux-en-y gastric bypass, laparoscopic sleeve gastrectomy, or laparoscopic gastric banding for adolescents with a BMI above 40 kg/m^2 and comorbidities or a BMI above 35 kg/m^2 and severe comorbidities; a multidisciplinary team with experience in childhood obesity and bariatric surgery should be involved; requires lifelong monitoring and nutritional supplementation

the use of logs to track behavior changes. Stage 3 increases the intensity of behavior changes, the frequency of visits, and a multidisciplinary weight management program with a dietitian, psychologist, and physician. Stage 4 treatment is implemented for obesity complicated by other comorbidities and is offered within a multidisciplinary specialty weight loss program supervised by a physician.

The use of pharmacology, very-low-calorie diets, and bariatric surgery all aim to promote weight loss and reverse comorbidities. Currently, Orlistat is the only drug approved by the US Food and Drug Administration for obesity in children above the age of 12 years. In one trial, Orlistat used in combination with a behavioral intervention resulted in a drop of 0.55 kg/m^2 BMI points when compared to a placebo group.[12] Orlistat causes fat malabsorption and thus fat-soluble vitamin supplementation may be warranted. Although not approved for obesity treatment, treatment of obese adolescents with Metformin XR 2000 mg daily showed a 0.9 kg/m^2 decrease in BMI points at 48 weeks compared to an increase of 0.2 kg/m^2 in a placebo group.[13]

Approaches to nutrition education should be individualized to the child's treatment goals and lifestyle. To date, however, there is little consensus about the optimal composition of weight loss diets. A large study conducted among adults showed no difference in body fat loss in diets differing in fat, protein, and carbohydrates,[14] whereas a study conducted among young adults suggests that a low glycemic index diet may be superior for some individuals.[15] In general, "restrictive dieting" should be discouraged, because very-low-calorie diets can run the risk of slowing height velocity and maturation in children at early stages of puberty.[16]

IMPLEMENTATION

The complexity of obesity prevention and treatment lies less in the identification of target health behaviors and more in the implementation. Traditional models involving a brief education and giving advice in which recommendations are provided are rarely effective. Utilizing patient-centered counseling techniques such as motivational interviewing helps the family identify their own motivation for making changes and is an effective strategy for moving ambivalent

families into action planning while improving their success. Motivational interviewing is fundamentally different from educational approaches in that motivation for change is elicited from individuals rather than imparted by a health care provider. This approach has been shown to improve results in weight loss counseling.[17]

Younger children are dependent on parents and adult care givers (PAC) to structure their home environment and daily lifestyles, which includes diet and physical activity. Parental adherence to core behavioral change strategies (Table 32–6) predicted better child weight outcomes after two to five years, whereas no particular parenting strategy is found to be superior to others. However, a restrictive parenting style with regard to a child's eating is discouraged as this may lead to eating in the absence of hunger.[18]

Table 32–6 Implementation of Core Behavior Change Strategies[22]

Behavior modification

1. Identify target behavior: The parents and adult care givers (PAC) and child identify a specific behavior that family members can change. Although there may be other changeable behaviors, PAC believes that his/her child can have initial success with this particular behavior
2. Stimulus control: Internal and external cues and triggers associated with a particular behavior are considered
3. Self-monitoring: The PAC and/or child keep a daily record of food consumed and physical activity expended. This can include type and amounts, who else was present, where, time of day, and how they felt
4. Reinforcement: PAC encourages healthy behavior changes with reinforcers, rewards, and behavioral contracts. Acknowledge and celebrate child's progress toward goal rather than focusing on child's "failures"
5. Self-efficacy and Self-management: The PAC develops a sense of confidence in his/her ability to implement core behavior change strategies

TREATMENT OUTCOMES AND PROGNOSIS

Establishing permanent changes to lifestyle behaviors may produce long-term health benefits and should be considered a good outcome, regardless of weight change. Unfortunately, obesity is a chronic disease and most cases of obesity during childhood persist into young adulthood. Most comprehensive medical and behavior interventions of medium-to-high intensity produce a decrease in BMI of only 2–3 kg/m^2 points in children and adolescents after one year.[19] However, frequent follow-up for the overweight and obese child, particularly for nutritional and behavioral counseling, is recommended to optimize successful health behavior changes and prevent BMI escalation.

ADOLESCENT BARIATRIC SURGERY

For children and adolescents suffering from severe obesity, dietary and behavioral interventions are only modestly successful (BMI reduction of 3%).[12] As such, more aggressive weight control strategies such as bariatric surgery are warranted in adolescents with extreme obesity and associated comorbidities who cannot reduce their BMI significantly and reverse comorbidities with intensive lifestyle and/or pharmacologic treatments.[20] Referral guidelines for adolescent bariatric surgery include adolescents with a BMI > 40 kg/m^2 with comorbidities or a BMI >35 kg/m^2 with severe comorbidities who have medically recalcitrant obesity that is not responding to a multidisciplinary medical treatment plan (see Table 32–7).

There are three main bariatric surgery procedures; laparoscopic adjustable gastric banding, laparoscopic sleeve gastrectomy, and Roux-en-Y gastric bypass (RYGB). RYGB is considered the gold standard operation for long-term weight control in the United States in severely obese adolescents.[21]

Table 32–7 Referral Guidelines for Adolescent Bariatric Surgery Evaluations[21]

Selection Criteria for Weight Loss Surgery in Adolescents	
BMI (kg/m^2)	**Comorbidities**
>35 with one serious comorbidity	• Serious: type 2 diabetes mellitus, moderate or severe obstructive sleep apnea (AHI = Apnea-hypopnea index >15 events/h), pseudotumor cerebri, and severe steatohepatitis
>40 with one other comorbidity	• Other: mild obstructive sleep apnea (AHI ≥5 events/h), hypertension, insulin resistance, glucose intolerance, dyslipidemia
Eligibility criteria	
Tanner stage	• IV or V (unless severe comorbidities indicate Weight loss surgery (WLS) earlier)
Skeletal maturity	• Completed at least 95% of estimated growth
Lifestyle changes	• Demonstrates ability to understand what dietary and physical activity changes will be required for optimal postoperative outcomes
Psychosocial	• Evidence for mature decision making, with appropriate understanding of potential risks and benefits of surgery • Evidence for appropriate social support without evidence of abuse or neglect • If psychiatric condition (e.g., depression, anxiety, or binge

(*Continued*)

Table 32–7 Referral Guidelines for Adolescent Bariatric Surgery Evaluations[21] (*Continued*)

Selection Criteria for Weight Loss Surgery in Adolescents	
BMI (kg/m²)	**Comorbidities**
	eating disorder) is present, it is under treatment • Evidence that family and patient have the ability and motivation to comply with recommended treatments pre- and postoperatively, including consistent use of micronutrient supplements • Evidence may include a history of reliable attendance at office visits for weight management and compliance with other medical needs

Adults who undergo bariatric surgery achieve clinically significant and sustained weight loss with improvement or reversal in obesity-related comorbidities leading to reduced cardiovascular morbidity and mortality.[22]

Early adolescent bariatric studies mimic the positive adult outcomes, thus bariatric surgery is now the primary treatment recommendation for adolescents with clinically significant obesity who are medically recalcitrant to treatment within a multidisciplinary medical supervised weight loss program. Despite the severity of obesity upon presentation to undergo bariatric surgery, all adolescents showed a 37% mean BMI reduction after 1 year post a RYGB procedure in one study.[23] A multicenter teen study is ongoing to assess the safety and outcomes of bariatric surgery in adolescents (TEEN LABS).

A comprehensive nutrition evaluation, nutrition education and meal planning, and pre- and postoperative diet education and monitoring are required for adolescents undergoing bariatric surgery.[24] Nutrition education should be provided in a minimum of six preoperative nutrition sessions. Nutrition information should start with the basics of weight loss surgery nutrition principles, including the elimination of sugar-sweetened beverages, meeting a baseline daily fluid requirement, consuming regularly scheduled protein containing meals (3–6) per day, and taking vitamins as directed. Food records and self-monitoring are initiated to assist in weight maintenance, aid in identification of daily caloric intake, and are used in postsurgical monitoring. Education in very-low-calorie, high-protein liquid supplementation for the perioperative period is discussed as well as the dietary texture progression post operatively from clear liquids to full liquids to smooth then to soft then regular textured foods (see Table 32-8). Education in limiting portion size is important, as postoperatively only very small portions (2–4 ounces) of food may be tolerated at a meal time. Frequent 1-oz portions of fluids are needed initially following surgery to maintain hydration and meet at least maintenance fluid needs of adolescents.

Special attention to identify dietary inadequacies leading to micronutrient deficiencies [thiamin (B_1), cobalamin (B_{12}), iron, vitamin D, calcium, and folate] is necessary and a daily general multivitamin is recommended preoperatively. Lifelong nutritional monitoring and nutritional supplementation is required postoperatively to prevent micronutrient deficiencies based on laboratory testing and the type of bariatric surgery procedure performed (see Table 32–9).[24]

Table 32–8 Diet Advancement Recommendations by Stage and Procedure[24]

Stage 1: ice chips, water, sugar-free clear liquids Roux-en Y: 1 oz/h for the first 24–48 h, then for 3–7 d ad lib Gastric band: 1 oz/h for the first 24–48 h Sleeve gastrectomy: 1 oz/h for the first 24–48 h, then for 3–7 days ad lib	• 4–6 oz of water or sugar-free clear liquids per hour (48–64 oz/d) • Acceptable sugar-free clear liquids include water, clear broth or bouillon, sugar-free gelatin, sugar-free fruit-flavored drinks, fruit ice made with sugar-free fruit-flavored drink, sugar-free popsicles • Sugar-free clear restrictions: no carbonated beverages, no caffeine, no red dye
Stage 2: high-protein full liquids Roux-en Y: 2–4 wk Gastric band: First 2 wk after surgery Sleeve gastrectomy: 1–5 wk	• Calories: 500–600 kcal • Protein: 50–60 g • Fluid: 80–90 oz or based on estimated requirements • New foods introduced: skim or 1% milk, low-fat soy or lactaid milk, high-protein drinks, light yogurt (plain or vanilla) thinned out with milk • Meal pattern: 3–6 meals per day • Volume: ½ cup per meal for solid foods
Stage 3: smooth consistency, high-protein foods Roux-en Y: 4–6 wk Gastric band: 3–4 wk Sleeve gastrectomy: 5–8 wk	• Calories: 500–700 kcal • Protein: 60 g • Fluid: 80–90 oz (or based on estimated requirements) • New foods introduced: scrambled eggs, blenderized/minced turkey, chicken, flaked fish or mashed tofu, tuna, melted low-fat cheese low-fat

	cottage cheese (small curd only), low-fat ricotta cheese • Consistency of food: smooth • Try new foods 1 at a time (¼ cup) every 2–3 d • Meal pattern: 3–4 meals per day • Volume: ½ cup per meal for solid foods or 5–6 oz per meal of protein drink
Stage 4: soft foods—other protein foods, fruit, vegetables, and grains Roux-en Y: 7–9 wk Gastric band: 5–6 wk Sleeve gastrectomy: 9–12 wk postop	• Calories: 700–800 kcal • Protein: 60 • Fluid: 80–90 oz (or based on estimated requirements) • New foods introduced—protein foods: shaved delicatessen meats, low-fat cheese, lean pork, cooked beans • Fruit: soft or canned in own juice, no skin • Vegetables: soft cooked or canned • Grains: toast, low-sugar cereal, crackers, oat meal, rice, pasta, mashed potatoes (choose mainly whole-grain products, foods) • Meal pattern: 3–6 meals per day • Volume: ½–1 cup per meal solid foods or 1 cup (8 oz) protein drink
Stage 5: healthy foods for life Roux-en Y: Begins at wk 9 and for life Gastric band: wk 7 and for life Sleeve gastrectomy: At wk 13 and for life	• Calories 800–900 kcal • Protein: 60 g • Fluids: 80–90 oz (or based on estimated requirements) • New foods introduced: all healthy food choices • Meal pattern: 3–6 meals per day • Volume: Up to ¾ to 1½ cup per meal

Table 32–9 Postoperative Vitamin Supplementation in Bariatric Surgery[24]

MVI Supplement	Gastric Band	RYGB	Sleeve Gastrectomy	Comment
General Multivitamin (MVI)	100% daily value	200% daily value	200% daily value	Begin day 1 postop
Elemental iron	As needed	18–27 mg/d	18–27 mg/d	Begin day 1 postop, may require more
Elemental Calcium	1500 mg/d	1500–2000 mg/d	1500 mg/d	Begin day 1 postop
Vitamin D	As needed	As needed	As needed	To keep levels >30
Vitamin B_{12}	NA	100 mcg/mo IM or 350–500 mcg/d orally	NA	Begin if deficiency
B complex	1 tab/d	1 tab/d	1 tab/d	Include if vomiting

Abbreviation: RYGB, Roux-en-Y gastric bypass.

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33 Oncology and Stem Cell Transplantation

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INTRODUCTION

Cancer in children is a group of diseases of abnormal cell growth. The most common type of pediatric cancer is acute lymphocytic leukemia (ALL), which accounts for 25% of cancer in children younger than 20 years of age, followed by central nervous system (CNS) tumors which account for 22% of pediatric cancers.[1] Advances in treatment of children with cancer have increased survival rates considerably; 5-year survival rates of all cancers exceeded 70% for children diagnosed from 1975 to 1994.[1] Treatment for refractory or high-risk cancers may include hematopoietic stem cell transplantation (HSCT). HSCT may also be indicated in various nonmalignant diseases including immunologic disorders, bone marrow failure syndromes, and storage diseases.[2]

Up to 46% of children and young adults experience some form of malnutrition related to tumor burden and/or cancer-associated treatments; however, malnutrition per se need not be accepted as an unavoidable consequence of the diagnosis.[3] While weight loss related to treatment side effects remains of concern among children with cancer, obesity is a rising problem

among survivors of childhood cancer.[4] Physical activity and healthy lifestyle habits should be emphasized to help attain appropriate body weight and optimize quality of life.

NUTRITION RISK FACTORS

Cancer treatment in children includes chemotherapy, radiation, and surgery. A combination of agents is often used to treat pediatric cancers. Since the type and stage of neoplasm largely determine the prescribed treatment, nutritional risk can be also characterized by disease (Table 33–1).

Side effects of cancer treatment as well as the manifestations of the disease itself can cause nutritional complications. Cachexia is defined as a state of ill health, malnutrition, and wasting caused by malignancy with or without weight loss.[5] The multifactorial causes of cancer cachexia are shown in Figure 33–1. Cancer treatment includes many medications that have a variety of side effects on nutritional intake and metabolism, including chemotherapy, corticosteroids, and immunosuppressive agents. Radiation and surgery are frequently components of treatment for pediatric cancer.

Table 33–1 High Nutritional Risk Pediatric Cancer Subtypes

Advanced stages of solid tumors, including
Wilms' tumor
Neuroblastoma
Rhabdomyosarcoma
Non-Hodgkin's lymphoma
Acute myeloblastic leukemia
Ewing's sarcoma
Medulloblastoma and other high-grade brain tumors
Head and neck tumors
HSCT

Source: Adapted from Bauer et al.[3]

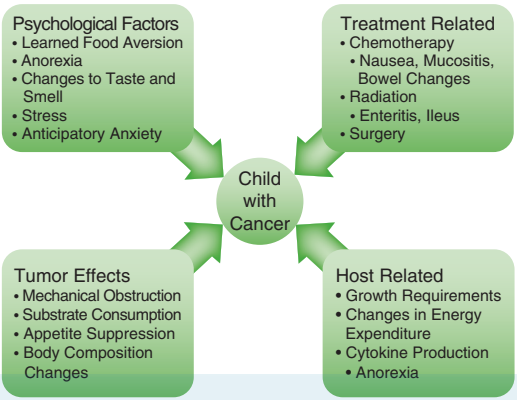

Figure 33–1: Contributors to cachexia in pediatric cancer. Adapted from Alexander et al.[6]

Surgery often involves placement of central venous catheters for access, placement of enteral feeding devices, or resection of tumor. Combined with the effects of chemotherapy, radiation can cause gastrointestinal toxicity leading to significant nutritional risk for many children undergoing aggressive treatment. Common treatments for cancer and nutrition-related side effects are shown in Table 33–2.

Table 33–2 Nutrition-Related Side Effects of Common Treatment Agents in Pediatric Oncology

	Chemotherapy	Radiation	Surgery
Anorexia	×	×	×
Mucositis	×	×	
Nausea/vomiting	×		
Diarrhea	×	×	×

	Chemotherapy	Radiation	Surgery
Constipation	×		×
Dysgeusia	×	×	
Hyperlipidemia, hyperglycemia	×		×
Dysphagia		×	×

SPECIAL ASPECTS OF NUTRITIONAL ASSESSMENT

The nutritional assessment of a child with cancer involves a thorough diet and symptom history and anthropometric evaluation as well as a review of the current stage of disease and treatment. Psychosocial considerations and medical interventions are important when addressing nutritional intake. The determination of an appropriate route for nutrition support may depend on the planned treatment course. Although most patients are well nourished and in remission when presenting for transplantation, the preparative regimen for HSCT generally causes substantial gastrointestinal toxicities and often precludes oral intake for extended periods.[7] Many patients receiving HSCT will require parenteral nutrition (PN) support to avoid acute malnutrition.

Weight, height, and BMI should be measured at baseline and at follow-up points with consideration to comparative standards and any change, expected or unexpected, in nutritional status. Fluid retention, tumor mass, and body composition changes may confound the interpretation of weight changes during treatment. Before initiating cancer treatment and up to three days after, patients are at risk for tumor lysis syndrome. Tumor lysis syndrome, a metabolic crisis situation, results from the destruction of tumor cells and the release of their contents into the circulation[8] (Table 33–3).

Table 33–3 Features and Management of Tumor Lysis Syndrome

Laboratory	Prevention and Treatment Strategies
Hyperkalemia	Minimize potassium intake
	Diuretics or potassium binders
	Insulin and glucose therapy
Hyperuricemia	Xanthine oxidase inhibitors (allopurinol) or urate oxidase (rasburicase)
	Urinary alkalinization with sodium bicarbonate (or acetate salts in parenteral nutrition solutions)
	Aggressive hydration to promote diuresis
	Dialysis
Hyperphosphatemia	Phosphate binders
	Minimize phosphorus intake
Hypocalcemia	Calcium gluconate, only if symptomatic (treatment may worsen calcium phosphate precipitation); correction of hyperphosphatemia

Source: Adapted from Fisher et al.[8]

SPECIAL ASPECTS OF NUTRITIONAL MANAGEMENT

Energy requirements of pediatric cancer patients are typically estimated by a calculation of basal energy expenditure (EE), with a broad range of 20%–100% added for the effect of activity, growth, and catabolic stress.[9] Acutely ill patients may require less energy due to reduced activity or greater energy during febrile illness. EE may be increased with a large tumor burden, lessened by reductions in lean body mass, or normal when disease is in remission.[5] Measurement of resting EE by indirect calorimetry is useful for determining suitable energy provision during the various phases of treatment.

A reduction in measured resting EE has been observed during HSCT.[10] Caution when estimating energy requirements should be exercised to avoid overfeeding during HSCT.[10] Adequacy of feeding is best judged by appropriateness of weight gain in the patient with normal fluid status.

Oral Nutrition

Several suggestions regarding oral nutrition may be helpful to the family and patient with cancer (Table 33–4). A diet low in bacterial content is often recommended during periods of profound neutropenia, particularly during HSCT. Sanitary

Table 33–4 Strategies for Improving Oral Intake During Cancer Treatment

Loss of Appetite
Small frequent feedings (6–8 meals/snacks per day)
Nutrient-dense beverages between meals
Favorite foods during treatment-free periods to prevent learned food aversions
Nausea and Vomiting
Feed 3–4 hours before therapy that typically causes nausea and vomiting
Offer small amounts of cool foods and encourage slow eating; avoid strong odors
Offer clear liquids between meals; using a straw in a covered cup may facilitate sipping
Mouth Sores
Serve soft or pureed bland food or liquids
Add butter, gravy, sauce, or salad dressing to moisten foods
Avoid highly seasoned or hard, rough foods
Altered Taste Perception
Use stronger seasonings; avoid excessively sweet foods
Experiment with salty tastes, e.g., hot dogs, pizza, pasta
Try new flavors of foods

food practices should be closely followed to minimize the risk of food-borne illness in immunocompromised states (Table 33–5).

Enteral Nutrition

The method of provision of nutrition support in patients at highest nutritional risk remains controversial. Provision of enteral nutrition is the preferred route of nutrition in any patient with a functioning gastrointestinal tract.[3] Nasogastric tube feeding is less expensive and associated with fewer life-threatening complications than PN.[3] Percutaneous endoscopic gastrostomy tubes have a high acceptance rate

Table 33–5 Sanitary Food Practices for Immunocompromised Patients

- Good hand washing before and after preparing and eating meals
- Do not share food with others
- Avoid foods from street vendors, salad bars, and shared bins of foods in grocery stores
- Wash raw fruits and vegetables well before eating
- Cook meat until well done
- Avoid raw eggs
- Avoid soft French style cheeses, pates, and uncooked hot dogs
- Avoid alfalfa sprouts and unpasteurized juices
- Keep foods at <40° F or >140° F to minimize growth of bacteria
- Clean all preparation items thoroughly before and after use to avoid cross-contamination
- Keep refrigerated leftovers for no more than 2 days

Source: Adapted from United States Department of Agriculture, Food and Drug Administration.[11]

and may be indicated when oral and/or nasogastric tube feeding is insufficient to maintain optimal nutrient intake.[3] Please see Chapter 14, "Enteral Nutrition" for enteral nutrition methods and formula choices.

Parenteral Nutrition

The use of PN in the pediatric oncology patient is well accepted in the setting of a poorly functioning gastrointestinal tract.[3] Even children who depend on PN for the majority of their nutritional intake may benefit from small amounts of enteral nutrition due to its stimulatory effects on the gastrointestinal mucosa. Limited evidence has shown that PN in the pediatric oncology patient improves weight gain, serum albumin, and adequacy of intake compared to EN.[12] PN is routinely used following HSCT, although further studies need to be done to evaluate its clinical impact, given its associated risks. Childhood cancer patients are often at greater risk for infection and toxicity due to the cumulative effect of their disease and treatments. More details of PN management are outlined in Chapter 15, "Parenteral Nutrition."

◆ LATE EFFECTS

Childhood cancer survivors face a wide variety of long-term side effects. Children treated for ALL are generally at a higher risk for overweight and obesity, especially those receiving radiation treatment, while survivors of other cancers have greater odds of being underweight.[4] Growth hormone deficiency leading to a reduction in height potential is also described in childhood cancer survivors, especially among those treated with radiation at a young age.[4] Other long-term problems associated with childhood cancer treatment include bone loss, cardiovascular disease,

and neurologic problems.[4] Attention directed to developing and maintaining healthy lifestyle habits is important, and ongoing nutrition assessment and intervention should be encouraged.

CONCLUSION

Nutritional assessment and intervention during pediatric cancer treatment is imperative to assure appropriate growth and development as well as optimal quality of life. While prevention and treatment of malnutrition remain important concerns for children with cancer, preemptive strategies for managing excessive weight gain and other late effects of survivorship are also essential tools for the nutrition clinician.

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34 Prematurity

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Advances in neonatology over the past several years have led to decreased mortality rates for premature infants surviving as young as 23–24 weeks gestational age. The premature infant is born with limited nutrient stores and increased energy needs (Table 34–1). Unfortunately, the physiologic demands of prematurity may lead to delayed or disrupted nutrient delivery, resulting in further nutritional deficits. Research has shown that postnatal growth restriction increases the risk for impaired neurological development.[1] Complications of prematurity such as osteopenia and respiratory distress put additional stress on the optimal delivery of nutrition (Table 34–2). Neonatal intensive care units continue to strive to maintain intrauterine growth rates despite these challenges.

Table 34–1 Nutritional Risk Factors in Prematurity

Increased nutritional demands
• Rapid growth phase
• Tissue development
• Stresses of medical/surgical course

• Prolonged illness • Poor temperature control, cold stress • Increased metabolic demand of SGA infants
Immature organ function • Immature GI tract • Use of nutrients may be decreased • Glucose instability • Renal immaturity
Poor nutrient stores • Cessation of placental nourishment interrupts natural fetal accretion • Delay in starting parenteral or enteral nutrition support
Altered feeding patterns • Suck/swallow/breathe coordination develops at 32–34 wk GA • Transition from nasogastric (NG) tube to feeding at breast—may be assisted by lactation consultant and occupational therapy • Prolonged nil per os (NPO) status for infants with chronic lung disease, CHD, and NEC

Abbreviations: SGA, small for gestational age; GI, gastrointestinal; GA, gestational age; NG, nasogastric; NPO, nil per os; CHD, congenital heart disease; NEC, necrotizing enterocolitis.

Table 34–2 Medical Risk Factors in Prematurity

NEC • Over 90% of cases occur in premature infants • Acquired ischemic GI disease of undetermined etiology, likely multifactorial • Cause may be related to feeding rate, volume, or substrate provided • Presents as mild feeding intolerance (NEC watch) to extreme necrotic bowel with perforation requiring surgical intervention • Treatment can include 10–14 days NPO, TPN, gradual reintroduction of feeds

(*Continued*)

Table 34–2 Medical Risk Factors in Prematurity (*Continued*)

BPD • Chronic lung disease secondary to extended mechanical ventilation and/or O_2 support • Potential for growth failure, increased metabolic demand • May require increased calories (130–160+ kcal/kg/d) • May require fluid restriction, increased caloric concentration of feeding • Steroids used in treatment may impede growth • Increased risk of osteopenia (diuretics, steroids, losses of Ca and PO4) • Increased WOB and/or decreased suck/swallow efficiency may increase energy needs
Osteopenia of prematurity • Decreased bone mass because of inadequate provision of mineral substrate • Ranges from mild demineralization to nontraumatic bone fractures • May impair linear growth • Risk increased with medications that cause mineral excretion, decreased absorption (diuretics, steroids), long-term TPN use because of low calcium/phosphorus allowed in solution, immobility
Developmental Delay • Multifactorial in cause—genetic, intraventricular hemorrhage, medications, long-term hospitalizations • Can impair oral intake, affect GI function • May increase nutritional needs and/or demands • Potential to disrupt appropriate growth

Abbreviations: TPN, total parenteral nutrition; BPD, bronchopulmonary dysplasia; WOB, work of breathing.

NUTRITIONAL ASSESSMENT

Nutritional assessment and therapy in premature infants must begin immediately after birth. The New Ballard Score, a revision of the original Ballard tool, is used to determine

gestational age (GA) through procedures developed by Jeanne L. Ballard, MD via neuromuscular and physical assessment of a newborn fetus. It was expanded in 1991 to include extremely premature neonates and increase accuracy of the original tool.[2] This information as well as measurement of birth weight, length, and head circumference provides the basis for the initial nutrition assessment (Table 34–3). There are many references available to assess the intrauterine and postnatal growth of a premature infant, but no single set is used exclusively. Intrauterine growth charts should be used to assess whether the infant has intrauterine growth restriction (IUGR), is small for gestational age (SGA), appropriate for

Table 34–3 Prematurity and Birth Weight Classifications

Maturity by GA
Preterm: <37 wk
Term: 37–42 wk
Postterm: >42 wk
Birth weight
Low birth weight: <2500 g
Very low birth weight (VLBW): <1500 g
Extremely low birth weight (ELBW): <1000 g
Birth weight for GA
IUGR: weight <third percentile (intrauterine growth restriction)
SGA: weight <10th percentile (small for GA)
- asymmetric SGA: weight only < 10th percentile - acute malnutrition or placental insufficiency, has potential for catch up growth
- symmetric SGA: w\eight, length, head circumference <10th percentile - prolonged malnutrition, genetic processes, or congenital anomalies, has less potential for catch up growth
AGA: weight 10th–90th percentile (appropriate for GA)
LGA: weight > 90th percentile (large for GA)

gestational age (AGA), or large for gestational age (LGA). Lubchenco intrauterine growth charts should be used at birth to assess intrauterine growth for infants born ≥36 weeks. Fenton growth curves combine intrauterine growth with postnatal growth, resulting in a "fetal-infant" growth curve and can be used for infants born at <36 weeks gestation to assess intrauterine growth and to plot postnatal growth until 50 weeks postmenstrual age (PMA).[3] Postnatal growth should continue to be monitored on World Health Organization (WHO) Child Growth Standards for infants born at >36 weeks. Infants born at <36 weeks should be transitioned to the WHO growth charts once they reach 50 weeks PMA.[4]

The "gold standard" for postnatal growth of premature infants remains the expected rate of weight gain seen in utero (Table 34–4). An infant's corrected age (CA) is the chronologic age adjusted by (i.e., "corrected by") the number of weeks of prematurity. For example, a premature infant who is born at 32 weeks GA is born 8 weeks early (40 weeks full term – 32 weeks GA = 8 weeks). At a chronological age of 12 weeks, this infant would have a CA of 4 weeks (12 weeks of age – 8 weeks premature = 4 weeks CA). This infant's weight, length, and head circumference should, therefore, all be plotted at the 4-week position on the WHO curves.

Table 34–4 Growth Parameters

Birth weight	Weight gain
<2 kg	15–30 g/d or 10–20 g/kg/d
<2kg	15–30 g/d
>2 kg	>20 g/d
Length gain: 0.7–1.1 cm/wk	
Head circumference: 0.5–1 cm/wk	
After CA of 40 wk/full term: weight gain may be similar to that of full-term infant	

NUTRITION THERAPY

The initiation of PN is indicated for premature infants during periods of bowel rest (>3–5 days) and with other GI malformations, whereas enteral feeding is contraindicated including severe hemodynamic instability, NEC, or other congenital bowel anomalies. PN support should begin within the first few hours of life, once urine output is established and electrolytes are stable, to prevent catabolism and hypoglycemia secondary to limited glycogen stores.[5] The solution should provide recommended fluid and nutrient estimates (Table 34–5) until enteral feeds can be established.

Table 34–5 Parenteral Nutrition in Premature Infants

Fluid requirements

- Premature infants have greater ECF volumes
- Initial diuresis occurs within first week of life
- 10%–15% loss of body weight for premature infants, can be up to 20% for ELBW infants
- Initial fluid requirements: 80–140 mL/kg/d
- ELBW infants may require up to 200 mL/kg/d
- Goal after fluid stabilization: 100–150 mL/kg/d
- Fluid restriction may be required for infants with PDA, BPD, CHF, renal failure, cerebral edema
- Insensible water loss increases with
  - increased skin permeability at birth
  - increased BSA to weight ratio
  - phototherapy
  - radiant warmer beds
  - respiratory distress syndrome
  - cold stress, increased activity

(*Continued*)

Table 34–5 Parenteral Nutrition in Premature Infants (*Continued*)

- Insensible water loss decreases with
  - heat shields
  - humidified incubators
- Fluid loss also results from
  - vomiting
  - diarrhea
  - ostomy output
  - chest tube drainage

Carbohydrate

- Initial glucose load: 4–6 mg/kg/min
- Adjust by 2 mg/kg/min as tolerated, advancing to meet nutritional need
- Limit to <14 mg/kg/min to prevent overfeeding, fatty liver, increased CO_2 production
- May require >14 mg/kg/min if on 1 g/kg lipid restriction to meet energy needs

Protein

- Infants <1500 g BW: begin at 2 g/kg/d, advance to goal of 4 g/kg
- Infants >1500 g BW: begin at 2 g/kg/d, advance to goal of 3 g/kg
- Research has shown that starting at 3 g/kg/d is safe and prevents negative nitrogen balance

Fat

- Begin at 1 g/kg/d and advance by 1 g/kg/d to goal of 3 g/kg.
- Maintain at 1 g/kg/d in patients who are anticipated to remain on PN > 3 wk to reduce risk of PN-associated liver disease
- May run lipid via central or peripheral access, over 12–24 hours
- Monitor with serum triglyceride, tolerate <250 mg/dL
- EFAD may occur in < 1 week without lipid source; provide minimum 0.5 g/kg/d to prevent

Total energy needs • 90–100 kcal/kg/d for VLBW and SGA infants • 80–90 kcal/kg/d for >28 wk and AGA
Additives Na 2–4 mEq/kg/d Ca: 60–90 mg/kg/d K 2–4 mEq/kg/d PO4: 47–70 mg/kg/d Cl 2–3 mEq/kg/d Mg: 4.3–7.2 mg/kg/d
MVI Pediatric: < 1 kg: 30% of standard 5 mL 1–3 kg: 65% of standard 5 mL > 3 kg: 100% of standard 5 mL

Abbreviations: ECF, extracellular fluid; PDA, patent ductus arteriosus; CHF, congestive heart failure; BSA, body surface area; BW, birth weight; EFAD, essential fatty acid deficiency; MVI, multivitamin.

Amino acid requirements in premature infants are different both qualitatively and quantitatively from term infants and older children. Many amino acids are considered conditionally essential and are not synthesized in sufficient quantities for the premature infant as they are in term infants. A specialized amino acid blend, designed to approximate the blood amino acid profile of the breast-fed infant, is used for the preterm infant.[6] Extreme premature and/or ELBW infants have increased rates of protein turnover, therefore, requiring higher protein intake compared to term infants to achieve ideal growth velocity.[5]

A 20% lipid solution is recommended as a high-density energy source as well as to supply the essential fatty acids (EFA), linoleic acid and its metabolites, and α-linolenic acid and its metabolites. Hypertriglyceridemia, fasting serum triglyceride level >250 mg/dL, may require a decrease in the infusion of lipids or cycling over 20 hours. Recent data

suggests that reducing parenteral fat intake to 1 g/kg/d and/or providing fish oil-based intravenous fat emulsions may reduce PN-associated liver disease, a common condition among premature infants with prolonged PN exposure. Serum fatty acid profiles should be closely monitored in infants receiving such restricted parenteral fat intakes, especially if enteral fat intake is minimal.[7,8] In addition, parenteral calories need to be maintained to achieve normal growth rates, which imply that high glucose infusion rates need to be tolerated. See also Chapter 16, "Parenteral Nutrition."

Protein, fat, and carbohydrate should be advanced daily while monitoring daily laboratory values until estimated needs are met. Thereafter, weekly nutrition panels that include chemistries, liver function tests, and a complete blood count, are used to evaluate the adequacy of the prescribed regimen. Macronutrients are calculated based on fluid volume as well as individual needs that are assessed using energy expenditure equations.

Enteral nutrition should generally begin in the first 24–48 hours of life.[1,9] The GA of the infant will affect the decision to feed by mouth or tube since suck/swallow/breathe coordination does not develop until 32–34 weeks gestation (Table 34–6). Feeding initiation and advancement is based on clinical status with close attention to feeding tolerance. Most premature infants begin with "trophic feeds," low-volume feedings of 10–20 mL/kg/d, to stimulate GI hormones, motility and maturation[(5,9)]. The typical practice is to advance the feeding rate slowly to prevent the development of NEC, although a recent Cochrane review found no evidence that slow feeding advancement reduced the risk of NEC.[10] The ability to take "full feeds" is dependent on many factors, including maturity of the GI tract, stomach capacity, and respiratory status (Table 34–7).

Table 34–6 Enteral Feeding Methods

Indications for nipple feeding
• Minimum 32–34 wk postconceptual age, although some infants may do well at the breast earlier • Coordinated suck/swallow/breathe pattern is present • Infant is free of apnea and bradycardia • Respiratory rate <60 breaths/min • Infant may benefit from gradual transition from gavage to nipple feeding • Consider partial gavage feeding if infant takes >30 min/feed to prevent excess energy expenditure
Indications for NG/orogastric (OG) tube feeding
• Infant <32 wk GA, poor suck/swallow/breathe coordination • Respiratory rate >60 breaths/min • No gag reflex evident • Continuous - may be better tolerated in smaller infants - for infants with previous intolerance to bolus feeds - requires less frequent tube change, less disruption to baby - may require less energy expenditure than bolus - may decrease risk of aspiration - may prevent increase in respiratory rate (vs. bolus) • Bolus - every 2–3 h - may improve gastric emptying - allows hunger/satiety, can alternate with nipple feeds - allows more mobility, parents can hold and provide care more easily
Indications for transpyloric feeding
• Consider for infants with intolerance to gastric feeding, GER, risk for aspiration, nasal CPAP • Requires continuous feeding • Placement of tube is more difficult

(*Continued*)

Table 34–6 Enteral Feeding Methods (*Continued*)

Indications for G-tube feeding
• For infants who will be unable to nipple feed for several months • May prevent oral aversion associated with long-term NG tube feeding

Abbreviations: GER, gastroesophageal reflux; CPAP, continuous positive airway pressure ventilation; G-tube, gastrostomy tube.

Table 34–7 Enteral Nutrition: Feeding Advancement and Goals

Feeding initiation and advancement
• 10–30 mL/kg/d based on clinical status
Warning signs of feeding intolerance
• Increase in gastric residuals to > twice previous hour's rate (continuous feed) or > half the previous bolus • Increase in abdominal distention/girth • Vomiting • Bilious residuals and/or vomiting • Heme positive/frank blood in stools • Reducing substances >0.5% • Increase in apnea/bradycardia with feeds
Energy goal
• 110–130 kcal/kg/d • Some infants may have increased needs up to 150–160 kcal/kg (BPD, SGA)
Protein goal
• 3.0–4.0 g protein/kg/d
Caloric distribution
• PRO: 8%–12% calories • CHO: 40%–55% calories • Fat: 35%–50% calories
Calcium
• 120–230 mg/kg/d

Phosphorus • 60–140 mg/kg/d
Multivitamin • Infants receiving unfortified breast milk or consuming <32 oz/d of infant formula should receive 400 IU daily of vitamin D • Infants receiving breast milk with human milk fortifier or premature formula do not usually require multivitamin supplementation • Preterm infants receiving breast milk exclusively should receive multivitamin supplementation including 400 IU vitamin D
Iron • Preterm infants are born with low stores and are subject to many blood draws • Infant should generally be at full feeds (150 mL/kg/d at 24 kcal/oz) before start of supplementation

Abbreviations: PRO, protein; CHO, carbohydrates; IU, international units.

Milk is the preferred feeding choice for nearly all infants, including premature infants (see Chapter 6, "Breastfeeding and Human Milk"). Fortification of breast milk with human milk fortifiers is recommended for all infants born <34 weeks GA or with a birth weight of <1500 g. Generally, human milk fortifiers are added when tolerance to breast milk has been established and feeds reach a volume of 100 mL/kg. It may also be necessary for premature infants who have been on PN >2 weeks (due to the risk of osteopenia from low Ca/PO4 ratio in PN), have suboptimal growth, and/or who are fluid restricted.[11] Further fortification may be required if poor growth is noted. A variety of additives can be used to meet estimated needs and should be prescribed on an individual

basis (Table 34–8). Ensuring appropriate macronutrient and micronutrient composition, including Ca, PO4, and iron, should be considered when deciding which additives to use.[12] If mother's breast milk is not available, the use of donor human milk should be considered. Donor human milk is preferred for high-risk neonates, including neonates <32 weeks gestation, <1500 g, infants with a history of NEC, or infants at risk of developing ischemic bowel.[13]

Table 34–8 Enteral Nutrition: Choice of Feeding Substrate

Breast milk may require supplementation for premature infants • Volume of breast milk required to meet protein, energy, Ca, PO4, Mg, and other vitamin and mineral needs is high • Fat in breast milk may adhere to the NG/OG tubing, which decreases available calories and EFA
Fortification of breast milk: • Powder human milk fortifier: - adds protein, carbohydrate, vitamins, and minerals - increases to 22 and 24 cal/oz - preferred when adequate amount of breast milk is available • Liquid human milk fortifier: - higher protein than powdered form - commercially sterile - increase to 22 and 24 cal/oz • Liquid concentrated donor milk fortifier: Prolacta - made from 100% human milk with additional Ca and PO4 - increase to 24, 26, 28, and 30 cal/oz • Tolerance - continue to monitor nutrition labs, especially Ca, PO4, and alkaline phosphatase - ELBW infants at increased risk for hypercalcemia

Breast milk fortifiers are indicated for:

- Infants born at <34 wk GA and/or <2 kg
- Infants with increased needs who are fluid restricted
- Hospital use only because of increased vitamin/mineral content
- Bottle or tube feeds until infant is:
  - taking sufficient volume at the breast
  - >34 wk GA and/or ≥2 kg
  - can use until infant reaches 3–4 kg or discharged if ELBW

Premature formulas

- Alternative to fortified breast milk when breast milk is not available
- Preferred for its composition, increased calories, protein, Ca, PO4
- Available in 20, 24, and 30 cal/oz, RTF
- PRO: whey predominant, 50% more than term formulas
- Fat: 40%–50% MCT oil may improve fat absorption and weight gain
- CHO: 40%–50% lactose, 50%–60% glucose polymers
- Same guidelines as breast milk fortifiers for transition off premature formula

Premature discharge formulas (transition formulas)

- Use when continued fortification is recommended for smaller, more premature infants
- Vitamin and mineral fortified
- Contain lactose and MCT oil
- Designed for home use up to 12 months of age
- RTF is 22 cal/oz
- Powder may be added to fortify breast milk
- Can transition to standard term formula when catch up growth is established

(*Continued*)

Table 34–8 Enteral Nutrition: Choice of Feeding Substrate (*Continued*)

Standard term, cow's-milk-based formulas • Not recommended for premature infants; does not meet nutritional needs for minerals, protein • May be provided for AGA infants >34 wk GA and >2.0 kg at birth • May be provided for growing premature infant >34 wk CA and >2.0–2.5 kg, who is ready for discharge home
Standard soy-based formulas • Not recommended for premature infants • Low bioavailability of Ca and PO4, adverse effects on bone • May be indicated for lactose intolerance, galactosemia, secondary lactose intolerance - would require vitamin/mineral supplementation - may require caloric concentration
Therapeutic formulas • Include protein hydrolysates, free amino-acid-based, or high MCT-containing formulas • Not recommended long term for premature infants because of suboptimal nutrient composition; may need to fortify if used
Modulars • When increased energy demands require further supplementation • MCT oil, corn oil, carbohydrate, and/or protein supplements may be added to 24 cal/oz fortified breast milk/formula • Attention must be paid to distribution of calories, osmolality, renal solute load

Abbreviations: RTF, ready to feed; MCT, medium chain triglyceride.

If human milk is not available, these infants will require a premature infant formula. These formulas have been designed to match some of the developmental aspects of

the premature human GI tract, including relative exocrine pancreatic immaturity, lowered lipase production, reduced bile acid pools, and possibly lower concentrations of lactase. The protein source is whey predominant and supplemented with taurine. Carbohydrates are provided in a mix of 40%–50% lactose and 50%–60% glucose polymers. Medium chain triglycerides provide 40%–50% of the fat source in these formulas. These formulas also contain higher concentrations of vitamins, minerals, and electrolytes to meet the demands of the preterm infant.

Growing preterm infants who are fed human milk require a source of elemental iron to provide 2–4 mg/kg/d after 1 month of age. This can be provided using iron-fortified complementary foods, or by using a supplement. Iron-fortified formulas provide 1.8 to 2.2 mg/kg/d when receiving 150 mL/kg/d. Low iron formulas are not recommended. There is no general recommendation at this time, but some preterm infants on iron-fortified preterm formula may need additional iron. Supplementing >2 mg/kg/d may be considered because of noncompensated blood loss or prolonged feeding intolerance.[14] Infants who received multiple blood transfusions during hospitalization may not need any iron supplementation.[15]

DISCHARGE PLANNING

Premature infant formulas and human milk fortifiers are not recommended for home use because of their higher concentrations of vitamins and minerals designed to meet the increased needs of infants who take smaller volumes of milk. Close to hospital discharge, nonbreast-fed infants should be transitioned to specially designed, so-called transition formulas for home. Transition formulas are designed to provide a higher concentration of protein, vitamins, and

minerals than normal term infant formulas but less than that found in premature infant formulas and human milk fortifiers to prevent excess intake. Transition to a safe and appropriate home feeding regimen is required. Referral to a community lactation consultant; Special Supplemental Food Program for Women, Infants, and Children; Early Intervention Program; and/or home-health nursing may be beneficial for assistance with feeding skills and weight checks and may help ensure optimal nutritional outcomes.[11]

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35 Renal Disease

Nancy Spinozzi, RD, LD

Chronic kidney disease (CKD) occurs when renal function has deteriorated, so that glomerular filtration rate (GFR) is reduced and progression to end-stage renal disease (ESRD) is inevitable. ESRD usually denotes the point at which conservative management of the patient is no longer effective and renal replacement strategies (dialysis and transplantation) are necessary. The major cause of ESRD in children is obstructive uropathy followed by aplastic, hypoplastic, and/or dysplastic diseases of the kidney (primarily in younger children, 0–4 years of age).[1] In 2008, the National Kidney Foundation, Inc. published updated Kidney Disease Outcomes Quality Initiative (KDOQI) pediatric nutrition clinical practice guidelines for practitioners treating children with CKD stages 2 to 5.[2] These included recommendations for nutritional evaluation and therapy. Table 35–1 lists the nutritional and metabolic consequences of CKD in children and provides guidelines for treatment.

Nutritional assessment of the child with CKD is complex and is necessary to perform on a frequent, regular basis.[3]

Table 35–1 Nutritional and Metabolic Consequences of Chronic Renal Failure

Problem	Etiology	Treatment
Protein/energy malnutrition	Anorexia/dysgeusia Caloric requirements >normal RDA	Protein/energy supplementation[4,5] Appetite stimulant[8] Tube feeding
Acidosis	Tubular dysfunction (bicarbonate loss)	Oral base solutions: sodium bicarbonate, Bicitra
Salt-wasting	1° (e.g., Obstructive uropathy, cystic diseases)	Sodium supplementation
Renal osteodystrophy[6]	Decreased PO_4 excretion leading to decreased serum Ca^{++} resulting in increased PTH secretion, ultimately leading to secondary hyperparathyroidism	Decrease PO_4 intake PO_4 binders(e.g., Ca^{++} carbonate, Ca^{++} acetate, sevelamer, lanthanum carbonate)[9]
	Decreased renal conversion of 25 hydroxycholecalciferol to 1,25-dihydroxycholecalciferol (calcitriol)	Provide active form of vitamin D (e.g., 1,25 dihydroxycholecalciferol, dihydrotachysterol)
Adynamic bone disease	Overdosing calcitriol may suppress osteoblastic activity	Avoid excessive reduction in parathyroid hormone
Hyperkalemia[7]	Decreased renal excretion	Decreased intake Sodium polystyrene sulfonate (Kayexalate/ Kionex)[10] Correct acidosis
Hypermagnesemia	Decreased renal excretion	Decreased intake Avoid Mg-containing antacids or laxatives

(*Continued*)

Table 35–1 Nutritional and Metabolic Consequences of Chronic Renal Failure (*Continued*)

Problem	Etiology	Treatment
Growth retardation	Growth hormone resistance	Growth hormone (rhGH)[11,12]
HTN or fluid retention[7]	Increased angiotensin II formation Volume-sensitive HTN	Decrease sodium intake (no-added-salt diet) ± fluid restriction Antihypertensives
Anemia	Decreased production of erythropoietin	Erythropoietin (rhEPO) Iron supplementation
Hypovitaminosis	Water soluble vitamins lost in dialysate Malnutrition	Supplement with water soluble vitamins only (e.g., Nephrocaps*, Nephronex†-both examples of dialysis vitamins) or MVI with the addition of 0.5–1.0 mg folate (for age)
Elevated homocysteine levels	Most likely because of antioxidant deficiency	Folate, B_6 and B_{12} supplementation
Hypervitaminosis A	Impaired retinol-binding protein excretion	Avoid vitamin A supplementation
Renal oxalate stones	Reduced clearance	Avoid vitamin C supplements and oxalate-rich foods
Dialysis-related carnitine disorder[13]	Reduced intake of carnitine-rich foods Reduced renal synthesis Continuous loss through maintenance dialysis	Use of intravenous levocarnitine only-Recommendations remain controversial at this time[2]

*Fleming Laboratories, Fenton, MO.
†Llorens Pharmaceutical Corp., Miami, FL.

Growth retardation is a common occurrence in CKD; therefore, all aspects of a child's potential growth characteristics must be taken into account. Table 35–2 outlines the specific aspects of nutritional assessment.

Once initial nutritional assessment is complete, recommendations must be consistent to ensure optimal nutrition within the limitations of kidney function.[4,5] There are currently no data to show that a reduced protein intake (recommended-dietary allowance (RDA) for age) will delay the progression of ESRD in pediatric patients. Protein and

Table 35–2 Special Aspects of Nutritional Assessment in Renal Disease

History
Diagnosis
Primary disease, if known
Current renal replacement modality (conservative, dialysis, transplant)
Diet recall
Calories
Protein
Electrolytes (Na^+, K^+, Mg)
Vitamins, minerals (Ca^{+2}, PO_4)
Fluid intake
Medications
Physical
Height
Weight-fluid dependent; must determine "dry" weight
Head circumference
MAMC and TSF
Laboratory
BUN, Cr, Na, K, glucose, PO_4, Ca^{++}, Mg, albumin, CO_2, hematocrit, triglycerides, cholesterol

Abbreviations: MAMC, mid-arm muscle circumference; TSF, triceps skinfold.

energy recommendations are based on the RDA for height age.[2] Tables 35–3 and 35–4 review some critical issues related to providing adequate enteral nutrition.

Table 35–3 General Considerations for Enteral Feedings in Renal Disease

Determine fluid allowance and metabolic status, GFR.
Formula feedings will likely need to be calorically dense, since infant's complete nutrition source is fluid.[14,15]
Increase caloric density of formula and feeds through carbohydrate and fat modules vs. concentration (which will increase renal solute load)[4]
Gastroesophageal reflux can be a major problem for infants with CKD.[16] Tube feedings are often necessary to ensure adequate intake of nutrients. Continuous nighttime infusions are usually well tolerated.
Monitor weight, blood urea nitrogen, electrolytes, albumin, and lipids and adjust feeds and diet as necessary (at least monthly).

Table 35–4 Nutritional Products Specific for Renal Patients

Product/Manufacturer	Comments
Similac PM 60/40 (Ross)	Infant formula reduced in electrolytes, Ca^{++}, PO_4
Amin-Aid (R&D Laboratories)	Low protein, calorically dense tube feeding with minimal electrolytes
Nepro (Ross)	Moderate protein, calorically dense supplement
Suplena (Ross)	Low protein, calorically dense supplement
Renalcal Diet (Nestle)	Low protein, calorically dense formula with minimal electrolytes
Osmolite (Ross)	Tube feeding with reduced electrolytes

PARENTERAL NUTRITIONAL (PN) CONSIDERATIONS IN RENAL DISEASE

Of major consideration when prescribing PN is the volume of fluid available to provide adequate nutrition. Fluid may be severely restricted because of oliguria/anuria, resulting in the need for very hypertonic solutions. As with enteral intake, energy and protein intake via PN should be guided by the RDA for height age. A mixed amino acid solution is well tolerated in renal patients. The utility of specially formulated amino acid solutions for renal patients is controversial.

CKD patients should begin with a parenteral solution without added K^+, Mg^+, and PO_4; these can then be titrated according to serum levels. Because of decreased intake of PO_4 and other cations, malnourished renal patients should be closely monitored for the refeeding syndrome (see Chapter 13, "Nutritional Assessment in Sick or Hospitalized Children"). Since some micronutrients (e.g., vitamin A, selenium) are excreted primarily through the kidneys, long-term use of standard parenteral multivitamins (MVIs) may lead to toxicities. Parenteral supplementation with folate, vitamin C, and B complex vitamins is recommended instead.

NUTRITIONAL CONSIDERATIONS IN THE POST-RENAL TRANSPLANT PATIENT

Transplantation is highly encouraged for all suitable children, eventually providing them a more normal lifestyle. It is important to monitor a patient's renal function after transplantation when planning nutritional support.[6,7] There may be a slow recovery of normal kidney function for a period of time after transplant; therefore, continuation of pretransplant diet restrictions may be indicated. Infants may develop a postoperative ileus; PN should be considered if feeding intolerance is anticipated to last for more than 5 days.

Table 35–5 Phosphorus Supplements

Supplement	Phosphorus Content
KPhos-Neutral	250 mg/tab
KPhos	114 mg/tab
Neutra-Phos	250 mg/packet

Immunosuppressive drugs may cause side effects that will impact on dietary recommendations, including hyperkalemia, hypophosphatemia, increased appetite, hypertension (HTN), glucose intolerance, gastric irritability/diarrhea, and hyperlipidemia. Most children, however, will initially require only a no-added-salt diet after transplantation (see Appendix 2, "Drug-Nutrient Interactions"). Hypophosphatemia is a common finding after transplantation, especially in older children, and usually requires PO_4 supplementation. Table 35–5 lists commonly prescribed phosphate supplements. In preparation for discharge, diet instruction should include a healthy diet for age and education related to food safety and immunosupression[2] (as per "Food Safety for Transplant Recipients" available from U.S. Department of Agriculture).

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APPENDIX 1
CONVERSION TABLES (APPROXIMATE)

Mass Weight

Avoirdupois to Metric Weight Conversions

1 ounce	=	28 g
1/4 pound	=	0.11 kg
1/2 pound	=	0.23 kg
3/4 pound	=	0.34 kg
1 pound	=	0.45 kg
1 g	=	0.036 oz
1 kg	=	2.2 lb

To convert ounces to grams, multiply by 28; grams to ounces, divide by 28. To convert pounds to kilograms, multiply by 0.45; kilograms to pounds, multiply by 2.2.

Length

1 inch	=	2.54 cm
1 foot	=	30.5 cm
1 yard	=	0.91 m
1 mile	=	1.61 km
1 mm	=	0.04 in
1 cm	=	0.4 in
1 m	=	3.3 ft
1 m	=	1.1 yd
1 km	=	1093.7 yd
1 km	=	0.62 miles
1 km	=	3281 ft

To convert inches to centimeters, multiply by 2.54; centimeters to inches, multiply by 0.4

Area

1 sq in	=	6.5 sq cm
1 sq ft	=	0.0929 sq m
1 sq yd	=	0.84 sq m
1 sq cm	=	0.16 sq in
1 sq m	=	1.2 sq yd
1 cu ft	=	1728 cu in
1 cu yd	=	27 cu ft

Liquid

Apothecary—Metric Equivalents

1 tsp	=	5 mL		
1 tsp	=	15 mL		
1 fl oz	=	30 mL		
8 fl oz	=	236 mL		
16 fl oz	=	473 mL	=	1 pt
32 fl oz	=	946 mL	=	1 qt
128 fl oz	=	3795 mL	=	1 gal
1 mL	=	0.03 fl oz		
1 L	=	1000 mL	=	1.06 qt

To convert milliliters to ounces, divide by 30; ounces to milliliters, multiply by 30.

Temperature

	Celsius (C)	Fahrenheit (F)
Water freezes	0	32
Room temperature	22	72
Body temperature	37	98.6
Water boils	100	212

To convert Fahrenheit to Celsius (centigrade), subtract 32, multiply by 5, divide by 9;

Celsius (centigrade) to Fahrenheit, multiply by 9, divide by 5, and add 32.

Energy

1 kilojoule (kJ) = 0.239 kcal

1 kilocalories (kcal) = 4.190 kJ

To covert kilocalories to kilojoules, multiply the kcal value by 4.2.

Nitrogen to Protein

$$\text{Grams of Nitrogen} = \frac{\text{Grams of Protein}}{6.25}$$

Milliequivalent-Milligram Conversion Table

Mineral Element	Chemical Symbol	Atomic Weight	Valence
Bicarbonate	HCO_3	61	1
Calcium	Ca	40	2
Chlorine	Cl	35.4	1
Magnesium	Mg	24.3	2
Phosphorus	P	31	2
Phosphate	PO_4	95	3
	HPO_4	96	2
	H_2PO_4	97	3
Potassium	K	39	1
Sodium	Na	23	1
Sulfur	S	32	2
Sulfate	$S0_4$	96	2
Zinc	Zn	65.4	2

$$\text{Milliequivalents} = \frac{\text{Milligrams}}{\text{Atomic Weight}} \times \text{Valence}$$

Example: convert 2000 mg sodium to mEq of sodium

$$\frac{2000}{23} \times 1 = 87 \text{ mEq sodium}$$

To change milliquivalents back to milligrams, multiply the milliequivalents by the atomic weight and divide by the valence.
Example: convert 20 mEq sodium to mg sodium

$$\frac{20 \times 23}{1} = 460 \text{ mg sodium}$$

Milliequivalents for Selected Salts

Salt	mEq/g Salt	mg Salt/mEq
Ammonium chloride	18.7	53.5
Calcium acetate	12.7	78.7
Calcium carbonate	20	50
Calcium chloride	14	73
Calcium glubionate	3.2	312.5
Calium gluconate	4	224
Calcium gluceptate	4.1	244
Calcium lactate	6	154
Magnesium chloride	9.8	102
Magnesium oxide	49.7	20
Magnesium sulfate	8.2	122
Potassium acetate	10	98
Potassium bicarbonate	10	100
Potassium chloride	13	75
Potassium citrate	9	108

Salt	mEq/g Salt	mg Salt/mEq
Potassium gluconate	4.3	233
Potassium iodide	6	166
Sodium acetate	7.3	137
Sodium bicarbonate	12	84
Sodium chloride	17	58.8
Sodium citrate	10	98
Sodium iodide	7	150
Sodium lactate	9	112
Zinc sulfate	7	144

Clinical Chemistry **SI Conversion Factors**

	Conventional Units	Conversion Factor (multiply)	SI Units
Alkaline phosphatase	IU/L	1.0	U/L
ALT	U/L	1.0	U/L
Albumin	g/dL	10.0	g/L
Ammonia (NH4)	µg/dL	0.5872	µmol/L
AST	U/L	1.0	U/L
Bilirubin	mg/dL	17.10	µmol/L
Calcium	mg/dL	0.25	mmol/L
Carbon dioxide	mEq/L	1.0	mmol/L
Chloride	mEq/L	1.0	mmol/L
Cholesterol	mg/dL	0.026	mmol/L
Copper	µg/dL	0.16	µmol/L
Creatinine	mg/dL	88.40	µmol/L

(*Continued*)

Clinical Chemistry **SI Conversion Factors *(Continued)***

	Conventional Units	Conversion Factor (multiply)	SI Units
Glucose	mg/dL	0.055	mmol/L
Magnesium	mEq/L	0.5	mmol/L
Osmolality	Osm/kg	1.0	mmol/L
Phosphorus	mg/dL	0.323	mmol/L
Potassium	mEq/L	1.0	mmol/L
Protein, total	g/dL	10.0	g/L
Sodium	mEq/L	1.0	mmol/L
Triglycerides	mg/dL	0.011	mmol/L

APPENDIX 2
DRUG-NUTRIENT INTERACTIONS

KATHLEEN M. GURA, PHARM.D., BCNSP

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Antiarthritic				
Adalimumab (Humira®)		N, abdominal pain	↑ Cholesterol, ↑ alk phos	
Anticoagulants				
Coumarins (warfarin, Coumadin®)	Vitamin K antagonist. Concomitant use of warfarin with vitamin K may decrease anticoagulant effects; high doses of vitamin A, E, or C may alter prothrombin time; fried or boiled onions may ↑ drug effect by ↑ fibrinolytic activity	N/V/D;* hemorrhage anorexiabalsa	Increased bleeding time	Consistent intake of vitamin K essential; breast-fed infants may be more sensitive to warfarin due to low amounts of vitamin K in breast milk; herbal teas/tonka beans/ melilot and woodruff contain natural coumarins and will ↑ warfarin effects

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Antidiabetic				
Acarbose (Precose®)	Do not take with pancreatic enzymes	Abdominal pain, diarrhea, flatulence	↓ Fasting glucose, ↓ postprandial glucose, ↓ HCT, ↓ HbA1c, ↑ AST, ↑ ALT	Take with first bite of each main meal. Titrate dose to ↓ GI side effects. Do not take with pancreatic enzymes
Antihistamine Drugs				
Cyproheptadine (Periactin®)	Appetite stimulant; increased weight gain and growth rate; administration with food increases drug bioavailability	Xerostomia; N/V/D abdominal pain, increased appetite	May interfere with response to diagnostic antigen skin tests; ↑ amylase; ↓ fasting glucose	
Loratadine (Claritin®)				
Anti-infective Drugs				
Antibiotics: General	Decreased synthesis of vitamin K by gut microflora; depletion of gut microflora can also lead to dysbiosis that can alter the digestion and absorption of nutrients; some antibiotics are folate and B12 antagonists	N/V/D; lactase deficiency	Anemia	

Aminoglycosides	Increased urinary excretion of potassium and magnesium; may also deplete sodium and calcium	Decreased appetite, N/V, increased salivation	↑ BUN, ↑ AST, ↑ ALT, ↑ LDH, ↑ bilirubin; ↓ calcium, ↓ magnesium, ↓ potassium, ↓ sodium	
Amoxicillin: Amoxicillin/Clavulanic Acid (Augmentin®)		N/V/D; incidence of diarrhea higher with Augmentin® vs. amoxicillin alone	Amoxicillin/clavulanic acid will result in high urine concentrations of amoxicillin; may result in false-positive reactions when testing for the presence of glucose in the urine using the Clinitest®, Benedict's solution, or Fehling's solution. Glucose tests based on enzymatic glucose oxidase reactions, such as Clinistix®, may be used	Take with food to reduce GI upset
Cephalosporins	Possible nephrotoxicity with vitamin K deficiency	GI mucosa damage; V/D	Prolongation of PT; ↓ potassium	

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Chloramphenicol (Chloromycetin®)	Decreased protein synthesis; increased need for riboflavin, B6, B12	V/D; stomatitis; enterocolitis, glossitis	Anemia	Take on an empty stomach
Clindamycin (Cleocin®)		N/V/D; esophagitis, pseudomembranous colitis	↑ LFTs	Take with a full glass of water to avoid esophageal irritation
Clofazimine (Lamprene®)	Food increases the extent of absorption	Constipation, abdominal pain, N/V/D, anorexia, GI bleeding, dysgeusia	↑ glucose	Administer with meals or milk to maximize absorption
Dapsone	Do not administer with alkaline foods or antacids (may decrease dapsone absorption)	Vomiting, anorexia, abdominal pain	↑ Potassium, ↓ albumin, ↑ alk phos, ↑ ALT, ↑ LDH, ↑ bilirubin	
Linezolid (Zyvox®)	Concurrent use of linezolid and foods or beverages containing large quantities of tyramine may result in a significant pressure response	N/D, dyspepsia, oral moniliasis, tongue discoloration, localized abdominal pain, constipation, pseudomembranous colitis	↑ ALT, may cause lactic acidosis	Patients receiving linezolid and tyramine-containing foods or beverages should be monitored for significant blood pressure increases. Avoid foods containing large amounts of tyramine (aged cheese, sour cream, red wine), <100 mg/meal

Macrolides	Rate and extent of GI absorption may be altered depending on the formulation.	Abdominal pain, cramping, N/V/D, stomatitis, dyspepsia	False-positive urinary catecholamines, 17-hydroxycorticosteroids, 17-ketosteroids, may elevate hepatic enzymes	Do not crush enteric-coated or delayed-release products
Azithromycin	Food does not affect bioavailability of the tablet formulation, immediate-release oral suspension, or the 1 g suspension regimen; however, extended release suspension ↑ absorption when given with a high-fat meal			Immediate-release suspension and tablet may be taken without regard to food; extended-release suspension should be taken on an empty stomach (at least 1 h before or 2 h following a meal)
Clarithromycin	Food delays rate, but not extent of absorption; Extended release: Food increases clarithromycin AUC by ~30% relative to fasting conditions			Immediate-release tablets and oral suspension may be given with or without meals, may be taken with milk. Extended-release tablets should be taken with food
Erythromycin	Erythromycin serum levels may be altered if taken with food (formulation dependent)			Avoid milk and acidic beverages 1 h before or after a dose; administer after food to decrease GI discomfort

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Metronidazole (Flagyl®)	Food decreases peak drug concentration	N/V/D, metallic taste, xerostomia, furry tongue	False-negative/ decreased AST levels	Disulfiram reaction with alcohol
Neomycin (Mycifradin®)	Decreased absorption of fat, MCT, vitamins A, D, K, B12, sodium, glucose, lactose, sucrose, xylose; may also deplete β-carotene, calcium, iron, magnesium, potassium	NV/D, colitis, cadidiasis, inactivation of bile salts, GI mucosal damage, decreased activity of disaccharidases, lipase inhibition	↑ BUN, ↑creatinine	
Penicillins	Increased urinary potassium excretion, may inactivate B6, food ↓ drug absorption	Decreased appetite, diarrhea	↓ Potassium, false-positive or -negative urinary glucose determined using Clinitest®, positive Coombs' (direct), false-positive urinary serum proteins	Administer with water on an empty stomach (1 h before or 2 h after meals); may take with food to ↓ GI upset
Quinolones	Dairy foods, mineral supplements, calcium fortified juices decrease drug concentrations; may increase caffeine concentrations	N/V/D; GI bleeding, abdominal pain, anorexia pseudomembranous colitis dyspepsia	Anemia, ↑ ALT, ↑ AST, ↑ alk phos, ↑ BUN, ↑ creatinine	Administer 2 h after meals, may take with food to ↓ GI upset

Sulfonamides	Decreased synthesis of folic acid, B vitamins, vitamin K; decreased iron absorption; increased urinary excretion of vitamin C; presence of food delays but does not ↓ absorption	Decreased appetite; N/V; stomatitis; pseudomembranous colitis, abdominal pain	↑ potassium; false-positive protein in urine, false-positive urine glucose with Clinitest®	Avoid large amounts of vitamin C or acidifying agents (cranberry juice) to prevent crystalluria
Tetracyclines	Chelate divalent ions; decreased absorption of calcium, iron, magnesium, zinc, amino acids; increased urinary excretion of vitamin C; absorption of tetracycline; hydrochloride ↓ by 50% when taken with milk/dairy products	N/V/D; anorexia; stomatitis, glossitis; antibiotic-associated pseudomembranous colitis; esophagitis, oral candidiasis	↑ BUN, ↑ alk phos, ↑ bilirubin, ↑ AST, ↑ ALT; false-negative urine glucose with Clinistix®; false-positive urine glucose using Clinitest®	Take on empty stomach 1 h before/2 h after dose; avoid milk/dairy products, polyvalent ions with 2–3 h of dose; doxycycline and minocycline may be given without regard to meals but best to avoid concurrent administration with milk/dairy products
Trimethoprim (Trimpex®, TMP)	Decreased folate concentrations	N/V; epigastric distress	Anemia, ↑ ALT, ↑ AST, ↑ alk phos, ↑ BUN, ↑ creatinine	Leucovorin may be given until normal hematopoiesis is restored
Antifungals				
Amphotericin B (Fungizone®)	Possible nephrotoxicity with increased urinary excretion of potassium and magnesium	Decreased appetite; N/V, steatorrhea, diarrhea with oral formulation	↓ Potassium, ↓ magnesium, ↑ BUN, creatinine	Monitor potassium, magnesium, supplementation usually necessary

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Caspofungin (Cancidas®)		N/V/D, abdominal pain, anorexia, mucosal inflammation	↓ Potassium, ↑ calcium, ↑ Cr, ↑ ALT, ↑ AST, ↑ alk phos, ↑ bilirubin	
Fluconazole (Diflucan®)	Food delays time of peak absorption but has no effect on total amount of drug absorbed	Mild–moderate GI upset (N/V/D), abdominal pain	↓ Potassium, ↑ cholesterol, ↑ triglycerides, ↑ AST, ↑ ALT, ↑ alk phos	
Flucytosine (Ancoban®)	Food ↓ rate but not extent of absorption; magnesium or aluminum salts delay rate of absorption	N/V/D; enterocolitis	↑ BUN, creatinine, ↑ ALT, AST, CK, LDH, ↑ alk phos, false ↑ in serum creatinine values if Ektachem analyzer used	May be taken with food
Griseofulvin (Grisactin®, Fulvicin®)	High-fat foods ↑ absorption rate	N/V/D; oral thrush	False-positive urinary VMA levels	Given with fatty meals to ↑ absorption and avoid GI upset
Itraconazole (Sporanox®)	Food ↑ absorption of capsule formulation; hypochlorhydria may ↓ absorption; grapefruit juice ↓ itraconazole AUC by 30%; absorption ↑ when taken with a cola beverage	N/V/D; abdominal pain; anorexia	↓ Potassium; ↑ ALT, ↑ AST, ↑ LDH, ↑ alk phos, ↑ triglyceride	Take capsules with food; take oral solution on an empty stomach

Ketoconazole (Nizoral®)	Food ↑ rate and extent of absorption; administration with an acidic beverage (cola, citrus juice) enhances absorption	N/V/D, abdominal discomfort, GI bleeding	↑ AST, ↑ ALT, ↑ alk phos	Take with food to ↓ GI upset
Micafungin (Mycamine®)		N/V/D, mucosal inflammation, constipation, anorexia, dyspepsia	↓ Potassium, ↓ magnesium, ↓ calcium, hypoglycemia, hyperglycemia, ↑ sodium, ↑ AST, ↑ ALT, ↑ alk phos	
Posaconazole (Noxafil®)	Adequate posaconazole absorption from GI tract and subsequent plasma concentrations are dependent on food for efficacy	N/V/D, anorexia, abdominal pain, constipation, dyspepsia	↑ AST, ↑ ALT, ↑ alk phos, ↑ bilirubin, hyperglycemia ↓ potassium, ↓ magnesium, ↓ calcium	Must be administered during or within 20 min of a full meal or oral liquid nutritional supplement; alternatively, may be given with an acidic carbonated beverage
Voriconazole (VFEND®)	High-fat meals reduce extent of absorption	N/V, anorexia, constipation, abdominal pain	↑ AST, ↑ ALT, ↑ alk phos, ↑ bilirubin, ↓ potassium, ↓ magnesium, ↑ creatinine	Take 1 h before or 1 h after meals
Antihelmintics				
Albendazole (Albenza®)	Bioavailability increased when taken with a fatty meal	N/V, abdominal pain	↑ LFTs	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Ivermectin (Stromectol®)	Bioavailability ↑ 2.5-fold when administered following a high-fat meal	N/D	↑ AST, ↑ ALT	Take on an empty stomach with water
Mebendazole (Vermox®)	Food ↑ drug absorption	N/V/D, abdominal pain	Transient abnormalities in LFTs	Administer with food
Antimalarials				
Artemether and Lumefantrine (Coartem®)		N/V, abdominal pain, anorexia	QT prolongation	Administer with a full meal for best absorption. Patients should be encouraged to take with a meal as soon as food can be tolerated. Patients who remain averse to food during treatment should be closely monitored as the risk of recrudescence increases
Chloroquine phosphate (Aralen®)		N/V/D, anorexia, stomatitis, weight loss	↓ Glucose has been reported	Take with food to ↓ GI upset; bitter taste may be masked by mixing with chocolate syrup

Hydroxychloroquine (Plaquenil®)	Food increases bioavailability	N/V/D, anorexia, abdominal cramps	↑ ALT, ↑ AST, ↑ bilirubin, ↑ PT, anemia	Take with food to ↓ GI upset
Primaquine phosphate		N/V, abdominal cramps, anorexia	Anemia	Take with food to ↓ GI upset; drug has bitter taste
Pyrimethamine (Daraprim®)	↓ Serum folate concentrations	Anorexia, abdominal cramps, V/D, atrophic glossitis	Anemia	Take with meals to ↓ GI upset; leucovorin may be given until normal hematopoeisis is restored
Sulfadoxine and Pyrimethamine (Fansidar®)	↓ Serum folate concentrations	Anorexia, gastritis, glossitis, V/D	↑ ALT, ↑ AST, anemia	Take with meals; leucovorin may be given until normal hematopoiesis is restored
Antiprotozoals				
Atovaquone (Mepron®)	Food increases bioavailability	N/V/D, abdominal pain, constipation, anorexia	↓ Sodium, ↑ amylase	Patients who cannot take with meals or have chronic diarrhea or GI problems at risk for drug malabsorption and treatment failure
Nitazoxanide (Alinia®)	Food increases AUC	N/V/D, abdominal pain		Administer with food

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Antiretrovirals				
Protease inhibitors				
Amprenavir (Agenerase®)	High-fat meals may decrease AUC; product contains vitamin E to improve bioavailability; may increase risk of bleeding if vitamin K deficient or on concomitant anticoagulant therapy	N/V/D, taste disorders	↑ Glucose, ↑ triglycerides hypercholesterolemia, ↑ LFTs	Fat redistribution and accumulation has been reported
Atazanavir (Reyataz®)	Bioavailability ↑ when taken with food	N/V/D	↑ Cholesterol, ↑ amylase, ↑ bilirubin, ↑ lipase	Administer with food; may cause redistribution of fat (e.g., buffalo hump, peripheral wasting with increased abdominal girth, cushingoid appearance)
Fosamprenavir (Lexiva®)	Tablets may be taken with or without food. Adults should take oral suspension without food; however, children should take oral suspension with food	N/V/D; abdominal pain; may cause transaminase elevations, hepatitis, and/or exacerbate preexisting hepatic dysfunction	↑ ALT, ↑ AST, ↑ alk phos, ↑ bilirubin, ↑ triglycerides, ↑ total cholesterol. Hyperglycemia; ↑ lipase increased	Take tablets with food if taken with ritonavir. May be administered without regard to food if not taken with ritonavir

				Adults should take oral suspension *without* food; however, children should take oral suspension *with* food.
				May cause redistribution of fat (e.g., buffalo hump, peripheral wasting with increased abdominal girth)
Indinavir (Crixivan®)	↓ absorption when given with high amounts of protein or fatty foods; grapefruit juice ↓ AUC by 26%	N/V/D; abdominal pain, metallic taste	↑ ALT, ↑ AST, ↑ alk phos, ↑ bilirubin, ↑ triglycerides, hyperglycemia (rare)	Ensure adequate hydration; take on empty stomach; if GI upset a problem, take with light meals or other liquids
Lopinavir and Ritonavir (Kaletra®)	Solution should be taken with food. Tablet may be taken with or without food	N/V/D; abdominal pain, altered taste, weight loss	↑ ALT, ↑ AST, ↑ alk phos, ↑ bilirubin, ↑ GGTP, ↑ triglycerides, ↑ amylase, ↑ lipase, hypercholesterolemia hyperglycemia alterations in sodium (↑↓)	Solution: Administer with food; if using didanosine, take didanosine 1 h before or 2 h after lopinavir/ritonavir
				Tablet: May be taken with or without food. Swallow whole, do not break, crush, or chew. May be taken with didanosine when taken without food

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Nelfinavir (Viracept®)	Food ↑ absorption	N/V/D; abdominal pain, anorexia, dyspepsia epigastric pain, mouth ulceration, GI bleeding, pancreatitis	↑ ALT, ↑ AST, ↑ alk phos, hyperlipemia, hyperuricemia, ↑ glucose, anemia	Powder formulation contains 11.2 mg phenylalanine per gram powder; do not administer with acidic foods or juices (results in bitter taste)
Ritonavir (Norvir®)	Food ↑ absorption; may cause avitaminosis	N/V/D, taste perversion, abdominal pain, pancreatitis	↑ triglycerides, ↑ cholesterol, ↑ creatine phosphokinase, hyperglycemia (rare), ↑ ALT, ↑ AST, ↑ alk phos, alterations in potassium (↑↓)	Administer with food to ↑ absorption; liquid formulations tastes unpleasant, reserve use for tube-fed patients or mix with chocolate milk or nutritional supplement
Saquinavir (Fortovase®, Invirase®)	High-fat meals maximize bioavailability; grapefruit juice ↑ saquinavir levels	N/V/D; abdominal discomfort, stomatitis	Hyperglycemia, ↑ creatine phosphokinase, ↑ ALT, ↑ AST, ↑ bilirubin, ↑ amylase, alterations in potassium and phosphorus (↑↓), ↑ calcium	Take within 2 h of a full meal; high-calorie/high-fat meals ↑ AUC and Cmax more than low-calorie / low-fat meals

Tipranavir (Aptivus®)	Coadministration with ritonavir is required. Administer with ritonavir capsules or solution without regard to meals; administer with ritonavir tablets with meals	N/V/D, abdominal pain, weight loss, dehydration, taste perversion	↑ Triglycerides, ↑ cholesterol, ↑ amylase, ↑ ALT, ↑ AST, ↑ GGT	Capsule contains dehydrated ethanol. Oral solution formulation contains vitamin E; additional vitamin E supplements should be avoided. May cause redistribution of fat (e.g., buffalo hump, peripheral wasting with increased abdominal girth, cushingoid appearance). May cause facial wasting
Nucleoside and Nucleotide Reverse Transcriptase Inhibitors				
Abacavir (Ziagen®)	Food does not affect AUC	N/V/D, anorexia, pancreatitis	Mild hyperglycemia, hypertriglyceridemia, lactic acidosis	Fat redistribution and accumulation has been reported
Didanosine (Videx®)	May alter GI absorption of various nutrients due to prolonged GI transient time; food may decrease oral bioavailability by 50%	N/V, constipation, xerostomia, dry throat, dysphagia	↓ potassium, hyperuricemia, ↑ triglycerides, ↑ glucose	Buffered powder for oral solution is inactivated in acidic juices/fluids

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Emtricitabine (Emtriva®)	May be administered with or without food	N/V/D; abdominal discomfort, gastroenteritis,	↑ CPK, ↑ amylase, ↑ lipase, ↑ triglycerides, ↑ glucose, ↑ ALT, ↑ AST, ↑ bilirubin, ↑ alk phos, anemia	May cause redistribution of fat
Lamivudine (Epivir®, 3TC)	Food may ↓ rate of absorption and peak serum concentrations, but does not significantly change the AUC	N/V/D; feeding problems, abdominal discomfort, pancreatitis, anorexia, stomatitis	↑ ALT, ↑ AST, ↑ bilirubin, ↑ amylase, ↑ glucose	May cause fat redistribution and accumulation
Stavudine (Zerit®, d4T)	Food ↓ peak serum concentrations by 45%, bioavailability not changed	N/V/D, abdominal pain, anorexia, pancreatitis	↑ ALT, ↑ AST, ↑ bilirubin	Take without regard to food
Tenofovir Disoproxil Fumarate (Viread®)	High-fat meals ↑ oral bioavailability	N/V/D; flatulence, anorexia, pancreatitis	↑ LFTs, ↓ phosphorus	Administer with meals to improve absorption
Zalcitabine (Hivid®, ddC)	Food ↓ rate and extent of absorption; AUC ↓ by 14%	N/V/D, oral/esophageal ulcers, dysphagia, anorexia, abdominal pain, constipation, pancreatitis, weight loss, anemia	↑ Glucose, ↓ calcium	Take on empty stomach

Zidovudine (Retrovir®, AZT, ZDV)	Folate/B12 deficiency increases zidovidine-associated myelosuppression; rate of absorption and peak serum concentration may ↓ when taken with food	N/V/D; anorexia	↑ AST, ↑ LDH, ↑ alk phos, anemia	May take with food; take capsules while in upright position to ↓ risk of esophageal ulceration; syrup is strawberry flavored
Reverse Transcriptase Inhibitor (Nonnucleoside)				
Delavirdine (Rescriptor®)	Patients with achlorhydria should take the drug with an acidic beverage	N/V/D, abdominal pain	↑ PT, ↓ hemoglobin	May be taken without regard to meals. Patients with achlorhydria should take the drug with an acidic beverage. 200 mg tablets should be taken intact. May cause fat redistribution and accumulation
Efavirenz (Sustiva®)	High-fat/high-caloric meals ↑ AUC and peak concentration and may ↑ adverse effects	N/V/D, abdominal pain	↑ Triglycerides, ↑ amylase, hypercholesterolemia, ↑ LFTs	Take with water on an empty stomach preferred, tastes peppery (grape jelly may be used to improve taste). Tablets should not be broken. Some clinicians recommend opening capsules and adding to liquid or food for patients who cannot swallow capsules; however, no pharmacokinetic data are available, and this is not recommended.

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Etravirine (Intelence®)	Food increases absorption of etravirine by ~50%	N/D	↑ Triglycerides, ↑ cholesterol, hyperglycemia, ↑ LDL, ↑ AST, ↑ ALT	Central redistribution of body fat. Take after meals. May disperse tablets in glass of water; stir well before drinking and rinse glass several times to ensure administration of complete dose
Nevirapine (Viramune®)	Can be given without regard to food	N/V/D, abdominal pain	↑ LFTs, ↑ triglycerides, ↑ HDL, ↑ GGT, ↑ AST, ↑ ALT. Most cases of nervirapine-associated hepatic toxicity occur during the first 12 wk of therapy. However, about one-third of cases occurred after 12 wk of treatment. In some cases, patients presented with nonspecific prodromal signs or symptoms of hepatitis and rapidly progressed to hepatic failure.	Central redistribution of body fat. Extended-release tablets must be swallowed whole and not crushed, chewed, or divided.

Rilpivirine (Edurant™)	Administer with a normal- to high-calorie meal. Absorption increased by ~40% when taken with a normal to high-caloric meal. Administration with a protein supplement drink alone does not increase absorption	Abdominal discomfort/pain, appetite decreased, N/V/D	↑ Cholesterol, ↑ LDL, ↑ triglycerides,↑ ALT, ↑ AST bilirubin increased, ↑ Creatinine	May cause redistribution of fat
Entry and Fusion Inhibitors				
Enfurvitide (Fuzeron®)		D/N, weight loss, abdominal pain, appetite decreased, pancreatitis, anorexia, xerostomia	↑ Transaminases, ↑ CPK	
CCR5 Antagonist				
Maraviroc (Selzentry®)	Absorption of maraviroc is somewhat reduced with ingestion of a high-fat meal; however, maraviroc can be given with or without food	Abdominal pain, altered appetite, constipation	↑ Transaminases, ↑ bilirubin	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Integrase Inhibitor				
Raltegravir (Isentress®)	May be administered without regard to meals; however, clinically insignificant variability in absorption exists depending on meal type	N/D	↑ CPK, patients with chronic active hepatitis B or hepatitis C are more likely to experience worsening AST, ALT, or total bilirubin than are patients who are not coinfected	May be taken without regard to meals. Some products may contain phenylalanine
Antitubercular Agents				
Cycloserine (Seromycin®)	B6 antagonist; ↓ absorption of calcium, magnesium, vitamin B12; decreased folate utilization and vitamin K synthesis; may increase B12 and folate requirements		Anemia; ↑ ALT, ↑ AST	Some neurotoxic effects may be prevented or lessened by pyridoxine supplementation. May administer without regard to meals
Ethambutol (Myambutol®)	May deplete copper and zinc	N/V; abdominal pain; anorexia	↑ Uric acid levels, abnormal LFTs	Take with food to ↓ GI upset

Ethionamide (Trecator®)	Neurotoxic effects may be prevented or relieved by the coadministration of pyridoxine	N/V/D, abdominal pain, anorexia, excessive salivation, metallic taste, stomatitis, weight loss	Hypoglycemia, ↑ bilirubin, ↑ LFTs	May be taken with or without meals
Rifabutin (Mycobutin®)	High-fat meal may decrease the rate but not the extent of drug absorption	N/V/D, anorexia, dyspepsia, abdominal pain, dysgeusia, flatulence	↑ LFTs	Take with food to ↓ GI upset
Rifampin	Food may decrease or delay amount of drug absorbed	N/V/D, anorexia, stomatitis	↑ LFTs, inhibits standard assay used to asses serum B12 and folate	Take on empty stomach
Antivirals				
Acyclovir (Zovirax®)	Food does not appear to impact absorption	N/V/D	↑ LFTs, ↑ BUN, ↑ creatinine	May administer with food
Amantadine (Symmetrel®)		N/V/D, xerostomia, anorexia, constipation	↑ LFTs, ↑ BUN, ↑ creatinine	
Cidofovir (Vistide®)		N/V/D, anorexia	Metabolic acidosis, ↑ LFTs, ↑ BUN, ↑ creatinine	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Famciclovir (Famvir®)	Rate of absorption or conversion to penciclovir and peak concentration are ↓ with food, bioavailability not affected	N/V/D, constipation, anorexia, abdominal pain		May take with food to ↓ GI upset
Ganciclovir (Cytovene®)	High-fat meal ↑ AUC	N/V/D, pancreatitis	↑ LFTs, ↑ BUN, ↑ creatinine	Administer with food; do not open capsules or crush tablets
Oseltamivir (Tamiflu®)	May be administered without regard to meals; take with food to improve tolerance. Capsules may be opened and mixed with sweetened liquid (e.g., chocolate syrup)	N/V/D, pseudomembranous colitis		Administer with food to ↓ GI upset
ValACYclovir (Valtrex®)	May administer with or without food	N/V/D, abdominal pain	↑ ALT, ↑ AST, ↑ alk phos	May be taken with or without food. Administer with food to ↓ GI upset
Valganciclovir (Valcyte®)	Coadministration with a high-fat meal increased AUC by 30%	N/V/D, abdominal pain, constipation, dyspepsia, ↓ appetite	Hyperglycemia, ↓ ↓↑ potassium, ↓ calcium, ↓ magnesium, ↓ phosphorus	Take with food

Miscellaneous Antiinfective Agents				
Clofazimine (Lamprene®)	Food ↑ extent of absorption	N/V/D, abdominal pain; constipation; bowel obstruction, GI bleeding, dysgeusia	Hyperglycemia	Administer with meals/milk to maximize absorption
Fuazolidine (Furoxone®)	Large doses or prolonged therapy ↑ risk of hypertensive effects if taken with tyramine containing foods	N/V/D	Hypoglycemia; false-positive urine glucose results with Clinitest®	Avoid tyramine containing foods
Methenamine (Hiprex®, Mandelamine®)	Foods/diets that alkalinize urine pH > 5.5 ↓ activity of methenamine; cranberry juice can be used to acidify urine and ↑ activity of methenamine	N/V/D, abdominal cramping, anorexia, stomatitis	Albuminuria, ↑ AST, ↑ ALT, ↓ urine pH	Administer with food
Nalidixic Acid (NegGram®)	Food delays absorption	N/V/D, abdominal pain	Anemia, false-positive urine glucose with Clinitest®, false ↑ in urinary VMA	Suspension is raspberry flavored
Nitrofurantoin (Furadantin®, Macrodantin®)	Food ↑ total amount absorbed. Cranberry juice or other urine acidifiers enhance drug action	N/V, anorexia, pancreatitis	Anemia	Administer with food or milk

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Pentamidine (Pentam®)		N/V/D; metallic taste, pancreatitis, anorexia, dyspepsia, xerostomia	Anemia, ↑ potassium, hypo-/ hyperglycemia, ↓ magnesium, ↓ calcium, ↑ BUN, ↑ creatinine	
Antihyperlipidemics				
Cholestyramine (Questran®)	Decreased absorption of fat, MCT, fat-soluble vitamins, B12, iron, folate, calcium, glucose, xylose, electrolytes	Constipation, nausea, anorexia, weight changes, abdominal distention	↑ Triglyceride, ↑ ALT, ↑ AST, ↑ phosphorus, ↑ chloride, ↑ alk phos; ↓ cholesterol, ↓ LDL, ↓ calcium, ↓ potassium, ↓ sodium	Administer before meals; to minimize binding, administer vitamins/ minerals 1 h before or 4–6 h after cholestyramine
Clofibrate	↓ Absorption of carotene, B12, iron, electrolytes, MCT, glucose, xylose	↓ Activity of intestinal disaccharidases; N/D	↑ ALT, ↑ AST, ↑ CPK	
Colesevelam (Welchol®)	↓ Absorption fat-soluble vitamins. Chronic use may be associated with bleeding problems due to hypoprothrombinemia from vitamin K deficiency	N, abdominal pain, constipation, dyspepsia, pancreatitis	↑ Triglyceride	Administer with meals. To avoid GI distress, do not take in dry form

Colestipol	↓ Absorption fat-soluble vitamins, iron; may bind to B12-intrinsic factor complex; may require folic acid, iron supplements	Anorexia, abdominal distention, N/V/D	Transient ↑ ALT, ↑ AST	
HMG-CoA Reductase Inhibitors ("statins")				
Atorvastatin; Cerivastatin; Lovastatin; Fluvastatin; Pravastatin; Simvastatin	Deplete coenyzme Q10; food ↑ drug absorption; serum drug levels may↑ when taken with grapefruit juice	Abdominal pain, constipation, N/V/D, dyspepsia, flatulence; regurgitation, xerostomia, anorexia, pancreatitis	Abnormal thyroid function tests; ↑ LFTs, ↑ CPK	Risk of myopathy and/ or rhabdomyolysis is ↑ with daily intake of large quantities of grapefruit juice (>1 quart/d)
Gemfibrozil (Lopid®)	↓ Coenzyme Q10, vitamin E	Epigastric pain, xerostomia, anorexia, constipation, abdominal pain, flatulence	↑ ALT, ↑ AST, ↑ CPK, ↑ LDH	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Antiarrhythmics				
Amiodarone (Cordarone®)	Food increases rate and extent of oral absorption; high-fat meals can increase AUC; grapefruit juice increases oral absorption	N/V, constipation, anorexia	↑ Ammonia. ↑ LFTs, ↑ bilirubin, ↑ triglycerides, hyperglycemia	
Digoxin (Lanoxin®)	Meals containing high fiber or bran or foods high in pectin may decrease digoxin absorption	N/V/D; feeding intolerance, abdominal pain		Avoid natural licorice; increased risk of digoxin toxicity in patients who are ↓ potassium, ↓ magnesium
Flecainide (Tampocor®)	Dairy products (milk, formula, yogurt) may interfere with drug absorption. Clearance of flecainide may be decreased in patients with strict vegan diets due to urine pH > 8	Nausea, xerostomia, metallic taste		Avoid concurrent administration with milk or milk-based formulas; monitor serum drug concentrations and decrease the dose when the diet changes to decreased consumption of milk
Verapamil (Calan®)	Grapefruit juice ↑ serum concentrations	Constipation, nausea, abdominal discomfort	↑ LFTs	

Antihypertensives				
ACE inhibitors; Benazepril; Captopril; Enalapril; Lisinopril	Food decreases the rate, but does not significantly decrease the extent of absorption. Limit salt substitutes or potassium-rich diet. Avoid natural licorice (causes sodium and water retention and increases potassium loss). May deplete zinc	N/D, ageusia	↓ Glucose, ↑ potassium	May result in a loss of sense of smell and taste; administer on empty stomach
Calcium Channel Blockers; Amlodipine (Norvasc®); Nifedipine (Procardia®)	Grapefruit juice increases oral absorption; avoid natural licorice products; administer with low-fat foods to minimize flushing	N/V/D, constipation, abdominal pain, dysphagia, xerostomia, weight changes, gingival hyperplasia	↑ LFTs	Administer without regard to food
Hydralazine (Apresoline®)	Inactivates B6	N/V/D; constipation; paralytic ileus, anorexia	↓ Hgb, ↓ WBC	Administer with food, avoid natural licorice
Methyldopa (Aldomet®)	Increased need for B12, folate	N/D, colitis, liver disorders, xerostomia, "black" tongue	Anemia, ↑ BUN, ↑ alk phos, ↑ AST, ↑ ALT, ↑ bilirubin, ↑ sodium, ↑ potassium	Dietary requirements for B12 and folate may be increased

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Antiinflammatory Agents				
Salicylates	Increased vitamin C requirements; possible iron deficiency; may ↓ serum folate levels	N/V/D; GI bleeding	Proteinuria, increased bleeding time; interferes with Gerhardt test, VMA determinators, 5-HIAA, xylose tolerance test	Administer with food to ↓ GI upset
Celecoxib (CeleBREX®)	Peak concentrations are delayed and AUC ↑ when taken with a high-fat meal	N/V/D, abdominal pain, dyspepsia, gastroesophageal reflux, flatulence, GI bleeding	↑ AST, ↑ ALT	May be administered without regard to meals
Ibuprofen (Motrin®, Advil®)	↓ Folate	N/V/D; GI bleeding, heartburn, dyspepsia		Administer with food to ↓ GI upset
Indomethacin (Indocin®)	Decreased absorption of amino acids, glucose, xylose; may deplete iron, folate	N/V/D, constipation, dyspepsia, GI bleeding, epigastric pain, anorexia	↑ Potassium, ↓ vitamin C, anemia, ↓ glucose (IV form)	

Ketorolac (Toradol®)	High-fat meals may delay time to peak by approximately 1 h and decrease peak level	Dyspepsia, N/V/D, GI pain, constipation	↑ LFTs	Administer with milk to ↓ GI upset
Corticosteroids	↑ Protein catabolism, ↓ glucose tolerance, ↑ sodium and water retention, ↓ absorption and ↑ excretion of potassium, zinc, vitamin C, calcium, and phosphorus; accelerated vitamin D metabolism; ↑ B6 and folate requirements; possible growth suppression and impaired wound healing	Increased appetite, xerostomia, dysgeusia, peptic disease, V/D, weight gain	↑ Glucose, ↑ triglyceride, ↑ cholesterol, ↑ sodium, ↓ potassium, ↓ calcium, ↓ T4, ↓ uric acid, ↓ zinc, ↑ prealbumin	
Budesonide (Entocort® EC)	Administration of capsules with a high-fat meal delays peak concentration, but does not alter the extent of absorption	N/V, abdominal pain, anorexia, diarrhea, dyspepsia, flatulence, gastroenteritis, glossitis, intestinal obstruction, oral candidiasis, taste perversion, tongue edema, weight gain, xerostomia	↓ Potassium	Avoid grapefruit juice when using budesonide oral capsules. Grapefruit juice may double systemic exposure of orally administered budesonide. Swallow whole; do not crush or chew caps

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
5-Aminosalicyclic acid derivatives; balsalazide, mesalamine, olsalazine, sulfasalazine	Folate depletion	Abdominal pain, cramps, flatulence, anorexia, gastritis, dyspepsia, N/V/D, constipation, hemorrhoids, anorexia	↑ ALT, ↑ AST	Take with food; consider folate supplementation
				Balsalazide: When sprinkled on food, may cause staining of teeth or tongue
Sulfasalazine (Azulfadine®)	Impairs folate absorption; increase dietary iron intake	N/V/D, anorexia, pancreatitis	↑ LFTs	Administer after meals or with food; consider folate supplementation
Antineoplastic Drugs				
Asparaginase (Elspar®)		N/V, abdominal cramps Pancreatitis, anorexia	↓ Albumin, ↑ uric acid, ↑ ammonia, hyperglycemia ↓ Thyroxine, ↑ bilirubin, ↑ hepatic enzymes	
Carboplatin (Paraplatin)		N/V/D, anorexia, hemorrhagic colitis, mucositis, metallic taste, constipation	↓ Calcium, ↓ magnesium, ↓ potassium, ↑ BUN, ↑ Cr	

Cyclophosphamide (Cytoxan®)		Anorexia; N/V, mucosal injury, dysgeusia	Anemia; ↑ uric acid, ↓↑ potassium; hyperuricemia, ↓ sodium; positive Coombs	Maintain high fluid intake; take with food only if GI distress occurs
Dactinomycin (Cosmegen®)	Decreased absorption of calcium, iron, and fat	Anorexia; N/V/D, stomatitis	↓ Calcium, hyperuricemia, ↑ LFTs	
Fluoruracil (5-FU)	Increased need for B1; malabsorption of glucose, xylose	Severe N/V/D; GI bleeding, anorexia, stomatitis, esophagitis	Anemia; ↓ albumin, ↑ alk phos, ↑ ALT, ↑ bilirubin, ↑ LDH	Increase dietary intake of thiamine; use of acidic solutions to dilute fluorouracil for oral use may result in precipitation of drug and ↓ absorption; maintain adequate hydration; do not eat 2 h before or after administration
Hydroxyurea (Hydrea®)	Supplemental administration of folic acid is recommended; hydroxyurea may mask development of folic acid deficiency	N/V/D, anorexia, constipation, gastrointestinal irritation mucositis, pancreatitis, stomatitis	↑ LFTs, ↑ BUN, ↑ creatinine	

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Imatinib (Gleevec®)	Avoid grapefruit juice (may increase imatinib plasma concentration)	N/V/D, abdominal pain, anorexia, weight gain, dyspepsia, constipation	↓ Potassium, ↑ ALT, ↑ creatinine, hyperglycemia, ↓ calcium, ↓ albumin, ↑ AST, ↑ alk phos, ↑ bilirubin	Should be taken with food and a large glass of water to decrease gastrointestinal irritation. Avoid grapefruit juice
Methotrexate (MTX)	Folate antagonist; ↓ absorption of fat, B12, lactose, carotene, cholesterol	GI mucosal injury; anorexia; N/V/D, stomatitis	Anemia; ↑ uric acid; ↑ ALT, ↑ bilirubin	Milk-rich foods may decrease absorption, folate may decrease drug response
Cytoprotectives				
Amifostine (Ethyol®)		N/V/D, metallic taste	↓ Calcium, ↓ magnesium	
Dexrazoxane (Zinecard®)	↑ Urinary excretion of iron, zinc, calcium	N/V/D	↓ Sodium, ↓ calcium, ↓ zinc, ↑ iron,↑ amylase, ↑ triglycerides,↑ AST, ↑ alk phos, ↑ ALT, ↑ bilirubin, ↑ LDH	
Leucovorin	Contraindicated in patients with pernicious anemia secondary to B12 deficiency			

Mesna		N/V/D, dysgeusia	↓ Potassium, false-positive urinary ketones with Chemstrip®, Multistix®, or Labstix®	Dilute well before oral administration to ↓ sulfur odor, dilute 1:1 to 1:10 in carbonated cola drinks, fruit juice or in milk; most palatable in chilled grape juice
Antirheumatic				
Abtacept (Orencia®)		N/D, abdominal pain, dyspepsia	May cause false ↑ glucose with some testing methods	Avoid echinacea (has immunostimulant properties)
Autonomic Drugs				
Anticholinergics (general)	Decreased absorption of electrolytes, iron, increased absorption of monosaccharides	N/V; constipation		
Central Nervous System Drugs				
Atomoxetine (Strattera™)	High-fat meals decrease rate but not extent of absorption	Weight loss, xerostomia, abdominal pain, N/V/D, decreased appetite, flatulence, constipation, dyspepsia		

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Anticonvulsants				
Phenobarbital; Phenytoin/ fosphenytoin; Primidone	Vitamin D deficiency; osteomalacia, ↓ absorption of folate, B12; ↑ vitamin K catabolism; may also deplete biotin. Dietary requirements for vitamins D, K, C, B12, folate may be increased with chronic use; high doses of pyridoxine may decrease effects of phenobarbital, pentobarbital	N/V/D, altered taste	↑ alk phos; ↓ calcium, ↓ magnesium, ↓ folate, ↓ B12, ↓ vitamins K, B6, C; megaloblastic anemia	Tube feedings ↓ phenytoin bioavailability; to ensure consistent absorption, administer at same time with regards to meals
Carbamazepine (Tegratol®)	Grapefruit juice increases the oral bioavailability by 40%. High-fat meals may increase rate of absorption and reduce time to peak levels of extended-release product but does not effect AUC	N/V/D. abdominal cramps	↓ Sodium	Administer with food to ↓ GI upset
Ethosuximide (Zarontin®)	Folate requirements may be increased	N/V, anorexia, abdominal pain, hiccups		Administer with food to ↓ GI upset
Felbamate (Felbatol®)		N/V/D, anorexia, constipation, dyspepsia, weight loss	↑ LFTs	

Gabapentin (Neurontin®)	Food slightly increases rate and extent of drug absorption; ↑ AUC	N/V, constipation, dyspepsia, weight gain	False-positive urine protein with Multistix®	Content of capsule bitter tasting
LamoTRIgine (LaMICtal®)	Food has no effect on absorption	N/V dyspepsia, abdominal pain, xerostomia, constipation, weight loss, anorexia, flatulence, weight gain		Lamictal® XR™ may be given without regard to meals. Swallow whole; do not chew, crush, or cut. Lamictal® chewable/ dispersible tablets may be chewed, dispersed in water, diluted in fruit juice, or swallowed whole
LevETIRAcetam (Keppra®)	Food may delay, but does not affect the extent of absorption	N/V/D, anorexia, constipation		May be taken without regard to meals
TiaGABine (Gabitril®)	Food reduces the rate but not the extent of absorption	N/V/D, abdominal pain, appetite increased, gingivitis,mouth ulceration, stomatitis, weight gain/loss		Take with food
Valproic acid (Depacon®, Depakene®, Depakote®)	May deplete carnitine and folate. Do not administer with carbonated drinks; do not administer tablet with milk	N/V/D, dyspepsia, constipation, pancreatitis, weight gain, taste perversion	↑ Ammonia, ↓ carnitine; false-positive urine ketones	Swallow delayed-release capsules whole; do not crush, break, or chew. May administer with food to ↓ GI upset. Do not administer with carbonated drinks

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Vigabatrin (Sabril®)		N/V/D, weight changes, constipation, abdominal pain, dyspepsia	↓ AST, ↓ ALT	May be given without regard to meals
Zonisamide (Zonegran®)	May deplete biotin, B1, B2, niacin, pyridoxine, B12, vitamin K	N/V/D, anorexia, abdominal pain, dyspepsia, weight loss, constipation, xerostomia, taste perversion	↑ alk phos, ↑ transaminases, ↑ LDH, ↑ BUN, ↑ creatinine	
Psychotherapeutic Agents				
Alprazolam (Xanax®)	High-fat meals taken <2 h before dose of an extended-release tablet may increase peak concentrations by 25%. Note: Doses taken immediately after a high-fat meal may increase time to peak concentration. Extent of absorption/AUC not impacted by food	Xerostomia, constipation, N/V/D, may increase or decrease appetite	↑ Bilirubin, ↑ AST, ↑ ALT	Do not crush, break, or chew extended-release tablet Administer immediate-release tablet with food to ↓ GI upset; caffeine antagonizes effects

Aripiprazole (Abilify®)	↑ Weight, primarily w/baseline BMI < 23	Anorexia, ↑ salivation, N/V, constipation		May be taken with or without food. Some products may contain phenylalanine
BuPROPion (Wellbutrin®; Zyban®)		N/V/D, weight loss, xerostomia, constipation, abdominal pain, flatulence, anorexia, appetite increased, taste perversion, dyspepsia, dysphagia		May be taken without regard to meals. Extended release tablets should be swallowed whole; do not crush, chew, or divide. The insoluble shell of the extended-release tablet may remain intact during GI transit and is eliminated in the feces
BusPIRone (BuSpar®)	Food may delay oral absorption, decrease the first-pass metabolism, increase oral bioavailability; grapefruit juice may greatly increase buspirone concentrations	N/V/D, flatulence, xerostomia	↑ Prolactin	
Phenothiazines; Chlorpromazine; Prochlorperazine; Thioridazine; Thiohixene	Interferes with riboflavin metabolism; ↓ B12 absorption, ↑ riboflavin elimination and induce depletion. Increase dietary riboflavin	Constipation; increased appetite and weight; xerostomia	↑ Cholesterol, ↑ bilirubin; false positives for PKU, amylase, urophyrins, urobilinogen	Administer with food to ↓ GI upset; dilute oral concentrate solution in juice before administration (undiluted oral chlorpromazine concentrate may precipitate in tube feeding)

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Diazepam (Valium®)	Grapefruit juice significantly increases bioavailability	N, constipation, hiccups, salivation changes	False-negative urinary glucose with Clinistix® or Diastix®	Limit caffeine intake
Imipramine; Amitriptyline	May increase need for riboflavin	N/V/D, constipation, increased or decreased weight; altered taste	Increased or decreased glucose	Administer with food to ↓ GI upset
Selective serotonin reuptake inhibitors (SSRI); Citalopram (CeleXA®); Fluoxetine (Prozac®); Paroxetine (Paxil®)	May cause decreased growth (smaller increases in weight and height in children and adolescents). Tryptophan supplements may ↑ CNS and GI adverse effects	N/D, xerostomia, anorexia, dyspepsia, constipation, weight loss, anorexia, flatulence, gastritis	↓ Glucose, ↓ sodium	Administer with food to ↓ GI upset
Haloperidol (Haldol®)	Drug will precipitate if oral concentrate mixed with coffee or tea	Xerostomia, constipation, N/V/D. Dyspepsia, hypersalivation	↓↑ Glucose, ↓ sodium, ↓ magnesium, ↑ prolactin,	Administer with food to ↓ GI upset; dilute oral concentrate with >2 ounces water or acidic beverage
Lithium (Eskalith®, Lithobid®)	Decreased calcium uptake by bones; may inhibit magnesium-dependent enzymes; alters glucose tolerance	N/V/D; increased appetite; xerostomia	↑ Magnesium, ↑ glucose	Administer with food to ↓ GI upset; avoid changes in sodium content; ↓ in sodium can ↑ lithium toxicity

Cerebral Stimulants				
Atomoxetine (Strattera®)	High-fat meal decreases the rate, but not the extent of absorption	Weight loss, xerostomia, N/V abdominal pain, decreased appetite		Do not crush, chew, or open capsule; swallow whole with water or other liquids. May be administered without regard to food
Dextroamphetamine (Dexedrine®)	Acidic foods, juices, or vitamin C may decrease GI absorption	Appetite suppression and weight loss, growth suppression, N/V/D, xerostomia, metallic taste		
Methylphenidate (Ritalin®)	Food may increase oral absorption	Decreased appetite; depression of height and weight, nausea		
Sedatives				
Barbiturates	Increased excretion of vitamin C; folate and vitamin D deficiency; ↓ absorption of B1; may also deplete calcium and biotin; high doses of pyridoxine may decrease drug effect; may increase the metabolism of vitamins D and K, dietary requirements of vitamin B12, C, D, K, folate, and calcium may be increased with prolonged use	N/V/D, taste perversion	↑ alk phos; ↓ calcium, ↓ magnesium, ↓ folate, ↓ B12, ↓ vitamins K, B6, C; megaloblastic anemia	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Electrolytes and Water Balance Drugs				
Diuretics; Acetazolamide (Diamox®)	Avoid natural licorice (causes Na^+ and water retention, ↑ excretion of potassium)	GI irritation, anorexia, N/V, xerostomia, melena, dysgeusia, metallic taste, black stools, may cause growth retardation	↓ Potassium, ↑ glucose, hyperchloremic metabolic acidosis, may cause false positive for urinary protein with Albustix®, Labstix®, Albutest®	Do not crush or chew long-acting capsules Administer with food to ↓ GI upset. Tablet may be crushed and mixed with chocolate or cherry syrup to mask bitter taste of drug
Amiloride (Midamor®)	Avoid natural licorice (causes Na^+ and water retention, ↑ excretion of potassium) and salt substitutes; food decreases absorption by 30%	N/V/D, abdominal pain, appetite changes, GI bleeding, heartburn, dyspepsia, flatulence, xerostomia, constipation	May alter LFTs, ↑ potassium, hyperchloremic metabolic acidosis	

Loop Diuretics; Bumetanide (Bumex®); furosemide (Lasix®)	↑ Excretion of magnesium, calcium, potassium, zinc; ↓ carbohydrate tolerance	N/V/D; anorexia, xerostomia	↓ Calcium, ↓ magnesium, ↓ potassium, ↓ chloride, ↑ glucose, ↑ BUN, ↑ uric acid	Avoid use of salt substitutes, administer with food
Metolazone (Zaroxyln®)		Abdominal bloating, GI irritation, bitter taste, N/V, anorexia, xerostomia	↓ Sodium, ↓ magnesium, ↓ potassium, ↓ chloride, ↑ glucose, hyperuricemia	Avoid natural licorice; administer with food
Spironolactone (Aldactone®)	Potassium sparing; ↑ calcium excretion, avoid diets high in potassium	N/V/D, anorexia, gastritis, cramping, GI bleeding	↑ Potassium, ↑ BUN, ↑ creatinine, ↑ magnesium, ↑ uric acid, ↓ sodium, ↓ chloride	Avoid natural licorice; administer with food
Thiazides	↑ Excretion of potassium, magnesium, zinc, riboflavin; glucose intolerance; ↓ calcium excretion	N/V/D; constipation; anorexia, cramping	↑ Uric acid, ↑ calcium, ↓ potassium, ↓ magnesium, ↓ chloride, ↓ bicarbonate, ↓ phosphorus, ↑↓ glucose	Avoid natural licorice; administer with food

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Triamterene (Dyrenium®)	Potassium sparing; avoid salt substitutes and diets high in potassium	N/V/D, xerostomia	Abnormal LFTs, ↑ potassium, ↓ sodium, ↓ magnesium, ↑ chloride	Administer with food
Gastrointestinal Drugs				
Antacids; Aluminum hydroxide	↑ Calcium absorption; can form insoluble salts with dietary phosphorus; may cause hypophosphatemia, ↓ absorption of vitamins A,C; inactivates B1	Constipation, anorexia; N/V, bezoar, or fecalith formation	↓ Magnesium; ↓ phosphorus	
Magnesium hydroxide		Diarrhea, abdominal cramps	↑ Magnesium	Take with water
Sodium bicarbonate	Concurrent administration with iron may ↓ iron absorption. Prolonged and excessive consumption of calcium/ dairy products can cause high calcium concentrations (i.e., milk–alkali syndrome).	Gastric distention, flatulence	↓ Potassium, ↓ calcium, ↑ sodium, ↑ osmolality	Administer 1–3 h after meals

Antihyperammonemic Agents; Lactulose (Cephulac®, Chronulac®)	Contraindicated in galactose restricted diets	N/D; constipation	↓ Ammonia	Administer with juice/milk
Sodium phenylbutyrate (Buphenyl®)	Do not mix with acidic beverages (cola, fruit juices) as drug may precipitate	Anorexia, abnormal taste, N/V, weight gain, abdominal pain	↑ Cholesterol, ↓ ammonia, ↓ potassium, ↑ sodium, ↑ chloride, ↑ phosphorus, ↓ albumin, ↑ LFTs, ↑ bilirubin	Administer with food, feedings
Cathartics; Bisacodyl (Ducolax®)	↓ Absorption of glucose	N/V/D, abdominal cramps, rectal burning	↓ Potassium; ↓ calcium	Administer on empty stomach, do not administer within 1 h of ingesting milk or dairy products (causes GI irritation)
Docusate sodium	Alters intestinal absorption of water and electrolytes	Diarrhea, abdominal cramping, intestinal obstruction, throat irritation	↑ Glucose, ↓ potassium	Administer liquid (not syrup) with milk/juice to mask bitter taste
Magnesium sulfate	↓ Nutrient absorption	↑ Intestinal transient time; N/V/D	↑ Magnesium	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Mineral oil	May ↓ absorption of fat-soluble vitamins, impairs calcium, carotene, and phosphorus absorption	Decreased weight; anorexia; N/V/D, abdominal cramps, anal itching	↓ β-Carotene	Nonemulsified mineral oil may be taken on an empty stomach; emulsified mineral oil may be administered with meals and is more palatable
Phosphate enema (Fleet®)	May deplete calcium, magnesium, potassium, sodium			
Antisecretory Agents; H_2 antagonists; Cimetidine (Tagamet®); Ranitidine (Zantac®); Famotidine (Pepcid®)	↓ B12, may deplete zinc; limit xanthine containing foods and beverages	N/V/D; constipation; loss of sense of smell and taste, mild diarrhea, xerostomia, dysgeusia, anorexia	↑ AST,↑ ALT, ↑ BUN, ↑ creatinine	
Proton pump inhibitors; Esomeprazole (Nexium®); Lansoprazole (Pevacid®); Omeprazole (Prilosec®); Pantoprazole (Protonix®)	↓ B12; absorption is decreased up to 50% when taken with food	N/V/D, abdominal pain, constipation, flatulence, dyspepsia, dysphagia, epigastric pain, melena, anorexia, dysgeusia, taste perversion, taste loss	↓ Sodium, hyperuricemia; ↑ LFTs, ↑↓ glucose, hyperlipemia	For G/NG tube administration: dissolve in an acidic fluid; for NJ/J tube administration: dissolve in a basic fluid; do not crush or chew capsule/ tablet contents

Sucralfate (Carafate®)	↓ Absorption of fat-soluble vitamins; aluminum salt may accumulate in renal failure	N/D; constipation gastric discomfort, xerostomia	↑ Aluminum (in renal failure)	Take on empty stomach
Octreotide (Sandostatin®)	May ↓ absorption of dietary fats, may ↓ vitamin B12; administer injections between meals to ↓GI side effects	N/V/D, abdominal pain, constipation, flatulence, xerostomia, dyspepsia, steatorrhea, biliary sludge, pancreatitis	↓↑ Glucose, ↑LFTs	
Hormones and Synthetic Substitutes				
Oral contraceptives	↓ Absorption of water soluble vitamins, ↓ magnesium, ↓ zinc; ↑ copper absorption	N/V; ↑↓ weight, bloating	Megaloblastic anemia, ↑ glucose, ↑ triglyceride, ↑ vitamin, ↑ vitamin E, ↑ iron, ↑ copper, ↑ alk phos, ↑ bilirubin, ↓ folate, ↓ calcium, ↓ magnesium, ↓ B6, ↓ B12, ↓ zinc	
Danazol	Food delays time to peak; high-fat meal increases plasma concentration	N/V, appetite changes, constipation, pancreatitis, weight gain	Glucose intolerance, ↓ HDL, ↑ LDL	

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Immunosupressants				
Azathioprine (Imuran®)		N/V/D, anorexia, stomatitis, pancreatitis, steatorrhea	False ↑ creatinine	Administer with food
Cyclosporine (Neoral®, SandImmune®, Gengraf®)	Grapefruit and grapefruit juice may affect cyclosporine metabolism (↑ cyclosporine levels)	N/V/D; abdominal discomfort, anorexia, hiccups, weight loss	↓ Magnesium, ↑ potassium, hyperuricemia, ↑ BUN, ↑ Cr, ↑ triglycerides (with IV form)	To improve palatability, dilute with milk, chocolate milk, orange juice, apple juice, stir well and drink at once, do not allow to stand, rinse glass with diluent to ensure entire dose is taken
Muromonab (OKT3)		N/V/D	↑ BUN, ↑ creatinine	
Mycophenolate (CellCept®)		N/V/D, constipation, abdominal pain, dyspepsia, anorexia	↓↑ Potassium, ↑ cholesterol, ↓ phosphorus, ↑ glucose	Do not open contents of capsule or crush tablets

Sirolimus (Rapamune®)	Avoid grapefruit juice; may ↓ clearance. Ingestion with high-fat meals ↓ peak concentrations but ↑ AUC	N/D, constipation, abdominal pain, weight loss	↑ Triglycerides, ↑ cholesterol, ↑↓ calcium, ↑ phosphorous hyper/hypoglycemia, ↓ potassium, ↓ magnesium, ↓ sodium	Should be administered consistently (with or without food) to minimize variability. Do not crush, split, or chew tablets. Solution should be mixed with at least 2 ounces of water or orange juice. No other liquids should be used for dilution
Tacrolimus (Prograf®, FK506)	Food decreases rate and extent of absorption; grapefruit may ↑ serum tacrolimus	N/V/D, constipation, dyspepsia, pancreatitis	↓ Magnesium, ↑ potassium, ↑ BUN, ↑ Cr, ↑ glucose, ↑ calcium, ↑ AST, ↑ ALT, ↑ LDH, ↑ cholesterol	Give on empty stomach
Antiasthmatics				
Albuterol (Proventil®, Ventolin®)		GI upset, xerostomia, N/V, heartburn, unusual taste	↓ Potassium, metabolic acidosis	Caffeinated beverages may increase albuterol's side effects

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	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Aminophylline/ Theophylline	Food does not impact absorption; high protein, low carbohydrate meals and charcoal broiled meats will decrease theophylline levels	GI upset, GI reflux, N/V/D, abdominal pain, cramping	↑ Uric acid	Limit intake of charcoal broiled meats, caffeinated beverages; maintain consistent intake of protein and carbohydrates
Terbutaline		N/V, dysgeusia	↓ Potassium, ↑ glucose, ↑ CPK	
Zafirlukast (Accolate®)	Food ↓ absorption by 40%	N/V/D	↑ ALT	Should be taken on an empty stomach (1 h before or 2 h after meals)
Chelating Agents				
Deferoxamine (Desferal®)	When taken with high doses of vitamin C, patients may develop impaired cardiac function, which is reversible on discontinuation of vitamin C supplements	Abdominal discomfort, diarrhea, N/V		Avoid vitamin C in patients with preexisting cardiac failure, start vitamin C supplementation only after the first month of deferoxamine, do not exceed vitamin C doses of 50 mg/d in children <10 y of age, 100 mg/d in older children, 200 mg/d in adults

Deferasirox (Exjade®)	Bioavailability increased variably when taken with food	N/V/D, abdominal pain	↑ ALT	Do not chew or swallow whole tablets. Completely disperse tablets in water, orange juice, or apple juice. Rinse remaining residue with more fluid; drink. Administer at same time each day on an empty stomach, 30 min before meals
Dimercaprol		N/V, salivation, may cause burning sensation to lips and mouth	False-positive ketones	
Edetate calcium disodium		N/V/D, abdominal cramps, anorexia	↓ Magnesium, ↓ potassium, ↓ calcium. hyperuricemia	
Penicillamine	Do not administer with milk or food; iron and zinc may decrease drug effectiveness, for Wilson's disease: ↓ copper in diet; for lead toxicity: ↓ calcium in diet	N/V, oral lesions, epigastric pain, dysgeusia, ageusia, pancreatitis, sore throat, weight gain	↓ Iron, ↓ glucose, false-positive ketones	Administer on empty stomach

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Suuccimer	Administer with fruit juice to mask odor	N/V/D, anorexia, metallic taste, breath may smell of sulfur, sore throat	↑ alk phos, ↑ ALT, ↑ AST, ↑ cholesterol; falsely ↓ CPK, falsely ↓ uric acid; false-positive urine ketones with Ketostix®)	Ensure adequate hydration, capsules may be opened and sprinkled on soft foods
5-HT3 Receptor Antagonists				
Dolasetron; Granisitron; Ondanestron		Taste perversion, diarrhea, abdominal pain, constipation, dyspepsia, anorexia	↓ Potassium, transient, ↑ ALT, ↑ AST, ↑ bilirubin	
Replacement Solutions/Mineral Supplements				
Calcium salts	High calcium intake interferes with phosphorus absorption; may also interfere with iron absorption. Caffeine may decrease calcium absorption and increase calcium excretion. Do not give orally with bran, whole grain cereals, or foods high in oxalates (will ↓ calcium absorption)	N/V, constipation, xerostomia	↑ Amylase, ↑ calcium, ↓ phosphorus, ↓ magnesium	Oral dosage forms should be administered with meals to be effective when treating hyperphosphatemia

Cysteine	May chelate copper in parenteral nutrition solutions			
Fluoride	Do not administer with milk. Magnesium, aluminum, and calcium containing supplements may decrease fluoride absorption	GI upset N/V		Some products contain tartrazine, which may cause allergic reactions
Iron salts	Milk, cereals, fiber, eggs, tea, coffee decrease iron absorption. Concurrent administration with >200 mg vitamin C per 30 mg elemental iron will increase absorption of oral iron	GI irritation, epigastric pain, N/V, constipation	False-positive guaiac test	Liquid preparations may stain the teeth. Administer with water or juice for maximal absorption. Do not administer with milk or dairy products
Magnesium salts	High magnesium intake may impair calcium absorption; may also decrease phosphorus absorption	N/V/D, ileus	↑ Magnesium, ↑ potassium, ↑ calcium, ↓ phosphorus	
Potassium chloride	↓ Absorption of B12	N/V/D, abdominal pain, GI lesions	↑ Potassium, ↑ chloride	Administer with food
Phosphorus	High intake decreases magnesium absorption; avoid giving with oxalate or phytate-containing foods	N/V/D, flatulence	↑ Phosphorus, ↓ calcium, ↑ potassium with potassium salts, ↑ sodium with sodium salts	Administer with food ↓ diarrhea

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Sodium chloride		N/V	↑ Sodium, ↑ chloride	
Zinc salts	Coffee, foods high in phytate, and dairy products ↓ zinc absorption; avoid foods high in calcium or phosphorus	N/V, indigestion		
Ascorbic acid (Vitamin C)	Increases iron absorption, impairs copper absorption, impairs cyanocobalamin absorption	N/V/D, heartburn	False-positive urinary glucose with cupric sulfate reagents, false-negative urinary glucose with glucose oxidase method; false negative with amine-dependent occult blood test	
Cyanocobalamin	Use in folic acid–deficient patients may improve folate-deficient megaloblastic anemia and obscure true diagnosis. Hematologic response antagonized by chloramphenicol	Diarrhea	↓ Potassium	Administer intranasal product at least 1 h before or after ingestion of hot foods or liquids; hot foods can cause nasal secretions that can result in medication loss

Folic acid	Hematologic response antagonized by chloramphenicol. Large doses may mask the hematologic effects of B12 deficiency, obscuring diagnosis of pernicious anemia. May interfere with zinc absorption	GI upset, bitter taste		Not contained in oral liquid vitamin products due to stability issues
Niacin	Concomitant administration with hot drinks or food will increase flushing or pruritus	N/V/D, GI upset, heartburn, anorexia	↑ Glucose, hyperuricemia, ↓ phosphorus, abnormal LFTs false urine glucose (+) with Benedict's reagent	Should be taken with meal; low-fat meal if treating hyperlipidemia. Avoid hot drinks around the time of niacin dose
Vitamin A	Mega doses may interfere with iron, iodine, copper, and calcium absorption; can also interfere with absorption of ascorbic acid, vitamins K, D, E	V/D, gingivitis seen with long-term use	↑ alk phos, ↑ bilirubin, ↑ AST, ↑ ALT	Administer with food or milk
Vitamin D	Reduced intake impairs calcium and phosphorus absorption and utilization	N/V, constipation, anorexia, xerostomia, metallic taste, weight loss	↑ Calcium, ↑ cholesterol	May be administered without regard to meals
Vitamin E	Inhibits the reticulocyte and hemoglobin response to iron	N/D, intestinal cramps	↑ Cholesterol, ↑ triglycerides, ↑ creatinine kinase	

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Vitamin K	Vitamin K absorption ↓ when taken with Olestra-containing foods		↑ Bilirubin seen in neonates	
Miscellaneous Agents				
Allopurinol (Zyloprim®)	Increases risk of kidney stone formation when taken with large doses of vitamin C	GI irritation, dyspepsia, N/V/D, abdominal pain, gastritis	Elevated hepatic enzymes, hyperbilirubinemia	Administer after meals with plenty of fluid
Biguanides; Metformin (Glucophage®)	May deplete coenzyme Q10, folic acid, B12	N/V/D. anorexia, flatulence, abdominal discomfort, constipation, heartburn, metallic taste, dyspepsia	↓ Glucose	
Colchicine	↓ Absorption of B12, vitamin A, folate, potassium, fat, sodium, nitrogen, lactose	Intestinal mucosal damage; N/V/D, constipation, GI bleeding, steatorrhea	↑ alk phos, ↑ AST, ↓ B12, ↓ vitamin A, ↓ cholesterol	Administer without regard to meals; maintain adequate fluid intake

Clonidine (Catapres®)		N/V/D, abdominal pain, anorexia, constipation, parotid gland pain, parotitis, pseudoobstruction, taste perversion, throat pain, weight gain, xerostomia	Hyperglycemia (transient)	May be administered without regard to meals. Swallow extended-release formulations whole; do not crush or chew
Diazoxide (Proglycem®)		N/V/D, abdominal pain, anorexia, ileus, pancreatitis, pancreatic necrosis, taste loss (transient)	↑ alk phos, ↑ AST, hyperglycemia, sodium retention	Administer on an empty stomach 1 h before or after meals
Endothelin Antagonist Bosentan (Tracleer®)	Food does not affect bioavailability	Weight gain	↑ transaminases (dose dependent)	May be administered with or without food. Avoid grapefruit and grapefruit juice.
GuanFACINE (Tenex®)	Extended-release formulation: high-fat meal ↑ peak concentration and AUC	N/V/D, abdominal pain, appetite decreased, constipation, stomach discomfort, xerostomia, weight gain		Swallow extended-release tablet whole with water, milk, or other liquid; do not crush, break, or chew; do not administer with high-fat meal

(*Continued*)

	Nutritional Considerations	Possible Gastrointestinal Side Effects	Possible Effects on Lab Values	Comments/ Recommendations
Isotretinoin (Accutane®)	Food or milk ↑ bioavailability. Vitamin A supplements increase toxic effects	Xerostomia, anorexia, N/V, IBS, acute pancreatitis	↑ Triglycerides, ↑ alk phos, ↑ AST, ↑ ALT, ↑ glucose, ↑ calcium	
Sevelamer (Renagel®)	Reduced levels of folic acid and vitamins D, E, and K may occur	Abdominal pain, flatulence, constipation	↑ Calcium	Take with meals. Tablets must be swallowed whole; do not crush, chew, or break
Sildenafil (Revatio®; Viagra®)		Diarrhea, dyspepsia	↑ LFTs	Administer tablets without regard to meals at least 4–6 h apart; avoid grapefruit juice
Levodopa	High protein diets may ↓ efficacy of levodopa. Avoid foods high in pyridoxine content	N/D, constipation, anorexia, GI bleeding, xerostomia	↑ Homocysteine	Administer with food
Levothyroxine (Synthroid®)	Iron supplements increase thyroid requirements. Limit intake of goitrogenic foods. Dietary fiber may decrease absorption	Diarrhea, weight loss, abdominal cramps, increased appetite		Administer on empty stomach

Orlistat (Xenical®)	Reduces the absorption of vitamins D and E and β-carotene	Gastric discomfort, nausea, fatty/oily stool, diarrhea	Increased levels of urinary oxalate	Patients should be advised to adhere to dietary guidelines; gastrointestinal adverse events may increase if taken with a diet high in fat (>30% total daily calories from fat)
Paricalcitol (Zemplar®)		N/V/D, GI bleeding, constipation, abdominal pain, dyspepsia, xerostomia	Hypoglycemia	Excessive vitamin D administration may lead to oversuppression of PTH, hypercalcemia, hypercalciuria, hyperphosphatemia

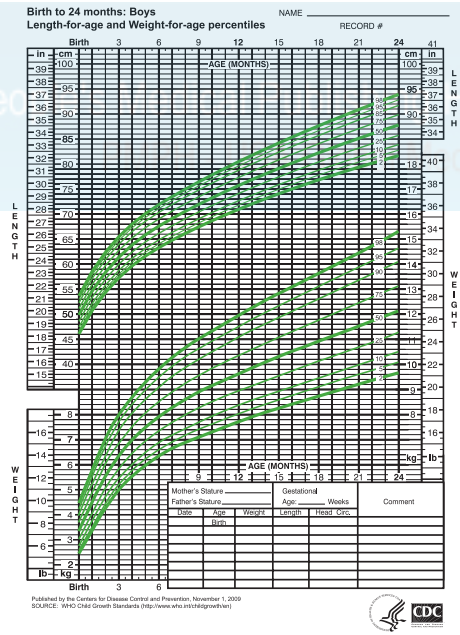
*N = nausea
V = vomiting
D = diarrhea

APPENDIX 3:
GROWTH CHARTS

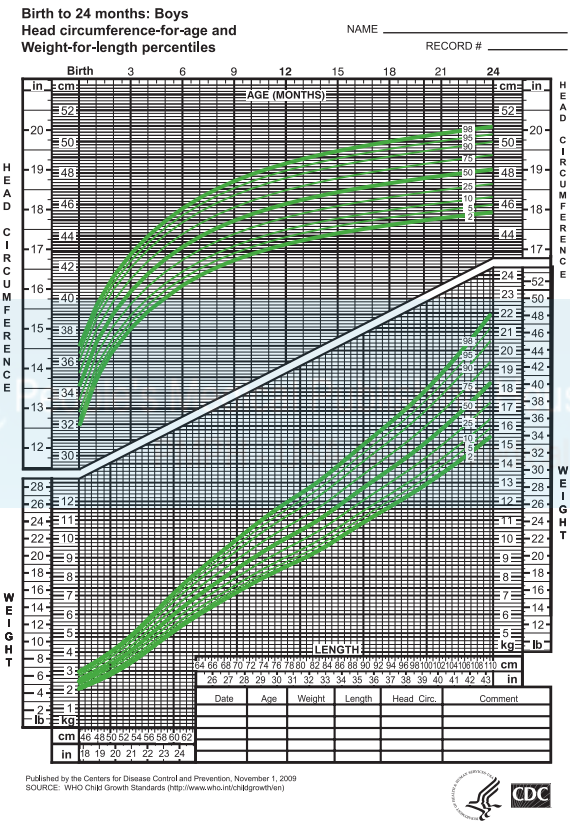
STACEY TARRANT, RD, LDN

The WHO growth standards that should be used for healthy infants and children from birth to 2 years of age and the CDC growth charts that should be used for children from 2 to 20 years of age are included below.

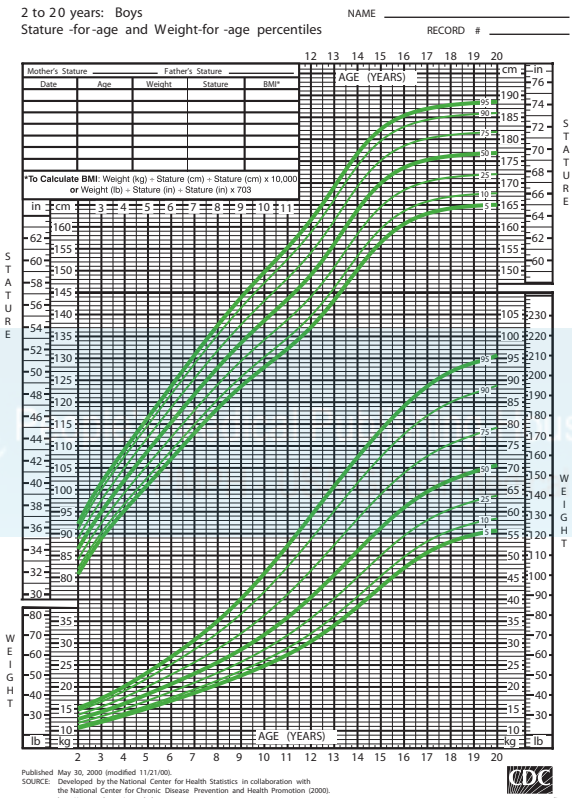
Birth to 24 months: Boys length-for-age percentiles and weight-for-age percentiles



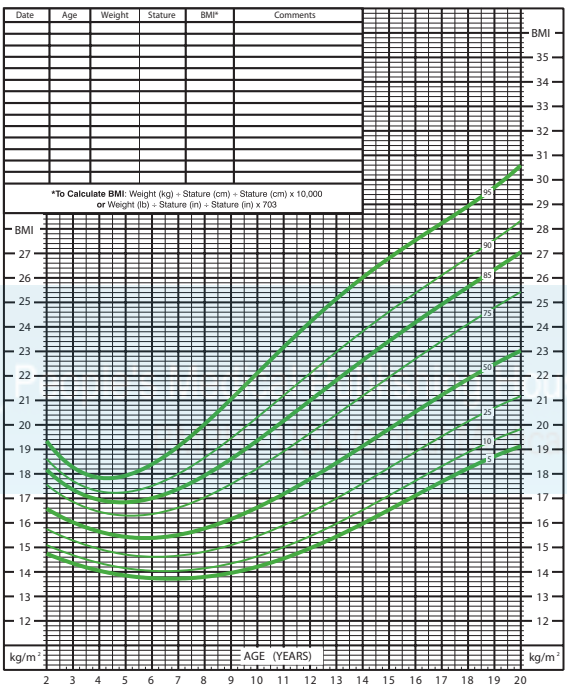
Birth to 24 months: Boys weight-for-length percentiles and head circumference-for-age percentiles



2–20 years: Boys stature-for-age and weight-for-age



2–20 years: Boys BMI-for-age



Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000). http://www.cdc.gov/growthcharts

CDC
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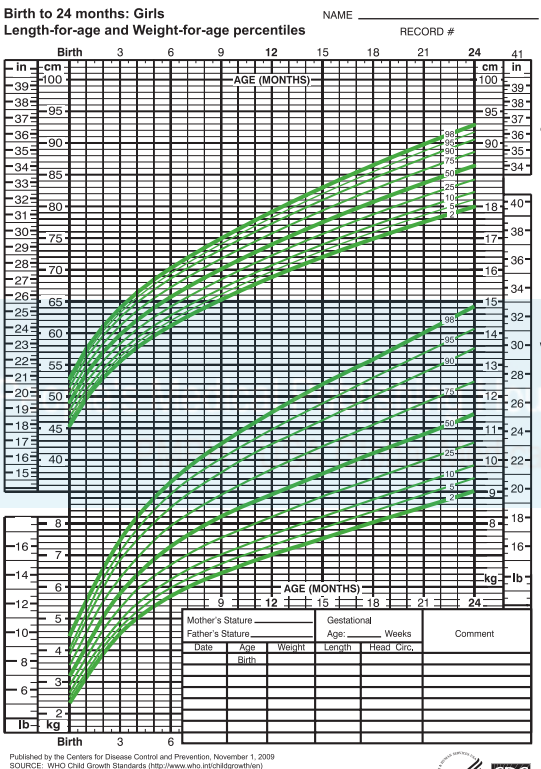
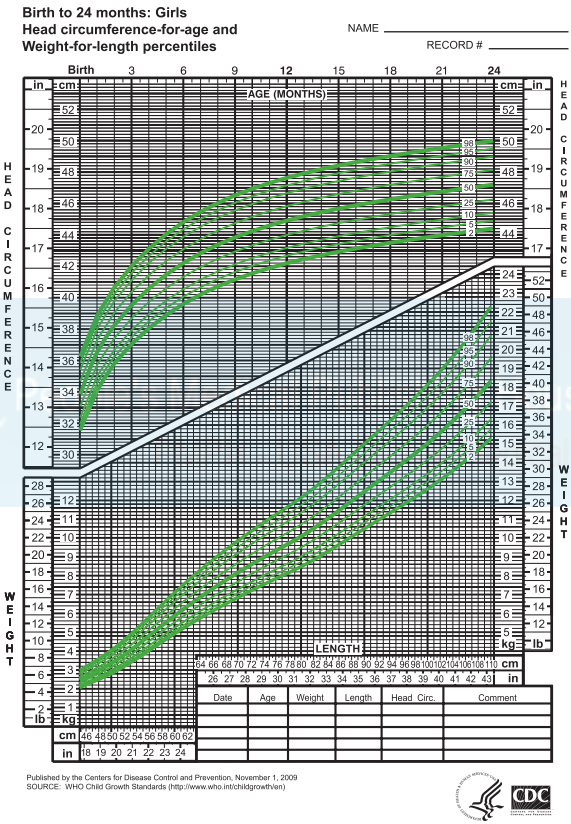
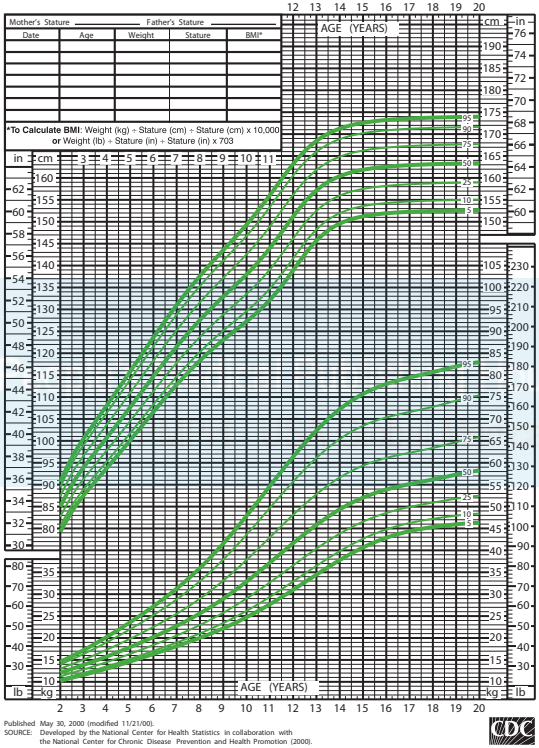
Birth to 24 months: Girls length-for-age percentiles and weight-for-age percentiles



Birth to 24 months: Girls weight-for-length percentiles and head circumference-for-age percentiles



2–20 years: Girls stature-for-age and weight-for-age



2–20 years: Girls BMI-for-age

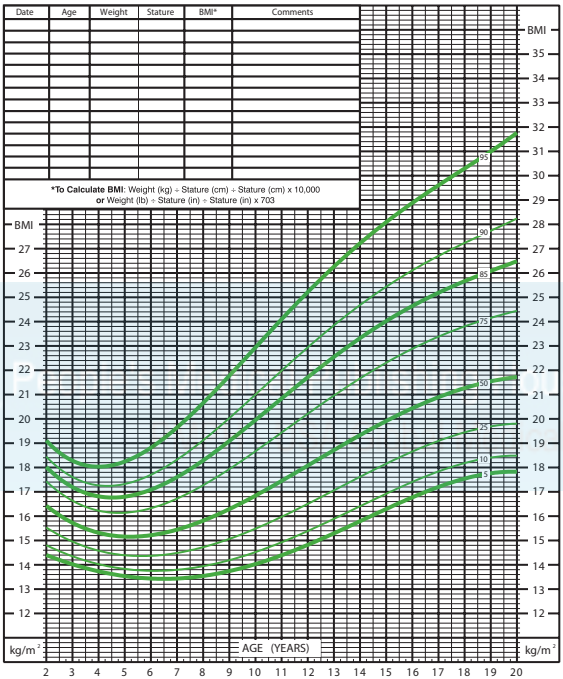
2 to 20 years: Girls
Body mass index-for-age percentiles

NAME _____

RECORD # _____

Date	Age	Weight	Stature	BMI*	Comments

***To Calculate BMI:** Weight (kg) ÷ Stature (cm) ÷ Stature (cm) x 10,000
or Weight (lb) ÷ Stature (in) ÷ Stature (in) x 703



Published May 30, 2000 (modified 10/16/00).
SOURCE: Developed by the National Center for Health Statistics in collaboration with the National Center for Chronic Disease Prevention and Health Promotion (2000). http://www.cdc.gov/growthcharts

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Anthropometric assessment of the nutritional status of patients with genetic and other medical conditions can be difficult using the WHO and CDC charts. To help evaluate the growth patterns of these patients, special weight and height curves for several syndromes have been published. Below is a list of references for growth curves for specific syndromes. For growth charts that are available electronically, the website references have been included.

Appendix 3–1 Special Growth Charts[a]

Condition	Reference(s)
Achondroplasia	Horton WA, et al. *J Pediatr.* 1978;93:435. Stature, growth velocity, head circumference, upper and lower segments. Hunter AGW, et al. *Am J Med Genet.* 1996;62:255. Weight-for-height. Hoover-Fong JE, et al. *Am J Med Genet Part A.* 2007;143A:2227. Weight-for-age from birth to 16 years. Electronic versions of these charts may be accessed at: http://qbdc.org/growth-charts/
Brachmann (Cornelia) de Lange syndrome	Kline AD, et al. *Am J Med Genet.* 1993;47:1042. Length- and weight-for-age birth to 36 months, height- and weight-for age 2 to 18 years, and head circumference-for-age birth to18 years. Electronic version of these charts may be accessed at: http://www.cdlsusa.org/docs/growth-charts-boy.pdf http://www.cdlsusa.org/docs/growth-charts-girl.pdf
Cerebral palsy (quadriplegia)	Krick J, et al. *J Am Diet Assoc.* 1996;96:680. Stature- and weight-for age and weight-for-stature age birth to 10 years.

Condition	Reference(s)
	Electronic versions of these charts may be accessed at: http://www.kennedykrieger.org/patient-care/patient-care-centers/cerebral-palsy-neurodevelopmental-medicine-phelps-center/cp-growth-references
Down syndrome	Cronk CE, et al. *Pediatrics*. 1978;61:564 and *Pediatrics*. 1988;81:102. Length-for-age and weight-for-age birth to 36 months; stature-for-age and weight-for-age 2 to 18 years. Until new growth charts are developed for Down syndrome, the American Academy of Pediatrics (AAP) recommends using the standard growth charts of the National Center for Health Statistics (NCHS) or the World Health Organization (WHO), as the previously used Down syndrome-specific growth charts no longer reflect the current population styles and body proportion. (Bull MJ, et al. Pediatrics. 2011;128:393.)
Marfan syndrome	Erkula G, et al. *Am J Med Genet*. 2002;109:100. Height- and weight-for-age 0 to 36 months and 2 to 18 years. Weight-for-height.
Myelomeningocele	Ekvall SW, Ekvall VK, editors. Appendix 2. In: *Pediatric Nutrition in Chronic Diseases and Development Disorders: Prevention, Assessment, and Treatment. 2nd ed.* New York: Oxford University Press; 2005. pp. 403–404. Height- and weight-for-age 0 to 20 years.
Noonan syndrome	Witt DR, et al: *Clin Genet*. 1986;30:150–153. Growth curves for height in Noonan syndrome.
Prader Willi syndrome	Butler, et al. *Pediatrics*. 1991;88(4):853. Weight, height, sitting height, head circumference, triceps, and subscapular skinfold (plus other measurements) for age 2 to 22 years.

(*Continued*)

Appendix 3–1 Special Growth Charts[a] *(Continued)*

Condition	Reference(s)
	Butler, et al. Pediatrics. 2011;127:687. Weight, length, weight/length, and head circumference for non-growth hormone-treated infants 0 to 36 months.
Sickle cell disease	Thomas PW, et al. *Arch Dis Child.* 2000;82:204. Height- and weight-for-age birth to 18 years.
Silver-Russell syndrome	Tanner JM, et al. *Pediatr Res.* 1975;9:611. Height- and height velocity-for-age 2 to 19 years (includes periods of treatment with human growth hormone).
Turner syndrome	Lyon AJ, et al: *Arch Dis Child.* 1985:60:932. Height-for-age birth to 18 years (girls).
Williams syndrome	Morris CA, et al: *J Pediatr.* 1988;113:318–26. Natural history of Williams syndrome: physical characteristics.

[a]Unless otherwise specified, charts are available for both girls and boys.

INDEX

Note: Page numbers followed by f, or t indicate material in figures, or tables, respectively.

A

B

C

D

E

F

G

H

I

J

K

L

M

N

P

Q

R

S

T

U

V

W

X

Z