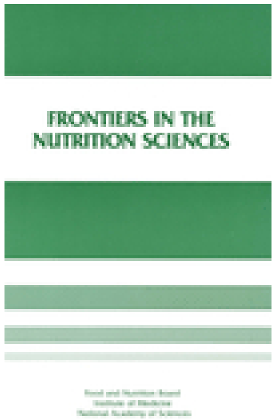

Frontiers in the Nutrition Sciences: Proceedings of a Symposium

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Frontiers in the Nutrition Sciences

Proceedings of a Symposium

Food and Nutrition Board
Institute of Medicine

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This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

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PREFACE

In 1987, the Food and Nutrition Board selected "Frontiers in the Nutrition Sciences" as the topic for its annual symposium. It symbolizes the Board's concern about declining attention to nutrition as a focal point in our universities and medical schools; but more importantly it expresses the Board's conviction that nutrition research has a bright and challenging future. Realization of this potential, however, requires cognizance of advances in molecular biology and related biological and physical sciences that form the basis of nutrition and ascertaining how this new knowledge in the basic sciences can be applied advantageously to uncover potential frontiers in nutrition research and training.

The symposium program was a preliminary step to determining the nature and extent of scientific advances that relate to nutrition, barriers to progress in the nutrition sciences, and the opportunities that lie ahead. Therefore, the primary objective of the symposium was to examine the current status of nutrition research and training at medical schools, other institutions of higher education, government-sponsored programs such as those at the U.S. Department of Agriculture's Human Nutrition Research Centers and other relevant facilities, and to identify future directions for research and training in the nutrition sciences. Sessions I and II provided an overview of advances in certain basic and applied sciences that offer opportunities for developing programs and undertaking collaborative nutrition research both domestically and internationally. Session III offered insights into trends and directions in research and training in university nutrition departments, medical schools, and schools of public health. A panel discussion focused on factors that have constrained progress and those that might enhance opportunities for research and training in the nutrition sciences.

The Food and Nutrition Board intends to use this symposium as a starting point for an in-depth study of opportunities in the nutrition sciences. Our ultimate objective is to draw attention to the field, point to barriers, highlight opportunities, and generate enthusiasm among young researchers and teachers for this indispensable component of biology.

RICHARD HAVEL, Chairman
SUSHMA PALMER, Director
Food and Nutrition Board

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I

FRONTIERS IN THE NUTRITION SCIENCES

Molecular Biology and Nutrition Research

Richard W. Hanson, Maria Hatzoglou, Mary M. McGrane,
Fritz M. Rottman, and Thomas Wagner

Metabolic research is the foundation of the science of nutrition, and progress in one area is linked to the vitality of the other. Metabolic research has not prospered over the past decade, when compared with research in fields such as genetics, due in part to a limitation in the techniques applied to metabolic problems. For too long metabolic research has focused on redefining problems of regulation without developing new methods powerful enough to provide definitive answers to these problems. The result has been a general demise of metabolism as an area of modern biology. With its research base contracting, nutritional science has become a more descriptive and less vital scientific field.

The revolution in molecular biology has brought new opportunities and a fresh challenge for metabolic research. To date, research in molecular biology has focused on the characterization of specific genes and on the processes that alter their expression. Many genes have been sequenced and their promoter-regulatory regions have been delineated, and various mutations involved in disease processes have been described. However, the ability to isolate and characterize a gene of interest is the first step in a process that can involve the modification and expression of that gene in cells and animals. It is here that the opportunities for the direct application of molecular biology to the field of metabolic research has the potential for its greatest impact. This brief review outlines some of the techniques in this rapidly evolving field and speculates on their application to metabolic research.

ISOLATION AND CHARACTERIZATION OF GENES OF METABOLIC INTEREST

The first area in which molecular biology will have an impact on metabolic research is the isolation and characterization of genes that code for proteins of metabolic interest. To date, understanding of the regulation of a key metabolic enzyme, such as the pyruvate dehydrogenase complex, phosphofructokinase, or P-enolpyruvate carboxykinase (PEPCK), has been limited by a total lack of knowledge of the primary or three-dimensional structures of these proteins or the configuration of the ligand-binding domains, which are critical to their functioning. As the list of genes of this type that have been sequenced grows, there will soon be a complete series of structures on which to base experimental approaches to understanding the regulation of key enzymes. This initial phase of characterization of metabolically important genes is well under way, and it is safe to predict that within the next 5 years, most of the major regulatory enzymes in important metabolic pathways such as glycolysis and gluconeogenesis will have been cloned, sequenced, and studied further.

The availability of complementary DNA (cDNA) clones for specific regulatory enzymes will permit their overexpression in bacteria and purification of the protein. Coupling of these techniques with site-directed mutagenesis of the DNA will permit a detailed analysis of structure-activity relationships for individual enzymes. This level of analysis requires knowledge of the complete crystal structure of the protein to accurately assign specific amino acids within the protein. At this point, the determination of the crystal structure of a protein is the rate-limiting step in studying its function by site-directed mutagenesis. This fact is reflected in the current demand for (and shortage of) X-ray crystallographers. It is ironic that it is now easier to isolate, clone, and sequence a gene than it is to characterize it by established physical methods.

An excellent example of the great power of the combined techniques discussed above is the work of Robert Fletterick and colleagues on the characterization of glycogen phosphorylase (Sprang et al., 1987; S. Sprang, E. Goldsmith, and R. Fletterick, unpublished data). This dimeric enzyme, which is present in muscle and liver tissues (Krebs and Fisher, 1956), has been purified and its crystal structure determined (Sprang et al., 1987, unpublished data). The enzyme is regulated by two parallel mechanisms. The first of these involves its phosphorylation by a glycogen, phosphorylase kinase, which converts the enzyme from the inactive b-form to the active a-form (Krebs and Fisher, 1956). Glycogen phosphorylase kinase is, in turn, phosphorylated (and activated) by a cyclic AMP (cAMP)-dependent protein kinase. This mechanism of liver glycogen phosphorylase regulation is directly linked to the level of blood glucose via alterations in the concentration of glucagon. The second type of regulation involves control of the activity of the enzyme by a series of intracellular intermediates, including AMP, ATP, and glucose-6-phosphate. These two mechanisms of regulation working together ensure a coordinated response to changes in energy metabolism and to the carbohydrate status of the organism. Such control is central to metabolic regulation and forms the basis of the nutritional response to carbohydrate intake.

Glycogen phosphorylase b, the unphosphorylated form of glycogen phosphorylase, binds AMP at a site on one of the subunits, which in turn promotes further binding of this ligand to a site on the second subunit. Glycogen phosphorylase b is inactive in the absence of AMP and is 80% as active as glycogen phosphorylase a when AMP is bound to the enzyme (Green and Cori, 1943; Morgan and Parmeggiani, 1964). Both ATP and glucose-6-phosphate inhibit glycogen phosphorylase b by competing with AMP and stabilizing the catalytically inactive conformation of the enzyme. An understanding of the nature of the complex interaction between these regulatory molecules has been limited by the absence of a detailed structure-function analysis of glycogen phosphorylase.

In a recent publication, Sprang et al. (1987) presented a detailed analysis of the structure of the glycogen phosphorylase nucleotide activation switch. That study elegantly demonstrated the power of the combined techniques of molecular biology and protein chemistry when they are applied to a regulatory enzyme of metabolic interest. Since the cDNA for the enzyme was cloned and the primary sequence of the phosphorylase was deduced from the nucleotide sequence, a detailed map of the amino acids at the enzyme's active site was determined. From the crystal structure of the protein, Sprang and coworkers showed that the subunit interface of glycogen phosphorylase is composed of a catalytic and a regulator, domain (Figure 1). The catalytic site of the enzyme was mapped to a crevice in the protein between the two domains, while the regulatory domain was found at the interface of the two subunits. The amino acid residues involved in nucleotide binding were identified, and their relative affinities for AMP and ATP were determined. A reaction mechanism based on the structure of both the

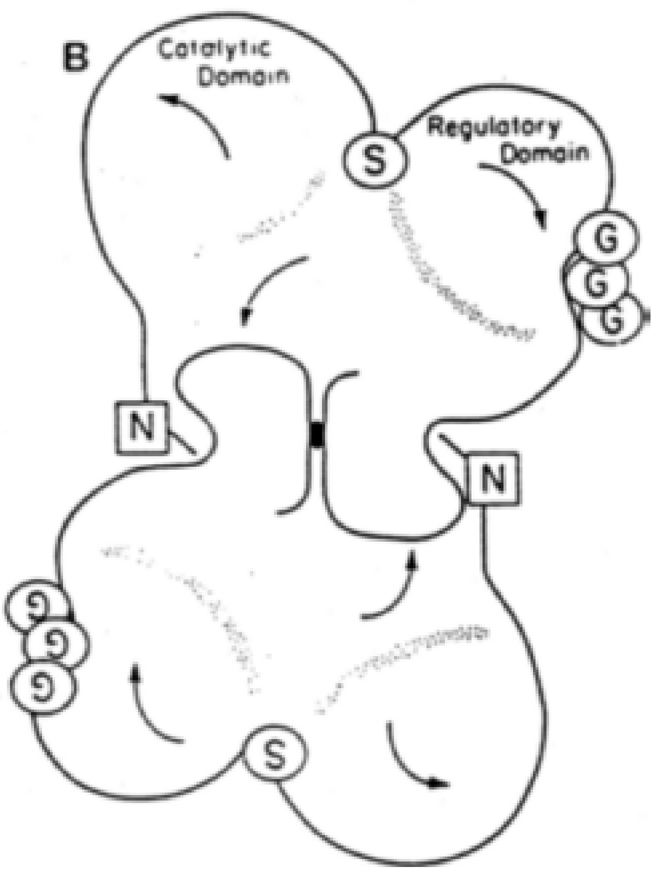

Figure 1 Schematic representation of changes in the dimeric glycogen phosphorylase a molecule. Abbreviations: S, Ligand-binding sites for glucose and glucose-1-P; G, glycogen and oligosaccharides; and N, AMP and ATP. SOURCE: From Sprang et al. (1987), with permission of the authors.

regulatory and catalytic sites on glycogen phosphorylase can thus be derived, and the conformational changes that occur in the enzyme after ligand binding can be described.

A detailed presentation of these studies is beyond the scope of this review; however, the work of Sprang et al. (1987) is an example of the refined analysis of enzyme regulation that will provide a molecular basis for the next generation of metabolic studies. Because of this work, it is now possible to discuss the regulation of glycogen phosphorylase in terms of its molecular interactions with regulatory molecules and to alter the metabolic function by site-directed mutagenesis based on an understanding of the reaction mechanism. Information of this type for other enzymes can be expected to increase rapidly as the sequencing and crystal structure analyses become available. A knowledge of the enzyme structure at this level also permits the rational design of modified proteins for metabolic studies involving gene transfer to cells and animals. This is discussed below in more detail.

THE INTRODUCTION OF GENES INTO CELLS AND ANIMALS

Construction of Chimeric Genes

Many structural genes that code for proteins of metabolic interest have been isolated and characterized (Goodridge and Hanson, 1986), including genes that code for key regulatory enzymes in metabolic pathways, hormones such as growth hormone, and insulin and a variety of receptors, to name only a few genes of interest. The number of proteins that have been isolated and characterized is growing rapidly and is likely, ultimately, to include virtually all of the important proteins involved in metabolic processes.

At the same time, the control regions within the 5´-flanking gene sequences are being isolated and studied. It is this promoter-regulatory region of a gene that controls its expression. Specific sequences contained in this complex region of a gene interact with transcriptional regulatory factors, which are often intermediates in hormone action, to control the tissue-specific expression of the gene in animals. It is now possible to construct genes that contain a chimeric promoter-regulatory region that contains, for example, selected hormone-responsive elements, a promoter element with appropriate strength, and a tissue-specific element that directs expression of the gene to a tissue of interest. This chimeric promoter-regulatory region can then be ligated to a segment of DNA coding for a structural gene of interest and can be introduced into cells or animals.

As the techniques for stably introducing genes into cells and animals improve, it should be possible to reproducibly target genes for selected tissues in animals by using these chimeric genes. This is a new tool with great potential for metabolic studies, since it will permit, for the first time, a modification of an enzymatic step in a complex metabolic pathway without the use of inhibitors or other compounds that have a broad spectrum of action in cells or animals. It also provides the potential to correct metabolic defects in humans, if the technology can be perfected to ensure a predicted site of integration into the human genome, as well as a normal level of expression of the newly introduced gene. We review here some aspects of this field and use as an example our own studies with the PEPCK gene, since its promoter-regulatory region has proven useful in driving the expression of a variety of structural genes in a regulated and tissue-specific manner. We also review the techniques currently being used to introduce genes into cells and animals in order to demonstrate both the limitations of and potential for these techniques.

Properties of a Regulated Promoter

The selection of an appropriate promoter-regulatory region for use with a linked structural gene in metabolic studies depends on the tissue in which the gene is to be expressed and the type and level of regulation of gene expression that is required. The promoter-regulatory region of the gene coding for the cytosolic form of PEPCK (GTP) (EC 4.1.1.32) contains a highly regulated promoter sequence, with regulatory elements for cAMP (Short et al., 1986; Wynshaw-Boris et al., 1984, 1986), glucocorticoids (Wynshaw-Boris et al., 1984, 1986), insulin (Magnuson et al., 1987; McGrane et al., 1988), and thyroid hormone (M. Hatzoglou, W. Lamers, A.

Wynshaw-Boris, and R.W. Hanson, unpublished observations), all within 550 base pairs (bp) of flanking DNA at the 5´ end of the gene. This gene also has a very high level of transcription (3,500 parts per million after administration of cAMP) (Lamers et al., 1982; Meisner et al., 1983) in transgenic mice and tissue-specific sequences are present in the promoter that directs gene expression, to the liver and kidney (McGrane et al., 1988). The messenger RNA (mRNA) for PEPCK has a half-life of 30 minutes (Granner et al., 1983; Tilghman et al., 1974), so that the level of mRNA for the enzyme is largely dependent on alterations in the transcription rate of the gene. Hormones such as glucagon (acting via cAMP), glucocorticoids, or insulin have a very marked and rapid effect on PEPCK gene transcription.

The administration of Bt_2cAMP to an animal causes an 8-to 10-fold induction in the rate of transcription of the gene within 20 minutes (Lamers et al., 1982). This effect can be blocked in cells if insulin is administered together with the cAMP (Granner et al., 1983; Wynshaw-Boris et al., 1986b). The PEPCK promoter thus has many advantages for use as a vehicle to drive the expression of linked genes in animal tissues; it is expressed in a tissue-specific manner and is regulated acutely by hormones, and its promoter strength is great enough to ensure sufficiently high levels of gene product.

The various hormone response elements in the promoter have been identified by gene transfection experiments in which chimeric genes containing segments of the promoter-regulatory region of the PEPCK gene were ligated to the structural gene for a selectable marker, such as the amino-3´-glycosyl phosphotransferase gene, which makes cells resistant to the cytotoxic compound, G418, or the Herpes virus thymidine kinase (TK) gene (Short et al., 1986; Wynshaw-Boris et al., 1984, 1986b). Figure 2 shows the locations of sequences in the PEPCK promoter that confer sensitivity to cAMP and glucocorticoids in the chimeric PEPCK-TK gene. Two cAMP response elements have been mapped by DNA-protein footprinting to the region between positions-82 to-90 and-135 to-142 (Roesler et al., 1989). The entire region of DNA between positions-61 and-416 can act as a hormonally sensitive enhancer and can regulate expression when it is

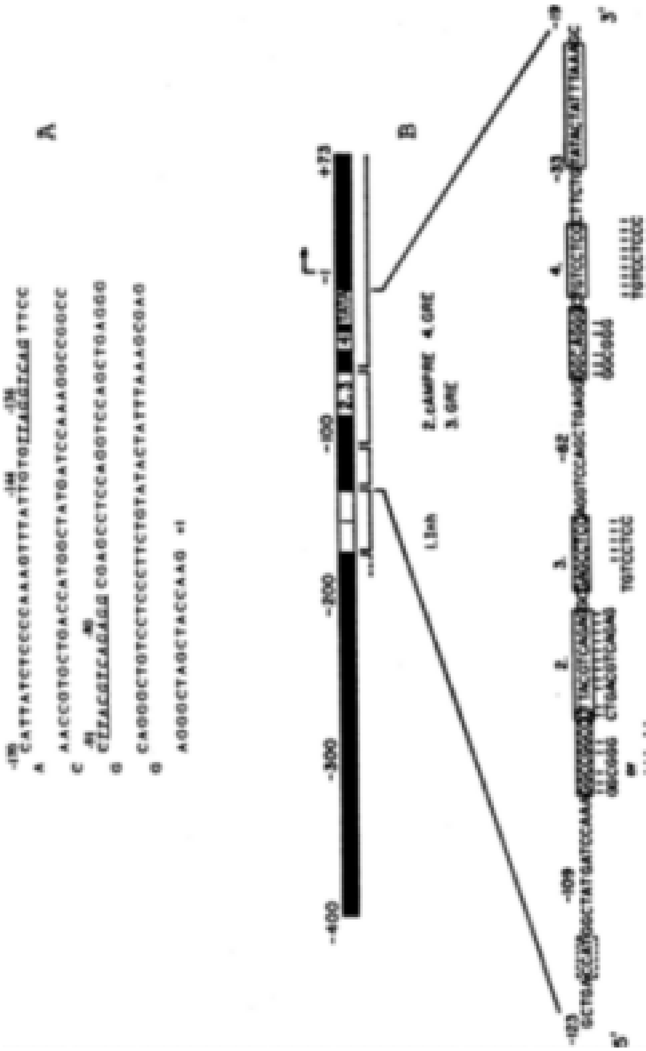

Figure 2 The promoter-regulatory region of the PEPCK range. (A) Nucleotide sequence from positions -170 to +1, showing the putative cAMP regulatory regions present between positions -91 to -80 and positions -144 to -136. (B) Position of the proposed regulatory elements in the PEPCK gene; Inh, inhibitory regulatory element; GRE, glucocorticoid-regulatory element; cAMPRE, cAMP-regulatory element. SOURCE: Short et al., 1986; Wynshaw-Boris et al., 1986b.

introduced into the chimeric gene in either transcriptional orientation or at a distance from the start site of transcription of the gene (Figure 3; Wynshaw-Boris et al., 1986b).

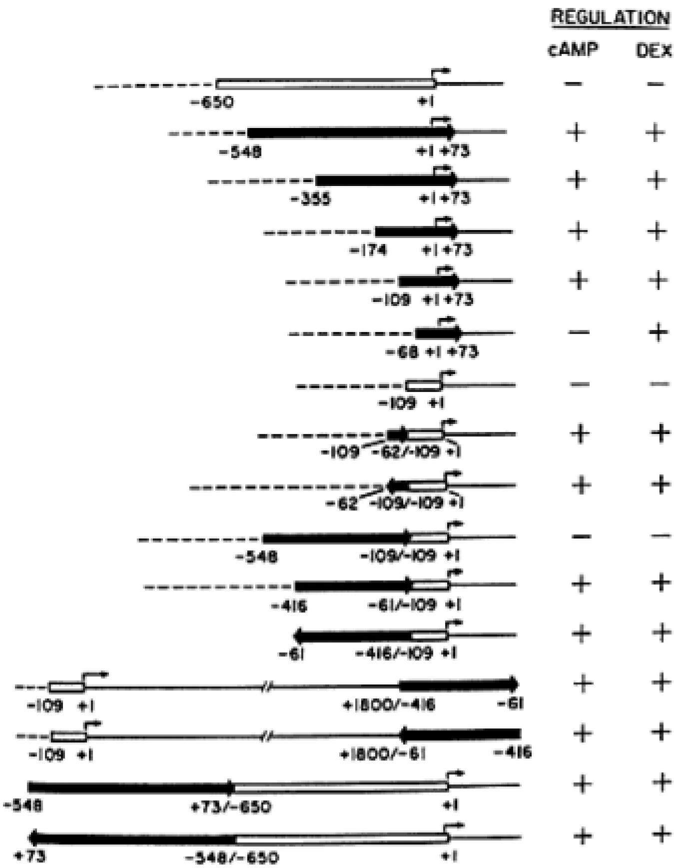

Figure 3 Functional analysis of the PEPCK promoter-regulatory region for cAMP and glucocorticoid regulatory elements. Rat hepatoma cells deficient in TK

were transfected with the genes shown on the left. These chimeric genes contain segments of the PEPCK promoter-regulatory region ligated to the structural gene for Herpes virus TK from the region noted in the figure. RNA was isolated from hypoxanthine-aminopterin-thymidine (HAT)-resistant cells that were either treated with Bt_2cAMP (cAMP) or dexamethasone (DEX) or not treated, and the level of TK mRNA was determined by quantitative S1 nuclease mapping. An induction (+) or lack of response (-) of TK mRNA within 3 hours after the addition of cAMP or DEX is indicated on the right. The PEPCK promoter-regulatory region is represented by filled boxes, with arrows indicating the direction of ligation relative to the direction of PEPCK gene transcription. Open boxes are the TK promoter sequences retained in the chimeric gene in the indicated constructions. The direction of chimeric gene transcription is noted by the arrow at position +1. The numbers below either the PEPCK or the TK promoter-regulatory regions indicate the position of the fragment relative to the start site of the gene of origin. The thin line represents TK structural gene sequences. SOURCE: Wynshaw-Boris et al. 1986a); the figure is based on a variety of published studies (Short et al., 1986; Wynshaw-Boris et al., 1984, 1986b), in which the methods used are described in detail.

The number of tissue-specific promoters that have been isolated and characterized in both cells and transgenic animals is growing rapidly. One of the most intensively studied elements is the promoter for the rat elastase I gene, which is expressed in the acinar cells of the exocrine pancreas. Hammer et al. (1987) have reported that 134 bp of 5´-flanking sequence in the elastase I gene is sufficient to direct gene expression in the pancreas of transgenic mice. This element, which extends from positions-72 to-205, is highly conserved in all species studied and confers the correct developmental and regulatory properties on a linked structural gene. It has even been possible to induce neoplasia of the exocrine pancreas in fetal transgenic mice that contain a chimeric gene composed of 4.5 kilobases (kb) of the rat elastase I promoter, ligated to the structural gene for the oncogene c-H-ras (Quaife et al., 1987). The tissue-specific expression of the immunoglobin, globin, actin, and *a*-fetoprotein genes has also been studied by using transgenic animals; and sequences that are responsible for their tissue-specific expression have been identified in the 5´-flanking regions of these genes. It is thus possible to select promoters containing sequences that direct the expression of a linked structural gene to a tissue of choice in an animal.

Methods for Introducing Genes into Cells and Animals

Genes can be introduced into cells by transfection, particle-mediated gene transfer, microinjection, electroporation, or viral infection and can be introduced into animals by microinjection of DNA into the male pronucleus of fertilized eggs or retroviral infection of embryonic tissue prior to development. A detailed discussion of each of these techniques is presented in detail by Wynshaw-Boris et al. (1986a). We concentrate on three of the most widely used techniques relevant to metabolic studies: DNA transfection, retroviral infection of cells and animals, and nuclear DNA microinjection.

DNA Transfection. DNA transfection is the most commonly used technique for introducing genes into cells. DNA is layered onto cells as a calcium phosphate precipitate; it is then taken up by endocytosis and is transported to the nucleus. The DNA is retained in the nucleus for a relatively short time (24 to 48 hours) before it is degraded. A small fraction of the gene introduced by this procedure is transiently expressed, and about 0.01% is integrated into the genome of the host cell. It is possible to use selection techniques (see Wynshaw-Boris et al. [1986a] for a detailed review) to isolate and subclone cells that have stably incorporated functional copies of the transfected gene into their genome and to establish clonally isolated lines of these cells. Alternatively, transient expression of the gene can be measured and used to monitor gene function. Despite its limitations, this procedure is widely used to measure the function and regulation of specific promoter elements in any cell line that can be maintained in culture. The usefulness of DNA transfection for metabolic studies is limited by its low efficiency of gene transfer and by the need to isolate and establish cell lines in order to carry out the more long-term experiments required for the replication of metabolic measurements.

Retroviral Vectors. Retroviruses have several features that make them ideal vectors for the introduction of genes into cells and animals. Retroviral infection is highly efficient and produces cells that have integrated into their genomes a single copy of the provirus containing the gene of interest. In certain cases, this obviates the need to subsequently select from a large population of cells individual cells that functionally express the transfected gene. A wide variety of species-specific retroviral vectors are available that can accommodate DNA segments ranging from 1 to 15 kb. Finally, retroviral vectors can be used to infect both cells and animals, which makes retroviruses useful vectors for the introduction of genes into differentiating tissues in animals during development (Johnson et al., 1985; Soriano and Jaenisch, 1986; Van der Putten et al., 1985). There have been several excellent recent reviews that document the usefulness of retroviral vectors for gene transfer (Bernstein et al., 1985; Gelboa et al., 1986).

The retroviral life cycle involves four steps. First, the virus binds to and infects the host cell. This process is species specific in that the virus recognizes determinants on the surface of the cell to be infected. Second, the RNA of the virus is converted to DNA by reverse transcriptase. This DNA enters the nucleus and integrates into the host cell genome as a provirus. Third, the provirus acts as a template for the synthesis of RNA, which yields viral proteins and additional copies of the retroviral genome. Finally, the genomic RNA and the retroviral proteins recombine into a mature virus that is released from the cell to initiate a new round of infection. These steps are illustrated in Figure 4 and have been described by Bernstein et al. (1985) and Gelboa et al. (1986).

The retroviral genome contains the information needed for transcription of the proviral DNA (cis functions), as well as the genes coding for proteins that are necessary for the normal life cycle of the virus (trans functions), such as the envelope protein (env gene) or reverse transcriptase (pol gene). The cis functions in the retrovirus include the promoter sequences required for

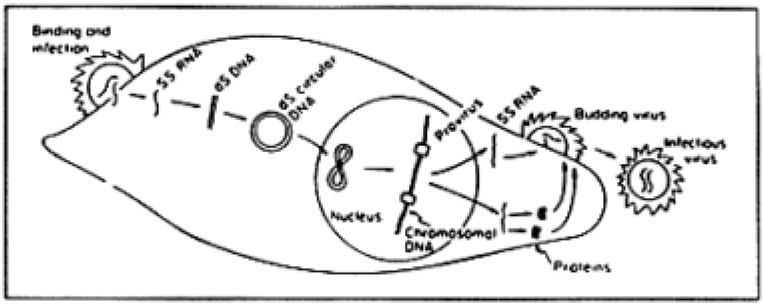

Figure 4 Retroviral life cycle. The process of retroviral infection is outlined. The figure traces the integration of proviral DNA into the genome of the host cell. Details are given in the text. (Reprinted with permission from Bernstein et al. [1985, p. 235]).

the initiation of gene transcription, various enhancers, and the sequences needed to guide the integration of the provirus into the host cell genome. These are contained within regions of the provirus termed long terminal repeats (LTRs). There is also an important segment of DNA that encodes the information needed for encapsidation, or viral packaging (ψ sequences.)

Many retroviral vectors that retain these cis functions within the vector have been constructed. An example is the retroviral vector pLJ, shown in Figure 5A, which is derived from the Moloney murine leukemia retrovirus (Korman et al., 1987). To be functional, retroviral vectors of this type rely on the availability of trans functions from helper cells that have been infected with retroviruses or from a specially constructed cell that contains these functions stably integrated into its genome. One such cell line, ψ2, was constructed by Mann et al. (1983) and is widely used to produce a high titer of retrovirus that is capable of only a single round of infection.

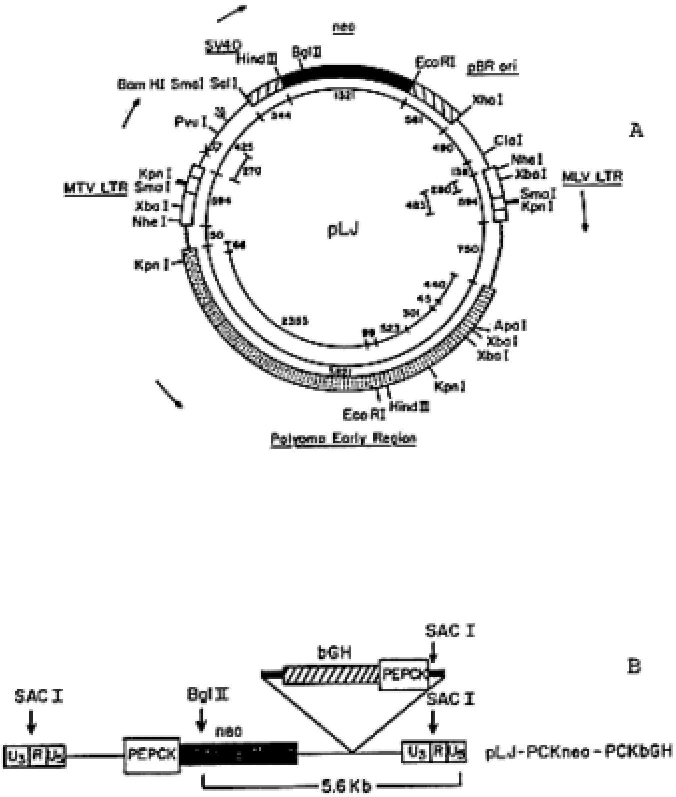

Figure 5 The murine retroviral vectors pLJ and pLJPCKneo-PCKbGH used to introduce genes into cells and animals. (A) pLJ was a generous gift of Dr. Richard Mulligan (Massachusetts Institute of Technology, Boston, Mass.). The vector is composed of the Moloney murine leukemia virus LTRs and includes the y sequences and the simian virus 40 (SV40) promoter linked to the structural gene for amino-3´-glycosyl phosphotransferase (neo). (B) pLJPCKneo-PCKbGH. The SV40 promoter from pLJ was removed and replaced by a 550-bp segment of the PEPCK promoter-regulatory region. A new chimeric gene composed of the same region of the PEPCK gene ligated to the bGH structural gene (without its own promoter) was inserted at the unique ClaI site in an orientation opposite the direction of transcription from that of the 5´ LTR.

Alternatively, a series of avian retroviral vectors that are replication competent and that infect virtually all of the tissues of the bird are available (Hughes and Kosik, 1984). Use of these retroviral vectors results in viremic birds. This type of virus is a powerful tool for the introduction of a foreign gene of interest into avian cells.

DNA Microinjection. The methods for the development of transgenic mice are theoretically straightforward, but they are technically demanding and require a large financial investment in expensive, specialized equipment. A recent detailed review by Camper (1987) provides an excellent summary of both the technique used for producing transgenic animals and the equipment needed to initiate such an undertaking.

In practice, female animals are induced to superovulate by injecting follicle-stimulating hormone; they are mated with fertile males. The fertilized eggs are collected from the oviducts, and approximately 300 copies of the gene of interest, in a volume of 1 pl, is microinjected into the male pronucleus. The microinjected eggs are implanted into the oviducts of pseudopregnant females and allowed to develop to term (Wagner et al., 1981). It is customary to wait until the animal is born and nutritionally independent from the mother before initiating the analysis of integration of the microinjected DNA in the genome of the animal. However, analysis of the host animal's genome can be carried out during fetal development or immediately after birth if specific developmental or metabolic questions are involved. Normally, a segment of the animal's tail is removed, and the DNA is extracted and analyzed by dot-blotting with a specific DNA probe, usually a fragment of the transgene that was microinjected. Camper (1987) estimated that of 60 eggs that survive microinjection, 6 of the implanted zygotes develop to term, and of these, 1 to 2 are transgenic.

METABOLIC STUDIES USING GENETICALLY MODIFIED CELLS AND ANIMALS

The most common use of genetically modified cells and animals is for the analysis of gene expression control. This is relevant to metabolic studies, since many of the adaptations caused by diet are mediated by hormonally induced alterations in the expression of genes of metabolic importance. Also, understanding of the mechanism of action of hormones such as insulin, glucagon, and glucocorticoids has advanced significantly since the advent of these new techniques for genetically modifying cells and animals. Elements in the promoter-regulatory regions of genes that are required for their response to these hormones have been identified, and specific binding proteins that regulate gene transcription are being isolated and characterized.

The major impact of this new technology on nutrition, however, is likely to come in the next phase of research, when genes of metabolic interest are modified, reinserted, and studied in animals. This type of experimental model will be invaluable for research in a broad variety of areas of nutrition and metabolism.

Introduction and Regulation of Genes Introduced into Hepatoma Cells via Retroviral Vectors

A major point that must be established in proving the usefulness of the techniques available for programming metabolic processes in cells is the level of expression and regulation of genes introduced into cells and animals. The usefulness of retroviral vectors for this type of study is illustrated by a series of experiments in which two chimeric genes, PEPCK-neo and PEPCK-bovine growth hormone (bGH) contained in a single retroviral vector (Figure 5B), were infected into hepatoma cells in culture. The 550-bp segment of the promoter-regulatory region of the PEPCK gene used to construct these chimeric genes contains both the cAMP and glucocorticoid regulatory elements (Short et al., 1986; Wynshaw-Boris et al., 1984, 1986). When Bt_2cAMP or glucocorticoids were added to hepatoma cells (rat FTO-2B cells and mouse Hepa 1-6C cells) infected with this virus, there was a two-to threefold increase in the output of bGH in the culture medium within 2 hours (Figure 6).

Furthermore, the PEPCK-neo gene was regulated in a parallel fashion in the cells. It is worth noting that the concentration of bGH released by mouse hepatoma cells after Bt_2cAMP stimulation is 0.5 μg/ml of culture

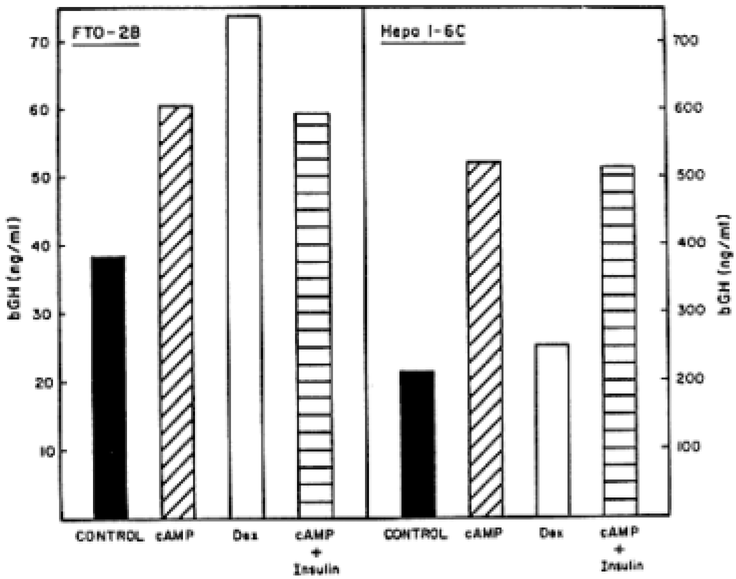

Figure 6 Effect of hormones on the production of bGH by FTO-2B and Hepa 1-6C hepatoma cells infected with the retroviral vector pLJPCKneo-PCKbGH. Cells were incubated with Bt_2cAMP (cAMP), dexamethasone (DEX), and insulin (Ins) for 24 hours; the bGH in the culture medium was determined.

medium. This is a high level of expression of an infected gene and indicates that the 550 bp segment of the PEPCK promoter-regulatory region used in this chimeric gene may be useful in future studies in which a strong, regulatable promoter is required for producing high levels of a specific gene product for metabolic studies.

Use of Retroviral Vectors to Introduce Genes into Animals

Retroviral vectors have been used to introduce genes into mammalian tissues, both during development and after differentiation. Embryonic stem cells, such as the XY stem cell line EK.CCE (Robertson et al., 1986) or preimplantation mouse embryos (Soriano and Jaenisch, 1986), have been infected with various murine retroviruses, often containing a marker gene of interest. This has resulted in the detection of viral sequences in specific tissues of adult animals. This technique allows the construction of transgenic animals containing a specific gene that was introduced into the germ line by retroviral infection (Van der Putten et al., 1985). Retroviral vectors have also been used to introduce genes into hematopoietic stem cells, which have been reimplanted into the bone marrow of recipient mice (Magli et al., 1987; McSvor et al., 1987). This allows investigators to track the fate of these cells during stem cell maturation (Magli et al., 1987). These techniques have a clear application to gene therapy, and their usefulness in treating a variety of human diseases and is being studied intensively.

Metabolic and nutritional research would benefit greatly from the development and general application of these techniques since they afford a potential method for introducing genes of metabolic interest into tissues of intact animals. It would be possible, for example, to design nutritional studies by using a modified gene that is responsive to dietary and hormonal stimuli in an animal species of interest. The potential for these techniques for metabolic studies is illustrated by a series of experiments in which the murine retroviral vector, pLJPCKneo (see Figure 5B), was injected as an infectious retrovirus into the peritoneal cavity of fetal rats between 16 and 20 days of gestation while the animals were still in utero (Hatzoglou et al., unpublished observations). During this period the liver is undergoing differentiation from a largely hematopoietic tissue into a hepatic organ (Jones, 1982). This is accompanied by a high level of cell division and hepatic growth. The retroviral vector integrates into the liver of these animals, introducing the regulatable PEPCK promoter linked to a structural gene for a marker protein such as neo or bGH, the latter of which can be assayed in the blood of the animal.

The chimeric PEPCK-neo and PEPCK-bGH genes are expressed in the livers of host animals; the level of expression of these genes appears to be regulated by cAMP, glucocorticoids, and thyroid hormone (Hatzoglou et al., unpublished observations). The relative level of RNA synthesized from these newly introduced genes was an order of magnitude lower than the level of PEPCK mRNA synthesized by the endogenous gene (Figure 7). The ability to direct the expression of a chimeric gene into the tissues of an animal relatively late in development, however, holds promise as a technique of potential usefulness for broader metabolic studies aimed at introducing modified genes of interest into animals to alter various metabolic and nutritional parameters.

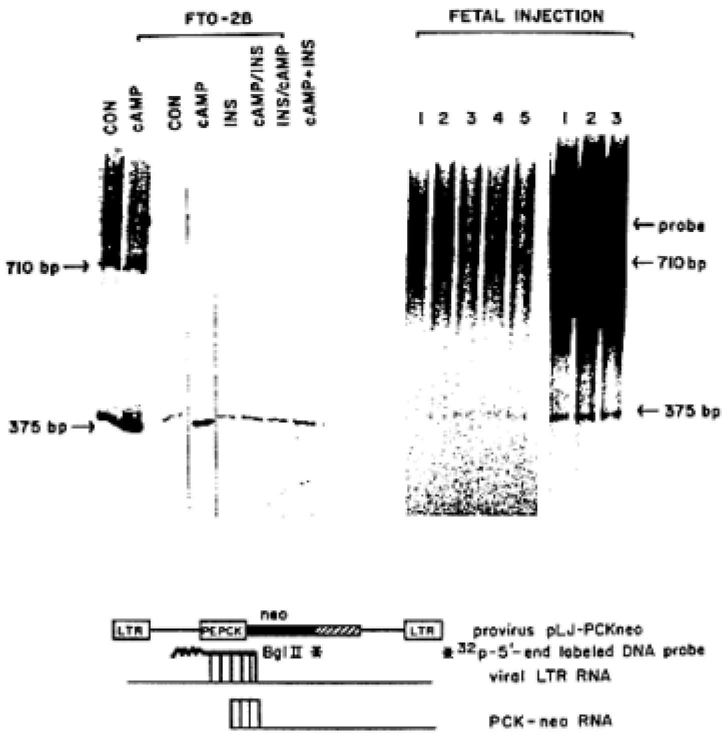

Figure 7 Expression of the <u>neo</u> gene introduced into FTO-2B hepatoma cells and in rat liver by retroviral

infection and its induction by Bt_2cAMP. The infectious retrovirus pLJPCKneo was introduced into FTO-2B hepatoma cells and into the peritoneal cavities of 19 fetal rats in utero. The virus had a titer of 8 x 10^7 G418-resistant colonies of NIH 3T3 cells per ml of virus-containing medium. Fetal rats were injected with 100 *m*1 of virus of the same titer at 19 days of fetal life and were then killed at 3 months after birth. A quantitative S1 nuclease analysis of neo mRNA in FTO-2B cells after treatment with Bt_2cAMP is presented on the left. The band present at 375 bp is a protected fragment corresponding to the predicted size of the neo gene probe used in these studies and indicates the mRNA transcript from the PEPCK promoter of the infected retrovirus. The diagram under the panels shows the orientation and size of the hybridization probe used, as well as the size of the predicted fragments protected from S1 nuclease. The 710-bp band represents mRNA transcribed from the 5´ LTR of the vector. Bt_2cAMP (0.1 mM) was added to the medium, and RNA was extracted from the cells 3 hours later. Insulin (10-8 units) was added at the same time as the Bt_2cAMP or 2 hours later (next to the last lane in the left panel). Rats were injected later with Bt_2cAMP 3 hours prior to death. Their livers were removed, and the RNA was extracted and analyzed for neo sequences. The two panels on the right are the result of two separate exposures of the bands protected during S1 nuclease mapping of RNA from the liver. The three lanes on the far right were exposed to X-ray film for 48 hours, and the five bands on the left were exposed for 24 hours. The relative intensities of the bands are proportional to the concentration of neo mRNA present in the cells.
SOURCE: Data from Hatzoglou et al. (unpublished observations).

Tissue-Specific Expression and Dietary Regulation of a Chimeric PEPCK-bGH Gene Introduced into the Germ Line of Mice

A series of transgenic mice were produced by the microinjection of a chimeric PEPCK-bGH gene into the male pronucleus of fertilized mouse eggs by the technique outlined above and as described by Wagner et al. (1981).

The microinjection experiments were performed by Drs. June Yun and Thomas Wagner (Edison Animal Biotechnology Center, Ohio University, Athens, Ohio). The promoter-regulatory region of the PEPCK gene contained 450 bp of 5´-flanking sequence, which included the cAMP and glucocortic regulatory elements. The concentration of bGH in the serum of animals that contained the gene stably integrated into their genome and ranged from a low of 5 to more than 2,300 ng/ml of serum (McGrane et al., 1988). Mice with high levels of bGH grew at twice the rate of their littermates but were normal in all other respects.

A detailed Northern blot analysis of animal tissues indicated that the chimeric PEPCK-bGH gene was expressed in only the liver and the kidney. This mirrors the expression of the endogenous PEPCK gene, which is also highly expressed in liver and kidney and only marginally in other animal tissues (Hanson and Garbers, 1972). The level of bGH mRNA in the livers of these transgenic animals was regulated by hormones and diet in a manner similar to that of the endogenous gene. When starved animals were fed a diet high in carbohydrate for 1 week, there was a 95% decrease in the concentration of bGH in the serum of the mice (Figure 8). This suggests that the expression of the PEPCK-bGH chimeric gene in these animals is sensitive to the insulin released after glucose ingestion. When the mice were refed a diet high in protein but devoid of glucose, the levels of bGH in serum were increased 30-fold after 1 week on the diet. This inductive effect of a high protein and carbohydrate-free diet on the levels of hepatic PEPCK is part of the response of the animal to the need for enhanced gluconeogenesis. The transgenic mice also responded to the administration of Bt_2cAMP by increasing the level of bGH in their serum two- to threefold in 90 minutes (see Figure 8).

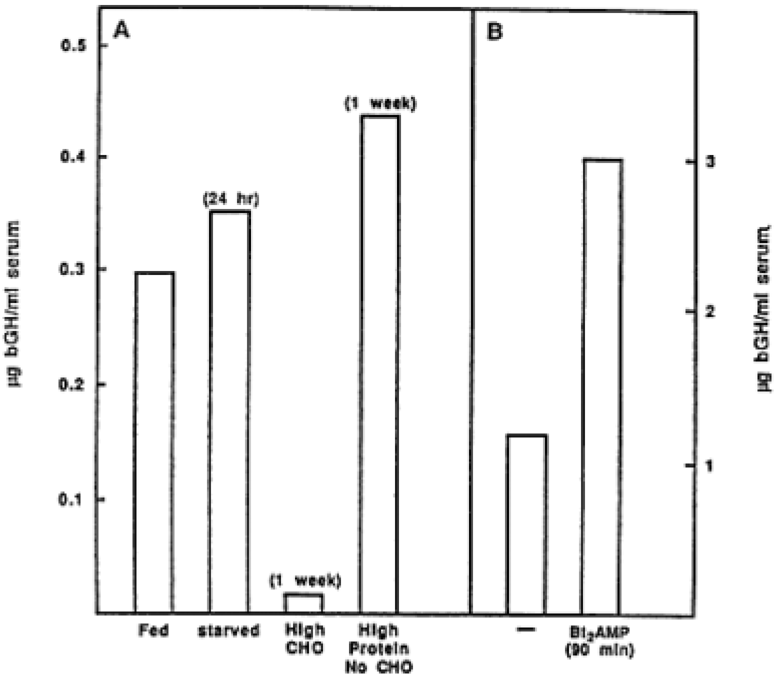

Figure 8 Regulation of the bGH concentration in the blood of transgenic mice by diet and Bt_2cAMP administration. (A) A transgenic Mouse expressing 300 ng of bGH per ml was starved for 24 hours and then fed a diet composed of 82% sucrose, 12.2% casein, 0.3% dl-methionine, 4% cottonseed oil, 2% brewer's yeast, and a 1% mineral mix plus vitamins for one week. Blood was drawn from the tail vein; the animal was then fed a diet containing 64% casein, 22% a-cell nutritive fiber, 11% vegetable oil, 2% brewer's yeast, and 1% mineral mix with vitamins (synthetic diets were from Nutritional Biochemical Corporation) for 1 week. The concentration of bGH in the blood was determined. (B) A mouse expressing 1.4 μg of bGH was injected with Bt_2cAMP and theophylline (both 30 mg/kg of body weight) at three consecutive intervals. At 90 minutes the mouse was bled from the tail vein and the concentration of bGH was measured (McGrane et al., 1988).

The acute responsiveness of the PEPCK promoter-regulatory region to induction by diet and hormones and its tissue-specific expression in the liver and kidney makes it an ideal tool for targeting the expression of various structural genes of interest to these tissues. It is also possible to modulate the level of expression of the structural gene over a broad range by altering the carbohydrate content of the diet fed to transgenic animals. Since the gene for the cytosolic form of PEPCK is normally not expressed until birth (Ballard and Hanson, 1967), the developing fetus is not exposed to a high level of protein that would result from expression of the structural gene. This has clear advantages with hormones such as bGH, which have the potential of interfering with the normal development of the fetus. We have noted a normal developmental pattern for the transgenic animals that we have studied to date. It should also be possible to use a segment of the PEPCK promoter, when it is linked to a structural gene of interest that contains its own core promoter but that lacks homologous tissue-specific elements, to direct the expression of this chimeric gene to the liver and kidney.

POSSIBLE APPROACHES TO GENETICALLY BASED ALTERATION IN METABOLIC PROCESSES

There are many metabolic models that can be used to test the potential of the techniques described above. An example is the role of the mitochondrial isozyme of PEPCK in the regulation of hepatic gluconeogenesis. Since the discovery of PEPCK in chicken liver mitochondria by (Utter and Kurahaski, 1954), as well as its cytosolic isozyme in the livers of a variety of species (Nordie and Lardy, 1963), the metabolic roles of the two forms of PEPCK have remained unresolved (Hanson and Mehlman, 1976). This has been compounded by the fact that species vary in the relative amounts of the two forms of the enzyme that are present in their livers. In birds, for example, 100% of the hepatic PEPCK is the mitochondrial isozyme, while in rodent species such as rats and mice, 90% of the enzyme is the cytosolic enzyme. The majority of species studied to date, including humans, have equal amounts of the two forms of PEPCK (Hanson and Garbers, 1972). These enzymes are distinct, but related proteins that have approximately 60% sequence identity and are coded for by different nuclear genes (S.M. Weldon, S.

Savon, W.C. Merrick, and R.W. Hanson, unpublished observations).

The only gluconeogenic tissue known to have a single form of PEPCK is the liver of the chicken, which contains only the mitochondrial isozyme (Watford et al., 1981). This distribution of the enzyme creates metabolic restrictions on the ability of the chicken to synthesize hepatic glucose. The lack of cytosolic PEPCK in the avian liver has been cited as a reason for the low rates of gluconeogenesis noted with oxidized substrates such as pyruvate or alanine in this tissue (Williamson, 1976). Lactate conversion to pyruvate in the cytosol provides the NADH required by the glyceraldehyde-3-phosphate dehydrogenase reaction during gluconeogenesis. In the liver of the chicken, the restricted synthesis of P-enolpyruvate in the mitochondria necessitates a continuous supply of NADH from oxidation-reduction reactions in the cytosol. However, for gluconeogenesis from pyruvate or alanine, the transfer of reducing equivalents, as well as carbon, from the mitochondria is required. In tissues that possess a cytosolic form of PEPCK, this is accomplished by the transport of malate into the cytosol, which is then converted to oxalacetate, generating NADH (Williamson, 1976). In tissues that lack cytosolic PEPCK, the carbon for gluconeogenesis must leave the mitochondria as P-enolpyruvate without the transfer of reducing equivalents. In chickens, glucose, systhesis in the liver is restricted to the Cori cycle, whereas net gluconeogenesis from amino acids occurs in the kidney, a tissue that contains both isozymic forms of PEPCK (Watford et al., 1981). Thus, birds recycle lactate from the muscle and red blood cells to the liver for gluconeogenesis.

It should be possible to test the metabolic role of the two forms of PEPCK directly in the hepatic cells isolated from chickens, in which the gene for the cytosolic form of the enzyme has been introduced via an infectious retrovirus by the techniques described above. The gene for the cystosolic form of PEPCK from chickens has been isolated, and a full-length cDNA is available (Hot et al., 1984 a, b). Since the gene can be inserted into the liver via infection of fertilized eggs with the replication-competent retrovirus described above, the levels of gene expression can be measured both by determining the concentration of PEPCK mRNA present in the liver and by aasaying for enzyme activity in the cytosol present in the liver. The effects of this genetic modification of the cellular localization of the rate-limiting enzyme in hepatic gluconeogenesis should have dramatic effects on glucose homeostasis in chickens. Therefore, a method is available to test the precautions of the metabolic model discussed above.

Alternatively, it should be possible to target the mitochondrial isozyme of PEPCK to the hepatic mitochondria in mice. This would involve the construction of a chimeric gene consisting of the promoter-regulatory region of the gene for the cytosolic form of PEPCK, which contains both hormone regulatory elements as well as sequences directing the tissue-specific expression of the gene to the liver and kidney, linked to the structural gene for the mitochondrial form of PEPCK from chickens, which also contains the signal sequences necessary to direct the protein to the mitochondria of murine liver. A cDNA coding for this isozyme has recently been isolated (Weldon et al., unpublished observations). Alternatively, the availability of a hepatoma cells line with minimum deviation that can grow in a glucose-free medium, such as the Fao cell line isolated and characterized by Weiss and colleagues (Deschatrette and Weiss, 1974), will be an invaluable tool in these types of studies, since it permits infection with the murine retroviral vectors already developed and has been shown to effectively introduce functional and regulatable genes into other hepatoma cells. Since the cells are able to synthesize glucose from the gluconeogenic precursors contained in the culture medium, their growth in the absence of added glucose should be directly dependent on the efficiency of gluconeogenesis. Finally, once these genetically modified cells are constructed and characterized, they are a permanent resource for other investigators who are interested in related metabolic problems.

The scenario presented above represent only one of many matabolic questions that might be approached by using the techniques outlined here. We anticipate rapid growth in this field as the number of genes that are isolated and characterized increases. It should be possible, for example, to introduce receptors for hormones such as insulin into the membranes of cells in which these receptors are either present in low number or missing. Such an approach has already been accomplished with the human placental insulin receptor, which has been introduced into rodent CHO cells (which have a low number if insulin receptors) and has been shown to respond to added insulin by greatly increasing the transport of glucose into the cells (Ellis et al., 1986). However, the metabolic consequences of altering the uptake of glucose in these cells was not considered. There currently is a unique opportunity to extend the usefulness of studies of this type into the area of metabolism and nutrition.

THE NEED FOR NEW EDUCATIONAL PROGRAMS COMBINING METABOLISM AND MOLECULAR BIOLOGY

The important advances that have occurred in molecular and cellular biology over the past 15 years have great potential for metabolic and nutritional research. A core technology centered around the ability to introduce specific genes into cells and animals in a directed and regulatable fashion is now developing. This technology will be generic in its usefulness in biology and medicine and will extend from the possible correction of genetic defects to the genetic patterning of cells and animals for metabolic studies. The field of nutrition has a vast potential as a research area in which this technology will find application. As discussed above, it will soon be possible to alter specific steps in a complex metabolic pathway in intact animals to determine the animals' responses to individual dietary components or to target the expression of hormone receptors to tissues that are normally unresponsive to a specific hormone.

For the potential of these new approaches to be fully realized in the nutritional sciences, a new generation of investigators who are familiar with molecular biology, as well as with metabolism and nutrition, must be trained. Without these individuals, the potential application of many of these techniques will be needlessly delayed. Unfortunately, among graduate students who are attracted to the fast pace and high visibility of molecular genetics, there is a diminished interest in metabolism and nutrition as a research area. There is also a gulf between faculty in the nutritional sciences and those in molecular biology in most universities. Two cultures have arisen that have different languages, different traditions, and different approaches to science. Unfortunately, these differences continue to grow. The information contained in this volume based on the symposium "Frontiers in the Nutrition Sciences" could make an important and timely contribution to the development of a program for education in nutrition. We hope that the nutritional sciences will share in the excitement of the new advances in molecular and cellular biology by participating in a revitalization of metabolic research, the basis for all nutritional science.

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The Genome: Nutrition and Human Variation

Arno Motulsky

This paper presents an overview of the role of genetics in nutrition and nutritional policy. It includes discussions of human individuality and how it is controlled by genetics, some examples of common and rarer diseases in which genetics plays an important interactive role, and some of the problems of public policy raised by our current knowledge of genetics and how these problems will compound as our knowledge of genetics increases over the next 10 to 20 years.

HUMAN VARIABILITY

Human variability, or genetically controlled variability, is very common. All people who are not twins look different; clearly, this is genetically controlled. We also tend to resemble our relatives more than we do our nonrelatives, and these similarities in physiognomy are controlled by genes. The similarity in physiognomy is also carried over in the ways that people, for example, hold their hands or make gestures. Thus, aspects of behavior that we do not ordinarily think of as being under genetic control are, in fact, controlled by genes. Although we do not know which genes are involved in physical or behavioral resemblance, we do know that genes are involved.

Over the past 20 years or so, internal genetic variability has also become apparent. For example, blood groups and various enzyme and protein types are now known to be genetically determined. The HLA variants also show tremendous genetic variability. More recently, chromosomal variants have shown considerable variability at the DNA level. Since most human DNA does not code for protein, the variability of DNA is usually not expressed phenotypically. However, such variability can be used, and is being used increasingly, as a marker for genes lying next to these DNA variants that are expressed. What this research indicates is that if we take just a few markers (but not DNA markers or HLA markers), we can show that the chance that two randomly selected people will have the same genetic type becomes extremely small. If we then add all known markers to the equations, we can establish mathematically that all people, except, of course, identical twins, are unique internally in respect to their various genetic markers.

The question therefore arises: How important is this variability in nutrition and health? To answer this, we must consider the nature of internal variability. If we assume that a gene is fully expressed and look at those that carry the gene and those that don't (i.e., homozygotes), there are found to be two distinct populations or distributions. If we assume that some people are heterozygotes and if we can distinguish between the two homozygotic and one heterozygotic populations, then there will be three separate distributions or curves. Since many genes interact with a variety of other genes (the so-called polygenetic situation), however, we most often get a single Gaussian distribution curve that is very common for all kinds of biological phenomena. This can be observed in the case of a very simple genetic interaction of just two pairs of additive genes. For example, the variability of enzyme levels within the normal ranges often has a simple genetic basis, because different alleles at a gene locus that specifies the structure of a given enzyme may be associated with slightly different mean enzyme levels. Thus, the widely variable quasi-Gaussian distribution of activity for a given enzyme in a population may be the result of few overlapping curves, each of which is characteristic of its underlying allele.

What is the relevance of this variability to nutrition? As is well known, there are many intrinsic processes of nutrition. These include absorption of nutrients, as well as their distribution, catabolism, uptake by receptors, transport across cells, storage, and excretion. It would therefore be surprising if the high degree of variability in the human biochemical makeup did not affect these processes, thereby influencing nutritional requirements and interactions.

Another point to consider is common variability. Several hundred inborn errors of metabolism, in which a variety of enzymes are absent or deficient, are known to us; many of these are known to lead to gross abnormalities in the organism. For example, phenylketonuria (PKU), a relatively common condition marked by the absence of the enzyme phenylalanine hydroxylase, occurs in the homozygous state in about 1 of 12,000 to 1 of 15,000 people. This disease, which leads to mental retardation if unchecked, can be prevented by restricting phenylalanine in the diet. It takes a double dose of the gene to produce PKU (as it does for most inborn errors of metabolism), and that is why recessive diseases such as PKU are relatively rare. From what we know of genetic arithmetic (i.e., the Hardy Weinburg Law), however, for every rare homozygote in the population, there are many heterozygotes or carriers of the gene. Thus, for an autosomal recessive disease like PKU in which 1 in 12,000 people is affected, we can estimate that approximately 2% of the population carry the gene.

What, then, are the implications of this common carrier state for nutrition and health? In general, people who are affected with such inborn errors have very little to no activity of the involved enzyme, while normal people have about 100% activity and carriers have about 50% activity. Under most conditions, a 50% level of enzyme activity is sufficient for adequate function and carriers remain in good health. Under conditions of growth, stress, illness, or malnutrition, however, a 50% level of enzyme activity may not be sufficient to maintain health, and specific abnormalities related to the underlying enzyme activity could result.

Familial hypercholesterolemia is an example of how a heterozygotic or carrier state for a metabolic condition can cause a relatively high disease rate. Another example of variation that affects food likes and dislikes, and, thus, probably nutritional status, is phenylthiocarbamide (PTC) nontasting. PTC nontasting is an example of a common monogenic trait that makes a significant proportion of the affected population unable to taste bitter substances. There are also less well-studied examples, such as variability in the ability to taste artificial sweeteners. Such subtle differences undoubtedly affect food preferences.

Genes do not act in a vacuum, and the action of a specific gene may depend not only on other genes but also on the environment. This principle is well illustrated by the field of pharmacogenetics. Certain inherited enzyme variants are harmless per se but they may cause untoward effects in the presence of a drug that requires the normal variety of that enzyme for its inactivation. In such cases, the presence of the enzyme variant by itself without the drug or the administration of the drug to people with the normal enzyme levels may cause no harm. If the drug is given to carriers of the enzyme variant, however, a drug reaction may ensue. Examples of this phenomenon include hemolytic anemia from glucose-6-phosphate dehydrogenase (G6-PD) deficiency, prolonged anemia from pseudocholinesterase variation, and various drug reactions associated with defective acetylation of drugs such as isoniazid.

EXAMPLES OF THE INTERACTIVE ROLE OF GENETICS

The concept of pharmacogenetics can also be applied to ecogenetics, that is, the interaction of specific genetic traits with any environmental agent to produce a given effect. Some ecogenetic examples of nutritional interest include (1) the development of gastrointestinal symptoms upon drinking moderate quantities of milk among the many individuals with genetically determined lactose intolerance; (2) the development of hemochromatosis in susceptible individuals who consume moderate dietary levels of iron; and (3) the development of hypertension in genetically predisposed people who migrate from a less developed, primitive environment to a more industrial Westernized environment.

For example, lactose intolerance, a common trait in which there is a persistence of the lactase enzyme in the intestine, is an excellent example of a simple genetic trait that affects absorption of commonly used foods, namely, products containing lactose. At the time of birth, all humans (as all other mammals) are able to make and use the intestinal enzyme lactase to break down the main constituent of milk, lactose, into glucose and galactose. In most humans, the ability to digest lactose disappears after weaning, but some individuals do not lose this ability and have persistent intestinal lactase activity (Lisker, 1984). Symptoms in lactose malabsorbers occur because undigested lactose in the gastrointestinal tract is decomposed by bacteria, causing bloating, diarrhea, intestinal rushes, flatulence, and even nausea and vomiting in severe cases. The lactose persistence is controlled by a gene (L) that may occur in the heterozygote (Ll) or homozygote (LL) state. People who do not carry the L gene, and who therefore cannot digest lactose after weaning, are homozygotes (ll) at this locus, which is the usual status for most of the world's population. Milk drinking does not induce lactase activity in those who no longer have this capacity, nor does lactose restriction reduce the intestinal lactase activity among those who never lost it. Lactose absorption (Ll or LL) or malabsorption (ll) is an inborn trait. Acute or chronic gastrointestinal disease may cause secondary hypolactasia among individuals with persistence of lactase activity, but intestinal lactase activity returns after the illness. Members of most populations have hypolactasia of the genetic variety. Only people from central and northwest Europe and from areas in Africa with a long history of dairy activity have high frequencies of persistence of lactase activity. Presumably, the gene for lactase persistence had a survival advantage in cultures with dairy activities, and over the generations it has increased in frequency because individuals who were able to absorb milk as children and young adults were either more fertile or less likely to die.

Another example of how genetic variation influences nutrition is the condition hemochromatosis. Those people who are affected are homozygotes for a gene that facilitates increased iron absorption and is carried on the short arm of chromosome 6, which is closely linked to the HLA-A locus. The homozygous state affects about 1 of 600 to 1 of 1,000 individuals in the United States and Western Europe, indicating that about 10% of the population is a heterozygote for or carrier of the condition. Clinically apparent disease is more common among males, since females can eliminate some excess iron in their periodic menses. Since iron deficiency is common among the population at large, supplementation of flour with iron has been recommended by public health authorities and is practiced in Sweden. The onset of clinical hemochromatosis in homozygotes presumably would be hastened by such a process. However, since the proportion of people with the homozygous hemochromatosis genotype is at most 1 in 500, some observers think that the merits of iron supplementation benefit a much larger fraction of the population and outweigh the damaging effects of excess iron in homozygotes. A crucial issue in this connection is related to the iron absorption status of the very common hemochromatosis heterozygotes (i.e., close to 1 in 10 people). However, current data suggest that while liver iron stores are somewhat increased among male heterozygotes as they get older, there is no evidence that heterozygotes are at risk for clinically apparent iron toxicity.

Another example of ecogenetics is that of high blood pressure and salt. Hypertension is an ecogenetic trait in that populations from less developed locales have little or no hypertension. High blood pressure develops in some migrants to a Western-type environment when the diet includes a high salt intake. Populations of African origin in the U.S. have a higher mean blood pressure and a higher frequency of hypertension than those of European origin. Recently discovered differences between black and white hypertensive populations include the absence of elevated red blood cell sodium and lithium countertransport in blacks--a finding that is also common among white hypertensives. This transport trait appears to be under monogenic control. This and other evidence suggests that hypertension is a heterogenous entity with different genetic mechanisms.

The fact that blood pressure levels are under strong genetic control is shown by studies in families, adopted children, and twins. Evidence for the role of sodium in the causation and maintenance of high blood pressure is also good. On a population level, the frequency of high blood pressure in different populations is related to their average sodium intake. However, sodium loading does not cause elevation of blood pressure in all individuals, and sodium restriction lowers blood pressure in many, but not all, hypertensives. Salt restriction has been advocated to reduce the frequency of high blood pressure, but it may not be helpful for the entire population. Currently, we lack clinical or laboratory criteria to differentiate those individuals who are salt resistant from those who are salt sensitive.

Another trait that is important for public health is obesity. Obesity clearly is related to food intake, although a variety of studies indicate that food intake alone does not explain all the variation in obesity. Studies done in twins have been useful in this regard. Assuming that all human variation is genetic, we would expect correlations between identical twins who share 100% of their genes to be 1.0, while we would expect it to be 0.5 between unidentical twins, who share half of their genes. In the case of body mass index, the correlation for identical twins is 0.8, while that for nonidentical twins is 0.42. This suggests that genetics plays a major role in the risk of obesity. In addition, studies have shown that children seem to have a body weight that resembles that of their biological parents more than that of their adoptive parents. This again suggests that genetic factors are involved. The exact mechanisms that make some people obese and others not are not yet known.

Lastly, I would like to consider how genetics modulates hyperlipidemia and coronary heart disease. Both genetic and environmental factors influence a variety of different lipid parameters that are involved in hyperlipidemia and heart disease. Cholesterol levels in serum as well as low high-density lipoprotein levels, high apolipoprotein B levels, and low apolipoprotein A1 levels have all been implicated as risk factors for coronary heart disease. Various alleles at the apolipoprotein E locus have a significant effect on raising or lowering cholesterol and apolipoprotein B levels. Monogenic defects causing hypercholesterolemia (i.e., familial hypercholesterolemia due to a low-density lipoprotein receptor defect) have been carefully defined, whereas the evidence for single-gene inheritance of some other lipid abnormalities has been less certain but suggestive. Regardless of the genes involved, genetic factors of some sort play a role in most of the hyperlipidemias. A common condition known as familial combined hyperlipidemia appears to be transmitted as a monogenic autosomal dominant trait and is usually associated with elevation of apolipoprotein B levels. Various DNA markers of the apolipoprotein loci have been associated with hyperlipidemia and with coronary heart disease but the results have not always been consistent. Considerable research work is being carried out in these areas and is likely to clarify the exact contribution of genetic factors to hyperlipidemias.

PROBLEMS OF PUBLIC AND GENETICS

What, then, are the nutrition policy implications of genetic variability? Given the probable effects of biological variability on nutritional requirements and chronic disease, we should first ask whether different dietary guidelines might be required for different populations or individuals. If variability is small and it can be overcome with general nutritional guidelines that are easy and acceptable to everyone, then one can ignore genetic variability and make a single recommendation for everyone. For example, we know that there is genetic variability in caries susceptibility, but fluoride is still given to everyone anyway.

The situation becomes less clear when we know that a general guideline helps many but may hurt a few. The fortification of foodstuffs with iron, increasing the risk of hemochromatosis in susceptible heterozygotes, is one such example. Another point bears on this issue of individual versus population recommendations. Some argue that a lowering of the cholesterol level of Western populations by dietary modifications would substantially reduce the frequency of coronary heart disease, regardless of genetic variaticholesterol level from 226 to 210 mg/dl, as might be achieved with dietary modification, would reduce the absolute risk of mortality from coronary heart disease only slightly. However, a small reduction in absolute risk for any individual may have a major effect when it is translated into the very large number of individuals that constitute the population. This is the so-called prevention paradox named by the British epidemiologist Geoffrey Rose. In a hypothetical example, assume that a person can reducetuation becomes less clear when we know that a general guideline helps many but may hurt a few. The fortification of foodstuffs with iron, increasing the risk of hemochromatosis in susceptible heterozygotes, is one such example. Another point bears on this issue of individual versus population recommendations. Some argue that a lowering of the cholesterol level of Western populations by dietary modifications would substantially reduce the frequency of coronary heart disease, regardless of genetic variati the risk of having a myocardial infarct in a given time span from 1 in 80 to 1 in 100 by altering his or her diet. If these figures were applied to 100,000 individuals, the expected frequency of 1,250 myocardial infarcts (1 in 80) would be reduced to 1,000 heart attacks (1 in 100). This reduction of 250 heart attacks per 1,000 individuals at risk would be of substantial public health importance. Although little is known about the effect of nutrition-genetic interactions on lipids, however, it is likely that some individuals are sensitive to dietary lipids while others may be resistant. The roles of the low-density lipoprotein receptor, structural variation in apolipoproteins B and E, the regulation of hepatic apolipoprotein B synthesis, and many other factors need to be studied to resolve these issues.

Public health policies have largely ignored genetic variation and have used an "average" human being in their formulation. Thus, nutritional recommendations have usually been set to provide a sufficient amount of a nutrient even for those with the highest requirements. With relatively small variation for a given nutrient, such a policy appears sound. Also, if special dietary requirements affect a few individuals with inborn errors of metabolism, policy recommendations can ignore such outliers since these individuals can be identified and will be treated by physicians. In many instances, however, the true extent of genetic variation is still unknown. We are indeed all different. We taste things differently; we smell things differently; and as noted earlier, it is likely that these differences influence the nutritional metabolic processes, requirements, and interactions that can lead to chronic disease. Judging from the frequency of genetic variants in enzymes and proteins and their effects on enzyme activity, significant variations in nutritional requirements or in genetic-nutrition interactions may often exist.

Thus, while population-based guidelines may, for the most part (at present), be sound, each nutritional topic must be considered on its own merits. In addition, since there are sizable racial or ethnic differences in disease frequencies, it is conceivable that a recommendation for one group of the population may need to differ from that for the other groups. Such differences among races may raise difficult policy questions because they can easily be misunderstood. However, there are precedents from a nonnutritional setting. Ashkenazi Jews are already screened for Tay Sachs disease, Mediterraneans and Southeast Asians are screened for thalassemia, and blacks are screened for sickle cell disease and trait.

Under ideal circumstances, we could tailor dietary recommendations to each individual, depending on his or her genetic makeup or susceptibility. Although we have an inkling of the extent and type of human variation, however, much more work is needed to elucidate the descriptive, metabolic, and biochemical bases of this genetic variation. Sensible dietary recommendations can be made for the general population, although we must not ignore individual needs. What we must remember is that the population approach and the individual approach are complementary, not opposite, and that both are necessary if we are to approach the resolution of the problems of nutritional requirements and nutritional disease.

Biotechnological Developments: Potential for Improvements in Food Formulation, Nutrient Delivery, and Safety

John E. Kinsella

This overview describes some biotechnological developments in the food production and processing sector, with emphasis placed on nutrients, and discusses these in the context of optimizing diet composition. Most nutrients consumed in the United States are derived from foods that have been processed to some extent. The food processing industry is immense, with retail sales of foods approaching $400 billion in 1987, and becoming increasingly sophisticated while it undergoes consolidation via mergers and acquisitions. Currently, some 50 companies account for approximately 60% of consumer food sales in the United States (Messenger, 1987a).

The modern food processing industry increasingly influences what consumers eat, that is, nutrient intake, although the availability of many products is largely determined by what the majority of consumers buy. Because overall domestic market expansion is limited by population growth to only about 2% per annum, food companies must be very competitive to be successful (Behnke, 1983; Pehanich, 1987). Hence, progressive food companies must be responsive to consumer concerns and needs in order to capture a larger market share, while at the same time they must adopt new technologies to cut costs and facilitate innovation. Nutrition has therefore become an integral criterion in product development, and the current problem areas of nutrition are of interest in terms of developing consumer products that provide a more balanced array of nutrients. This interest encompasses all facets of food from producer to consumer.

NUTRITIONAL STATUS OF THE AMERICAN POPULATION

Vital statistics indicate that the American population is generally healthy and well nourished but aging, with overt symptoms of nutritional deficiencies being relatively rare (Harper, 1987; McGinnis, 1987). However, a number of diet-related chronic degenerative diseases that reduce the quality of life afflict a significant number of people and cause extensive morbidity and mortality (McGinnis, 1987). The major contemporary nutrition-related health problems include obesity, hyperlipidemia, hypertension, coronary heart disease, atherosclerosis, thrombosis and stroke, diabetes, arthritis, and cancer. Genetic factors may play a complicating role in many of these health problems, for example, hypertension and hyperlipidemia (Motulsky, 1987). According to the Joint Nutrition Monitoring Evaluation Committee, many of these nutrition-related health problems may result from consumption of excess calories, fat, saturated fatty acids, cholesterol, and sodium. There is evidence that certain subgroups of the population (especially young females) may consume inadequate levels of iron and vitamin C and that dietary calcium may be deficient, resulting in osteoporosis in older women (Federation of American Societies for Experimental Biology, 1984; National Institutes of Health, 1986a).

Data summarizing the incidence of nutrition-linked diseases in various segments of the U.S. population and the magnitude of the excesses or inadequacies in intake of nutrients (compared with the generally recommended levels) have been collated recently (NRC, 1988). The relationships between dietary fats and several chronic diseases have been reviewed (NRC, 1989; Perkins and Visek, 1983).

Coronary Arterial Diseases

Hyperlipidemia is associated with an increased incidence of atherosclerosis, heart disease, and thrombosis and stroke, which are the major causes of morbidity and mortality in the United States (American Heart Association, 1986; Levy et al., 1979). When excess calories are consumed as fat, especially as saturated fatty acids (SFAs), low-density lipoproteins (LDLs), which exacerbate these diseases, are increased (Keys, exacerbate these diseases, are increased (Keys, 1970;

Levy et al., 1979; Shaefer and Levy, 1985). Reduction of SFAs or their substitution by polyunsaturated fatty acids (PUFAs) results in decreased plasma cholesterol and reduced incidence of heart disease (American Heart Association, 1986; Federation of American Societies for Experimental Biology, 1984; Keys, 1970). Current intake of SFAs are about 13-14% of calories (National Institutes of Health, 1985). A reduction in total fat, SFAS, and cholesterol intake has been recommended consistently (Federation of American Societies for Experimental Biology, 1984).

Obesity

Increased consumption of fat and sugar are associated with increased obesity and about 30% of the U.S. population between 27 and 74 years is overweight (National Center for Health Statistics, 1983). Obesity may adversely affect health and longevity and is frequently associated with hypertension, hypercholesterolemia, non-insulin-dependent diabetes, increased incidence of certain cancers, and other health-related problems (National Institutes of Health, 1985). A reduction in caloric intake, especially fat, is recommended for people who are 20% or more overweight (National Institutes of Health, 1985).

Non-insulin-dependent diabetes (insulin resistance) is frequently associated with obesity. In rats, dietary PUFAs of the n-6 family (safflower oil) reduced insulin potency, whereas dietary n-3 PUFAs in fish oil potentiated responsiveness to insulin (Storlien et al., 1987). This observation may be relevant to human diabetes and suggests a role for dietary n-3 PUFAs in modulating the insulin receptor.

Cancer

Diet plays an important role in cancer, the second major killer disease in the United States (Pariza and Simopolous, 1987). There is a strong correlation between caloric intake, especially from fat, and the incidence of many common cancers (American Cancer Society, 1984; Doll and Peto, 1981; Wynder, 1976). Available evidence suggests that fat intake may be more relevant and variable than calorie intake (National Research Council, 1982; Willett and MacMahon, 1984).

In addition, there appears to be an association between unsaturated fatty acids, especially n-6 PUFAs, and growth of certain tumors. This may be partly related to increased production of the prostanoid PGE_2, which can exert immunosuppressive effects. In animal studies this is counteracted by n-3 PUFAs, which also reduce the growth of certain tumors (Karmali et al., 1987; Welsch, 1987). This underscores the potent and pervasive physiological effects of dietary n-6 unsaturated fatty acids via eicosanoids and the need to recognize that in making recommendations to reduce the risk of one particular disease that others are not being exacerbated.

Hypertension

Hypertension afflicts approximately 20% of the population and has genetic, environmental (stress), and dietary etiologies. Excess dietary sodium has been strongly implicated (Federation of American Societies for Experimental Biology, 1979). Consumption of sodium varies widely, with average intakes generally exceeding the recommended daily intake of 3 g (Federation of American Societies for Experimental Biology, 1979).

Because of the linkage between sodium intake and hypertension, efforts to reduce the use of sodium in foods are being made. Sodium chloride enhances flavor perception (Gillette, 1985), but in addition, it performs a number of important functions in conventional food processing (Dunail and Khoo, 1986). In meats, dairy products, and soups, it controls microbial growth and may be a selective inhibitor of pathogenic or toxigenic microbes; in cheeses, it affects the activity of ripening enzymes and controls the microflora; and in processed meats, it functions in solubilizing myofibrillar proteins, which are required in the formation of the final product (Federation of American Societies for Experimental Biology, 1979). Hence, sodium chloride cannot be summarily replaced or substituted. However, its use in processed foods can be reduced, and potassium chloride (which imparts a bitter taste to foods) can be substituted in limited amounts (<25%). The reduction of sodium chloride in certain foods can be facilitated by adding herbs, spices, and other strong flavors such as monosodium glutamate. Certain hydrophobic dipeptides possess a salty taste. The dipeptides ornithine-glycine, lysine-glycine, ornithine-β-alanine, and ornithine-γ-aminobutyric acid are approximately twice as salty as sodium chloride, while ornithine-taurine and lysine-taurine are equivalent to salt (Tada et al., 1984). These dipeptides warrant further study as possible substitutes for salt in the diet of subjects with hypertension.

DIETARY FAT AND FATTY ACIDS

The genetic basis of human nutrient requirements evolved millions of years ago, presumably reflecting the nutrients available during the evolution of metabolic pathways (Eaton and Konner, 1985). The adaptability of the human metabolic system to dietary changes is considerable, but it has limits, as evidenced by the need for around 45 essential nutrients. While the metabolic system has built-in feedback regulators, they can be overridden; it is conceivable that excesses or imbalances in the intake of certain nutrients can perturb the system and induce pathophysiologies to which humans are predisposed. Leaf and Weber (1987) suggested that relatively recent dietary changes (especially the increased fat intake and changes in types of fatty acids) exceed the biochemical (genetic) capacity of the system to adjust, and consequently, they are conducive to some of the familiar chronic diseases discussed above. These degenerative diseases become more obvious with increased longevity and are exacerbated by dietary imbalances.

With the reduction in manual labor, much less dietary energy is needed; hence, less fat is required in the diet (American Heart Association, 1986). In addition, with the elucidation of the important roles of eicosanoids in a number of chronic inflammatory and immune diseases, a reassessment of the quantitative importance of dietary n-6 PUFAs in the human diet may be warranted (Lands, 1986a,b). A number of chronic diseases (arthritis, asthma, psoriasis, allergies, and immune and inflammatory diseases) that afflict an enormous number of Americans, especially older people, may be affected by dietary components, and there is accumulating evidence that dietary PUFAs may directly and indirectly affect the etiology and severity of these diseases by influencing the production of eicosanoids, both prostanoids (PG) and leukotrienes (LT) (Table 1). High intakes of n-6 PUFAs may increase the severity of some of these diseases, while consumption of n-3 PUFAs may ameliorate them (Lands, 1986a,b, 1987). The current high consumption of n-6 PUFAs is a relatively recent phenomenon reflecting innovative oilseed processing technology and the promotion of n-6 PUFAs in high-fat diets to reduce plasma cholesterol. Historically, mankind was accustomed to a

TABLE 1 Some Diseases Associated with Disturbances in Eicosanoid Metabolism

Disease	Eicosanoid[a]	Cell or Tissue
Hyperaggregatability	TXA_2	Platelets
Increased adherence of platelets	TXA_2	Platelets, macrophages
Excess bleeding or bruising	PGI_2, PGI_3	Blood
Immunosuppression	PGE_2	Macrophages
Asthma	TXA_2, LTs	Lungs
Inflammation	LTs, PGE_2	Polymorphonuclear leukocytes
Psoriasis	LTs, HETEs	Skin
Rheumatoid arthritis	PGE_2, LTs	Monocytes
Diabetes	TXA_2	Platelets
Autoimmune disorders	PGE_2, LTs	Spleen
Hypercholesterolemia	TXA_2	Platelets
Chronic placental insufficiency	PGI_2	Umbilical cord

[a] TXA_2 = thromboxane; PG = prostaglandin; LTs = leukotriene;
HETE = hydroxyeicosatetraenoic acid.

relatively low-fat diet rich in both n-3 and n-6 PUFAs, mostly from plant foods (Crawford, 1987; Leaf and Weber, 1987). Hence, the contemporary diet in which PUFAs are preponderantly of the n-6 family may be predisposing the system to a hypersensitive proinflammatory state by synthesis of excessive eicosanoids (Lands, 1986a,b). Some dietary n-3 PUFAs may be desirable to modulate the metabolism of n-6 PUFAs and to down-regulate eicosanoid synthesis (German et al., 1988; Kinsella, 1987b; Lands, 1986a,b, 1987). The apparent beneficial effects of dietary n-3 PUFAs of fish oils on numerous parameters (Table 2) are consistent with this (Lands, 1987; Simopoulos et al., 1986) and suggest that n-3 PUFAs from green leaves and seafoods should be included in the diet (Kinsella, 1989).

TABLE 2 Some Common Diseases That May Be Ameliorated by Dietary n-3 PUFAs

Arthritis	(Asthma?)
Atherogenesis	Atherosclerosis
Autoimmune diseases	Blood pressure resistance
Burns	Diabetes (insulin)
Hyperlipidemia	Inflammatory disease
Ischemic heart disease	Psoriasis
Thrombosis	Tumor growth
Vasospasm	

The minimum requirement for linoleic acid to prevent deficiency symptoms and apparently to provide ample arachidonic acid for normal eicosanoid synthesis is 1 to 2% of calories (Lands, 1986a). Hence, the current intake of linoleic acid (6 to 7% of calories) may be overtaxing to the human system. Because n-3 PUFAs are effective hypolipidemic agents and down-regulate eicosanoids, a mixture of n-6 and n-3 PUFAs may be desirable and perhaps should be present at levels below the currently recommended 10% of dietary calories. Low-fat diets containing both n-6 and n-3 PUFAs typical of vegetarian diets may be more representative of the desirable pattern of dietary PUFAs, especially as total fat intake is reduced (Crawford, 1987; Dyerberg, 1986; German et al., 1988; Leaf and Weber, 1987).

The gradual elucidation of the role of the immune system in health and disease and the potential role of food components in modulating the immune system will become of increasing importance to food scientists and nutritionists (Chandra, 1985; Pestka and Witt, 1985). Recent research demonstrating the key roles of eicosanoids in intercellular signaling and modulation of lymphocyte, monocyte, and neutrophil functions strongly implicates dietary PUFAs in immunocompetence (Chandra, 1985; Kunkel and Chensue, 1986). The increased tendency of macrophages to produce more immunosuppressive PGE_2 in animals fed increasing amounts of n-6 PUFAs is significant (German et al., 1988). The capacity of n-3 PUFAs of fish oils to suppress eicosanoid synthesis in cells of the immune system needs to be studied more extensively as n-3 PUFAs are introduced into foods (Kinsella, 1989).

Fat Consumption

The current intake of fat is about 38% of calories, down from approximately 41% in 1977. Food intake data indicate that this is made up of approximately 15, 14, and 7% of calories from saturated, monoenoic, and polyunsaturated fatty acids, respectively. Actual consumption of dietary fat may be about 85 to 90 g/day (Rizek et al., 1983). Approximately 50% is from animal sources, with 25, 12, 9, 5, 3, and 0.7% being derived from red meat, dairy foods, butter, lard, poultry, and seafoods, respectively. The remainder is derived mostly from salad, frying, and cooking oils; shortenings; spreads; and fat consumed as components of various prepared foods, for example, bakery products, fruits, and vegetables.

Approximately 30, 25, 35, and 5% of saturated fatty acids are derived from dairy foods, meat, vegetable oils, and eggs, respectively. Dietary cholesterol is obtained preponderantly from animal (30% meat, 15% dairy) and avian products, with eggs being the major source (NRC, 1988).

Data concerning quantitative intake of dietary fat and fatty acids, however, are questionable, and many calculations are based on supply, which overestimates intake. Data on muscle foods tend to be for raw untrimmed products and tend to overestimate the intake of animal fats and cholesterol. On the other hand, deep-fried foods (e.g., french fries, fish sticks, and doughnuts), and especially breaded products, are major sources of fat and contain up to 20 to 30% fat by weight (Kinsella, 1988).

In light of the association of dietary fat with many of the major chronic diseases, there is universal agreement that dietary fat intake should be reduced to match energy output and should not exceed 30% of total calories (Federation of American Societies for Experimental Biology, 1984; National Institutes of Health, 1986b; NRC, 1989; DHHS, 1988). In addition, the fatty acid composition of dietary fat should meet certain guidelines. Thus, saturated fatty acids should not exceed 10% of total calories and PUFAs (not defined) should be included but should not be more than 10% of total calories. The remainder should be composed of monoenoic fatty acids. In addition, cholesterol intake should be 100 mg/1,000 kcal (<300 mg/day), sodium intake should be <3 g/day, and dietary fiber intake should be about 25 g/day (National Institutes of Health, 1986b).

To meet the guidelines (less fat, cholesterol, and saturated fatty acids), all actual and potential sources of dietary fat need to be considered. Thus, traditional commodity foods, meats, dairy foods, contemporary fabricated foods, franchise foods, prepared meals, shortenings, spreads, and fried foods should be examined in the context of reducing their dietary fat levels and modifying their fatty acid compositions. The replacement of SFAs and perhaps some n-6 PUFAs with hypolipidemic monoenoic fatty acids (Grundy, 1987) and the inclusion of n-3 PUFAs as a partial replacement for n-6 PUFAs may be desirable (Kinsella, 1988b).

With respect to nutrients or food components, the tendency to single out a specific compound and overemphasize its importance or overdramatize its potential danger results in confusion among the public. The necessity of consuming a range and variety of foods from different sources is generally recognized. However, the emphasis on dietary cholesterol and saturated fat and the concomitant proscription of animal products as sources of cholesterol and SFAs (which is not valid for such foods as trimmed meats, milks, and yogurt) may contribute to problems emanating from inadequate iron, calcium, and vitamin B_{12} intakes in certain subgroups of the population. A balanced comprehensive perspective is important when dietary recommendations are made in the context of ameliorating chronic degenerative diseases that may be only marginally responsive to dietary modifications. Because animal products provide significant quantities of essential nutrients, appropriate modification of their fat content is a practical and prudent approach (Briggs, 1985).

APPROACHES FOR MODIFYING FATS IN FOOD PRODUCTS

Reduction of the fat and cholesterol contents of foods and modification of the fatty acid composition is the goal of a number of current production and processing technologies in conventional agriculture that are being facilitated by developments in biotechnology.

Animal Products

Established practices and pricing systems have traditionally placed a premium on fat production in animals for both meats and milk. In response to nutritional and marketing pressures, however, the situation is changing, and producers and researchers are exploring various alternative approaches (Table 3) for reducing the fat content of animal products.

The fat content of animal tissues can be reduced by restricting energy (starch) in the diet, especially during the finishing period and by selecting for leaner strains of animals. To facilitate these measures and selection for leaner animals, new techniques for measuring body composition and fat levels are important. Thus, ultrasonic methods, X-ray-based computerized automated tomography, nuclear magnetic resonance imaging, and total body electrical conductivity are modern nondestructive methods being evaluated for sire selection and for determining the fat content and market readiness of animals (NRC, 1988).

TABLE 3 Some New Technologies That Provide Options for Producing Leaner Meats

Strain selection
Nutritional plane or finishing diets (less starch)
Noncastration of male animals
Growth hormones (somatotropin)
β-Agonists (epinephrine analogs)
Immunological suppression of adipocytes, growth inhibitors, etc.
Transgenic animals

Advances in the knowledge of factors affecting muscle growth and partitioning of nutrients are being explored for use in altering the composition of animal products. Adrenergic amines, especially those that bind to β-receptors (*β*-agonists), mobilize fat from adipose tissue; enhance its oxidation; and favor the deposition of muscle proteins in swine, beef, sheep, and fowl. Analogs of *β*-agonists or repartitioning agents are effective in increasing muscle mass and reducing fat deposition by directing nutrient flow to muscle growth (Dalrymple et al., 1986). The administration of somatotropin or growth hormone to animals markedly enhances muscle growth (Chung et al., 1985) and significantly increases milk yields in cows (Bauman et al., 1985). These new agents are being investigated intensively, and bovine growth hormone is being produced routinely by recombinant DNA techniques.

In addition, immunological techniques are being explored; for example, the generation of antibodies that might bind biologically active molecules such as somatostatin (ST) and that might allow somatotropin to function continuously is being explored in cattle by using autoimmunization with conjugated ST (Spencer and Mallett, 1985). Also being evaluated is the feasibility of immunizing animals against preadipocytes to prevent their differentiation into mature adipocytes and thus to reduce fat deposition. Further research to characterize endocrinological and humoral peptide regulators of cell metabolism and growth should provide new methods for manipulating animal growth and controlling body composition.

Transgenic animals that contain exogenous functional genes for desirable functions or antisense RNA for unwanted functions may be possible in the future. The concept of incorporating genes coding for growth-promoting agents, for example, somatotropin, or antisense genes (Green et al., 1986) to fatty acid synthetase or acyltransferase into animals warrants investigation. Such developments (Greenberg, 1987) would be compatible with current methods for both meat and milk production.

The intensive methods used for poultry production favor the fast-growing lean birds that contain about 15% (mostly subcutaneous) fat that is easily removed during processing or cooking or prior to consumption. The fatty acid composition of poultry and swine reflects dietary fatty acids, and thus can be manipulated to provide a more appropriate fatty acid composition for human consumption (NRC, 1988).

Aquaculture (e.g., of catfish, trout, Atlantic salmon, tilapia, crayfish, and shrimp) is a burgeoning new technology that is providing increasing quantities of lean muscle foods with a desirable lipid content and fatty acid spectrum. Dietary manipulation can increase the n-3 PUFA content of cultured fish (Kinsella, 1988).

Postharvest Modification of Animal Products

Beef cuts may contain from 5 to 20% fat, depending on the cut and grade. Research has shown that the palatability of beef cuts containing from 3 to 7% fat is equally acceptable (NRC, 1988), suggesting that much of the fat can be trimmed from prime cuts without a loss in quality. Trimming can be most easily accomplished at the time of slaughter (hot trimming). This is undesirable for the producer or processor, however, because it would alter the yield, and under current regulations of the U.S. Department of Agriculture (USDA), a carcass must have a yield grade to receive a quality grade. If a carcass is trimmed at slaughter, it is disqualified from receiving yield and quality grades. Because hot trimming can remove 80 to 90% of the fat and provide a leaner cut, the American Meat Institute has petitioned the USDA to allow, at the buyer's option, the separation of the yield and quality grades for beef. Approval of this now provides more lean mean cuts for consumers. The meat industry is currently providing a much wider selection of trimmed, low-fat meat cuts and is combining this with an informative educational effort on the nutrient contents of different cuts of meat.

Several advances in meat processing technology are facilitating fat reductions. These include the successful development of low-fat, restructured meat products (e.g., turkey hams). These are made by vigorously mixing pieces of meat in the presence of salt to solubilize the myofibrillar proteins that act as adhesive agents and bind the pieces together in an appropriate mold. Other proteins (e.g., egg white) can be added, and polysaccharides (e.g., alginates) can be used to improve adhesion and reduce the salt levels in re-formed meat products (Mittal and Usbonne, 1985). Surimi (a crab meat analog) is a gelled, restructured muscle food made from insoluble myofibrillar proteins, usually from fish (pollack), by gelation in the presence of binder proteins, starch flavors, and sorbitol. This low-fat product (<1% fat) can be colored and flavored to simulate a range of seafood products (Lee, 1986).

Comminuted and processed meat products (e.g., hamburgers and frankfurters) tend to be high-fat products, but there is interest in reducing the fat levels in these products. Advances in the knowledge of meat emulsions and gels are facilitating the formulation of acceptable products with reduced fat and increased amounts of water or in which fat is partly replaced by polysaccharides or other proteins (Kinsella, 1987a).

Milk

Milk has approximately 3.5% fat, of which 0.2% is cholesterol (approximately 10 mg/100 ml). The fat exists in globules and can be readily removed by centrifugal separation (Webb et al., 1974). This is now routinely practiced to reduce the fat content of fluid milks and products manufactured therefrom. Most fluid dairy products have relatively low amounts of fat and cholesterol. Traditional hard cheeses (Cheddar and Colby, for example) contain about 30% fat, and dairy creams represent products with relatively high amounts of fat. Research to develop low-fat cheeses is being pursued; however, it is a major challenge to simulate the flavor, texture, body, and mouth-feel of normal cheeses. More information concerning the physical and chemical contributions of milk fat to cheese quality is needed in order to produce high-quality, low-fat cheeses.

With respect to cultured dairy products (cheeses, yogurts, sour creams, etc.), the potential to reduce fat and cholesterol and modify fatty acid composition by using strains of genetically engineered culture microbes is in the initial stages of exploration (Harlander, 1987). Thus, cloning of genes coding for desirable enzyme systems (e.g., β-oxidation, cholesterol oxidation, and fatty acid desaturation) into microorganisms in starter cultures represents a possibility for the future. Such research is warranted because of the importance of milk and dairy foods in the diet as sources of calcium, protein, and vitamins.

Edible Oils

Vegetable oils represent a major dietary source of calories in the U.S. diet, mostly as visible fats (salad oils, shortenings, frying oils, spreads), but in addition, they are used extensively in food formulations. Edible oils are composed mostly of soybean oil, are generally rich in linoleic acid, and contain limited amounts of SFAs. Olive oil contains 70% oleic acid, while palm oil and especially lauric oils (coconut and palm kernel oils) are rich in SFAs. Advances in oil processing technology, especially better selectivity and control of hydrogenation, have resulted in a reduction of trans-fatty acid isomers in shortenings and margarines made from processed vegetable oils (Erickson, 1980). Improvements in hydrogenation coupled with a reduction of autoxidation (by removing traces of catalytic transition metals, by using antioxidants and packaging under inert gas) has facilitated much greater use of high vegetable oils with levels of linoleic acid in the U.S. food supply.

The apparent beneficial effect of n-3 PUFAs has stimulated commercial interest in the use of oils containing these fatty acids. Vegetable oils containing α-linolenic acid (LNA), that is, rapeseed oil with low levels of erucic acid (Canola oil), which has 10% LNA, and refined unhydrogenated soybean oil, which has 6 to 7% LNA, may be useful in this regard. Linseed oil, with approximately 50% LNA, is a potential rich source if the LNA can be stabilized against autoxidation. The new Canola rapeseed oil contains 60% oleic acid, 20% linoleic acid, and 10% LNA. This may represent a desirable ratio of dietary unsaturated fatty acids.

Fish oils represent a good source of long-chain n-3 PUFAs, usually containing 10 to 20% of these (mostly eicosapentaenoic and docosahexaenoic acids (Kinsella, 1989). Effective stabilization of these fatty acids in foods and edible oils remains a major challenge, and currently, their use in foods is limited by their chemical instability (Kinsella, 1987b).

The development of new information concerning the metabolic interrelationships of dietary unsaturated fatty acids (Lands, 1986a,b), the beneficial hydrolipidemic effects of oleic acid (Grundy, 1987), the potent effects and actions of eicosanoids, and the modulatory effects of n-3 PUFAs (Lands, 1987) may suggest that changes in the amounts and mixtures of unsaturated fatty acids used in food formulation and processing should be reassessed. As a result of developments in oil processing and stabilization together with the increasing capacity (especially via biotechnology) to produce edible fats and oils with desirable composition, a range of oils varying in physical and nutritional properties should become available. In this regard, the production of nonabsorbable food-grade edible oil substitutes is of significance (Haumann, 1986).

BIOTECHNOLOGICAL DEVELOPMENTS: POTENTIAL IMPACT ON NUTRIENTS

Developments in biotechnology may facilitate the production and processing of designed edible oils, food materials and ingredients by plant, animal, and microbial processes. This should permit the formulation of foods with balanced nutrients for optimum nutrition and health. Some of these developments that may have an impact on such things as production, commodity composition and properties, and processing (Figure 1) are surveyed below.

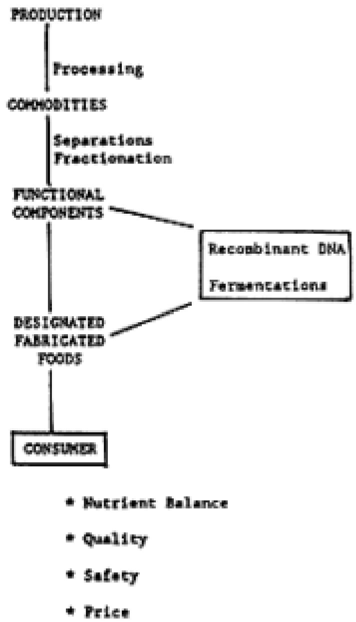

Figure 1 Major points or phases in food production and processing that can be affected by ongoing innovations in technology. Recombinant DNA and genetic engineering can improve production efficiencies and facilitate the rational design of components, and fermentations using genetically engineered microbes can become a significant source of functional ingredients. These developments will facilitate the production of formulated food products that more closely meet consumer criteria (i.e., nutrient balance, quality, costs, etc.). In that context the consumer increasingly may influence the sources of food components.

Biotechnology, that is, the application of modern techniques of molecular biology, biochemistry, and chemical engineering to the production of plant, animal, and microbial materials, can have a major impact on conventional food production and the nutrient content of foods. Genetic engineering connotes the successful transfer of DNA or genes coding for specific compound(s) from one cell to another. Considerable success has been achieved in producing pharmaceutical products (insulin, interferon, somatotropin, and vaccines), enzymes, and diagnostic agents by recombinant DNA techniques in microbes; and some limited success has been achieved in plants and animals.

Plants

Extensive research is being conducted to improve the efficiency of photosynthesis and to impart the capacity for nitrogen fixation into various food crops. Success in these areas should contribute to improved food production (Frawley et al., 1986).

The traditional breeding and selection techniques for new plant cultivars with greater resistance to pests and diseases and improved yield and quality characteristics are rapidly being superseded by more rapid tissue culture and protoplast fusion techniques to obtain genetic diversity (Frawley et al., 1986). In addition, recombinant DNA is being used to introduce into plants new genetic materials from other plant, animal, or microbial sources. The success of this approach depends on the regeneration of plants from cultured cells, which is a challenging obstacle with many plant species. Genetic engineering in plants is more complex than it is in prokaryotes because plants contain nuclear, mitochondrial, and chloroplast genetic material that interacts and controls different traits; cloning and vector systems are very limited; cell replication is slower; and finally, the transformed cell must regenerate into a plant. In addition, gene regulatory mechanisms and rate-limiting enzymes in important metabolic pathways are not yet well understood (Frawley et al., 1986; Zaitlin et al., 1985).

Cell culture techniques have greatly accelerated plant cultivar development. The newer techniques (Table 4) being applied to the selection of new plants include somaclonal variation in plants regenerated from cells, gamete culture, protoplast fusion, and gene transfer (transgenic plants) (Evans, 1985; Sharp, 1986). These methods are mostly being used to select favorable production traits but can also be used to improve the functional and nutritional properties of the products, with transgenic modification being most appropriate in this respect (Sharp and Evans, 1986; Zaitlin et al., 1985).

TABLE 4 The Major Techniques Used to Improve the Quality of Edible Plants via Plant Biotechnology

Method	Example
Genetic selection	Rapeseed corn
Tissue culture, somaclonal propagation	Potato, palm oil, tomato, asparagus
Gametoclonal variation (anther culture)	Cereals (corn, wheat, rice)
Protoplast fusion	Hybrid plants
Recombinant DNA technology	Herbicide and insect resistance

Routine clonal propagation of plants from cell culture is now used in plant breeding to propagate crop plants (Zaitlin et al., 1985). Somaclonal variation in plants regenerated from cells has been widely exploited in establishing new cultivars of tomatoes, carrots, and potatoes with different phenotypic characteristics (Whitaker and Evans, 1987). In addition, this method can be manipulated to obtain products with altered compositions (fruits, tubers, or seeds), for example, carrots with higher levels of β-carotene, tomatoes with more solids, red peppers with more pigment, or soybeans with a different range of fatty acids (Evans, 1985; Sharp, 1986).

Intensive research on methods that can be used to develop strains of oilseeds, especially soybean and rapeseed with different levels of oil and containing different fatty acids (i.e., more oleic acid, less palmitic acid, and zero to 15% linolenic acid), is in progress (Haumann, 1987; Horsch et al., 1987; Nielsen, 1987; Sharp, 1986). The dramatic successes in developing Canola oil (rapeseed), that is, replacing erucic acid by oleic acid (presumably from the loss of oleyl elongase) and sunflower cultivars with high levels of oleic acid derived from linoleic acid-rich cultivars (presumably from the loss of a desaturase) indicate that there is considerable genetic flexibility in the types of oil that can be synthesized by oilseeds. Green (1987) recently developed a flaxseed in which the LNA was reduced from 60% to approximately 1%, and linoleic acid was concomitantly increased to greater than 50%. Backcrosses of these flaxseeds gave intermediate levels of these two fatty acids. This crop could become a significant source of LNA for use in foods and as an edible oil. The various cell culture techniques in use should facilitate selection of cells with altered fatty acids. However, rapid methods are needed to diagnose desirable changes in the original cell rather than depending on plant regeneration and seeding (Frawley et al., 1986).

Gametoclonal variation in cultured anther cells (haploid and double haploid) provides a novel approach for producing new potato wheat, rice, rye, pepper, barley, and corn genotypes in a short time (Whitaker and Evans, 1987). This method is extremely promising for plant breeders and could be exploited more effectively if rapid screening methods were available.

Protoplast fusion techniques can be used to produce somatic hybrids and to introduce new gene combinations from different species and genera. Hybrid plants have been regenerated from carrots, rapeseeds, and potatoes (Evans, 1985). These techniques are of value as they allow integration and combination of cytoplasmic (chloroplast and mitochondrial) genetic materials into the hybrid, and hence, they may be useful in manipulating cytoplasm-linked factors (Frawley et al., 1986).

Gene transfer or gene modification is the most precise approach for introducing desired traits or product synthesis into plants. Genetic material can be introduced into many plant cells by using a plasmid from Agrobacterium tumefaciens as a vector to transfer and insert foreign DNA into the plant chromosome. This system has been successfully used to transfer foreign genes into a number of dicotyledonous plants (Jaworski, 1987). Thus, single-function genes for insect luciferase, soy conglycinin, and other proteins have been successfully transferred and expressed in other species of plant cells. The cloning of the gene for the insect toxin from Bacillus thuringiensis has been successfully cloned into plants and is expressed, as evidenced by insect resistance. This can have a major impact in increasing the production of plants used for food, but it may also enable a wider range of plant cultivars to be cultivated (Lawrence, 1987). However, the safety of this Bacillus toxin in human foods needs to be ascertained.

A number of transgenic plants containing foreign genes (mostly for herbicide resistance) have been propagated experimentally. However, more information concerning gene promoter sequences, transcription, and expression factors is needed. In recent years crop plants (e.g., rapeseed, tomatoes, potatoes, and lettuce) have been successfully transformed by using the A. tumefaciens plasmid vector (Frawley et al., 1986; Lawrence, 1987).

More recently, the direct microinjection of foreign DNA into plant protoplasts has been achieved (Jaworski, 1987). This method is particularly relevant to monocotyledonous plants (e.g., cereals) that are not amenable to transfection by A. tumefaciens and with the exception of rice, have been difficult to regenerate from cells (Cocking and Davey, 1987). Recently, the direct incorporation of DNA (which was injected into tillers of rye plants) into progeny cells and its expression in the progeny plants was reported (de la Pena et al., 1987). This method circumvents the problem of regenerating plants from protoplasts and should be a boon to the improvement of cereals.

Of the oilseeds, rapeseed, which readily regenerates from somaclonal, gametoclonal, or protoplast cells, is currently most promising in terms of oil modification (i.e., increasing its LNA content) (Knauf, 1987).

Recombinant DNA techniques hold promise for modifying the nutrient content (e.g., increasing the essential amino acid content) of many food plants. The insertion of the appropriate base sequences corresponding to essential amino acids into genes coding for seed protein synthesis is feasible, and these genes can be inserted into protoplasts or cells by direct microinjection or by the A. tumefaciens system. The plants regenerated from these cells can thus be modified. For example, the proteins of cereals (e.g., rice and corn) can be enriched in lysine, and legumes (e.g., soybean) can be enriched in methionine by using multicopy insertions if necessary. In addition, the insertion of foreign genes coding for proteins rich in essential amino acids or amplifying the transcription of endogenous genes for proteins rich in amino acids may become feasible (Bruening et al., 1987). Recently, Jaynes et al. (1986) successfully introduced a synthetic gene rich in essential amino acids into potato cells by using plasmids of A. tumefaciens and Agrobacterium rhizogenes as vectors. Similar strategies can be used in other plants (e.g., corn) to provide proteins with the appropriate amino acid balance (Messing, 1983; Rao and Singh, 1986). The content of other important nutrients, e.g., β-carotene, tocopherol, and certain B vitamins, should be amenable to manipulation.

However, multigenic traits are still difficult to transfer (Rao and Singh, 1986; Zaitlin et al., 1985). Detailed knowledge of the rate-limiting enzymes in biosynthetic pathways (for oil, protein) in plants is necessary in developing and applying a strategy for modifying products. Most pathways (e.g., fatty acid synthesis) require many enzymes, and hence, multigene manipulation may be required to alter a product. If one particular enzyme is rate limiting, however, the introduction of the gene for that enzyme may be sufficient to enhance synthesis of the product. On the other hand, if a particular product (e.g., trypsin inhibitor or lipoxygenase) is unwanted, then transgenic modification with an antisense gene for the rate-limiting step in the synthesis of that product can be used (Ecker and Davis, 1986). Elimination of lipoxygenase from soybeans has been shown to improve the flavor quality of soy products (Nielsen, 1987). Antisense genes (Ecker and Davis, 1986) eventually may be used to suppress the synthesis of undesirable multigene products (e.g., tannins in sorghum, trypsin inhibitors, saponins, thiocyanates, and goitrogens) in food plants.

In addition to the use of biotechnology to improve the nutrient content of plant products, increasingly it will be used to improve the physical and functional properties of plant (and animal) components to meet the exacting needs of food manufacturing. As the food industry fabricates new foods de novo, ingredients such as starches, proteins, polysaccharides, and fats with particular physical properties will be required in particular products (Kinsella, 1982). This will require knowledge of the relationships between the structure and physical properties of these macromolecules (Table 5) and rather sophisticated genetic engineering of such

TABLE 5 Intrinsic Factors That Affect Protein Structure, Function, and Behavior in Food Systems

Amino acid composition (major functional groups)
Amino acid sequence (segments or polypeptides)
Secondary or tertiary conformation
Surface charge, hydrophobicity, polarity
Size, shape (topography)
Intramolecular stabilizing forces
Disulfide and sulfhydryl content
Quaternary structures
Secondary interactions (intra-and interpeptide)
Substituent groups (phosphorylated, glycosylated)
Bound or prosthetic groups

multigenetic functions. Thus, rational modification of plants to produce more soluble polysaccharides and fiber, more heat-stable proteins, or a stronger gluten will be pursued as the food processing industry seeks more consistent functional ingredients (Lawrence, 1987).

Animals

Much of the emphasis in animal biotechnology has focused on reproduction (superovulation, embryo manipulation, multiple embryo generation, culture and transfer, and sex determination), the development of animal health care products (vaccines, interferon, hormones, and somatotropin), and veterinary diagnostic products by monoclonal and recombinant DNA techniques (Evans and Hollander, 1986; Ratafia, 1987; Smith et al., 1986). These can all markedly enhance the productivity of animal products and should thereby improve the quality and safety of the food supply.

The use of growth hormone (somatotropin) has been very effective in growth stimulation and in enhancing muscle growth in steers and milk yields in cows (Bauman et al., 1985; Evans and Hollander, 1986). The recent successful transfer and expression of exogenous genes in animals has greatly enhanced the potential of developing transgenic animals with improved growth, health, etc., that can also be manipulated to produce better quality meat and, possibly, milk containing desirable products of cloned genes that are activated by lactogenic hormones. The use of milking animals for the cloning of genes activated by lactation-specific regulators is particularly practical because the product is secreted and can be recovered or left in the milk for consumption.

The successful cloning of foreign DNA into the mammalian genome was developed in mice. Usually, DNA is microinjected into the pronucleus of a fertilized unicellular egg that is allowed to develop in the oviduct. Some 10 to 20% of the eggs survive, and following implantation some 20% of the neonates carry one or more copies of the original microinjected DNA, which is capable of tissue-specific expression for the production of a protein (Brinster and Palmiter, 1986). Other less successful methods involve the use of retroviruses to transfect animals (Van der Patten et al.,

1985) and embryonic stem cells (Bradley et al., 1984; Smith et al., 1986). Clark et al. (1987) have recently described the successful development of transgenic animals by microinjection of DNA into the ova of farm animals (e.g., sheep). Their observations indicated that microinjection of the complete intact gene sequence ensures tissue-specific expression in the transgenic animal. Alternatively, the gene segments comprising the promoter, coding sequence, and some extra nucleotides can be fused with an endogenous tissue-specific gene (e.g., the casein gene for mammary tissue expression) prior to injection. Appropriate signals for splicing and polyadenylation are required for transport and stability of the messenger RNA (mRNA) (Clark et al., 1987).

In mammary tissue the mostly single-copy genes coding for milk proteins are expressed at very high levels, reflecting promoter sequences that are very active. Fusion of these sequences with exogenous genes should ensure high rates of synthesis and secretion into milk. The possibility of using this approach to modify the nutrient composition of milk has been discussed. This modified composition could include caseins with higher amounts of methionine (Kang et al., 1986), milk with greater concentrations of transferrin or lysozyme, low-lactose milk, and β-lactoglobulin with a rich array of essential amino acids and better functional properties. Eventually, it may be possible to clone additional acyl desaturases into bovine mammary tissue and increase the degree of unsaturation of fatty acids in milk, to introduce antisense RNA into fatty acid synthetase, and to reduce milk fat.

This approach has already been used successfully to produce tissue plasminogen activator in the mammary tissues of transgenic animals (Clark et al., 1987). More information is needed concerning appropriate signal sequences and posttranscriptional modifications for the successful production of proteins in animal cells.

Microbial Fermentation

The most promising biotechnology developments have occurred in the microbial fermentations arena (Table 6), although few products are in use because of cost and

TABLE 6 Examples of Some fo the Major Products That Can Be Produced for the Food Industry by Biotechnological Innovations

Product	Uses
Amino acids	
Glutamic acid	Food additive
Aspartic acid	Aspartame (NutraSweet)
Phenylalanine	
Methionine	Animal feed
Lysine	
Tryptophan	
Enzymes	
α-Amylase	High-fructose corn syrup
Glucoamylase	
Glucose isomerase	
Amylogalactosidase	Light beer
Pullulanase	
Proteases	Protein modification
Rennin, Lysozyme	Cheeses
Improved organisms	
Yeasts	Wine and beer
Lactic acid bacteria starters	Milk fermentations, cheeses
Low-caloric sweeteners	
Aspartame	Non nutritive sweeteners
Thaumatin	
Monellin	
Stevioside	
Modified triglycerides and fatty acids	Cooking oil and food additives
Microbial polysaccharides	Thickeners and gelling agents
Flavors, fragrances, and colorants	Fabricated foods
Food testing	
Monoclonal antibody kits	Salmonella, Listeria
DNA Hybridization	aflatoxins, clostridia
Microbial proteins	Animal and human food supplements
Vitamins B_2, B_{12}, C, and E	Human and animal dietary supplements

regulatory constraints. Recombinant DNA techniques are most advanced for prokaryotic systems and to a lesser extent for yeasts. Basically, the gene or DNA sequence coding for an enzyme is isolated (or in the case of eukaryotic genes, the complementary DNA [cDNA] made from isolated mRNA, i.e., devoid of introns) is placed in a vector (usually a plasmid, phage, or virus) and is thereby incorporated into the microbial cell, which is then propagated (cloned); the transformants are then isolated and cultured for product generation (Lin, 1986). For high levels of expression, the cloned DNA sequence should be placed after the promoter and ribosome-binding site sequence and an appropriate transcription terminator sequence should be inserted in the plasmid. Ideally, the host cell should not degrade the message or the product, which, for most purposes, should be secreted (Lin, 1986).

Advances are being made in the application of recombinant DNA to the modification and improvement of functions of food-grade microbes used in food and beverage fermentations (Batt, 1986a,b; Follette and Sinskey, 1986; Harlander and Labuza, 1986; Knorr 1987; Stewart, 1984; Stewart and Rutsell, 1987). However, knowledge of, for example, the genetics, plasmid-linked traits, suitable cloning vectors, effective gene transfer mechanisms, and expression in food microbes is limited compared with what is known about Escherichia coli. Nevertheless, extensive research is focusing on these food organisms to amplify and improve their metabolic efficiencies, to introduce Additional stable traits, and to enhance the nutrient content of fermented foods (Kinsella, 1986b). There is a precedent for exploiting microbes approved for use in foods because several of the ingredients and nutrients currently used in the food industry are produced by microorganisms (Harlander and Labuza, 1986). These normal endogenous products of selected microbes include amino acids, flavor enhancers (monosodium glutamate), acidulants (gluconic, lactic, and citric acids), flavor compounds (yeast extracts and nucleotides), pigments, sweeteners (fructose and aspartame), stabilizers, thickeners (xanthan gum), and a range of enzymes. Current research is focusing on extending the number of functional ingredients (colors, flavors, essences, enzymes, gums, antioxidants, fatty acids, n-3 PUFAs, and vitamins) and developing transformed microbial organisms and plant cell cultures to improve productivity (Harlander and Labuza, 1986; Knorr, 1987; Lin, 1986; Whitaker and Evans, 1987).

Elucidation of the biochemical pathways identifying the rate-limiting enzymes and then cloning these into the cell or organism can greatly increase the production of multienzyme products (Lin, 1986).

By exploiting recombinant DNA techniques, microbial biotechnology has the potential to greatly supplement traditional sources of food materials and to manipulate the structure and physical properties of functional ingredients. Some examples are discussed below.

Molecular Design: Proteins and Enzymes

Computer modeling of functional macromolecules (proteins, enzymes, and polysaccharides) to elucidate structure-function relationships in foods and to assess the effects of genetic modification at specific sites is being increasingly exploited (Blundell and Sternberg, 1985; Lin, 1986). This facilitates molecular engineering via a single point mutation or substitution and subsequent cloning of the modified gene. Because the functional properties of proteins in foods reflect particular structures and secondary interactions (Kinsella, 1982), the rational modification of proteins by altering specific genes for functional uses may now be feasible (Hol, 1987). Because they are mostly single gene products and many are unmodified posttranscriptionally (via glycosylation or phosphorylation), proteins and enzymes have been used most successfully in molecular cloning to date. Point mutations and cassette insertions or substitutions can be used to alter the amino acid sequence, structure, and functional properties of proteins and enzymes produced in transformed microorganisms. The thermal stability of proteins can be improved by introducing arginine, lysine, and new disulfide bonds. This approach has been successfully used to modify the stability and properties of enzymes (Perry and Wetzel, 1984; Pitcher, 1986). The possibility of improving the nutritional value of proteins by genetically incorporating more essential amino acids while concurrently enhancing functional properties should also be feasible.

In addition, proteins that can be used in conventional food processing may be produced. Thus, in hard cheeses (e.g., provolone and emmenthal), late blowing, that is, gas formation caused by <u>Clostridium butyricum</u> , causes irregular vacuoles. This can be inhibited by nitrate (which is not allowed) or it can be controlled by lysozyme, which is currently isolated from egg whites. Recently, Perry and Wetzel (1984) isolated and cloned the thermally unstable T4 lysosome. By site-directed mutagenesis, they replaced isoleucine with a cysteine that could form an extra intramolecular disulfide link to produce a stable lysozyme. This lysozyme may have antimicrobial applications in foods and perhaps can be exploited in fermentations. Similarly, the cloning of other proteins (e.g., bovine lactoferrin) is of interest for use in baby formulas and feeds as an antimicrobial agent.

Scarce and expensive enzymes can now be cloned into microbes and produced in quantity (Table 7). Successes

TABLE 7 Examples of Common Food Enzymes That Can Be Produced by Genetic Engineering

Enzyme	Substrate	Uses
α-Amylase	Starch	Liquefaction to dextrins, brewing, baking
Catalase	Hydrogen peroxide	Milk sterilization
Cellulase	Cellulose	Juice clarification
Glucoamylase	Dextrins	Hydrolysis to glucose
Glucose isomerase	Glucose	High-fructose corn syrup
Glucose oxidase	Glucose and oxygen	Elimination of browning discoloration
Invertase	Sucrose	Production of invert sugar
Lactase	Lactose	Hydrolysis of lactose for low-lactose milks
Lipase	Lipids	Cheese ripening
Pectinase	Pectin	Wine or juice clarification
Protease	Proteins	Meat tenderizer, sausage curing, dough conditioning, beer clarification
Rennet	Casein	Casein coagulation, cheese manufacture

SOURCE: Harlander (1987).

to date include chymosin (rennet for cheese making), amylase, glucose isomerase (for corn sweetener), alkaline proteases, glucoamylase, and a broad array of other enzymes used in small quantities (Lasure, 1986; Lin, 1986). The microbial enzyme β-galactosidase is routinely used to hydrolyse lactose in milk and thereby render it suitable for consumption by lactase-deficient consumers. Cloning and site-directed mutagenesis to improve enzyme function is now feasible, but the relative costs and Food and Drug Administration approval for food uses are current obstacles (Pitcher, 1986).

In food processing, the traditional approach of trying to accommodate a process to suit the available ingredient or enzyme can now be changed so that ingredients or enzymes are redesigned to suit a particular process. Thus, enzymes that remain active in particular or unusual environments (i.e., apolar media, lipids, etc.) can be generated. An example is a lipase that catalyses the transesterification of fatty acids into glycerides in an organic or glyceride phase (Gillis, 1987). Such enzymes can be exploited to make triglycerides with the appropriate fatty acid composition and physical properties to meet particular nutritional or functional criteria.

Microbial Polysaccharides

Hydrocolloid gums are widely used in the food industry as viscosity modifiers, for gelling and emulsion, or as stabilizing agents that can impart desirable tactual and sensory properties to foods (Table 8). These are derived from seaweed, algae, plants, seeds, and microbial sources and show a wide range of properties. Most are nonmetabolizable, indigestible fibers that exert desirable physiological effects (Pilch, 1987). Microbial sources of homo-and heteropolymers that are being developed as functional ingredients include xanthans (glucuronic acid), dextrans (glucose), pullulans (glucose), alginates (mannuronic acid), and curdlan (glucose) polymers. These are examples of the range of hydrocolloids with different properties (Sinskey et al., 1986a,b) that can be used to substitute for fats in some processed foods.

TABLE 8 Examples of Types, Sources, and Structures of Food Polysaccharides and Gums Used in Food Formulations

Gums	Sources	Structures
Agar	Marine algae of the class Rhodophyceae	Heterogenous chains of β-(1,3)-d-galactose and α-(1,4)-3, 6-anhydro-l-galactose
Alginate	Brown seaweed (Macrocystis pyrifera)	Linear polymers of β-(1,4)-linked d-mannuronic acid and α-(1,4)-linked l-guluronic acid
Arabic	Exudate produced by acacia tree in response to injury	Spiral chains of β-galactopyranose linked β-(1,3) with side chains of (1,6)-linked galactopyranose, arabinopyranose, rhamnose, and glucuronic acid (molecular weight-500,000)
Carrageena n	Red seaweed such as β-(1,3)-linked Chondrus crispus	Linear chains of alternating β-d-galactopyranosyl and (1,4)-linked α-d-galactopyranosyl units sulfated at 2, 4 and 6 positions (molecular weight-200, 000)
β-Glucan	Aleurone cell wall and endosperm of oats and barley	Linear polymer of β-(1,3)-and β-(1,4)d-glucopyranosyl units (molecular weight-30,000 to 130,000)
Guar	Endosperm of seeds from two annual leguminous plants (Cyamopsis tetragonolobus and C. psoraloides	Linear chain of β-d-mannopyranosyl units linked α-(1,4), with single members of α-d-galatopyranosyl linked (1,6) as side branches (molecular weight-220,000)
Pectin	Midlamella between cells of apple pomace and citrus peel	Mostly an α-linked linear polysaccharide of d-galacturonic acid esterified with methoxyl groups from 0 to 85% (molecular weight-50,000 to 180,000)
Xanthum	Microorganism (Xanthomonas campestris)	Main chain of β-(1,4)-linked β-glucose with side chains of mannose and glucoronic acids (molecular weight2,000,000)

SOURCE: Ink and Hurt (1987).

Vitamins

Many vitamins are produced by microbial fermentation (Knorr, 1987). The successful cloning of a critical enzyme in the synthesis of vitamin C from glucose was reported recently (Anderson et al., 1985); with the cloning of gluconolactone oxidase, the final enzyme in vitamin C synthesis, a microbial system for the complete synthesis of vitamin C may be available presently. With advances in molecular cloning, the synthesis and production of vitamins via bioengineering will increase. The possibility of eventually cloning vitamin C synthesis into microbes used in food fermentations might improve food stability, and in processed meats it could reduce the need for nitrite.

Culture Organisms

Biotechnology, as epitomized by food fermentations (i.e., the rational use of microbes for improving the stability, quality, safety, and indirectly, the nutritional value of food products), has been exploited for thousands of years to preserve milk and to produce bread and alcoholic beverages. The molecular biology and genetics of the microorganisms used in food fermentations are elucidated to improve their applications. Research to improve lactic acid starter cultures for cheese and dairy fermentations is in progress in several laboratories (Batt, 1986a,b; Chassy, 1985; McKay, 1986; Venema and Kok, 1987). This includes research to enhance lactose metabolism to lactic acid, increase resistance to phage infection, and control proteolytic activity. In addition, the idea of incorporating additional plasmid-linked genetic capabilities into lactic acid streptococci is being explored. This includes, for example, the modification of cholesterol and the use of temperature-activated proteases and/or lipases to enhance flavor development and the ripening rates of cheese. The gene for the sweet protein thaumatin has been cloned and expressed in fermentative organisms (Kluyveromyces lactis), although it was not secreted (Edens and van der Waals, 1983).

Ideally, the cloning of genes for desirable functional ingredients and nutrients for human consumption should be conducted by using food-approved microbes. Hence, research on the genetics and molecular biology of lactic acid bacteria is particularly important because of their long history of use and safety. Information to improve their successful exploitation as host microbes for heterologous proteins should accelerate their use (Venema and Kok, 1987). In addition, the transformation of starter microbes with an increased ability to synthesize B vitamins, ascorbic acid, etc., may be feasible in the future.

The direct effects of viable food microorganisms on health is also of interest. The putative beneficial effects of Lactobacillus acidophilus in fermented dairy foods (acidophilus milk, yogurts, etc.) in reducing the production of enzymes (β-glucuronidase and nitroreductase) that are known to convert procarcinogens into carcinogens in the large intestine (Goldin and

Gorbach, 1984) deserve study from a molecular genetics viewpoint. Elucidation of this effect may be of significant value to public health.

Flavors

In addition to nutrition, contemporary consumers are concerned about safety, and in this regard natural ingredients are perceived as being safer than ingredients produced by chemical methods. Hence, there is a keen interest in exploiting biotechnology as a source of natural food ingredients. This is particularly true of flavors for which there are limited supplies and costs are high. Hence, plant, animal, and microbial cell cultures are being exploited and enzymes are being used to transform flavors to meet the criteria of natural food products. Genetic engineering of generally recognized as safe (GRAS) microbes with the appropriate enzymatic pathways for the synthesis of organic flavor compounds is at a premium, even for compounds such as acetaldehyde, benzaldehyde esters, and vanillin, which can be synthesized inexpensively by chemical methods. Plant tissue culture techniques are being used as a source of flavors (e.g., vanilla, strawberry, tomato, and mint), as a method for the biological transformation of flavor intermediates, and as a source of precursors that generate desired flavors when used in processing (Evans, 1983, 1985; Knorr, 1987).

Food Safety

Advances in molecular biology have resulted in the development of a number of new sensitive methods for the rapid detection of pathogenic and toxicogenic food-borne microbes (Harlander, 1987). This is particularly significant as new strains of infectious microbes are encountered in food systems. In view of the high priority of food safety, the improvement of rapid methods represents a major contribution to public health. Because of the need to monitor the safety of foods before they are released into the market, rapid and sensitive methods for the reliable detection of pathogenic or toxigenic microbes are at a premium. New methods based on enzyme immunoassays with monoclonal antibodies and, more recently, DNA hybridization techniques are becoming available (Table 9). Immunoassays with monoclonal antibodies have been used for the detection of Salmonella and Staphylococcus enterotoxins in foods; DNA-DNA hybridization probes provide a new technology for detecting various food-borne organisms. For example, Escherichia coli and Yersinia, Salmonella, and Listeria species (Fitts, 1985) have greatly improved the specificity of these tests (Fitts, 1985, 1986; Mattingly et al., 1985).

TABLE 9 Some Examples of DNA Probes Being Developed for Detecting Food-Borne Pathogens

Organism	Component Detected
Staphylococcus aureus	Enterotoxins A, B, and Cl
Clostridium botulinum	Neurotoxins A, B, and E
Yersinia enterocolitica	Invasiveness
Vibrio parahaemolyticus	Thermostable hemolysin
Vibrio cholerae	Enterotoxin, hemolysin, and cytotoxin
Salmonella spp.	Species specific
Escherichia coli	Heat-labile and heat-stable enterotoxins
Listeria monocytogenes	Hemolysin

SOURCE: Harlander (1987).

Algal Culture

Interest in algal culture as a source of nutrients (e.g., β-carotene and tocopherol) is burgeoning. This has been accentuated by the ability of certain algal strains to produce very high concentrations of n-3 PUFAs, and some strains can produce either eicosapentaenoic acid or docosahexaenoic acid preponderantly (Kinsella, 1989). Because of the therapeutic potential of n-3 PUFAs and the limited sources of relatively pure n-3 PUFAs (eicosapentaenoic and docosahexaenoic acids) produced by algae represent a potential source of these important nutrients (Pohl, 1982).

Comment on Biotechnological Developments

The potential of genetic engineering for revolutionizing food production by conventional (animal, plant, and avian) and nonconventional (microbial, algal, and marine) means is immense, and when coupled with advances in human nutrition, it should facilitate the formulation of a wide selection of high-quality foods with the appropriate balance of nutrients, calories, and fiber. The ability to design genetically macromolecules with the proper physical and nutritional properties, to simulate fats, to generate flavors, and to selectively eliminate antinutrients will accelerate automated food assembly and fabrication processes. Ongoing basic research should help to elucidate the mechanism(s) underlying the regulation of gene expression and the factors modulating cell replication, differentiation, and tissue growth and development and to identify the rate-controlling enzymes in multienzyme pathways. The lack of such information is currently retarding progress in the application of these new techniques.

Biotechnology has great potential, but it will take time for the use of products because the path from success in the laboratory (i.e., detection of nanogram quantities of a product) through scaleup to production is a tortuous one with numerous technical, engineering, regulatory, and marketing challenges. There is already evidence of nascent success with drugs and vaccines in the medical arena. The potential is great and the promise is exciting; however, educating the public sector to ensure reasonable but prudent regulatory criteria is critically important. The new technologies are easily transferable and can be exploited worldwide to produce more foods and relieve people from hunger, malnutrition, and debilitating diseases.

FOOD PROCESSING

In addition to progress in material production, developments in food processing and handling are altering the quality and nutritional and safety characteristics of the food supply. The primary function of food processing is to ensure safety, especially from pathogenic microbes and toxins, and concomitantly, to improve quality and storage stability, remove antinutrients (both natural and incidental), and improve the digestibility of proteins and starch and the bioavailability of nutrients (Tannenbaum, 1979). In addition, contemporary food processing involves nutrient fortification and supplementation, product formulation on the basis of nutrient content and convenience, aseptic processing, and the production of new foods from ingredient blends.

Thermal Processing

Thermal processing results in the destruction of some thermolabile nutrients, especially thiamin, riboflavin, and vitamin C. The extent of destruction depends on the time, temperature, and pH of treatments, reflecting relative activation energies (Karel, 1979). Water-soluble nutrients may be significantly reduced during the washing, blanching, and canning of fruits and vegetables. Thiamin is particularly alkali labile. Water blanching, which is necessary for vegetable preservation (to inactivate enzymes and reduce microbes), removes water-soluble vitamins; but this can be minimized by steam or air blanching (IFT, 1986). New methods of microwave heating or quick blanching to reduce nutrient losses, especially in products that are a major source of a particular nutrient, may warrant further exploration.

The traditional methods of canning can result in the loss (10 to 90%) of vitamins unless heating times and temperature are carefully controlled (IFT, 1986). Commercial sterilization also causes destruction, especially when it is done in traditional cans or glass containers. However, recent developments, that is, high temperature, short time (HTST) heat treatments and aseptic processing, both of which are facilitated by innovative packaging, can improve the retention of nutrients. HTST processing exploits the higher energy of activation of microbial lethality compared with that of nutrient destruction; hence, microbial destruction is favored at higher temperatures (Karel, 1979). These aseptic and ultra-high-temperature treatment methods are now being applied to the thermal processing of solid food particles in which the use of thinner films allows faster heat penetration and the more rapid destruction of microbes, with subsequent improved nutrient retention. Technologies for improving heat transfer efficiency or the generation of heat internally, for example, by microwave radiation, need to be explored further.

Irradiation

Interest in preservation, pasteurization, and sterilization by irradiation has been revived in the United States. Low dose irradiation (<1 kilogray [kGy]) has been approved for use in fruits and vegetables to control maturation, in wheat and flour to control insects, in fresh pork (<0.3 kGy) to reduce trichinosis, in potatoes to prevent sprouting, and in herbs and spices for use as a disinfectant. It is used to sterilize foods for immunocompromised patients. Irradiation commonly involves gamma-rays from cobalt-60 or cesium sources, although electron beams are effective for the surface sterilization of products. Limited up-to-date data are available concerning the effects of controlled irradiation in nutrients (IFT, 1983). Irradiation is an effective method, but because of the public perception, its immediate future in food processing in the United States is uncertain.

Microwave

Microwaves can be used effectively for pasteurization and sterilization, microbial destruction, and enzyme inactivation in a variety of products. Microwave drying and pasteurization are efficient and are being applied to the drying of pasta and precooking of bacon for franchise and institutional trades (Svenson, 1987). With the development of appropriate materials for use in packaging and containers, microwaves may be more widely and more efficiently used for the pasteurization of foods and for improving the safety of products.

The use of microwave ovens (now in more than 70% of households) is significantly changing the eating habits and food selection of Americans (Messenger, 1987b; Svenson, 1987). Numerous new meals, many of them low in calories (lean or lite meals), are being successfully marketed, and microwave cooking has favored the grazing eating trend at the expense of the traditional family meal. This creates a new situation in terms of monitoring and controlling nutrient intake and underscores the need for manufacturers to provide complete nutrient data on their products.

The need for water and ions to accentuate heat generation from microwave dishes and the energy loss problem with fats (with limited dielectric polarity, fat is a very poor heat-generating medium) may discourage the use of fats in microwaveable foods and encourage the use of more water, salt, and polar, water-soluble ingredients (Schiffman, 1986). Because of the differences in the heating mechanisms (rates and directions) between conventional and microwave cooking methods and the markedly different microwaveable behavior of different food components (e.g., heating rate, energy diffusion, penetration, and radiation), the formulation of acceptable microwaveable foods in which all components cook evenly remains challenging to food processors (Best, 1987; Rosenberg and Bogt, 1987). In this regard it is important that technical problems not be solved at the expense of good nutrition. Progress in microwaveable foods has generated demands for new coloring and flavoring agents and an array of new functional ingredients (e.g., modified starches and gums) (Best, 1987; Messenger, 1987a,b). Biotechnology may be partly able to meet these needs.

Freeze-Drying

The use of improved drying techniques, especially large-scale freeze-drying, has grown rapidly and is used commercially for the preservation of such foods as diced vegetables, fruits, and spices.

Separations and Fractionation

Ultrafiltration, diafiltration, microfiltration, and reverse osmosis represent relatively new technologies that are changing a number of food processing operations concerned with the concentration, separation, clarification, and deionization of liquid foods. It is widely used in the dairy industry, in beverage processing, and in concentrating fluid foods (Kosikowski, 1986; Paulson et al., 1984). Ultrafiltration can be used to modify the composition of fluid foods and to fractionate foods (e.g., milk) for the preparation of functional ingredients.

Supercritical gas and solvent extraction technologies (Table 10) may provide additional options for selectively removing undesirable organic components from raw materials and foods (Rizvi et al., 1986). Supercritical carbon dioxide is currently used for decaffeination of coffee and extraction of hops flavor (Hoyer, 1985). Supercritical carbon dioxide extraction is effective as a delipidating method; by manipulating conditions and refluxes, selective fractionation or removal of saturated fatty acids or cholesterol from fats is feasible. It is effective in removing cholesterol from muscle (Hardardottir and Kinsella, 1988) and may eventually be applied to the selective removal of saturated fat and cholesterol from commodities and food products (e.g, egg yolks and organ meats). Supercritical technology also

TABLE 10 Some Current Applications of Supercritical Fluid Extraction to Foods

Decaffeination of coffee and tea
Deodorization of oils and fats
Extraction
Vegetable oil and fats from seeds
Food coloring from plant material
Flavors, fragrances, aromas, and perfumes
Hops and spices
Fruit juices
Drugs from plant material
Oil from potato chips and snack foods

provides an alternative method that avoids the use of organic solvents in the processing of edible oils. This method is very efficient in refining crude oils (e.g., fish or vegetable oils) and may provide an approach for the selective recovery of polysaturated fatty acid components from marine oils (Daniels et al., 1988).

Packaging

Developments in food and beverage packaging, particularly the range and versatility of packaging materials, have greatly facilitated the development of new products and have improved the range and safety of foods available in the marketplace (Sacharow, 1986). Aseptic barrier plastics, oxygen barrier plastics, and modified and controlled atmosphere packaging (based on selective barrier plastics composed of different laminated films of various polymers) are revolutionizing the food and beverage industry.

Thus, storage of individual vegetables and fruits for retail trade in a controlled or modified atmosphere is being used increasingly to extend the shelf life of vegetables and fruits, which should increase their year-round availability.

FOOD FORMULATION

In addition to ongoing consolidation and globalization, the food processing industry has undergone major changes in the past 20 years--from mostly a commodity-handling industry to a more sophisticated industry manufacturing consumer food products. This has changed the relationships among the producers, processors, and consumers. The most notable are the concerns about nutrition and safety, the increased influence of consumers on producers via the processors, and the growing integration of the technical needs of the processors with production protocols. This reflects the evolution of a food processing industry that increasingly uses traditional food commodities (milk, cereals, etc.) as raw materials from which functional ingredients are fractionated and isolated for use in product reformulation (Kinsella, 1987a).

The practice of new product development to meet market and consumer needs has placed a premium on the availability of a range of ingredients with precise physical and functional properties suitable for formulation into products designed to provide desirable physical, organoleptic, and nutritional properties; safety; and convenience to the modern consumer. The need for ingredients with precise physical properties is accentuated by the trend toward automation (Kinsella, 1987c). In this regard, biotechnology and genetic engineering, as applied to conventional ingredient production, are timely and will enable producers of both agricultural and nonagricultural products to supply market needs. The trend toward food fabrication will encourage the development and production of rationally designed molecules (proteins, polysaccharides, and lipids), processing aids (enzymes), ingredients (acidulants and flavors), and nutrients (amino acids and vitamins) by the most competitive production systems. The rapidity with which this will occur is greatly influenced by food regulations and standards of identity, both of which require continual updating.

Fat Substitutes

The fabrication of new foods, especially products low in fats and sugars, has been stimulated by the demand for foods with reduced calories. This is being facilitated by a range of new functional ingredients (sweeteners, low-calorie fat substitutes, and flavors). A consensus panel of the National Institutes of Health (1986b) recommended that the food industry actively develop new products that are lower in fat and cholesterol. A number of alternatives or substitutes for fat in foods have been promoted. Maltodextrins can be used to replace some of the oil (30 to 50%) in such foods as salad dressings, gravies, dips, frozen desserts, and ice cream (Kaper and Gruppen, 1987). Gums, soluble fiber (Ink and Hurt, 1987) (see Table 8), and dextrins can be used to impart a smooth mouth-feel to foods in which fat has been partly replaced. Polydextrose, a synthetic polymer, is a low-calorie functional ingredient that can be used to replace fat and add body, viscosity (thickener), and mouth-feel. Effective flavoring is important in such products because the fat components are usually the principal carriers of desirable flavors in foods.

Nonmetabolizable, nonabsorbable fats have been synthesized. These include acylated sucrose (sucrose polyesters), polyglycerol esters, glycerol ethers, and polycarboxylic acid esters, and they have physical properties similar to those of fats and oils in food products, but they are not absorbed (Haumann, 1986). However, ingestion is limited by their laxative effects and the elution of fat-soluble vitamins. Whereas triacyl esters of glycerol are readily hydrolyzed, the penta-and hexaacyl esters of polyhydric alcohols are not hydrolyzed and, hence, are not absorbed. Sucrose polyesters (olestra) consist of a mixture of hexa-, hepta-, and octaacyl esters of sucrose with fatty acids; are nondigestible; and reduce plasma cholesterol and low-density lipoproteins (Mattson et al., 1979); they may exert laxative effects in some patients, however. These fats can be readily substituted in products, but the anal leakage problem and regulatory criteria are still major obstacles (Haumann, 1986). Nevertheless, they may have a place in food products in limited amounts. Because oils absorbed by foods during deep frying in fat are a significant source of calories in the American diet, nonabsorbable fats can be useful as a cooking or frying media.

Sweeteners

The total consumption of sweeteners in the United States is about 125 lbs/capita/annum. Sugar provides about 17% of calories in the U.S. diet. The reduction of dietary calories can be aided by using the wide array of sweeteners on the market. Sucrose consumption (approximately 85 lbs/annum) is decreasing, while corn sweeteners (high-fructose corn syrup) have increased (to approximately 35 lbs/annum), saccharin is consumed at about 10 lbs/capita/annum, and noncaloric sweeteners are approaching consumption levels of 20 lbs/capita/annum (Dziezak, 1986; Newsome, 1987).

The successful use of glucose isomerase facilitated a major breakthrough in enabling the production of fructose from glucose derived from cornstarch hydrolysates (the most successful example of enzyme biotechnology). Fructose is sweeter than sucrose per unit calorie, and its adoption by soft drink producers greatly expanded its use and general acceptability in the U.S. food supply.

The concern with calories has resulted in the development of a major line of low-calorie foods for which there is a current estimated market that approaches $2 billion. Because of the continuing demand for low-calorie sweeteners, several new products are available (Table 11) (Gelardi, 1987). The dipeptide aspartylphenylalanine-methylester (aspartame) has been adopted for use in many foods, and current sales are burgeoning (>$700 million, or approximately lbs/capita/annum). Aspartame is 200 times sweeter than sucrose, is sensitive to heat, and is somewhat unstable in solution above pH 5.0. Xylitol, which is as sweet as glucose, is metabolized (4 cal/g) but is chemically very stable and is not cariogenic. Thaumatin is a protein that is more than 2,000 times as sweet as sucrose and acts as a flavor enhancer. This protein has been cloned and can be generated in fermented products by using transformed microbes (Edens and Van der Waals, 1983). Several other sweetening agents, for example, stevioside, glycyrrhizin, phyllodulcin, and sucralose (chlorinated sugar), are being studied for particular applications (Dziezak, 1986; Grenly et al., 1983).

TABLE 11 Some Currently Available Food Sweeteners

Sucrose	Acesulfame
Fructose (high-fructose corn syrup [HFCS])	Stevioside
	Glycyrrhizin
Aspartame	Neohesperidin
Glucose	Dihydrochalcone
Saccharin	Phyllodulcin
Xylitol	Monellin
Thaumatin (talin)	

In addition, research on the mechanism of taste perception is progressing, and Schiffman (1987) has summarized recent work in this area. Certain compounds that stimulate the activity of the sodium pump can elicit the sensation of sweetness. The growing knowledge of receptor mechanisms should accelerate developments in designing new no-calorie condiments and flavors.

CONCLUSIONS

Improvements in the diet should ensue from the numerous developments that are occurring in molecular biology, food production technologies, fermentations, and food processing technologies. Technical advances will come at an accelerated pace, but their exploitation and application may only develop at a "legal pace" (i.e., slowly) unless the benefits of innovation are clearly communicated to the public and legislators and appropriate actions are taken to rationalize regulations and expedite their execution.

It should become more feasible to provide optimum amounts of nutrients in high quality food products. However, continued research and closer attention to food safety, particularly the role of microbes and their products in the etiology of both acute and chronic diseases, is justified. The potential long-term effects of these products on the immune system and chronic diseases need more attention.

The burgeoning developments in biotechnology, foods, and nutrition (Figure 2) underscore the integrated effort that is required in developing nutritious and safe

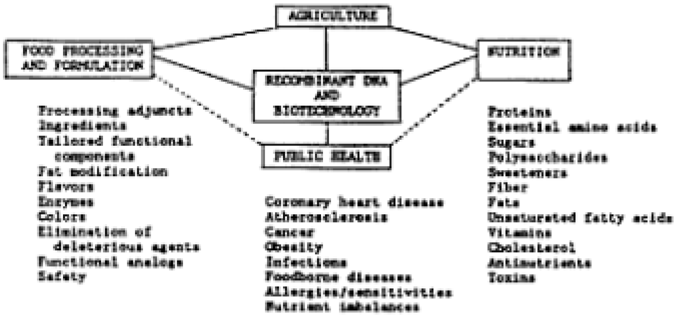

Figure 2 Scheme showing the manner in which biotechnology can have an impact on agriculture, food processing, nutrition, and public health via food and nutrient manipulation. In addition, genetic engineering can have an impact on public health via gene therapy and the production of vaccines, therapeutic agents, and drugs. Improvements may involve production of desired components or elimination of unwanted components by applying modern biotechnological techniques to food production and processing.

products and dramatize the innovations that are necessary in the education system to provide the appropriate and balanced training of scientists in the area of food science, nutrition, safety, diet, and public health. Research support to foster collaborative research in these areas is needed. The existence in academia of discrete departments that are each concerned with such areas as production, food processing, nutrition, and dietetics creates an atmosphere of reductionism and separateness and does not foster a complementary interdependence of these disciplines as they impinge on food, nutrition, and health.

Finally, these developments may provide more options for eliminating hunger and malnutrition around the world. Implementation of new developments requires commitment, a sense of balance in priorities, and humanitarian motivation in providing aid and training for those less fortunate around the world.

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From Ecologic Correlations to Metabolic Epidemiology: The Link with Nutrition

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The strengths of epidemiology for the study of the etiology of human disease are increasingly being recognized in the scientific community. Epidemiology not only focuses on humans, the species of interest, but also examines the effects of human exposures in their natural context. This means that epidemiologic analyses are necessarily based on the actual routes and levels of exposure occurring among the individuals at risk, can consider the impact of other interacting variables, and usually, encompass a sufficiently wide range of exposures to permit dose-response assessments. With regard to diet and disease relationships specifically, the epidemiologic approach has certain salient advantages:

- Epidemiologic studies can take into consideration some of the complexities of the human diet, including food sources, varieties, combinations, methods of preparation and preservation, temperatures, and additions (e.g., spices) that are unique to human populations and that may influence disease risk. These patterns are not easily reproduced in animal models.
- Dietary factors may interact among themselves or with other variables (e.g., exercise, medications, smoking, and other social habits). Epidemiologic studies have the potential to uncover such relationships, which would not likely be identified in animal studies.
- Because epidemiologic studies deal with actual levels of exposure, they can indicate the true magnitude of the effect of the dietary behavior and, therefore, its real public health significance. Thus, they are the primary basis for meaningful risk assessments among individuals.

- Since epidemiologic studies are carried out in free-living populations, they can identify the particular behavioral and sociocultural characteristics associated with diet-related illnesses, and thus can suggest practical and appropriate approaches to primary prevention. These approaches can be tested in well-controlled intervention trials before being implemented in the general population

Although epidemiologic studies provide the essential information on etiology, they are very limited in their ability to elucidate the mechanisms involved in pathologic changes. It is this latter aspect of the study of disease that is best carried out under controlled conditions in the laboratory with animal or human subjects. However, it is worth noting that precise knowledge about mechanisms is not essential to identify causal factors or to implement control measures that will prevent disease.

IMPORTANCE OF DIET IN CHRONIC DISEASE ETIOLOGY

Diet and nutrition are major factors in the risk of several chronic diseases. The two leading causes of death in the United States today, making up about 60% of all deaths, are chronic conditions: heart disease and cancer (Table 1) (Silverberg and Garfinkel, 1987).

TABLE 1 Ten Leading Causes of Death in the United States, 1984

Cause of Death	Mortality Rate/100,000 Population	% of Total Deaths
Heart disease	269.9	37.3
Cancer	170.7	22.2
Cerebrovascular disease	52.8	7.6
Accidents	36.3	4.6
Pneumonia/influenza	19.8	2.9
Chronic obstructive lung disease	17.4	2.4
Diabetes mellitus	13.0	1.8
Suicide	11.3	1.4
Hepatic cirrhosis	11.0	1.3
Arteriosclerosis	7.8	1.2

SOURCE: Data from Silverberg and Garfinkel (1987).

Through its influence on at least two primary risk factors for myocardial infarction, serum cholesterol level and obesity, diet makes a major contribution to the high incidence of coronary heart disease. Scientific data also suggest, although the evidence is less firm at present, that diet plays a significant role in the etiology of several leading cancers in the United States, including cancers of the large bowel, breast, and prostate, as well as several less frequent cancers, such as the stomach and pancreas (National Research Council, Committee on Diet, Nutrition, and Cancer, 1982). In addition, diet is a significant contributing factor to several other important chronic diseases in the United States, including hypertension, osteoporosis, diabetes mellitus, and dental caries. Thus, diet or nutrition is likely to be the major life-style factor affecting morbidity from chronic disease in the United States today, although the overall impact of cigarette smoking is better established at present.

DEVELOPMENT OF NUTRITIONAL EPIDEMIOLOGY WITH RESPECT TO CHRONIC DISEASE ETIOLOGY

The conclusion given above indicates that adequate assessment of dietary patterns and individual intakes is an essential part of much epidemiologic research into the causes of the major chronic diseases. Methods for conducting this research have been evolving continuously, but, as the following discussion shows, refinements are still needed.

Ecologic Correlations

Some of the earliest leads in the nutritional epidemiology of chronic disease came from simple correlations of food disappearance data with disease mortality rates. For example, researchers showed that mortality from heart disease in various countries was highly correlated with per capita consumption of dietary fat (Figure 1) (Jolliffe and Archer, 1959; McGandy et al., 1967). More recently, attention has been turned to cancer, and a similar high correlation has been seen for per capita fat consumption and cancers of the breast and large bowel (Carroll, 1975; Knox, 1977).

Such correlations suffer from the imprecision of food disappearance data as measures of food intake by individuals, not only because these data fail to account for such variables as storage and household waste, but also because they do not usually distinguish among even such heterogeneous groups as men and women or adults and children. Some investigators have attempted to overcome certain of these limitations in their ecologic studies. For example, Kato et al. (1987) used data from actual household surveys in Japan to correlate food and nutrient consumption with mortality from stomach and large bowel cancers in 12 geographic areas. Among their findings were positive associations in both sexes of stomach cancer with vitamin A intake, colon cancer with cheese intake, and rectal cancer with protein intake. In Hawaii, Kolonel and colleagues (1981) obtained diet histories on representative samples of the population and overcame several limitations of ecologic analyses by correlating nutrient intakes by sex, age, and ethnicity with corresponding cancer incidence rates. They found strong associations between dietary fat, especially saturated fat, and cancers of the breast, prostate, and endometrium (Table 2 and Figure 1) (Kolonel et al.,

TABLE 2 Significant Correlations of Mean Daily Lipid Intake and Cancer Incidence among Age-, Sex-, and Ethnic-Specific Groups in Hawaii

	Correlation Coefficient[a]			
Cancer Site	Total Fat	Saturated Fat	Unsaturated Fat	Cholesterol
Breast	0.94	0.95	0.90	
Corpus uteri	0.98	1.00	0.95	
Prostate		0.87		
Lung				0.94
Larynx				0.76

[a] Partial correlation coefficient, adjusted for sex where appropriate.

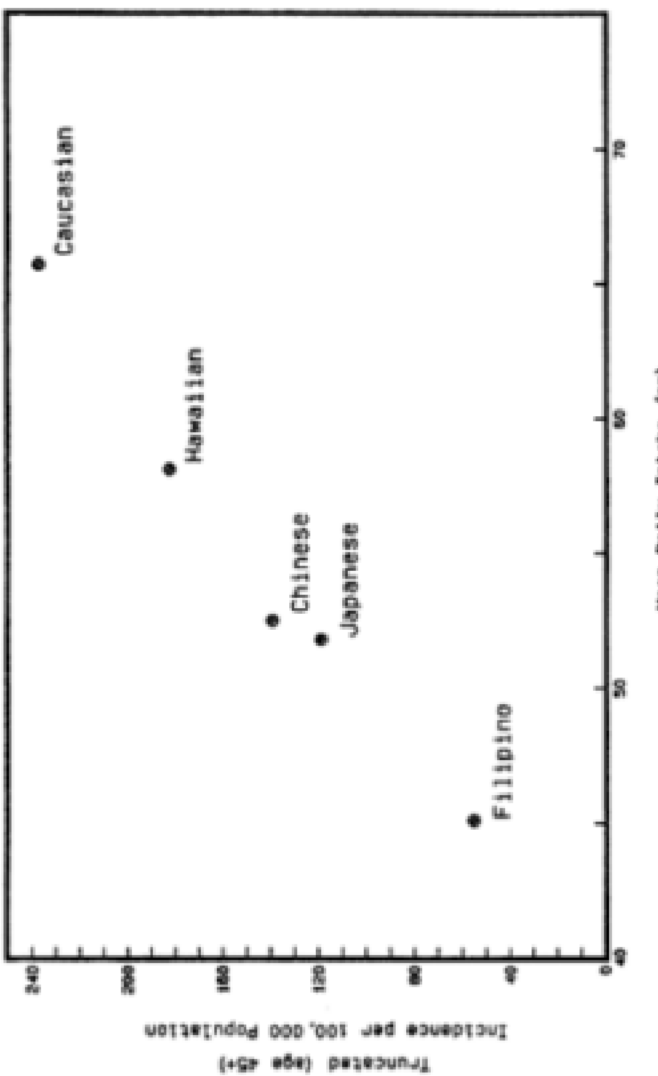

Figure 1 Mean dietary intake of total fat and female breast cancer incidence in five ethnic groups, Hawaii, 1977-1980.

1981). Because of the availability of a population-based tumor registry in Hawaii, they had the added advantage of working with morbidity rather than mortality data, which eliminated any concern that differences in survival, influenced by treatment and other factors, may have accounted for the observed correlations.

While ecologic studies based on individually collected intake data, with attention given to sex, age, and other possible confounding variables, represent an improvement of the per capita estimates from food disappearance data, the problem remains that the exposure and outcome groups are separately identified and may not overlap (ecologic fallacy). Thus, these studies have generally been thought of as hypothesis-generating only, needing confirmation with more analytic study designs. However, because of methodologic limitations in the assessment of individual diets (discussed below), there may be good reason to place greater confidence in the results of ecologic than of more analytic types of studies.

Case-Control and Cohort Studies

Studies based on diet histories. To explore particular dietary hypotheses, many epidemiologists have carried out case-control studies in which subjects were asked for their past intake of selected food items or of the total diet. These studies often relied on frequency data only (how often an item was eaten), and if nutrients needed to be estimated, standard portion sizes were assumed. For example, Lubin et al. (1981) compared the dietary habits of breast cancer cases and controls in western Canada based on a brief food-frequency questionnaire. They reported higher intakes of beef and pork and, using fixed portion sizes, of animal fat by the cases, in support of the hypothesis that fat is a risk factor for breast cancer.

In order to refine this method, other investigators have used certain props, such as geometric or plastic food models and colored photographs (Hankin, 1986; Morgan et al. and Jain, 1978), to estimate portion sizes. We prefer this approach, because it allows for greater variability in estimates and because usual portion sizes can differ substantially in heterogeneous groups such as the multiethnic population of Hawaii. For example, typical portion sizes of meat are much smaller for Filipinos than for Caucasians living in Hawaii, leading to greater differences in actual meat intake between these groups than would be estimated from frequency data alone. Nonetheless, at least in some other settings, there appears to be little difference in the findings regarding diet-disease associations whether frequency or frequency plus portion size is used. For example Humble et al. (1987) found similar odds ratios for the association of vitamin A intake with lung cancer among whites in New Mexico, a relatively homogeneous group, whether they used frequency data alone or frequency modified by portion size.

There are a number of additional limitations to the diet history method as applied in epidemiologic research. A major concern is the ability of individuals to recall accurately their food intakes in epidemiologic inquiries. Although several attempts have been made to assess the validity of such recall, with generally encouraging results (Block, 1982; Byers et al., 1987a, b; McKeown-Eyssen et al, 1986; Rohan and Potter, 1984), many investigators nevertheless remain skeptical about the reliability of such information. At best, one assumes that such recall data must reflect substantial measurement error (systematic as well as random), such that the diet-disease relationships are attenuated, in some instances, to the extent that true associations of modest magnitude may be missed altogether (Prentice, in press).

Errors of recall are made more likely by the fact that the diet in such developed countries as the United States is extremely varied in the number and nature of the foods eaten. Thus, the within-subject variability can actually exceed that between individuals. It has been reported, for example, that because of such variation in intake, one would need more than 6 weeks of daily food consumption records in order to classify 80% of individuals into only their appropriate tertile of intake of vitamin A (James et al., 1982). This observation points out one of the potential strengths of the diet history method, however. When subjects recall their usual intake of particular foods (for diet history, in contrast to a 24-hour recall or a 7-day food record, for example), they are actually accounting for this day-to-day variability in consumption by providing an average or representative intake. Such a diet history also permits the investigator to cover a wider spectrum of foods, thus providing a better reflection of intake than can be achieved from only a few days' records.

Although the more quantitative approach to the dietary history, that is, using variable portion size estimates, would seem to be desirable, this additional recall information may also add to the error in measurement, thereby lessening somewhat the gain in accuracy. This could be a reason for the failure of the New Mexico study (Humble et al., 1987) to find any significant difference in the nature and magnitude of the effect of vitamin A on lung cancer risk, whether variable portion sizes were included or excluded from the analysis. While this is only speculation at present, if confirmed, it would provide additional evidence that improved methods of quantification need to be developed.

In most instances, cohort studies are considered to be preferable to case-control studies, because they are less subject to bias (Lilienfeld and Lilienfeld, 1980). In dietary research, however, they often lack the representativeness of the case-control study, in that the intake information is usually based on consumption over a brief period surrounding the time of initial data collection (in some studies only 24 hours), which may not be even the most relevant period of life in terms of subsequent disease incidence. Furthermore, secular changes in the diet are usually not obtained in such groups, because of the considerable costs entailed in efforts to make repeated contact with the subjects to obtain additional information.

Despite the hazards of the diet history method, it has proven to be a successful tool in epidemiologic research. For example, as estimated from a diet history, saturated fat intake showed a significant association with serum cholesterol level in middle-aged American men, and unsaturated fat and dietary cholesterol showed significant associations (the former inverse) with coronary heart disease mortality (Shekelle et al., 1981b). Similarly, several studies using the diet history method have shown that the consumption of dietary sources of carotenes is inversely associated with the risk of lung cancer, especially among smokers (Table 3) (Bond et al., 1987; Byers et al., 1987; Hinds et al.,

TABLE 3 Epidemiologic Studies in the United States Showing an Inverse Association between Lung Cancer and Dietary or Serum Carotene

Year of Study (Principal Author)	Location of Study	Type of Study	No. of Subjects (Cases/ Controls)	Sex of Subjects
1981 (a,b) (Shekelle)	Illinois	Cohort	33/1,954[a]	Male
1984 (Hinds)	Hawaii	Case-control	364/627	Male and female
1985 (Samet)	New Mexico	Case-control	447/759	Male and female
1985 (Wu)	California	Case-control	220/220	Female
1985 (Nomura)	Hawaii	Cohort[b]	74/302[c]	Male
1986 (Ziegler)	New Jersey	Case-control	763/900	Male
1986 (Menkes)	Maryland	Cohort[b]	99/196[c]	Male and female
1987(a,b) (Byers)	New York	Case-control	450/902	Male and female
1987 (Bond)	Texas	Case-control	308/308	Male

[a] Number of cases/number of subjects in cohort.
[b] Based on serum measurements.
[c] Number of cases/number of controls analyzed from the cohort.

1984; Menkes et al., 1986; Nomura et al., 1985; Samet et al., 1985; Shekelle et al., 1981a; Wu et al., 1985; Ziegler et al., 1986).

On the other hand, certain diet-disease associations have been more difficult to establish with any consistency. For example, despite impressive ecologic correlations (shown earlier) and strong animal evidence, an association between dietary fat and breast cancer has been reproduced inconsistently and only weakly in case-control and cohort studies by diet history methods (National Research Council, Committee on Diet, Nutrition, and Cancer, 1982; Rohan and Bain, 1987). For many investigators, this has raised questions about the value of these methods, particularly in situations in which the true relative risks may be modest in magnitude. This concern has served as a major stimulus in recent years for efforts to find meaningful biochemical measures of dietary intake for use in epidemiologic research.

Studies based on biochemical measures. Suitable biochemical markers of dietary intake have not been easy to identify. To be useful, a marker (1) should be sensitive to (and relatively specific for) the particular nutrient (or other dietary constituent) of interest, (2) should vary in a definable manner in response to changes in dietary intake, (3) should achieve an integration of highly variable intakes, (4) should reflect the relevant period of exposure, and (5) should be easily and reliably measured. Such requirements are not readily met. For example, it has not yet been possible to find a marker of total fat intake that can satisfy all of these criteria. One can use biopsies of adipose tissue to provide information on fatty acid distributions, although not total fat intake. But even this procedure cannot be contemplated for the large numbers of subjects involved in most epidemiologic studies, especially healthy volunteers. Furthermore, in case-control studies, the marker levels may be influenced by the disease process itself, so that one is measuring a consequence, not a precursor, of the disease.

Nevertheless, some epidemiologic studies have used biochemical measurements. For example, at a group level, serum cholesterol has been positively associated with coronary heart disease mortality (Keys, 1980). However, since the serum cholesterol level is not greatly influenced by dietary cholesterol (Keys, 1984), this biochemical measure is not really a good marker for dietary cholesterol intake. Similarly, serum retinol has been examined relative to cancer risk. Since this parameter is under homeostatic control and only varies at the extreme ranges of intake, it does not satisfy any of the criteria for a marker noted above. Thus, as one would have expected, most studies have found no association between serum retinol levels and cancer risk (Bertram et al., 1987).

Willett et al. (1983) examined selenium levels in blood as a marker for dietary intake of this trace element. They found that low levels in serum, especially when combined with low levels of vitamins A and E, were associated with a higher risk for cancer. Since all three of these nutrients have antioxidant properties, this observation suggests that greater power in defining risk groups for a particular disease might be achieved if a single index for several factors that share a common mechanism of action could be developed.

There is yet another complexity to the study of dietary or nutritional factors in relation to human disease. This is the question of individual susceptibility. Even a biological marker that can be measured with considerable precision and does reflect usual intake might still not serve to distinguish high- from low-risk groups if individuals vary substantially in their susceptibilities to the effects of exposure. Such differences in susceptibility could be genetic in origin or could result from other environmental exposures. Thus, two individuals with similar exposures to a dietary risk factor of interest could have different rates of metabolism of the agent, which, in the case of a carcinogen precursor (procarcinogen), could result in the greater or lesser formation of an active carcinogen. This could be entirely hereditary, or it could result from another exogenous exposure that induces enzymes in the same metabolic pathway.

Intervention trials. Recently, diet has been the focus of intervention trials involving cancer and coronary heart disease (Greenwald et al., 1987; Multiple Risk Factor Intervention Trial Research Group, 1982). Such investigations are costly, require considerable nutritional expertise, and for ethical reasons, can only assess the effects of presumed beneficial dietary modifications. Unfortunately, incomplete knowledge or control of such factors as optimal levels of intake to achieve the desired effect, individual variation in susceptibility, compliance in the intervention groups, and dietary drift in the nonintervention groups all can easily undermine these research efforts.

FUTURE NEEDS AND DIRECTIONS

From this brief review of the interest in nutrition and the evolving use of nutritional methods in epidemiologic research, it is obvious that further methodologic developments must occur. No single investigative approach seems to be without its limitations with regard to nutritional assessment. For this reason, efforts in all areas of epidemiologic research, including ecologic analyses as well as case-control, cohort, and intervention studies, should be encouraged. A convergence of findings from many sources by a variety of approaches continues to offer the best hope for identifying meaningful etiologic relationships. Beyond this general statement, however, certain specific needs related to nutrition can be highlighted:

- Improvements in our ability to obtain accurate diet history information are very much needed. Although further validation of current methods can be one part of this effort, there is a need to develop techniques that can better distinguish among individuals with meaningful differences in their intake levels. Since the true relative risks for many diet-disease relationships that have not yet been established may be small, even moderate degrees of misclassification of consumption may be sufficient to result in false-negative results. The fact that such relative risks may not be impressive in magnitude should not lead to the conclusion that these relationships are of no public health importance, however. Since the combined incidence of diet-related illnesses is extremely high and the consumption of suboptimal diets is widespread, the number of individuals at risk is substantial; thus, even small relative risks can have very significant population impacts.
- As part of a total effort to advance this area of research, we should continue to seek biological markers of dietary intake. Such markers do not necessarily have to be direct tissue or serum analogs of the food components of interest. For example, a tissue enzyme that is influenced by changes in intake of a particular food constituent may serve as a better marker than the serum or target tissue level of the constituent itself (or even one of its metabolites). Similarly, the dietary factor that best reflects a biochemical measure of interest may not be the most obvious one. This is well

illustrated by cholesterol, the serum level of which is more clearly influenced by saturated fat than by cholesterol in the diet. Furthermore, other indices, not necessarily biochemical, such as central to peripheral ratios to adipose tissue or other anthropometric measurements, can be useful adjuncts in the evaluation of dietary exposures.

- Greater attention should be given to assessing individual differences in susceptibility to the effects of dietary exposures. This emphasis should include both genetic and nongenetic factors. Such a refinement in classification could offset a significant portion of the dietary measurement error, which probably will never be completely eliminated.
- Since different food components or nutrients may act in the same way to promote or prevent illness, consideration should be given to the development of indices that combine the separate effects of several agents. For example, vitamins A and E, selenium, and certain nonnutritive constituents in foods all have antioxidant properties. A single measure of the combined effect of all antioxidants in reducing cancer risk (using either a biochemical measurement or a computed value from dietary histories) might better account for differences among individuals than could any component alone.

Other needs related to data analysis should also be addressed, such as better means for assessing interactions among nutrients, more attention to eating patterns and food temperature, and greater accuracy of data in food composition tables.

- More nutritionists are needed to support this area of research. This is a special category of nutritionists who should have a basic understanding of the principles of epidemiology and biostatistics, since the focus in such studies is quite different from that in dietary counseling or in laboratory-based nutritional research. For example, such nutritionists must recognize certain limitations inherent in the conduct of field research on relatively large numbers of subjects or in designing practical methods of dietary assessment when individuals need to be classified precisely in a relative but not necessarily absolute sense.

CONCLUSION

Nutrition is receiving increasing attention by epidemiologic researchers, since many of the major diseases of public health importance today are ones that are likely to have a strong basis in dietary behavior. Research efforts to date have identified certain significant associations, such as that between saturated fat intake and coronary heart disease, between simple sugars and dental caries, or somewhat less definitively, between dietary fat intake and some cancers. Further advances are being constrained by methodologic limitations, however, including substantial errors of measurement in the diet history as these measurements are currently implemented, the lack of functional biological markers of specific dietary intakes, an inability to classify subjects into risk groups with sufficient refinement, and unmet needs related to data analysis. Nutritionists who are well trained for this area of research are rare and are very much needed. They could have a significant impact on the elucidation of important diet-disease relationships, leading to meaningful public health measures that could greatly reduce chronic disease morbidity in the future.

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II

FUTURE OF DIETARY INTERVENTION

Introduction

William E. Connor

I would like to make several points in the way of introducing this section of the report, the future of dietary intervention. Dietary intervention to improve human health is older than recorded history. Usually, the intervention is a part of the folklore of the people and is informal rather than a matter of official policy. Aphorisms about food such as "a mackerel a day keeps the doctor away" or "fish is brain food" illustrate this folklore. Hippocrates suggested, "let thy food be thy medicine." Humans have always used food to prevent disease--it is not a new concept.

The necessity for continual nutritional intervention rests on the rather static genetic makeup of humans coupled with an ever-changing world and technology. Basically, twentieth century humans have the same genetic makeup as Stone Age people, who obtained food only by hunting, fishing, and gathering from nature. They had limited technology and lived on the precarious edge of survival. The problem was to get enough food.

Successive agricultural revolutions have provided us today with an abundance of foods, both natural and highly processed. The maldistribution and overconsumption of food have led to new diseases, some in epidemic proportions. There is a wealth of scientific evidence that faulty nutrition is responsible for a host of disease processes in people who live in underdeveloped and impoverished parts of the world, as well as in people who live in developed parts of the world. Some are listed in Table 1.

TABLE 1 Diseases of Affluence and Poverty

Diseases of Affluence	Diseases of Poverty
Coronary heart disease malnutrition	Protein-calorie
Obesity	Xerophthalmia (vitamin A deficiency)
Hypertension	Anemia (iron deficiency)
Diabetes mellitus (adult)	Pellagra (niacin deficiency)
Cancer (e.g., breast, colon, prostate)	
Gallstones	

It is noteworthy that both the diseases of affluence and the diseases of poverty so prevalent in the developing countries have occurred because human cultures have strayed considerably from the dietary patterns developed over hundreds of thousands of years, particularly during the hunting and gathering stages during which the genetic makeup of modern man was developed. During the hunting and gathering stages, the diet characteristically included almost completely unprocessed food from both plant and animal sources. The animals and fish, as well as the plant foods and insects, that humans consumed had a relatively low fat content and were rich in nutrients such as vitamins, protein, and minerals. The food supply of the hunters and gatherers was diverse, with hundreds of individual foods gathered from nature. In particular, the animals were lean and their meat had a much more polyunsaturated fatty acid composition as compared with the saturated fat of the feedlot animals consumed by humans today. The rich diversity of the food supply meant that diseases of poverty, including vitamin and mineral deficiencies, were undoubtedly much less common. The main point I wish to make here is that both present-day diseases of affluence and diseases of poverty have resulted from technological advances. In the Western world the human diet is too rich and in developing countries the diet is stereotyped, for the most part, with there being a great dependence on single or several foodstuffs without the widely varied supply that our ancestors, the hunters and gatherers, consumed.

Technology has provided problems and opportunities. The agricultural revolution meant that given the proper distribution, all peoples of the world, including those of the United States, can have an ideal diet that will help them to produce healthy children and healthy adults free from the diseases of civilization with which so many are now afflicted. Technology means a safe, and tasteful, food supply. Both the diseases of overconsumption and diseases of poverty can be ameliorated by modifying the nutritional life-styles of both the relatively affluent and the poor.

Before I stress official public policy, important as it is, I want to emphasize the importance of the private, informal networks of dietary intervention. Take, for example, atherosclerosis and coronary heart disease. The private network that is of the opinion that dietary cholesterol and fat are bad for the heart began in the 1940s and 1950s in the United States. Remember Paul Dudley White, Louis Katz, Ancel Keys, William Dock, and Isadore Snapper? They said it all. The public listened, but it is impossible to change food habits without recipes, so low-fat cookbooks appeared. Dobbin and Goffman published one in 1952, and even today it is up to date. The American Heart Association issued a formal statement with dietary recommendations to prevent coronary heart disease in 1960. By the late 1970s, it was apparent that the mortality from coronary disease in the United States was 20 to 30% less. People had changed their diets. This did not please the egg producers. The informal networks operating in a literate and individualistic society had worked. In contrast, in Great Britain there were few medical leaders who said anything about diet and coronary disease--there was only skepticism. The press and the communications network in that country were silent, and the incidence of coronary disease increased in England while it decreased in the United States.

The United States is now at the stage of history of nutritional intervention when public policy by government can provide a further impetus for proper nutrition, especially for those of our citizens, the underclass, who are not in touch with these informal educational networks that provide so much nutritional guidance--for those who don't read Jane Brody in the New York Times or attend lectures by distinguished physicians. It is this group, the underclass, that particularly needs the benefits of governmental action to help them change their faulty nutritional life-styles, a matter that this section of the report emphasizes.

Nutrition and Public Health--New Dimensions

J. Michael McGinnis

Changes are occurring at a rapid pace in the nutrition sciences. This paper discusses various ways in which these changes will shape future public policy and practice related to nutrition.

Those who watch the literature and who attend the numerous scientific symposia held annually around the country receive the more than $200 million a year the National Institutes of Health pours into nutrition-related research. Indeed, those who merely read the daily newspapers can sense a biological revolution that will have a vast impact on the way nutrition affects the health of Americans. Yet, for society, scientific accomplishment is only as praiseworthy as its successful application for the betterment of the human condition.

It is therefore important to emphasize several of the challenges to be faced in making changes in public health policy, irrespective of the pace of change in the biomedical knowledge base. The following may help to put things into perspective:

> By many indications, this country's major needs in nutrition today are as follows: 1) control of obesity, 2) elucidation of the role of nutrition in the chronic diseases, 3) assessment of nutritional status as a step toward control of borderline deficiencies, 4) means of complete intravenous alimentation, and 5) additional knowledge regarding nutrition in the aged, those under stress, and in the convalescent (Sebrell, 1953).

This comment was made 35 years ago this month by the then director of the National Institutes of Health, W. Henry Sebrell, on the occasion of his receipt of the Joseph Goldberger Award in Clinical Nutrition. Advances in the science base, such as those described in papers by R.W. Hanson et al., A. Motulsky, and J.E. Kinsella in this volume, have provided the technical means of addressing many of these needs; but the persistent timeliness of Sebrell's observations of another generation is a poignant reminder of the difficulties of moving progress out of the laboratories and into the community. This is a fact that we should keep firmly in mind as we seek to explore future prospects for harnessing scientific insights more effectively for public health progress.

The issues that will shape the public health nutrition agenda of the future can be explored from three perspectives:

1. a summary of some of the major factors influencing the substance of the U.S. nutrition policy agenda,
2. a review of how those factors play on elements of the agenda, and
3. a brief look to the future.

FACTORS INFLUENCING NUTRITION POLICY

The factors most likely to influence our nutrition policy agenda include the national disease profile, the development of scientific insights, the advent of new technologies, the U.S. demographic profile, economics, changing meal source patterns, and public and professional awareness.

Disease Profile

Fundamentally, any public health agenda is driven to a substantial extent by the population's profile of disease and disability, the nature of the problems at hand, and the rate at which they are changing. Table 1 illustrates the selected causes of death for which diet may offer important contributions. The list includes 5 of the 10

TABLE 1 Selected Causes of Death, 1985

	Rate/100,000	
Cause of Death	Population	Number
Heart disease	323.0	771,169
Cancers[a]	193.3	461,563
Infant immaturity[b]	86.6[c]	3,257
Stroke[d]	64.1	153,050
Diabetes mellitus	15.5	36,969
Chronic liver disease	11.2	26,767 and cirrhosis
Atherosclerosis	10.0	23,926
Undernutrition[e]	0.1	134

[a] Cancers are malignant neoplasms, including neoplasms of lymphatic and hematopoietic tissues.
[b] Infant immaturity is disorders relating to short gestation and unspecified low birthweight.
[c] Per 100,000 live births.
[d] Stroke includes cerebrovascular diseases.
[e] Undernutrition is combined total for 1985 deaths from the lack of food and Kwashiorkor.
SOURCE: National Center for Health Statistics (1987) and unpublished data from the Division of Vital Statistics, National Center for Health Statistics (1988).

leading causes of death, 3 of which--heart disease, stroke, and cancer--account for more than 70% of all deaths in the United States (NCHS, 1987). For some of these, solid nutrition-related factors have been identified (Consensus Conference Statement, 1985; U.S. Department of Health and Human Services, 1988; Levy et al., 1979). We have begun to see impressive progress in their control, although it is far short of what ought to be possible. Some of the most intractable causes of death, like cancers and infant mortality associated with prematurity or low birthweight, have nutrition components that are less clear (DHHS, 1988; IOM, 1985; NRC, 1982). Of course, some must be on the list not because of their size, but--as in the case of undernutrition--because of their nature, because of their very presence in our society.

This list represents only a sampling of our health challenges. It does not include problems like acquired immune deficiency syndrome (AIDS), Alzheimer's disease, and arthritis, which are growing rapidly but have no clearly defined nutritional components, or nonfatal sources of disability with dietary elements, like osteoporosis. Nor is this necessarily representative of the picture a generation or even a decade hence. If a new or newly recognized disease with nutritional correlates should break onto the scene, things could change dramatically. For the present, however, the list in Table 1 is reasonably reflective of how disease profiles contribute to the public health nutrition agenda.

Scientific Insights

New scientific insights can change the role of nutrition in public policy. A good example is what is happening in the National Cholesterol Education Program (Cleeman, 1986; Lenfant, 1986, 1987), based on more than half a century of research about the relationship between blood lipids and cardiovascular disease. The future may hold much more as the nutritional sciences embrace the tools of molecular biology and genetics (A. Motulsky and R.W. Hanson et al., this volume). Some of these are discussed below.

Table 2 illustrates the research areas identified as being of particular importance by the federal Interagency Committee on Human Nutrition Research. They include the following:

- Nutrient requirements throughout the life cycle, because of the importance of identifying how age-related metabolic changes have an impact on nutrient needs;

TABLE 2 Interagency Committee on Human Nutrition Research Priorities

Nutrient requirements throughout the life cycle
Nutrient interactions and bioavailability
Nutrition and chronic diseases
Energy regulation, obesity, and other related eating disorders
Nutrition surveillance and monitoring methodology
Nutrition education techniques

SOURCE: ICHNR (1986).

- Nutrient interactions and bioavailability, in recognition of the integrative nature of human diets and the need to be cognizant of the broader systemic effects of secular trends related to fiber and supplement consumption;
- Nutrition and chronic diseases, because of growing appreciation of the central importance of nutritional factors to chronic disease occurrence, but residual uncertainty as to the nature of the mechanisms;
- Energy regulation, obesity, and other related eating disorders, because of the disproportionate prevalence of obesity in the United States and its likely association with various health problems;
- Nutrition surveillance and monitoring methodology, in recognition of the substantial deficiencies in the ability of the United States to reliably assess the population's nutritional status; and

- Nutrition education techniques, because of the fact that progress in nutrition is essentially dependent on motivating informed choices conducive to health prospects.

Major breakthroughs, or even accumulation of a number of more subtle changes, in any of these areas, could have a substantial impact on public health nutrition policy.

Technologies

Closely related to and, indeed, derived from the world of new scientific insights is the dazzling array of technologies that present both instruments and challenges for public health nutrition. Table 3 lists several technologies that can be predicted to have a considerable influence on the future course of nutrition policy.

TABLE 3 Nutrition-Related Technologies

Gene characterization
Genetic engineering
Food and ingredient synthesis
Food composition assays
Body composition techniques
Micro/computerized bioassays
Automated personal diet profiles
Automated analysis of food usage

Gene Characterization. Mapping of the human genome has yielded the identification of the region of the DNA pathology responsible for sickle cell anemia, β-thalassemia, Tay Sachs disease, galactosemia, and more than 30 other inherited diseases (Stanbury et al., 1983). Of the approximately 200 inborn errors of metabolism, almost one-third affect the digestion, absorption, transport, metabolism, or excretion of nutrients and therefore can be at least potentially responsive to diet therapy (Nestle, 1985). Inborn variations in metabolism with a potentially much broader public health impact are also being characterized (Motulsky, 1987; this volume). Brown and Goldstein's work on familial hypercholesterolemia is a now classic example (Brown and Goldstein, 1984, 1986; Sudhof et al., 1985).

Genetic Engineering. As a logical outgrowth of gene characterization these insights can be applied in efforts to change the offending DNA structure. This may ultimately hold promise for correcting those inborn errors of metabolism mentioned above. But already the technique of engineering genetic change is being put to work in the development of new types of food products. Examples range from manipulation of sperm, ova, and embryos to produce genetically improved animals (Polge, 1985; Van Raden and Freeman, 1985); to the use of gene transfer systems to develop herbicide-tolerant, insect-resistant, and viral disease-resistant plants (Goodman et al., 1987); to development of new probes to identify contaminated food.

Food and Ingredient Synthesis. As new technologies increase the possibility of modifying traditional foods and developing new foods, an accompanying set of unique problems of food safety, quality, and labeling has emerged (Miller and Stephenson, 1987). For example, the U.S. Food and Drug Administration (FDA) is increasingly faced with new issues presented by new products like the protein-based fat substitute Simplesse (Anonymous, 1988) or a nonabsorbable, chemically synthesized sucrose polyester fat substitute that may have cholesterol-lowering properties (Glueck et al., 1983; Grundy et al., 1986), or by modified products like the higher oleic acid-, less saturated fatty acid-containing canola oil and the olive oil-enriched Sunola oil (Anonymous, 1987). The food industry is currently pouring substantial sums of money into the development of new and reformulated food products--more than 7,000 products were projected for 1986 alone (Albrecht, 1986)--that are targeted to a public apparently fascinated by them. This shows that the old industry axiom, "You can't sell nutrition," is no longer true.

Food composition assays. Despite the fact that food composition analysis is the oldest of the food-related technologies, we still are relatively ignorant about the precise makeup of a sizable share of our food supply, particularly with respect to the various ways in which foods are prepared and served. A leap in our ability to conduct such assays could well have a considerable influence on the conduct of our public health programs.

Body composition techniques. The ultimate physiologic effect of the nutrients we consume is a central issue in nutrition. New techniques to make such assessments, like total body electrical conductivity, neutron activation analysis, and magnetic resonance imaging (described in Lukaski, 1987), may help usher in important capabilities in this regard.

Microcomputerized bioassays. A related technology with substantial potential to enhance our understanding of the physiologic effects of dietary patterns, as well as the individual variation in the nature of those effects, is the development of automated techniques with widespread applicability to the conduct of our national health and nutrition surveys. For example, the Centers for Disease Control has developed methods for the analysis of vitamins A and E and iron in serum using very small samples (DHHS and U.S. Department of Agriculture [USDA], 1987).

Automated personal diet profiles. The cornerstone of the current approach to dietary guidelines is balance. The questions are "what constitutes balance" and "when are we accomplishing it?" Current methodologies for assessing personal diet profiles have considerable weaknesses, but with the increased availability of microcomputers and with advances in the quality of available software for assessing daily diets, we should anticipate an improvement on this dimension. The third National Health and Nutrition Examination survey (begun in 1988), for example, uses an automated 24-hour recall instrument for data collection.

Automated analysis of food usage. A vulnerable component in the National Nutrition Monitoring System is its inability to track food usage patterns reliably. We simply do not know how much of any given product produced by American agriculture or imported from abroad is actually consumed in any given year or over time (DHHS, manuscript in review). Knowing the form in which it is presented is yet another challenge altogether. Nonetheless, automation may well yield substantially enhanced capabilities for monitoring patterns for food usage.

Demographic Profile

Public policy is generally more responsive to groups whose numbers are growing than those whose numbers are shrinking. Here the dominant theme is "older", as shown in Table 4. Over the course of the twentieth century, the median age of the U.S. population increased by nearly 16 years, from 23 to 39, with a 1,200% increase in the share of people over age 85 and a 40% decrease in the

TABLE 4 U.S. Population Age Profile

Age Group	1900	1980	2010	2040
Under 25 (%)	54.0	41.3	32.7	29.6
65 and over (%)	4.0	11.3	13.8	21.7
85 and over (%)	0.2	1.0	2.3	4.2
Median age (yr)	22.9	30.0	38.5	41.6

SOURCE: U.S. Bureau of the Census (1955, 1975, 1984, 1987); U.S. Senate, Special Committee on Aging, et al., (1988).

share of people under age 25. Indeed, if a projection is made to the year 2040, the population over age 85 will have nearly doubled again relative to that in 2010 and will represent about 4.5% of the total U.S. population (U.S. Bureau of the Census, 1984). The nutrition concerns of older people are going to move quickly up the public health agenda.

Economics

One cannot forget the role of economics as a major determinant of public policy. In fact, it is not uncommon for advocacy organizations to define policy simply as a six-letter word spelled "b-u-d-g-e-t." With the food sector accounting for about 10% of the domestic economy (U.S. Bureau of the Census, 1986), it is clear that food is big business. As shown in Table 5, the

TABLE 5 Economics of Food, 1985

Expenditure	$ (billions)
Sales of farm products	142.1
USDA farm programs[a]	7.7
USDA food programs	18.4
Processed food industry	83.0
Food and eating out	461.0
Nutrition research	0.292

[a] Direct payments to farmers for farm-related activities.
SOURCE: U.S. Bureau of the Census (1986) and ICHNR (1988).

United States spent, for example, $461 billion for food (groceries) and eating out in 1985 (U.S. Bureau of the Census, 1986). The processed food industry accounted for $83 billion of the national economy in 1985, farm product sales accounted for $142 billion, and farm and food program expenditures in the USDA alone accounted for over $26 billion. With amounts of this magnitude, economic forces will do much to shape the ways in which nutritional issues are presented in public health.

Meal Source Patterns

A very practical consideration for public health programs in nutrition is the places people eat. Both as a determinant of nutrient intake profiles and as a possible locus for education and intervention on those profiles, the ways in which meals are taken present special opportunities. These days the watchword for meal taking is "convenience." For example, in 1985 more than half (57%) of American households had microwave ovens (Hotelmen, 1986), which were being used to prepare a new generation of prepackaged meals. And increasingly, people are eating out or purchasing prepared food for consumption off the premises. This is reflected in eating place sales,* which make up two-thirds of total food service industry sales (National Restaurant Association, 1987) and which increased from $104.5 billion in 1984 to $128.6 billion in 1987--a 23% increase in just 3 years. Sales are forecast to reach $138.2 billion in 1988- -another 7.5% increase (National Restaurant Association, 1987). As Table 6 indicates, limited-menu restaurants, the so-called fast-food restaurants, continue to be one of the fastest growing segments of the industry, with forecasted sales of $60.4 billion in 1988. Children under age 18 and adults aged 25 to 34 are frequent patrons, accounting for half the share of takeout restaurant meals in 1987 (National Restaurant Association, 1987).

* Eating places include restaurants, lunchrooms, social caterers, commercial cafeterias, and limited-menu restaurants, as well as ice cream and frozen custard stands.

TABLE 6 Where People Eat (Food and Drink Sales, $ in billions, rounded)

	Estimated		Projected		% Change	% Real Growth Change
Eating Place[a]	1984	1985	1987	1988	(1987-1988)	(1987-1988)
	104.5	111.6	128.6	138.6	7.5	3.3
Restaurants[b]	55.1	58.4	66.1	70.6	6.7	2.5
Fast food	43.7	47.2	55.7	60.4	8.5	4.3
Cafeterias	3.2	3.3	3.7	3.9	6.4	2.2
Social caterers	1.2	1.3	1.5	1.6	7.4	3.2
Ice cream stands	1.3	1.4	1.6	1.7	7.1	2.9

[a] Data are from restaurants, lunchrooms, fast-food restaurants, commercial cafeterias, social caterers, and ice cream and frozen custard stands.

[b] Includes lunchrooms

SOURCE: National Restaurant Association (1987) and National Restaurant Association Research and Information Service Department (1987).

Data from the USDA indicate that whereas in 1977 only about 45 percent of women recalled eating away from home on the day before they were surveyed, that figure was 57 percent by 1985 (USDA, 1985). When asked about their eating out activities over 4 days in 1985, 88 percent of the women reported eating out at least once (USDA, 1987). Not surprisingly, increases in out-of-home meals were also noted for children and for men, who tend to eat the most meals away from home (USDA, 1985, 1986).

A statistical analysis of USDA data sheds some light on the nutritional quality of the food consumed away from home, at least by women (Guenther and Ricart, 1987). This analysis controlled for household and other sociodemographic characteristics that might have masked any associations between the extent of food service eating and nutrient quality. Moreover, on average, 16 percent of calories consumed by the women aged 19 to 50 were taken outside the home in restaurants, fast-food establishments, or cafeterias (Guenther and Ricart, 1987). The analysis also showed that women who obtained more than 20% of their food energy from these three types of food service establishments (high users) had lower densities of iron, calcium, vitamin C, carbohydrate, and fiber and higher densities of total fat and saturated fat, suggesting a slightly negative influence of the three types of food service establishments on nutritional quality (Guenther and Ricart, 1987). Presumably, the effect of children's diets on nutritional quality would be similar. While the health implications of these trends are unclear at present, it has the potential to be a sizable public health issue.

Public Awareness

Public awareness serves as both a challenge and a stimulus to public health. There is little question that the public is increasingly interested in nutrition and is aware of the central issues. Table 7, compiled from several DHHS surveys, indicates the increase in public awareness over the last decade with respect to cardiovascular disease and some of the dietary correlates. There was greater than a threefold increase in awareness of the relation between high blood pressure and likelihood of a heart attack (Lenfant and Roccella, 1984; Roccella et al., 1986), greater than a fourfold

TABLE 7 Public Awareness of Cardiovascular Disease and Dietary Correlates

	% Awareness[a]	
Causative Factor and Disease	Mid 1970s	Mid 1980s
High blood pressure and heart disease	24	91
Sodium and high blood pressure	12[b]	59
Dietary fat and heart disease	45	80

[a] Percentage of respondents indicating awareness of cardiovascular risk factors.
[b] Data for 1982.
SOURCE: DHHS (1986), Lenfant and Roccella (1984), and Rocella et al. (1986).

increase in awareness about the link between sodium and high blood pressure (U.S. Department of Health and Human Services, 1986; Roccella et al., 1986), and almost a doubling in understanding of the link between fat and heart disease--the latter occurring in just a 5-year period (U.S. Department of Health and Human Services, 1986; Rocella et al., 1986). Indeed, Table 8 from the jointly sponsored National Heart, Lung, and Blood Institute (NHLBI) and FDA national cholesterol Awareness Surveys shows that in just a 3-year period, from 1983 to 1986, there where 8 to 10% increases in adult attitudes, beliefs, and actions on lowering blood cholesterol to reduce the risk of heart disease (Schucker et al., 1987b) Judging from the public response to the Kellogg All-Bran campaign, interest is perhaps even more keen in other areas of nutrition as well (Levy and Stokes, 1987).

TABLE 8 Changes in Public Attitudes, Knowledge, and Behaviors Relating to Cholesterol and Heart Disease, in Percent

	Percent of Population Surveyed	
Characteristic Surveyed	1983[a]	1984[b]
Adults who believe that lowering high blood cholesterol will have large impact on heart disease	64	72
Adults who had blood cholesterol checked	35	46
Adults who changed their diet to lower their blood cholesterol	14	23
Adults diagnosed as having high blood cholesterol	7	8

[a] Total number surveyed was 4,007.
[b] Total number surveyed was 4,004.
SOURCE: Schucker et al. (1987b). Data from the NHLBI and FDA Cholesterol Awareness Survey.

Professional Awareness

One of the more curious aspects of health enhancement efforts is that if an effort is viewed as falling within the public domain--if it is public health or health for the public--then a large share of practicing health professionals somehow feel absolved of any responsibility, or expertise for that matter. Table 9, for example, which was also drawn from the Cholesterol Awareness Survey data (Schucker et al., 1987a, b), shows the pace at which physicians have come to be interested in peoples' blood cholesterol levels, which is the single greatest risk factor outside of heredity for heart disease, the dominant killer of nonsmoking, normotensive

TABLE 9 Cholesterol Awareness, in Percent

Positive Response[a]	1983	1986
Public	64	72
Physicians	39	64

[a] Response to query on preventive effect of reducing high blood cholesterol. The percentage of the public and physicians responding that lowering of a high blood cholesterol level will have a large effect on coronary heart disease. In 1983, the total number surveyed was 4,007 members of the public and 1,610 physicians. In 1986, the total was 4,004 members of the public and 1,277 physicians.

SOURCE: Schucker et al. (1987 a, b). Data from Cholesterol Awareness Survey.

adults in their prime (DHHS, unpublished). In 1983, nearly twice as many of the general public as physicians believed in a salutary effect of reducing high blood cholesterol. By 1986, the gap had narrowed, but the public was still in the lead. Data on the nature of physician gains over that period indicate that 25% more physicians surveyed in 1986 believed that lowering high blood cholesterol would have a large effect on heart disease, 12% more believed that low-fat diets will affect blood cholesterol, and 36% more initiated diet therapy at the levels approximating the recommendations of a National Institutes of Health (NIH) Consensus Conference (Consensus Conference Statement, 1985) on the subject (Schucker et al., 1987a). So physician attitudes are changing, but they have a way to go.

In sum, myriad factors are converging from various perspectives to affect the U.S. agenda for nutrition policy. In many cases, like those of technologic change, economics, and public demand, they are pressing hard for rapid changes.

PUBLIC HEALTH NUTRITION INTERVENTIONS

The kinds of interventions important for any public health activity, whether it be occupational health, AIDS control, or nutrition policy, include agenda setting (identifying the priorities); public education and information (getting the word out to people); direct services delivery (making sure that people are provided with the tools to make the change); reimbursement policies (payments to health care providers with special capabilities to deliver the services); tax policies (to establish economic incentives for change); health protection regulation (using the regulatory system to safeguard the public against abuses); strengthening multisectoral capacities (enlisting participation at state and local levels as well as from other sectors); training health professionals (and keeping them current in new techniques); research; and finally, monitoring and surveillance.

Various factors influence the activities in these intervention categories.

Agenda Setting

Certain issues, such as caloric balance and dietary fat, cholesterol, sodium, fiber, and calcium, have emerged prominently as a result of the interaction of several of the factors described earlier in this paper. Attention is also beginning to be refocused on micronutrients and protein. In each case the closer scrutiny is producing a deeper appreciation of the physiologic and metabolic complexities. Inevitably, the resulting insights influence the agenda by requiring a stratification of the goals and guidelines beneath the population level to accommodate group and individual variations. It is important for the society, however, to ensure that no single factor, whether it be economics, technology, public demand, or a quest for some undefinable standard of scientific purity, be allowed to overwhelm the process of crafting the U.S. national nutrition policy agenda.

Public Education and Information

Several things are clear about how information and education efforts are being affected. First, they are becoming more innovative. No longer are posters and pamphlets the only communication vehicle. They still have their place for health care professionals, but Madison Avenue and the news media are the first to capture the public's attention--they have become the front lines of the new public health. Second, and relatedly, many more sectors are involved in the educational process. Health care and nutrition professionals are finding new opportunities (and challenges) not just through the media but with employers, teachers, public personalities, and of course the food industry. Third, as the impact of both science and demographics is felt, greater and more specific attention will be directed to subgroups in the population (e.g., the elderly, pregnant women, and minorities).

Direct Services Delivery

At a minimum, each of these factors will compel more attention to the kind of food that is provided to people in public programs like congregate and home-delivered meals for the elderly, supplemental food and food vouchers for the poor, and school cafeterias. The commercial sector also plays a roles however. The major services are financed by people themselves in supermarkets, employee cafeterias, restaurants, and fast-food restaurants, and internal and external pressure is building for a greater involvement of these commercial providers in the promotion of nutrition principles. Public demand provides the greatest impetus, but guidance from the nutrition community is needed.

Reimbursement Policies

Reimbursement for a service through an insurance mechanism, whether public or private, can be a major stimulus to any public health intervention. Except for isolated examples related to therapeutic interventions in cases like diabetes, cardiac rehabilitation, and end-stage renal disease, nutrition services are largely uncovered. One of the reasons for this is that reimbursement policies largely focus on physicians, and in a procedure-oriented payment system like the one in the United States, physicians have shown no great interest in providing nutrition services. This may change (for some of the wrong reasons) with the advent of the technologies discussed earlier: body composition techniques, microcomputer bioassays, and automated dietary profiles. Regardless of whether it is driven by technology, the science base, or public demand, it is not unreasonable to expect some sort of nutrition services ultimately to be provided as part of a reimbursable preventive services package.

Tax Policies

Taxes can be used in a variety of ways to provide incentives to public objectives. Whether to encourage implementation by industry of safety procedures, to encourage development of employee health promotion programs, or to discourage consumption of tobacco, tax policies have proven to be potentially powerful influences. Currently, the applications of taxation to nutrition are largely limited to the provision of incentives for nutrition services at work sites, although some other Western countries have begun experimenting with the use of preferential excise taxes as a means of influencing choices of more healthful food products.

Health Protection Regulation

Some of the greatest challenges in the field of public health are now in the regulatory arena and will remain there in the future. Issues related to how products are graded and labeled, to the safety and efficacy of new food products, to ways of assessing risk, to whether health claims are allowed in the entrepreneurial efforts to reach the hard-to-reach populations are all critical questions whose complexities are growing on a daily basis.

Strengthening Multisectoral Capacities

When contemplating interventions to change individual behavior, it is clear that federalization of the effort is neither effective nor appropriate. Leadership and support for these efforts must derive from a point as close as possible to that at which the individual can make his or her own personal decision. A major public health challenge will therefore be the need to strengthen the capacities of other sectors--state and local, business and labor, and education and media--to carry forward these efforts.

Implications and actions in training health professionals, research, and monitoring and surveillance should be obvious. As intervention approaches become more sophisticated, the training of health professionals in their use will be important. And research and monitoring are fundamental to charting, tracking, and refining the course of progress.

FUTURE DEVELOPMENTS IN NUTRITION AND HEALTH

Predicting the future is always hazardous in any event, because we tend to view it through essentially linear lenses, yet it inevitably unfolds exponentially to our great confusion. This review has touched some of the major elements of future developments. It is helpful, however, to focus on a few that suggest what we might be facing in the year 2000. We can take as an example what might be in store in the categories of the ICHNR research priorities given in Table 3.

- Instead of general patterns of nutrient requirements throughout the life cycle, we should focus more definitively on individual variations in those requirements.
- Instead of undertaking assays of nutrient interactions and bioavailability, we will be titrating ways to use those phenomena to affect disease outcomes.
- Our understanding of the relationships between nutrition and chronic diseases will begin to allow us to move more confidently in using diet as an intervention tool against those diseases, from approaches that are now oligodimensional in character to those of a more polydimensional nature--in effect, to begin to deploy a kind of matrix management to the use of dietary tools in chronic disease control.

- Our progress in this respect should be enhanced by a deeper understanding of the relationships between patterns of inheritance and patterns of behavior in predisposing individuals to disease outcomes.
- We should anticipate a time when nutrition education will not derive just from global homilies but rather from sophisticated and dynamic automated analyses of predispositions and preferences.

The results of these advances in the research base will have major implications for the kinds of objectives we will be setting in the twenty-first century.

- It is possible that after the year 2000 we will develop targets not for aggregate serum cholesterol levels but for some more precise index, perhaps a target ratio of nutrient intake:cellular receptor sites.
- It is possible that rather than deal crudely with the balance between caloric intake and exercise levels, we will target individual metabolic setpoints.
- It is even conceivable that we will target dietary accomplishment of central nervous system levels of certain neural peptides as measured by some over-the-counter metabolic probe.
- In the agricultural sciences, presumably we will be able to target even more powerfully the use of genetic engineering to enhance changes in crops and livestock.

In some version, all these are at least imaginable. Some are already unfolding. And the present offers our most compelling challenges. About 1,400 people die each day as a result of coronary heart disease; death rates from heart disease among blacks are about one-third higher than those among whites, and death rates from stroke are nearly double those among whites (NCHS, 1987); and twice as many black babies as white babies die (NCHS, 1987).

While we do not have all the answers to these problems, we do have some answers and important hints about others. Nutrition plays a role, and it is possibly quite a large role. It may be that the biggest gap we face today is not a knowledge gap but an application gap, at least application in an equitable fashion, for all members of society. The dictum premium non nocere, first do no harm, applies to inaction as well as to action. If W. Henry Sebrell were asked today to comment on the state of nutrition sciences, he might marvel at the scientific accomplishments but be more than a little chagrined at the sluggishness--relative to the potential--of society's ability to capture the clues available 35 years ago. He might suggest that as we ponder these new dimensions for nutrition and public health, we not ponder too long before we act.

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The National Cholesterol Education Program

DeWitt S. Goodman

The National Cholesterol Education Program is providing new impetus for a change in nutrition education for medical students and for physicians. This program, launched approximately 2 years ago by the National Heart, Lung, and Blood Institute, involves collaboration among more than two dozen private and public organizations that have grouped together to develop a coordinated attack on many fronts related to high blood cholesterol levels and high rates of coronary heart disease in this country.

The work of the National Cholesterol Education Program is being done by four panels, two of which have been working for some time. One of them--the Expert Panel on Detection, Education, and Treatment of High Blood Cholesterol in Adults--prepared a report that was officially endorsed and made public on October 5, 1987 (The Expert Panel, 1988). Since its release, this report has received a very large amount of publicity and has led to the launching of programs by a number of organizations. The authoring panel (also called the Adult Treatment Panel) consisted of 22 members and 7 ex-officio members with a wide range of expertise and experience and produced its report after almost 2 years of hard work.

This report will have an impact on nutrition education in medical schools and among physicians. It deals with the high risk or patient-based approach--not with the public health strategy, which is being dealt with by a different panel. This panel's charge was to identify individuals at high risk who will benefit from intensive medical intervention. The goals of the report are to establish criteria for identifying candidates for medical intervention, to recommend ways to detect these people, to establish goals for treatment, and to monitor the subjects.

The report deals with two basic questions: Who should be treated in a medical setting to lower cholesterol and how should they be treated? Therefore, the report first consists of sections on the classification of patients according to total cholesterol levels and then according to low density lipoprotein, or LDL, cholesterol levels. Following are sections on dietary treatment, which is described in considerable detail, and on drug treatment.

This report was developed with certain principles in mind. One was to develop a set of guidelines that were as simple as possible and consistent with current knowledge. Another was to provide enough specific detail to guide a physician in dealing with an individual patient, that is, to provide a detailed primer for physician practice in this area.

The report classifies people according to total cholesterol level: 200 mg/dl or less is called desirable blood cholesterol, 200 to 239 mg/dl is designated as borderline high-blood cholesterol, and 240 mg/dl and above is classified as high blood cholesterol. These 200-and 240-mg/dl levels were based somewhat arbitrarily on a very large body of quantitative epidemiologic data (e.g., the Multiple Risk Factor Intervention Trial, or MRFIT study), which provide an enormous data base showing that the increasing cholesterol levels throughout the U.S. population lead to increases in the risk of coronary hear disease. The cholesterol cutpoint that defines high blood cholesterol--240 mg/dl- -is believed to be a level at which the risk among people with different backgrounds is sufficiently high to warrant medical care.

The follow-up recommended for people with total cholesterol levels below 200 mg/dl is that they should be given information about coronary heart disease and reexamined within 5 years. Most people with borderline high levels--200 to 239 mg/dl--and, specifically, those who do not have definite coronary heart disease or other major coronary heart disease risk factors, should be given dietary and other risk factor information and reevaluated annually. People with high levels, and those with borderline high levels who do have definite coronary heart disease or two other major risk factors, should have lipoprotein analyses; further action should be based on LDL cholesterol levels.

The classification by total cholesterol levels thus identifies those patients who should undergo lipoprotein analysis. The focus of attention should then turn to LDL cholesterol levels, which serve as the key index for clinical decision making about whether or not someone needs treatment. LDL cholesterol is really the more primary etiologic risk factor associated with coronary disease, and programs to lower cholesterol are really aimed at lowering LDL cholesterol levels, which are classified as follows: desirable, if below 130 mg/dl; borderline-high-risk between 130 and 159 mg/dl; and high-risk at 160 mg/dl and above. The cutpoints of 130 and 160 mg/dl were chosen because they correspond roughly to the total cholesterol cutpoints of 200 and 240 mg/dl.

The report contains very specific algorithms and charts that a physician can follow in first encounters with a patient and then use in deciding what to do and how to proceed in the evaluation, and ultimately in treatment. For example, the recommendations for people with desirable LDL levels are the same as those for people with desirable total cholesterol, namely, that a cholesterol test should be repeated within 5 years. Those with high-risk LDL cholesterol levels and those with borderline-high-risk levels and other risk factors for coronary heart disease should have a full clinical evaluation and then should be brought into cholesterol-lowering therapy.

The report and its recommendations very strongly emphasize dietary therapy--the primary modality and the cornerstone of treatment for people with high blood cholesterol. This is not a trivial statement, because if these recommendations are followed, at least one-quarter of the adult U.S. population, which is at least 40 million people, will be brought into medical treatment to lower their cholesterol levels. This creates an enormous market of patients who need to have dietary treatment, and most physicians providing primary care do not know how to prescribe this. Therefore, this report was written to provide a great deal of information for physicians about dietary counseling. This is done first with regard to nutrients, then to foods, and then to food patterns; the information given should enable physicians to take the first step toward delivering dietary information and treatment to patients. There is an emphasis on the importance of interaction with registered dietitians and others who have more professional expertise. The report states that treatment should be aimed minimally at lowering cholesterol levels below those levels that brought a patient into therapy, and it contains detailed descriptions of diets. There is a Step-One Diet and a Step-Two Diet designed to progressively reduce intakes of saturated fatty acids and cholesterol and to keep total calories at a desirable level. These kinds of recommendations conform to those of the American Heart Association and other major organizations that have dealt with this topic before.

The report recommends that once patients are brought into dietary therapy, they should be followed carefully and their cholesterol remeasured at 4 to 6 weeks and at 3 months. Monitoring can initially be limited to total cholesterol, which is much simpler to measure. If the goal is achieved, then there should be confirmation that the LDL goal is achieved and the patient brought into long-term monitoring. If the goal is not achieved, then a registered dietitian should be consulted for more intensive dietary treatment of the patient, and the patient may be then counseled about the Step-Two Diet or alternatively be given a more intensive trial on the Step-One Diet. Ultimately and hopefully the patient will thus achieve the cholesterol goal. If the goal is not achieved, drug treatment should be considered.

In the final chapter of this report, drug treatment is discussed in considerable detail, again to provide a detailed educational primer to physicians. Cutpoints are provided for drug treatment, and there are goals for creating what is called a protective barrier against the inappropriate overuse of cholesterol-lowering drugs. There are extensive exhortations in this report about the use of drugs only in the most severely and substantially elevated cases that persevere despite dietary therapy, which is again emphasized. The various drugs available are discussed.

Since the report's formal endorsement in October 1987, substantial programs have been launched by the American Heart Association, the American College of Cardiology, nurses organizations, dietitians, and family practitioners. The American Medical Association has also endorsed the report and is beginning an educational program. We are very gratified that this tremendous momentum for change in medical practice has followed in the wake of this report. Once this degree of acceptance has taken hold, we will find that doctors will feel obliged to try to implement, to try to put into practice, these guidelines because it will be considered proper medical care. We hope that there will follow appropriate reimbursement and other incentives that would encourage this kind of practice. This should have an impact on the need for nutrition education of physicians.

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The International Dimension: Nutrition's Role in World Food and Population Concerns

Marian F. Zeitlin

The state of the art in international nutrition interventions improved dramatically in the 10-year period from 1977 to 1987. During this time most types of nutrition interventions improved in design as they went from being marginally or questionably effective to being demonstrably beneficial in improving either the nutritional status of vulnerable groups or the food consumption of the poor.

At the same time, the world hunger problem has steadily worsened, particularly in Africa, where the toll of combined deaths from starvation and the acquired immune deficiency syndrome (AIDS) by the end of this century could dwarf any disaster in recorded history. Moreover, history may view our excuses for not preventing these massive losses of human life as rather thin, given that we live less than 24 hours away by airplane from the victims and that the victims have done nothing to deserve their disentitlement to the world's resources.

The net transfer of resources from industrialized countries to developing countries, where the malnourished are concentrated, has decreased gradually and systematically from a positive transfer of about $39.4 billion in 1980 to a negative transfer of minus $31 billion in 1985. Simultaneously, over this period, the rates of malnutrition in developing countries outside of South and East Asia have systematically worsened and are continuing to deteriorate (Cornia et al., 1987). Given this state of the world economy, nutrition programs in developing countries are, by definition, compensatory.

Closer to home, the level of funding that enables the United States to assist developing country governments to develop nutrition programs has decreased. This level is now in danger of dropping below a critical threshold. Below this critical threshold it would be impossible to sustain the recent U.S. contribution to the growth of effective nutrition intervention models or the commitment of developing country leadership to the implementation and expansion of these models.

In 1977, I was working at the Harvard Institute for International Development (HIID) as associate director of a project for the U.S. Agency for International Development (AID) to distill the state of the world's knowledge about nutrition programming into a set of guidebooks. Directed by James Austin of the Harvard Business School, this project produced the HIID Nutrition Intervention in Developing Countries series (Austin and Zeitlin, 1981) and seven other studies (see below). In this paper I review how we have progressed since that time and discuss future directions.

THE DIMENSIONS OF THE PROBLEM

Depending on the indicator used to define malnutrition, the manner in which the indicator is calculated, and the age groups on which the calculation is based, estimates of rates of malnutrition in poor countries vary anywhere from 5 to 90%. Global estimates of the numbers of malnourished individuals vary from about 0.5 billion to 1.5 billion (Food and Agricultural Organization of the United Nations [FAO], 1985; Grigg, 1985; World Bank, 1986) and are expected to double by the middle of the next century. One of the difficulties in rallying assistance for malnutrition has been the lack of common standards for reporting malnutrition rates. According to any of these counts, the numbers of malnourished people in all developing regions of the world are increasing with population growth. In most countries of Africa, Latin America, West Asia, and the Middle East, both the proportions and the absolute numbers of malnourished people are rising. In South and East Asia, the proportions of the malnourished are declining, but not fast enough to reduce the absolute numbers (see McGuire, in press, for a detailed review of negative effects attributable to malnutrition).

The world hunger problem can be divided into the problem of periodic famine or food insufficiency and the problem of continual chronic undernutrition, particularly of young children and their mothers. Insufficient global food production or food production capacity are not the causes of either of these conditions, nor should food production be limiting in the future (Mellor and Johnston, 1987). According to projections, the size of the world's population will level off by the year 2100 at about 10.4 billion, according to the World Bank, or between upper and lower limits of 8 and 15 billion, according to the United Nations (Demeny, 1985). Most experts believe that at the global level food production per se can technologically keep pace with increasing population growth over this time period and beyond, given that we are entering a new era of agrobiotechnology with almost limitless possibilities for innovation and for expanding production on marginal lands (Lipton, 1985). In many poor countries, however, decreases in per capita subsistence food production, together with rapid population growth, are the immediate causes of hunger.

In the simplest terms, the cause of world hunger is the maldistribution of food, the resources needed to produce or acquire food, and the knowledge and motivation to utilize food adequately. Distribution problems exist at two levels: the macrolevel of politics and trade and the microlevel of public and private programs and household and community uses of food resources.

MACROLEVEL PRECONDITIONS FOR IMPROVEMENT IN INTERNATIONAL NUTRITION

The preconditions for nutritional improvement in developing countries lie outside of the realm of nutrition per se. Nevertheless, since the future outcome of nutritional programs depends on these conditions, it is important to note them in summary form. Several recent books on food and development policy detail the complex contributions of economic and historic forces to the present situation and its potential solutions (Biswas and Pinstrup-Andersen, 1987; Cornia et al., 1987; Eicher and Staatz, 1984; Gittinger et al., 1987; Timmer et al., 1983). The following list of preconditions for improving the nutrition of people in developing countries is taken primarily from Adjustment with a Human Face, edited by Giovanni Andrea Cornia, Richard Jolly, and Frances Stewart (Cornia et al., 1987):

- A steady expansion of world economic output.
- Restoration of long-term positive net resource flows from industrialized to developing countries, including increased direct aid or assistance to developing countries.
- Debt restructuring and/or relief for developing countries.
- Elimination of agricultural policies in industrialized countries that protect domestic producers by exporting below-market-price, subsidized surplus food grains and other agricultural products.
- Reduction of protectionist trade barriers in industrialized countries against importing primary commodities and manufactures from developing countries.
- Support of poor countries' real earnings for commodity exports during severe slumps in the international market.
- Reduction in real international interest rates.
- Improvement of international credit systems set up to provide loans as a buffer to hardship conditions in poor countries.
- Adoption of indicators that would rapidly reflect worsening conditions and would trigger eligibility for buffer loans.
- Economic adjustment policies in developing countries that combine adjustment with the restoration of economic growth and with the protection of the welfare of vulnerable groups.

THE ROLE OF NUTRITION AS A DISCIPLINE

The role of nutrition as a discipline is primarily to improve microlevel distribution, although nutritionists also educate policymakers concerning the severity of nutrition problems, their social consequences, and the need for social and political change. Many who enter the field with the vague hope that studying international nutrition will transform them into macrolevel political activists end up disillusioned. For example, a colored South African student who was completing her master's degree program at the Tufts University School of Nutrition realized with growing anger that research and proposed nutrition interventions did not attack the root causes of hunger. For those who remain in the field, the hope endures that good work at the micro level not only will alleviate suffering and lead to the development of basic services and skills but will have a leavening effect on macro level policymakers.

THE DANGERS OF CUTBACKS

The role that nutrition as a discipline will play in world food and population problems depends, to no small degree, on the commitment of the U.S. government to continuing to fund international nutrition activities. To date, the United States has provided most of the funding for technical assistance to international nutrition activities, with the result that most of the state-of-the-art knowledge in international nutrition interventions is U.S. based.

It can be argued that there is a critical threshold level of funding above which U.S. technical assistance to nutrition is needed to keep up the momentum in contributing toward development. So long as this momentum continues to grow and programs continue to expand, political leaders and professionals in developing countries gain increasing awareness of nutritional concerns and continue to advance their skills in nutritional problem solving. Above this level there is the hope of advancing the potential of the brightest and best of the next generation's leaders. There is hope of nurturing effective demand for a basic needs, or "human face," approach to development and, therefore, some hope of counterbalancing the negative macro-level flow of economic resources over which we have no control. By strengthening human resources and the commitment to ending hunger, we hope to empower developing country leadership to develop creative solutions to the economic dilemmas.

Over the past 20 years, Martin Forman provided the vision and political astuteness that made it possible for AID's Office of Nutrition to operate above this threshold level. The Office of Nutrition and nutritionists in AID's regional bureaus, in the Bureau for Program and Policy Coordination, and in other affiliated offices in the U.S. government succeeded in expanding the research, knowledge, and programmatic skills base of an international network of concerned leaders and scientists. By the early 1980s, however, this network and its funding base ceased expanding and started to contract.

If funding for nutrition continues to decrease, efforts to improve nutrition in developing countries might melt away or appear increasingly to be skillfully crafted window dressings for aspects of U.S. foreign policy over which nutritionists have no control. U.S. foreign policy, as it relates to food, appears to be increasingly driven by agricultural growers' lobbies. These lobbies are committed to withholding access from developing country farmers to the technology that they need to increase their production, out of fear that increases in developing country production would compete with U.S. agricultural exports.

The recently passed Bumpers Amendment (Section 209 of the 1986 Supplemental Appropriations Bill) prohibits both technical and financial assistance by AID to projects that may be intended to develop the exports of recipient countries, when those exports could cause substantial injury to U.S. producers. Invocation of this amendment by growers' lobbies has made it difficult for professionals in AID to even speak of providing aid to increase production without substituting terms such as consumption or self-sufficiency for the word production.

In Zaire, I evaluated a very small, exquisitely crafted U.S. Title II food program that sells milk powder to finance three excellent projects. One project provides for the upgrading of equipment and for increasing the capacity of a local commercial firm that produces a low-cost weaning food. The second project supports the distribution of subsidized cornmeal to Kinshasa's poorest markets by a local development group that uses profits from the sale of corn under Title II to provide a producer's subsidy to farmers who grow corn locally. The third project supplies cornmeal under Title II to a primary health care umbrella agency for use in the promotion and sale of the subsidized and targeted corn-soy weaning food in the city's poorest maternal and child health (MCH) centers. One of this project's overall goals is to create demand for corn instead of cassavah (on which diets are based in Kinshasa) as a nutritionally superior staple.

This project, which is run by the private and voluntary Organization for Rehabilitation and Training (ORT), is like a tiny jeweled watch, a tribute to the most clever and dedicated nutrition strategists and program developers. The watch tells time in a country half the size of the United States that is ravaged by poverty and social disruption. In Kinshasa, no detective work is required to understand that U.S. agricultural food surpluses function as one of the means by which the U.S. government props up and ensures the loyalty of an excessively corrupt regime; that this regime puts about 1% of its gross national product back into agricultural development when in some years it puts more than 30% into Swiss bank accounts for the private use of its president; and furthermore, that this regime is accused of operating through the village chieftain systems in rural areas to extort crops from farmers at such low prices that rural subsistence is barely possible.

Minute in size, the ORT Title II project is one of perhaps 50 or more illuminating models of creative ways in which U.S. technical assistance can work in developing countries to craft solutions to hunger. With funding cuts, the creative spark will die out of these projects. New projects will not be developed, and those that continue to exist will retract to a lackluster, token, maintenance status.

FUNDING AND PERSONNEL CUTS

Table 1 shows recent trends in funding for nutrition programs within AID. Both the absolute and percent

TABLE 1 Child Survival Interventions, All Accounts

	Millions of $ (% of total)				
	FY 85	FY 86	FY 87	FY 88	FY 89
Oral rehydration therapy	38.1 (29)	32.8 (21)	40.1 (23)	33.4 (21)	31.8 (21)
Immunization	30.3 (23)	48.0 (31)	57.5 (33)	56.3 (36)	53.0 (35)
Nutrition	25.8 (20)	20.7 (13)	24.4 (14)	13.9 (9)	16.8 (11)
Child spacing	6.3 (5)	7.2 (5)	7.8 (5)	8.3 (5)	10.2 (7)
Other child survival	30.0 (23)	47.1 (30)	43.7 (25)	44.6 (28)	41.2 (27)
Total attributions	130.5 (100)	155.9 (100)	173.5 (100)	156.5 (99)	152.9 (101)

NOTE: Includes attributions from Child Survival, Health, Sahel and ESF accounts, as well as small amounts from Population and ARDN accounts, where applicable. Attributions for fiscal year 1985 (FY 85) and FY 86 are derived from yearly reports from field HPN officers on program content and are gathered by means of a Health and Child Survival Reporting Schedule. Attributions for FY 87 to FY 89 are obtained from a combination of data from Child Survival Reporting Questionnaires and from FY 89 ABS (Table IV) submissions. FY 87 to FY 89 attributions will change as programs evolve and when reporting is completed at the end of each year.
SOURCE: AID.

Amounts allocated to nutrition have been decreasing. Since the early 1980s, the professional staff of the office of nutrition has decreased. The Africa Bureau of AID, which attend to the region where nutrition problems are most severe and volatile, does not have a directly hired nutritionist. The excellent regional nutrition adviser who was recently based with REDSO in Abidjan, Ivory Coast, and who generated nutrition programs throughout West and Central Africa, has left to serve elsewhere and has not been replaced.

Reasons for these cuts have to do with the pendulum swings of trends in technical assistance, the ever present desire for simple technological solutions, and the fact that nutrition as a field tends to lose ground in economically hard times. Since the World Health Organization (WHO) Conference on Primary Health Care at Alma-Ata in the Soviet Union (WHO, 1978), where sufficient food was defined as the first and most basic human need, the focus in assistance to mothers and children has shifted to child survival. The twin engines of immunization and ORT have produced rapid reductions in infant mortality but have overshadowed nutrition.

FUTURE TRENDS VERSUS IMMEDIATE DANGERS

The United Nations International Children's Emergency Fund (UNICEF), which has been a trend setter in providing assistance to vulnerable groups, may now be on the point of shifting back from the highly technological to a more holistic approach. The term, adjustment with a human face, which is also the title of a new book from UNICEF (Cornia et al., 1987), refers to the incorporation of a basic needs approach into adjustment, with a strong focus on strengthening the informal economic sector through participatory community-level interventions, including nutrition programs. Moreover, as certain child survival program goals are achieved, there should be more room for nutrition. The EPI immunization program has targets of immunizing 80% of children in 70% of the countries served by the beginning of the 1990s. As immunization programs approach these targets, there should be more room in the child survival agenda for nutrition and more emphasis on quality of life, in addition to survival.

The physiological effects of malnutrition on the immune system are proven and cannot be argued away (Chandra and Newberne, 1977). Malnourished children, who are protected from dying of dehydration by ORT and from measles by immunization, have a greater than average risk of succumbing to malnutrition or to other illnesses for which no vaccines are available (Mosley, 1986).

Nutrition programs may also be recognized as an effective medium for dealing with the troublesome issue of neglect or underinvestment in the care of specific children, which appears to be increasing along with social disorganization in developing countries (Bulterys and Davis, 1987). Malnutrition is the most sensitive available screening measure for detecting underinvestiment. Short of providing major material and psychological support to families practicing benign neglect of their infants, nutritional growth monitoring probably is the most useful programmatic action that can be taken to combat this problem. Growth monitoring provides potentially ambivalent caretakers with continuing social support and makes them publicly accountable for the growth and health of their children.

In the meantime, while awaiting a swing of the pendulum, we could lose not only our positive momentum but also the efficient program designs and other achievements that have been built up over the past years. Institutional memory is only as strong as the people who staff the institutions and keep up the files, records, and commitment to the continuity of professional excellence. Without sufficient professional staff, evaluations in a closet down the hall are just as lost to the programming process as if they had never been conducted. The accumulated wisdom from years of effort could disappear. There has been speculation in the Office of Nutrition that the Japanese might forge forward with technical assistance in nutrition if the United States gives up this line of endeavor. Yet, any other country or agency that took over the work the United States has been trying to achieve would probably have to reinvent the wheel.

ACHIEVEMENTS AND PREDICTIONS

The nutrition planning process has matured through AID-sponsored experimentation in more than a dozen countries. Although nutrition activities overall are diminishing from the lack of support, the nutrition planning movement exerted global influence in sensitizing governments to incorporate nutritional goals into their national plans. When nutrition planners remain active, nutrition planning has become pragmatic and goal oriented and, hence, increasingly effective (Berg, 1987). There is a sense that we have gone, in terms of the book Megatrends (Naisbitt, 1982), from using "high-tech" models for nutrition planning to using "high-touch" skilled human applications for planning and programming.

In the future, we can expect to see the following:

- Changing standards for assessing nutritional status in childhood, adjusting for the fact that normal breastfed infants do not grow according to the National Center for Health Statistics (NCHS) standards (Stuff et al., 1987) and that growth in height depends on the amount of animal protein in the diet.
- Increasing emphasis on maternal nutrition during pregnancy and lactation, on anemia, and on adequate child care.
- More efficient rapid appraisal methods for all types of nutritional needs assessments and program evaluations.
- Widespread use of nutritional surveillance indicators to sensitize policymakers to changing nutritional conditions and the linking of surveillance to growth monitoring.
- More effective operational research methods for program design.
- Compensatory nutrition plans linked to economic adjustment strategies and, in general, to the global economy.

- Increasing the movement of nutritional service delivery of all kinds out of government and into private, nongovernmental organizations and for-profit sectors, particularly in Africa.

TYPES OF INTERVENTIONS

The following summaries of intervention types outline the progress that has been achieved over the past 10 years and anticipated future directions, should funding be adequate. In general, the "high-touch" responses of extending and perfecting the applications of existing technologies will predominate.

Agriculture

Progress. In 1977 it began to be realized that increased agricultural production of food does not automatically lead to improved nutrition, and it was being emphasized that assistance to agriculture affects nutrition primarily through price, employment, and income effects (Goldman and Overholdt, 1981). Over the next 10 years the negative effects that agricultural projects sometimes have on women and on the nutrition of marginal populations were identified (Jiggins, 1986) and strategies for incorporating nutritional goals into agricultural projects and for attaching compensatory nutrition programs to agricultural assistance programs were elaborated (FAO, 1983). This period also saw the application of grass roots operational research to agriculture in the form of farming systems research (Caldwell, 1987), which, while labor intensive, provided a reliable method for incorporating concerns for nutrition and other basic needs into the design of agricultural technology packages.

Future trends. The "green gene" agrobiotechnological revolution is here, but the ways in which the first waves of the green revolution have failed to make technology beneficial to the poor are well documented (Pinstrup-Andersen and Hazell, 1987). Ignorance of how to increase the productivity of small farmers on marginal lands or of the benefits to national economic development by focusing on small farmers is no longer an excuse for not doing so (Mellor and Johnston, 1987; Messer, 1987).

Health

Progress. In 1977 the definitive case was made for integrating nutrition with health and family planning (Austin et al., 1981a.b). Since then there has been a revolution in health care services delivery introduced by primary health care. The definition of the role of nutritional status has been narrowed; this has been accompanied by nutrition education and counseling and by the distribution of food and specific nutrients in special cases. It has also been learned that the nutritional component of primary health care and primary health care itself can be attached to family planning, agriculture, or other infrastructures, so long as referrals to health care services can be arranged. There are increasingly sensitive growth charts (Pielemeier et al., 1987) and effective regional growth monitoring programs in a few countries.

Future trends. The efficiencies of self-financing models of primary health care service delivery, linked with other integrated services, should improve over time, when resources are not absolutely limiting. Local nongovernmental organizations, such as the Bangladesh Rural Advancement Committee, may increasingly assume a management role in large-scale grass roots development initiatives in which primary health care, weaning foods, and growth monitoring models will gel into forms that are adapted to socially, culturally, politically, and geographically diverse conditions. Communications research also can be applied to make the educational and promotional components of growth monitoring more effective.

Subsidies

Progress. Ten years ago the nutritional benefits of food price subsidies to the poor had just begun to be documented (Rogers et al., 1981). These benefits are now well known. There has been progress in targeting subsidies in a variety of ways: by subsidizing the types and qualities of foods eaten primarily by poor, by locating outlets for subsidies in areas with the lowest incomes, and by providing subsidized food or food coupons at health care centers to mothers and children who are at the greatest nutritional risk.

Future trends. Effective targeting will become increasingly important during periods of economic adjustment, so that cuts in government expenditures for food subsidies may have less of an impact on the poor and so that compensatory subsidies can be established on low budgets. A global-level food stamp program administered by an international agency may be on the horizon (Reutlinger, in press). The future should also see increasingly creative and effective combinations of providing subsidies with nutrition education, as in a pilot oil and rice subsidy scheme in seven poor villages in the Philippines (Garcia and Pinstrup-Andersen, 1987), and with other program activities in nutrition, health, and agriculture, as in the ORT Title II project in Zaire or in the PAN food coupon program in Colombia (Berg, 1987). In that program, food coupons were distributed through health centers to families with pregnant or nursing women or children under age 5 in the poorest geographic areas. Thus, the program simultaneously increased food consumption and participation in preventive health care services.

Nutrition Education

Progress. Nutrition education has experienced a great metamorphosis over the past 10 years. On the one hand, it has emerged from the domain of home economists, extension agents, and MCH public health nurses to become the new field of nutrition communications, behavioral change, and social marketing (Manoff, 1985). On the other hand, it has spawned subject-specific offspring in the form of weaning foods projects, growth-monitoring activities, breastfeeding promotion, and a forthcoming maternal nutrition project, which apply communications and methods of behavioral change to specific topics. More than any other type of nutrition intervention, nutrition education has become multidisciplinary and has allied itself with the applied social sciences. Moreover, it has grown from an activity that is believed to have little impact and that receives only token funding (Zeitlin, 1983) to an area in which significant investments are budgeted. For example, there is a $15 million project in nutrition communications and social marketing starting in AID's Office of Nutrition.

Future Trends. To the extent that funds permit, support will be made available in selected countries to achieve across-the-board changes in the dietary habits of vulnerable groups through social marketing in nutrition. Alliances with prestigious medical authorities to enlist food processors and manufacturers in developing countries to produce and market healthful foods will be a key to the success of these efforts, as it has been in the industrialized countries.

Formulated Weaning Foods

Progress. Ten years ago there was a stalemate on the use of food processing technology to develop successful low-cost weaning foods (Heimendinger et al., 1981). Over 100 such projects had been tried with very moderate success (Orr, 1977). While failures of these Products to reach the poor were blamed on price, the role of marketing and product image had been largely ignored. Today, there is evidence that such products can be successful if they are manufactured and/or marketed by the private sector, as in the case of CEREVAP, the weaning food produced by the VAP biscuit company in Kinshasa, Zarie, with assistance from the ORT Title II project.

Future trends. As the world's population becomes more urban and as urban mothers in developing countries continue to support their families by working in manufacturing and other jobs that keep them away from home, the use of processed infant foods will increase. Technical assistance is needed to ensure the nutrient adequacy of processed infant foods manufactured by the private sector in developing countries, since it tends to be more profitable for manufacturers to produce and market nutritionally inferior products.

Supplementary Feeding

Progress. More has been written about the lack of impact of large-scale feeding programs than has been written about their success in combating malnutrition, apart from their role in famine relief and in supporting refugees (Anderson et al., 1981). A municipal-level evaluation of the Philippines National Nutrition Program by Abt Associates (Kerpelman et al., 1982) found, for example, that the longer and the more intensively the municipality had received Title II foods in the targeted MCH feeding program, the higher the rate of second-and third-degree malnutrition, as measured by the community weighing exercise Project Timbang. Since children had to be second-or third-degree malnourished to qualify for the program, this finding was not surprising, nor was it encouraging. On the other hand, as evidenced by the Tamil Nadu (India) Nutrition Program (Berg, 1987) and the Zaire ORT MCH component, supplementary food distribution can be a valuable resource if it is embedded in a carefully designed and closely monitored integrated program. Historically, the availability of supplementary foods for mothers and children has served as an incentive for expanding MCH services in many countries.

Future trends. With the withdrawal of the Catholic Relief Services from Africa, the old-style programs in which food distribution was a major end in itself may be phased out. They may be replaced by the more strategic use of food in programs in which distribution is highly targeted and/or in which the food serves multiple goals with respect to behavioral change and complementary development activities.

Food Fortification and the Distribution of Micronutrients

Progress. The biggest innovation in micronutrient interventions has been in the breaking off of vitamin A distribution as a separate intervention type. Food fortification proved its value 10 years ago (Austin et al., 1981a,b) and was shown to be extremely dependent on the political will of the government in power. The strength of fortification, of which the greatest success remains the fortification of salt with iodide, is that it is largely invisible to consumers. This lack of visibility also is its weakness, in that fortification programs do not readily develop a local political constituency and are therefore overly dependent on the benevolence and consistent long-term planning of the central government. Countries such as Burma, for example, have seen goiter eradicated in one era, only to reemerge in another when the government decontrolled the sale of salt.

Future trends. All the evidence is in place for iron distribution to take on an importance equal to that now accorded to vitamin A. The scientific evidence implicating anemia in poor labor productivity (Basta et al., 1979) and reduced cognitive performance in children (Pollitt et al., 1981; Soemantri et al., 1985) is beyond dispute. Iron supplementation has proved that it can ameliorate these effects. Iron is therefore a known technical fix that is easier to promote than ORT and that is waiting for investments in operational research and social marketing.

CONCLUSIONS

There is currently a lack of fit in the United States between the increased knowledge and skills in international nutrition and the decreased funds available to implement programs. At the same time, economic conditions and the rates of malnutrition and hunger in most developing countries are steadily worsening. We are experiencing an advocacy and leadership vacuum in international nutrition and can only hope that the urgency of this situation will inspire new leaders and new advocates to step forward and speak in a language that politicians and the public can understand. Professionals and academics know what is happening in developing countries, yet their voices are muffled and they lack the forms of communication that would make the rising death tolls vivid and compelling, even to ourselves.

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III

ACADEMIA AND THE NUTRITION SCIENCES

Recent Trends and Future Directions

Malden C. Nesheim

A biochemist, a human geneticist, a food scientist, an epidemiologist, a physician/endocrinologist, a human biologist, a public health physician, and a sociologist have discussed aspects of the future of nutritional sciences in this volume. Perhaps it is not surprising, then, that educational institutions are in some confusion as to what to do about nutrition, a field that does not seem to have a neat and tidy academic niche. In this paper I discuss some observations relating to the challenges in nutrition that face educational institutions and raise issues for discussion.

Since the great age of discovery of essential dietary factors has been left behind, one could argue that the nutritional sciences have reached a high point in their history, particularly in the United States.

The number of individuals in this country who consider themselves to be professionally associated with the field approaches more than 70,000. The memberships of the major professional societies in the United States with a primary interest in nutrition are given in Table 1. The

TABLE 1 Major Professional Nutrition Societies in the United States

Society	Founded	Current Membership
American Dietetic Association	1917	56,300
American Public Health Association Food and Nutrition Section	1917	1,085
American Institute of Nutrition	1928	2,400
American Board of Nutrition	1948	400
American College of Nutrition	1959	980
American Society for Clinical Nutrition	1960	600
Society for Nutrition Education	1968	3,700
American Society for Parenteral and Enteral Nutrition	1975	4,450
Institute of Food Technologists, Nutrition Division	1975	1,600
American Association of Cereal Chemists, Nutrition Division	1981	300
Total		71,815

largest group, with more than 56,000 members is the American Dietetic Association (ADA), an association made up primarily of nutrition practitioners. Other individuals associated with various aspects of nutrition research or nutrition and medicine number in the many of thousands, and there have been six major nutrition societies founded in the United States since 1959. The growth of the ADA has been especially striking, with very rapid growth since about 1970 (Figure 1).

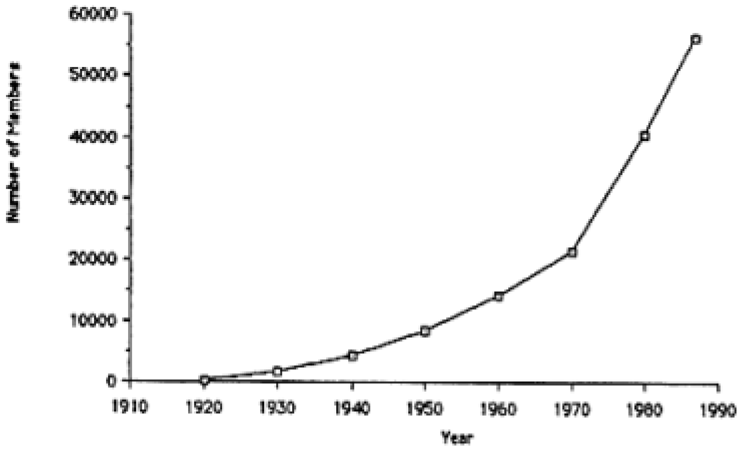

Figure 1 Membership of the American Dietetic Association, 1917 to Present.

There has also been a major increase in the number of nutrition science-related journals published both in the United States and worldwide. The number of titles in print began to grow significantly in about 1940, and this growth appears to have accelerated since 1970 (Figure 2). Journals published outside the United States seem to have increased at a greater rate than those published in the United States.

This increase seems to have closely paralleled the rise in funding for nutrition research (Nesheim, 1986). Prior to 1950, the principal support for human nutrition research was through federal formula funding to state agricultural experimental stations and through industry.

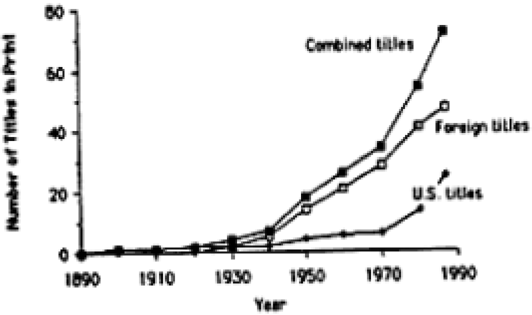

Figure 2 Major Nutrition-related Journals, U.S. and Foreign Titles in Print, 1890 to Present. SOURCE: Compiled from information in Ulrich's International Periodicals Directory (1987-1988).

The Nutrition Foundation played an important role from 1942 to 1963, providing about $6 million in grants for nutrition research over that period. The National Institutes of Health (NIH) has now become the major source of support, with over $200 million in extramural research related to nutrition. The U.S. Department of Agriculture (USDA) has over $50 million of expenditures in human nutrition research, although these funds are expended largely in support of five major human nutrition research centers. These centers represent a major commitment by the federal government to human nutrition research. The National Cancer Institute (NCI) has recently announced plans to open an intramural nutrition research laboratory to support research relative to diet, nutrition, and cancer.

All of these activities--the growth in the number of scientists and practitioners, the level of research funding, and the development of major government research centers--seem to indicate that nutrition science is a growing and robust component of the U.S. scientific community.

The growth of the nutrition sciences has also been accompanied by major changes that have affected U.S. educational institutions. Until about 1960, the principal focus of nutrition research was on the discovery, isolation, and identification of functions of the dietary essentials that are recognized today. It was an extremely exciting period and was clearly the domain of biochemists and physiologists. The practitioners of the nutrition sciences were primarily in the field of home economics, where the emphasis and application of nutrition principals were on the home and family.

Today, the research agenda is very different from that of 30 years ago. Nutrition scientists study aspects of metabolic regulation by modern techniques of molecular and cell biology. They are concerned with chronic diseases such as heart disease and cancer, and there are new and rather sophisticated applications of nutrition principles in aspects of clinical medicine. Also, individuals involved in intervention strategies often are concerned with a variety of population-based interventions. The organization of society has made the traditional, family-based approach to nutrition interventions less effective. Thus, in view of the many institutional changes in the field, it is not surprising that we are in a time of uncertainty for nutrition programs at many U.S. universities.

Over the years, there has been a waxing and waning of the contributions of various universities to the field of nutrition. Many early researchers traced their lineage to the laboratory of Osborne and Mendel at Yale and that of McCollum at Johns Hopkins. Strong and large programs in nutrition existed for many years at Harvard and the Massachusetts Institute of Technology, and it is fair to say that the nature of those institutions' commitment to nutrition has changed a great deal over the past several years.

Much of the institutional difficulties associated with nutrition today involve the nature of research and where it is done. For example, much of the research on nutrition and cancer, or nutrition and heart disease--which has dominated much of our research in the past several years--began in medical schools or in units outside of the traditional nutrition science organizations at universities. Thus, there are universities in which individuals or small laboratories are scattered throughout the institution and in which many research programs significantly related to nutrition have no institutional connection to units identified with the field. This problem is at the core of the institutional crises that have developed in U.S. universities in terms of nutrition organizations.

Perhaps a good illustration of where nutritionists work today can be obtained from examining the sources of papers published in the Journal of Nutrition and the American Journal of Clinical Nutrition (AJCN). The data in Table 2 show that in 1986, for the AJCN, most of the papers came from investigators based in medical schools, with a much smaller number coming from traditional nutrition departments. Many came from private or governmental research laboratories and from a large number of other academic centers. Similarly, for the Journal of Nutrition in 1986 (Table 3), researchers based in medical schools represented a major group of contributors, although the more traditional nutrition groups contributed more to this journal than to AJCN. There are papers in both journals from a broad range of

TABLE 2 Origin of Papers Published in the American Journal of Clinical Nutrition, Vols. 43 and 44, 1986

Origin of Papers	No. of Papers
Medical schools or hospitals	92
Medical schools and other units (university departments of nutrition, biochemistry, other)	44
Government or private research laboratories	27
University departments of nutrition, food science, or food and nutrition	25
Schools of public health	13
University departments of biochemistry, biophysics, or biomedical sciences	9
Other	5

TABLE 3 Origin of Papers Published in the Journal of Nutrition, Vol. 116, 1986

Origin of Papers	No. of Papers
University departments of nutrition, food science, or food and nutrition	76
Medical schools or hospitals	50
Animal science and veterinary medicine	35
Government or private research laboratories	31
University departments of biochemistry, biophysics, biomedical sciences, and agricultural biochemistry	22
Medical schools and other units (university departments of nutrition, biochemistry, other)	19
Schools of public health	2
Other	5

organizational entities. The concentration of medical school-based papers is of interest in view of the general lack of identity of nutrition units in many medical schools. Nutrition scientists publish in many other journals; however, the two journals discussed above, which are clearly identified as nutrition journals, probably reflect publications of individuals who wish their work to be clearly identified as nutrition related.

It is precisely the lack of focus, definition, and visibility of nutrition research and teaching programs in universities today that led to the development of the Pew National Nutrition Program. This program, funded by the Pew Memorial Trust of Philadelphia, has attempted to help a limited number of institutions develop new strategies for their nutrition programs over the next few years, in light of the modern agenda of the field.

When the program was announced in 1986, institutions interested in being considered for an institutional grant of up to $1 million were asked to submit a letter of intent outlining the ideas they wished to develop. Over 70 institutions in the United States responded. The distribution of these letters of intent was very interesting and provides a useful profile of the distribution of nutrition programs in universities throughout the United States. Some data relative to the letters of intent are given in Table 4.

TABLE 4 Nature of Applications to the Pew National Nutrition Program

Academic Unit of Principal Investigator	No. of Institutions
Medicine	29
Combined medicine and other unit(s)	11
Public health	5
Human ecology or home economics	11
Agriculture	12
Other	2
Total	70

Forty of the applications were submitted by principal investigators based in medical schools. Of those 40, 11 were submitted jointly, that is, by one principal investigator in a medical school and a second principal investigator associated with another organization on campus, most commonly a department of nutrition based in a college of agriculture or home economics (eight applications) or a school of public health or allied health (three applications). Of the medical schools that applied, 23 submitted applications for programs based essentially entirely within the school of medicine. The remaining 17 were collaborative programs between the school of medicine and many other units within the institution, including those related to allied health, agriculture, nursing, dentistry, pharmacy, home economics (human ecology), and even the liberal arts.

Five applications whose principal investigators were within schools of public health were received. The programs proposed in all but one of those applications were collaborative efforts with the school of medicine; and in two cases, several other departments ranging from nursing, dentistry, pharmacology, arts and sciences, and education were also involved.

Eleven of the letters of intent were submitted by schools or colleges of home economics or human ecology. Of these, 10 proposed a collaboration with a large number of other units within the institution. There were 12 applications whose principal investigators were based in a college of agriculture and associated with a variety of departments such as animal science, poultry science, food science, nutritional science, or agricultural chemistry. All of the agriculture-based applications proposed collaborations with multiple departments, ranging, it appeared, across the university. Two of the applications came from university units that did not fall in any of these categories: one was based within a particular department, and the other was a multidepartmental collaboration.

Although the original announcement of the Pew National Nutrition Program may have encouraged this multidepartmental approach, it was clear that the applicants were responding to the complex organizational arrangements in which individuals contributing to and interested in nutrition find themselves. Almost every proposal outlined a coordination mechanism that would be developed to bring together individuals interested in nutrition, but almost none of the proposals involved substantial institutional reorganization. In many cases, multiple groups with previous concerns for nutrition were present on the same campus, presumably competing for institutional resources that were allocated to support the subject.

The advisory committee for the Pew National Nutrition Program was somewhat disappointed by the institutional responses, and it is clear that the incentive that would be required to stimulate major organizational changes within institutions is far greater than the funds that were available through the Pew program. Five institutions were identified whose proposals were considered to be innovative and exciting, and the Pew program intends to work with these institutions over the next 5 years as they attempt to develop aspects of their nutrition programs that will accomplish the objectives of the Pew grants. In response to the general disappointment with the applications, however, some of the funds originally allocated to the program by the Pew Memorial Trust are being redirected into fellowship programs intended to develop skills and leadership in individuals within the nutrition community, as opposed to attempting to promote institutional change.

One could respond to the above discussion of the institutional organization of nutrition with the following question: "What difference does it make if the research in nutrition sciences is now scattered throughout institutions and if the focus and identity of nutrition as a subject is becoming lost?" This may be a desirable evolution of subject matter within universities, and there are a number of other areas that have lost identity over the years. As long as the particular research problems important to the field as a whole are being considered with sufficient expertise, perhaps there is no need for strong institutional identities and organizations for the subject within colleges and universities.

In contrast to many other fields that have gone in this direction, however, there are some unique factors affecting the field of nutrition that are important for universities to face. Several thousand individuals who are majoring in some aspect of nutrition are graduating from U.S. colleges and universities every year. They are becoming the grass roots nutrition practitioners throughout the United States. In U.S. land-grant colleges, there exists a national network of nutrition educators associated with the cooperative extension system in the United States. This represents one of the principal resources for nutrition education of the public at large. The dissociation of the units or departments that carry out this undergraduate training and nutrition education from the major researchers and research themes now occupying the field represents a long-term problem for the nutritional sciences that should be addressed at the institutional level.

Although researchers in human nutrition more often seem to be associated with medical schools, no strong organizational units associated with nutrition have appeared in many medical schools. Perhaps this is why it has been so difficult to increase the attention given to the teaching of nutrition in medical schools (National Research Council, 1985).

Some universities have been coming to grips with this problem and have been making changes in institutional arrangements or in faculty expertise that reflect the changing research agenda of the field. Progress has been rather slow, however, and institutions need to ensure that undergraduates are in contact with the subject matter most important and relevant to nutrition practice today. Care must be taken that professional organizations--which have been so concerned with developing the professionalism that would ensure a niche for practitioners in the field within the health system--do not unintentionally create barriers for institutions that make it difficult to respond to changes that are occurring within the field of nutrition.

I have no prescription that can be universally applied for the organization of nutrition in academic institutions. However, universities whose resources in nutrition are scattered throughout several areas of the institution are missing an opportunity to do many interesting and exciting things. Because of the breadth and depth of the subject matter currently making up nutrition, substantial resources are required that are managed in such a way that research, teaching, and public education can be dealt with logically and in concert. This is a challenge that those in the field of nutrition must meet if they are to provide the traditional association between high-quality research, training of graduate students, appropriate undergraduate instruction, and professional education of future nutrition practitioners.

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Critical Issues in Nutrition Sciences at the University Level

John A. Milner

Approximately 250 administrative units throughout the United States offer educational opportunities in nutrition. Many of these programs are part of a comprehensive university, and thus have as their primary mission the creation, perpetuation, expansion, and transmission of nutrition knowledge. However, these administrative units vary widely in their organizational programs, services, challenges, and opportunities.

Academic excellence in nutrition requires the effective coordination of teaching, research, and public service, not only for the development of future leaders in the nutrition sciences but also for the acquisition of knowledge aimed at improvement of the quality of life. It is recognized that inappropriate nutrition is a primary factor in unattained genetic potential, reduced productivity, and increased susceptibility to disease. Public recognition of the importance of nutrition to public health has led to an unprecedented interest in this discipline by scientists, legislators, health professionals, and consumers. Our ability to capitalize on this increased recognition will surely determine the fate of nutrition as a science. For nutritionists to continue to make contributions to improving the quality of life, several critical issues must be addressed. Each of these is briefly discussed below. Recognition of these issues offers exciting challenges and opportunities for those actively involved in this discipline. Likewise, exciting possibilities exist for universities that are willing to assume a leadership role.

IMAGE AND IDENTITY

Science is the systematized knowledge obtained from observations, examination, and experimentation performed to determine the nature or principles of specific processes. Thus, nutrition science is one that examines the sum of the biological processes that occur prior to and following the intake of food as they relate to growth, development, and the maintenance of health. Therefore, nutrition is not a pure science but draws extensively on root disciplines. The application of advances made within these root disciplines has been at least partially responsible for the awareness of the science of nutrition. This coupling with root disciplines, however, has also been at least partially responsible for the image and identity problems faced by those involved in nutrition. Nutritionists are invariably not easily pigeonholed into neat compartments within the hierarchical system that occurs on many university campuses. For nutritionists to make significant advances, they must interact not only with other nutritionists but also with individuals within root disciplines. This reliance on other disciplines can lead to nutritionists asking: "Where should I reside and what is my primary focus?" The problem of identity faced by nutritionists is by no means unique to this area, but it is probably magnified by the expectations imposed on them by the general population. Furthermore, at least part of the image problem possibly comes from the inability of nutritionists to sell or market nutrition, at least under most circumstances. For nutritionists to truly make progress, they must be the first to communicate to the public the impact that nutrition can, and does, have on health and the quality of life. Too often, when nutritionists address issues, they are placed on the defensive rather than the offensive.

PERSONNEL NEEDS

To ensure that the next generation of nutrition scientists includes creative minds, recruitment must take place at both the undergraduate and the graduate levels. It is surprising that a degree in nutrition sciences is not touted as an appropriate undergraduate program for entry into any of the health-related professional schools. Since nutrition can have an impact on the ultimate outcome of patient care, greater emphasis on nutrition as an undergraduate program appears to be appropriate.

Nutritionists must continue to focus on critical issues using state-of-the-art technologies. By continuing to be at the forefront of nutrition and the associated root discipline, the profession can be competitive in attracting quality undergraduate and graduate students. This continuation is not only critical for addressing issues of immediate concern but also for the development of future leaders in nutrition.

INTERDISCIPLINARY APPROACH

Strong linkages with various administrative units on a university campus are essential for meeting the mission and goals of a strong nutrition program. By highlighting critical issues faced by consumers, nutrition programs within a university can serve as a focal point for a coordinated campaign.

The responsibility for initiating, developing, and administering educational programs in nutrition is traditionally delegated to departments or other academic units within or across colleges. At the University of Illinois, an interdepartmental and intercollege graduate program in nutritional sciences, the Division of Nutritional Sciences, has been established. At present, 42 faculty are joined together through a common allegiance to the science of nutrition, but they reside within a home department in one of six colleges on the campus. The objective is to join forces with other units throughout the university to focus on nutrition issues, assist in the education of future leaders in nutrition, and address issues in nutrition through interdisciplinary research. By allowing faculty and students to remain closely aligned to a nutrition sciences interdisciplinary program, it should prevent unnecessary duplication of efforts in the nutrition sciences and allow for the maximum use of resources. While such interdisciplinary and multidisciplinary programs are often touted as having clear advantages, their creation is the exception rather than the general rule in most universities. This reluctance to develop such administrative units possibly reflects the inability of university administrations to recognize nutrition as an integrated science and to deal with administrative units other than departments that are committed to the mission and goals of an individual college.

It must be recognized that research serves as the cornerstone of the science of nutrition, which plays an essential role in medical practice, disease prevention, public health education, and the use of agricultural products. By virtue of the groups that can be influenced by nutrition research, an interdisciplinary approach appears to be extremely logical. Because of its complexity, nutrition research requires sophisticated designs and analytic capabilities that, again, are often best addressed in an interdisciplinary and multidisciplinary environment. In the future, nutrition objectives will surely require scientists to use extensive interdisciplinary approaches.

Figure 1 depicts the potential partnerships that can be developed between a nutrition sciences program and the various educational units that typically exist in a

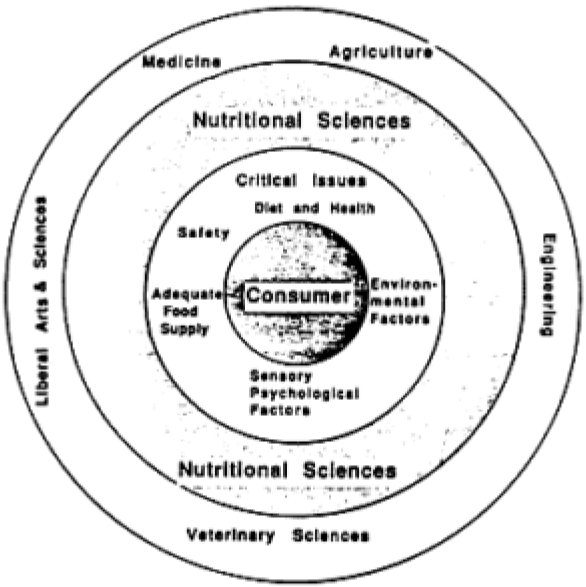

Figure 1 Relationship between nutrition sciences and other administrative units typically found in a comprehensive university in meeting consumer needs.

comprehensive university in order to address common concerns. It is the belief of many that making nutrition a campus-wide program, rather than limiting its scope to a single college, enhances the opportunities available to nutritionists and reduces possible image and identity problems. By focusing on the science of nutrition and not necessarily emphasizing the application of this knowledge, interdisciplinary programs are less likely to engage in turf battles with departments. An environment in which all participants in the program win must be established for an interdisciplinary nutrition program to survive. Faculty and students with commitments to either human or animal nutrition can work side by side on ventures of common interest.

By focusing attention on consumers, a variety of academic units can benefit from an interdisciplinary approach to nutrition (Figure 1). Many factors are known to influence the dietary habits of individuals. While diet and health are clearly involved, other considerations such as adequate food supply, sensory and psychological factors, and safety and environmental concerns may also regulate dietary habits.

We all recognize that money is needed for the conduct of research and that these costs are increasing at an unbelievable rate. Historically, research in agricultural production, food science, and nutrition has been rewarding and cost-effective. Although various studies have shown that there are higher returns following investment in research and development, the food and agriculture research and development system typically funds research at levels lower than those of virtually all other industries. The lower level of support may reflect the less well defined benefits of nutrition research. By capitalizing on the social and psychological factors regulating food intake and capitalizing on nutrition as a key factor in the quality of life, we may be able to enhance the present resources for nutrition research.

STRONG ACADEMIC INTERRELATIONSHIPS

Until recently, many nutritionists were only able to explain the metabolic derangement associated with inappropriate nutrient intake. However, dramatic advances in biotechnology promise to afford nutrition scientists the means of seeking the underlying mechanisms by which nutritional factors modulate growth and resistance to disease. Extensive evidence shows that inappropriate nutrition often leads to dramatic changes in specific cellular proteins and is therefore a primary factor in determining the genetic potential of an organism. To facilitate excellence in nutrition science programs, a strong educational and research bond with units offering expertise in cellular and molecular biology must be established and fostered.

The current public attention on health maintenance has stimulated interest in both diet and exercise. Mounting evidence supports a synergism between both of these factors in health maintenance. At least some dietary recommendations appear to be designed to overcome the adverse effects of a sedentary life-style. Although dietary manipulations will likely never compensate totally for inactivity, better understanding of the dynamic relationship between these factors is needed before general and widespread recommendations can be made to the public. Thus, again, a strong tie with kinesiology or related units must be developed and fostered.

Unfortunately, some of the underlying factors that control food preference are still not understood. It is evident that food selection is regulated by a variety of stimuli that are related to the individual's psychological, economical, sociocultural, and physiologic state, as well as to the chemical, physical, and sensory factors of the food to be consumed. Greater understanding of the complex process of food selection will come from the effective blending of expertise in the social, psychological, biological, and chemical sciences. With the demands on the nation's and world's food resources that are now occurring, and that will likely be magnified in the future, it is imperative that we join forces to enhance our understanding of food selection.

Since nutrition has both applied and fundamental components, nutritionists must continue to develop strong ties with the health professional community. The recognized association between inappropriate nutrition and health maintenance serves to emphasize the importance of fostering this linkage.

SUMMARY AND RECOMMENDATIONS

The modern-day nutritionist is facing many exciting opportunities and challenges, and this paper describes many of the challenges and opportunities that exist at the University of Illinois. Nevertheless, similar opportunities and challenges are available in many, if not most, universities where nutrition science is taught. Nutritionists must take advantage of the opportunities and address the challenges for continued progress to be made in the discipline. With the increased awareness of nutrition as a major contributor to health, the time to act is now.

Nutrition in Medicine: What Is Its Place?

George A. Bray

The threads of nutrition in medicine go back to the classic clinical studies of Lind in which oranges and lemons were found to prevent scurvy (Stewart and Guthrie, 1953). At nearly the same time, Lavoisier and de la Place (1780) and Crawford (1979) introduced the study of metabolism and showed that combustion by a candle and metabolism in the body produced similar amounts of heat. When Graham Lusk, one of the pioneers in nutritional science, wrote the first edition of The Elements of the Science of Nutrition in 1906 (Lusk, 1906), more than half of the book was devoted to the concepts of the energy metabolism and a smaller part was devoted to some of the endocrine glands. These important ideas about the way in which the body handles the major components of the diet are still a central theme in the nutrition education of the physician.

During the first half of the twentieth century, a second theme originating in the work of Lind was picked up to led to the identification, isolation, and synthesis of vitamins (Goldberger et al., Hopkins, 1912; 1926; Rickes et al., 1948; and Szent-Gyorgi, 1928). Thiamin and riboflavin led the way, followed by the other water-soluble vitamins and the fat-soluble vitamins. In 1948, vitamin B_{12}, cyanocobalamin, was the last of the vitamins to be identified and accepted. With the closure of the field active identification and isolation of the major vitamins, many people thought that nutritional problems had come to an end and that the scientific basis for nutrition could be taught to physicians through courses in biochemistry and physiology. Scientific and clinical developments in the last quarter century, however, have shown that there are still many unsolved nutritional problems with important clinical implications that need to be included in the curriculum.

Malnutrition, which is so prevalent in many underdeveloped and rapidly developing countries, came into prominence in the United States in the 1960s. The political arena was soon alive with examination of a subject as gripping as "hunger." As one indication of this political visibility, Senator E.G. Hollings published a book in 1970 entitled The Case against Hunger: A Demand for a National Policy (Hollings, 1970). To quote, "One of the nation's most appalling tragedies is the plight of millions of Americans for whom hunger is an every day fact of life" (Hollings, 1970). During much of the decade that followed, the U.S. Senate Select Committee on Nutrition and Human Needs, and more recently the U.S. Senate Subcommittee on Nutrition, have focused on the extent of malnutrition in the United States. One outgrowth of the political and public concern has been the increased activity in nutritional surveillance of the American people, as witnessed by the National Health and Nutrition Examination Survey (NHANES), which has now completed three major surveys and is beginning a survey of select segments of the population in which malnutrition may be more prevalent. The Ten State Survey from the Center for Disease Control (U.S. Department of Health, Education, and Welfare, 1972) was a second evidence of the heightened public concern with documenting and then eradicating the pockets of malnutrition that might exist.

As the search for malnutrition in this country increased, politicians gradually came to the conclusion that the major U.S. nutritional problems were associated with overnutrition and such illnesses as coronary artery disease, obesity, diabetes, hypertension, and dental disease rather than undernutrition (Bray, 1979). As a result of this concern, the U.S. Senate Select Committee on Nutrition and Human Needs (1977) published Dietary Goals for the United States. Concern about the desirability of national dietary goals was expressed from many quarters, including professional groups. Whatever the value of such goals, however, the scientific basis on which the relationship between dietary factors and disease rests comes from nutritional investigations undertaken by scientists and physicians.

The growing interest in the relation of nutrition to disease has posed a challenge to those interested in nutritional education in medicine. It has made it necessary for physicians in training to have a broader understanding of the human diet and its relation to the diseases that they treat. Following the publication of Dietary Goal for the United States, the U.S. Government released the Dietary Guidelines for Americans (U.S. Department of Health, Education, and Welfare, 1979). A second scientific review of the same data led to substantiation of the dietary guidelines in a new edition. The American Society for Clinical Nutrition (1979) has published a careful assessment of the data relating to diet and disease. More recently, the National Research Council's Committee on Diet and Health and Surgeon General of the U.S. Public Health Service developed reports on nutrition (DHHS, 1988; NRC, 1989). Any program of nutrition education for physicians must deal with the kinds of information on which these recommendations to the public are based.

A final element that impinges on the training of physicians, in both the undergraduate and the graduate years, is the rapid expansion of techniques for feeding patients through both parenteral and enteral routes. Although blood transfusions were well established by World War II, the use of other intravenous fluids was limited to volume expanders and isotonic solutions. During the past quarter century, the development of improved catheters, the ability to place such catheters in the major veins, and the potential for long-term maintenance of energy and nutritional needs have added a new dimension to the importance of nutrition education and clinical care for physicians. In the years ahead, the use of parenteral nutrition for a growing list of chronic problems will make understanding of nutritional principles important for all physicians.

Medicine must deal with this explosion of nutritional information in three different areas:

- It must provide knowledge of normal nutrition and the relation of abnormal nutrition to diseases of deficiency or surfeit.
- It must develop understanding of the relation of nutrients in the diet to the growing number of drugs that are used.

- It must prepare physicians to understand the nutritional problems associated with chronic parenteral and enteral feeding.

NUTRITIONAL IN UNDERGRADUATE MEDICAL EDUCATION

The need to teach physicians more about nutrition has been known for years. The American Medical Association (AMA) and the Nutrition Foundation sponsored a 1962 conference on the teaching of nutrition in medical schools, after an AMA survey found that "medical education and medical practice have not kept abreast of the tremendous advances in nutritional knowledge" and "there is inadequate recognition, support, and attention given to this subject in medical schools."

The quality of the nutritional curriculum in medical schools was reevaluated 10 years later. The conference at which this reevaluation took place was designed to "formulate realistic practical guidelines for incorporation of nutrition education into medical training in concurrence with the physician's responsibility" for health care. Many participants at the 1972 conference felt that little progress had been made during the intervening 10 years and that the quality and quantity of nutrition education in medical curricula were in need of improvement (White et al., 1972).

A third survey was conducted in 1976 when a questionnaire on nutrition education was mailed to 124 medical schools by the AMA and 123 schools, including 9 new schools, responded. Thirty medical schools reported that they required courses in nutrition; this encompassed just over 25% of the medical students. Elective courses were offered by 82 medical schools. Only 16 schools offered clinical clerkships in clinical nutrition. Of the 30 medical schools reporting that they required courses in nutrition, 25 of them offered these courses during the basic science curriculum, and 7 had requirements for course work during the clinical portion of the curriculum. Of the 82 schools reporting elective nutrition courses for medical students, 22 offered nutrition courses during the clinical years, 39 offered them during the basic science years, and 31 offered them at any time during the 4-year curriculum. In summary, then, in 1976, 64 medical schools offered nutrition courses in the basic science years, 72 offered nutrition courses in the clinical years and 31 schools offered nutrition courses throughout the curriculum. Two medical schools did not designate required nutrition course placement. Ninety-seven percent of U.S. medical schools incorporate instruction in nutrition throughout the curriculum (U.S. Senate, Subcommittee on Nutrition, 1979) of nutrition education in medical schools (White and Geiger, 1980).

The issue was taken up again in 1979 by the Senate Subcommittee on Nutrition, which requested a report from the General Accounting Office on the state of nutrition education in medical schools (U.S. Senate, Subcommittee on Nutrition, 1979). Six of the 10 leading causes of death in the United States (heart disease, cancer, cerebrovascular diseases, diabetes, arteriosclerosis, and cirrhosis) have been linked to poor nutrition. Various nonfatal conditions have also been traced to poor nutrition; dental decay is one example. "Although nutrition is important in medicine, it is not taught adequately in many U.S. medical schools. As a result, many physicians may not know as much as they should know about how to make nutritional assessments or counsel patients about diet. Medical schools train physicians primarily to look for and treat nutrition-related diseases after they occur rather than preventing them through nutritional assessment and dietary counseling" (U.S. Senate, Subcommittee on Nutrition, 1979).

The situation has not changed in the past decade. This was made clear in a recent report on Nutrition Education in U.S. Medical schools by a Food and Nutrition Board Committee (National Research Council, Committee on Nutrition in Medical Education, 1985). In 1979, 24% of medical schools had a nutrition course identified as such; this value increased to only 27% in 1983. Similarly, the percentage of schools offering electives in nutrition rose from only 54% to 64% over the same interval. Much of the nutrition education offered was available in the first 2 years of school. An outline of a core curriculum for the nutrition education of a medical school undergraduate is shown in Table 1. Of 39 schools that provided reliable information, the average total number of hours required for nutrition education was 21. However, 20% of the schools taught fewer than 10 hours and only 10% taught more than 40 hours. The

TABLE 1 Elements of a Core Curriculum

- Energy balance
- Specific nutrients and dietary components
- Nutrition in the life cycle
- Nutritional assessment
- Protein-energy malnutrition
- Nutrition in disease prevention and treatment
- Diversity of dietary practices

percentage of schools teaching various topics was also surveyed. Energy balance, obesity, undernutrition, protein carbohydrate, lipid metabolism, and the major vitamins and minerals were taught in more than 80% of the schools. However, the relationship of nutrition to the immune system, renal disease, cancer, the central nervous system, and various phases of the life cycle was taught in less than 60% and in some cases as little as 30% of the medical schools (National Research Council, Committee on Nutrition in Medical Education, 1985).

While some nutrition appears to be taught in more than half of the medical schools, strengthening of the nutrition curriculum is necessary. As recommended in the Food and Nutrition Board's report on nutrition education, one reasonable and logical way to do this would be for each school to engage a physician as a focal point for nutrition education, mentioned above, to pull nutrition training together so that any weaknesses in the teaching of this subject could be identified. This key individual should be placed in an existing department of the medical school and should be a physician with a special interest and capability in nutrition who would be available for teaching and research.

POSTGRADUATE CLINICAL NUTRITION TRAINING

The slow rate at which nutrition education has expanded in the undergraduate medical curriculum is mirrored in the progress in postgraduate nutrition education. Nearly 10 years ago, reports from the University of Alabama (Weinsier et al., 1979) and from the New England Deaconess Hospital (Bistrian et al., 1974, 1976) in Boston pointed out the frequency of malnutrition in patients on medical and surgical services. The data from the New England Deaconess Hospital are summarized in Table 2. There were significant abnormalities in this group of patients. There was a deterioration in the nutritional status in 50% or more of the patients, depending on the criterion selected. Patients who satisfied the criteria for malnutrition on admission had a greater likelihood of a longer hospital stay and increased mortality compared with those without these criteria (Weinsier et al., 1979). The likelihood of malnutrition in that study increased with the length of hospitalization. Butterworth (1974), in a paper with the catchy title "The Skeleton in the Hospital Closet," pointed out that as many as three-fourths of the patients with normal nutritional status at the time of admission to the hospital were found to have an abnormal

TABLE 2 Prevalence of Hospital Malnutrition

	Prevalance (%)	
	Surgical	Medical
Criterion	Service	Service
Triceps skinfold	46	76
Arm muscle circumference	48	55
Albumin	--	44

SOURCE: Bistrian et al. (1974, 1976).

nutritional status by the end of their hospital stay. Hill et al. (1977) pointed out that among 105 surgical patients, abnormalities in nutritional status were as high as 50% among those who were still in the hospital more than 1 week following major surgery.

The realization that malnutrition could occur in a substantial number of patients in American hospitals and the development of techniques for delivering nutritional support to medical and surgical patients by enteral and parenteral methods led to the expansion of postgraduate training programs in clinical nutrition. Data from the University of Pennsylvania Hospital showed that the number of patients receiving nutritional support in 1979-1980 totaled 13,749 patient-days, a figure that nearly doubled to 23,245 patient-days by 1983-1984 (American Society for Clinical Nutrition, Committee on Education and Training, Subcommittee on Postdoctoral Training, 1986). In 1979 and 1980 the outpatient component of this nutrition program was less than 25%, while by 1983-1984 the outpatient component rose to nearly 50%. This increase in the number of outpatients has occurred in many other hospitals where nutrition support teams are available.

The distribution of training programs for clinical nutrition is shown in Table 3 (Heymsfield et al.,

TABLE 3 Clinical Nutrition Programs

Programs	Total No.
• Medical schools thought to offer nutrition training	91
• Had no nutrition program	18
• Had a nutrition program	72
• Major focus	40
• Minor focus	27
• In planning stage	5
• M.D.s trained from 1976 to 1981	470

SOURCE: Howard and Bigaduette (1983).

1985). More than 60 programs can be identified throughout the United States, but there is less than one program for every two medical schools. When it is realized that several of these programs are attached to the same medical school, it becomes clear that the opportunities for training in clinical nutrition and the distribution of expertise in this area is geographically inappropriate. Between 1976 and 1981, 470 physicians were trained in 67 programs in the United States (Howard and Bigaduette, 1983). Of these, 40 programs had nutrition as a major focus and 27 had nutrition as only a minor component.

To establish criteria for effective nutritional programs at the postgraduate medical school level, a conference on clinical nutrition was sponsored by the American Society for Clinical Nutrition in 1984 (American Society for Clinical Nutrition, Committee on Education and Training, Subcommittee on Postdoctoral Training, 1986). Programs in clinical nutrition can be identified in departments of medicine, surgery, and pediatrics; but the majority are in internal medicine. Funding support for these programs comes through a variety of mechanisms, including local and federal sources. In the most recent survey published in 1987 (Merritt et al., 1987), there appears to have been very little further growth in the number of clinical nutrition training programs available at medical schools at the postgraduate level. In 1983, 67 programs were identified compared with 69 programs in 1987. Thus, like nutrition education at the undergraduate level, growth in nutrition training at the postgraduate level has nearly stalled. That there is a need to improve the quality of nutritional education is made clear by a recent report from the Johns Hopkins Hospital (Roubenoff et al., 1987). One house staff team was evaluated before and after a brief training program in nutritional assessment. Initially, only 12.5% of the patients who were at nutritional risk were appropriately diagnosed by the house staff. Following the intensive training program in nutritional assessment, 100% of patients deemed to need nutritional services were identified and treatment was initiated. The distressing part of this report, however, was that in a major teaching hospital, recent medical school graduates identified less than 20% of those patients who were in need of nutritional therapy!

QUALITY ASSURANCE

Identifying clinical nutrition training programs is one thing, but ensuring that those who come out of those programs are well-trained is another. Beginning more than 40 years ago, the American Board of Nutrition started a testing procedure by which physicians and scientists claiming nutritional competence could be evaluated critically. The American Board of Nutrition provides an annual examination for individuals with medical or doctoral degrees who wish to take the examinations certifying them for human or clinical nutrition. With support from the American Society for Clinical Nutrition and the American Society of Parenteral and Enteral Nutrition, the quality of the examination procedure has steadily improved.

SUMMARY AND RECOMMENDATIONS

- Nutrition education should be an identifiable component of all undergraduate medical education. This can best be done by identifying a physician scientist in each medical school who is committed to teaching and research in clinical nutrition.
- Nutritional assessment should be an integral part of the course on the introduction to clinical medicine.
- The National Board of Medical Examiners should be encouraged to increase the number and quality of questions in nutrition as a procedure for ensuring that undergraduate education in nutrition is of sufficient quality.
- Postgraduate training programs for physicians interested in clinical nutrition should become more widely available to meet the geographic and educational needs of the entire nation.
- Hospital malnutrition should be reduced by 50% by the year 2000 by implementing clinical nutrition teams, including a physician, in every hospital that receives Medicare funds.

- Nutritional services should be identified in the International Classification of Diseases (9th and subsequent editions) and should be compensated for by federal and nonfederal health care providers.
- Third-party providers of health care should require that those physicians and other support personnel delivering nutritional services meet minimum standards of training and that this be certified by an examination process.

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Critical Issues in Nutrition Education and Training at the University Level

Barbara Hansen

The lack of nutrition knowledge and of nutrition content in curricula of the health professions has Read's and my combined files (Cardullo, 1982; Hoting and Littlefield, 1982; NRC, 1985). Nevertheless, despite this continuing identification of this problem, it continues. A recent study (Weinsier et al., 1986) indicated that 85% of senior medical students were dissatisfied with the quantity of their nutrition education, while 60% were dissatisfied with the quality. Yet, 59% believed that nutrition training was "very important" to their careers. Nevertheless, in our own medical school, only about 15% of medical students elect to take a specific nutrition course. This relatively low level of course election is comparable to the 3 to 6% of medical students who elected a nutrition course in the study by Weinsier et al. (1986). On our second campus, one with 9,000 undergraduates and 1,200 graduate students, I was unable to identify by title any course with nutrition as its focus.

To illustrate the unusual situation in which nutrition education is desired and believed in, but neither studied nor internalized, another study, which examined family practice resident nutrition knowledge, found that significant fundamental concepts were not understood (Dappen et al., 1986). Surprisingly, 56% of the physicians surveyed thought that polyunsaturated fats were less fattening than saturated fats. Furthermore, only 36% of the residents understood that 2 g of sodium was equivalent to 5 g of salt. Thus, even the most practical concepts have, in many cases, not been sufficiently absorbed and utilized (Dappen et al., 1986).

In a recently completed study of family medicine residents and faculty, completed by Sobal and his associates on our campus, residents and faculty were surveyed for their respective views of the relative importance of various nutritional topics and their desire to have additional information. This specific needs assessment showed some interesting differences in the areas in which further information was desired by each group (Sobal et al., 1988). Faculty, interestingly, sought more information on the relationship of nutrition to cardiovascular disease, osteoporosis, cancer, and the elderly. Residents, on the other hand, sought more information about the relationship of nutrition to obesity and weight control, pregnancy, diabetes, parenteral nutrition, and vitamins and minerals. Although not suggested by the investigators, one might suspect some interaction of personalized nutrition issues with those of the clinical setting. Self-perceptions of actual involvement in nutrition teaching of patients may differ from the adequacy of the knowledge base, and perhaps by discipline. For example, 98% of public health nurses indicated that they used nutritional brochures or pamphlets in the education of patients, and 100% stated they included nutrition activities in their maternal health and infant health services (Sabry et al., 1987). There is clearly no shortage of nutrition education materials available for the instruction of the health professions (Read et al., 1987), as George Bray so well indicated in this symposium.

H.L. Mencken, the "Bard of Baltimore," has commented that for every problem, there is a solution that is simple, neat--and wrong. I wonder whether our neat solution might be wrong. Although it has been suggested that the need is for standardized teaching and performance expectations in the area of nutrition, the above information suggests two additional routes to the enhancement of nutritional knowledge in health professionals. The first is to tailor at least a significant portion of the nutrition information to the personal perceived needs of the learner as related to his or her own health. The second appears to be an apparent need for sophisticated marketing techniques. Although health professionals seem to believe they need nutritional knowledge and verbally indicate they desire it, they are not yet voting with their feet. Perhaps sophisticated marketing techniques aimed at appealing to their personal desires for better understanding of the impact of nutrition on their own health could produce more active participation and involvement.

The American Dietetic Association, in its 1986 House of Delegates Meeting, approved a position statement on the importance of nutrition education to physicians. Aggressive marketing of courses in basic nutrition was mentioned (American Dietetic Association, 1986). Interestingly, the student participant in the 1984 Conference on Nutrition Teaching in Medical Schools also noted the need for marketing (Shulman, 1984).

Another approach might be through a requirement of active involvement in nutrition research projects. Clearly, the observation of effects of nutrition clinically and of nutrition intervention can be a convincing approach to the internalization of the information. I believe our problem is one of this internalization--like the first time I looked in an ophthalmoscope: I saw, but I didn't perceive. Perhaps it is this aspect of nutrition education which deserves further attention.

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The Role of Undergraduate Research Colleges in the Education of Future Nutrition Scientists

M.R.C. Greenwood and Patricia R. Johnson

Nutrition is an old and distinguished science. It has evolved over the past century, beginning with early discoveries that living organisms, including humans, obeyed the laws of thermodynamics. In the late 1800s, nutrition scientists demonstrated that energy metabolism in man was not fundamentally different from the process of heat production by the oxidation of conventional fuels. This initial series of observations formed the basis of nearly a century of scientific investigation, which continues today, as modern nutrition scientists continue to strive to understand how the regulation of gene expression and metabolism are influenced by nutrient status.

An early definition of nutrition and its role in the basis of food selection was offered in 1927 by a prominent nutrition scientist, Ruth Wheeler, then a member of the Vassar College faculty:

"The only wise basis for food selection is a thorough knowledge of nutrition: the value of various foods in terms of the nutrients they supply; the importance of each nutrient in nutrition of the body; the nutritive requirements of people of different ages and different conditions of health and activity" (American Red Cross, 1927).

This definition differs little from many that have been offered over the more than 60 years since then, and indeed, it could be found with little alteration on the pages of most currently used nutrition textbooks.

Nonetheless, as pointed out below by a modern nutrition scientist, the same questions may remain, but the approaches are rapidly changing the power and the exactness of our possible understanding of a new nutrition science.

The major undertaking for the future will be a study of the impact of the environment on precisely described living systems. The genome is shaped, molded, expressed or repressed by events occurring during "windows" of developmental opportunity. Among these, the influence of nutrients which are pieces of the environment incorporated into the substance of living cells must surely figure prominently. This is the province of modern nutrition science. The new nutrition will utilize biological understanding at the most profound level to direct man to that selection of nutrients which will optimize health, comfort and social function. This is very little different from previous definitions of nutrition science; the goals are the same but the tools and investigative approaches are now very much more powerful and exact than in the past (Jules Hirsch, The Rockefeller University, 1987).

To ensure that the next generation of nutrition scientists includes the best creative minds, in all of the subdisciplinary areas intrinsic to nutrition in the twenty-first century, nontraditional resources will need to be more carefully examined and encouraged. One of the best, and frequently less obvious, of these resources for nutrition scientists of the twenty-first century is the graduate pool from our nation's top research colleges.

THE DEFINITION OF "RESEARCH COLLEGE"

Research colleges include the finest of our undergraduate colleges, which have traditionally produced large numbers of the nation's subsequent science scholars and leading clinical investigators. In research colleges, faculty members in the biological sciences and their colleagues in related science and mathematics departments are training nearly one-half of the next generation of biological science scholars and physicians. These biological science faculty members have trained in the finest research universities in the world (Table 1), and most newly recruited faculty members have had several

TABLE 1 Doctoral Degree Origins of the 1985-1986 Science Faculty

Harvard	Wisconsin	University of California, Berkeley
Yale	Illinois	Michigan
MassachusettsInstitute of Technology	Princeton	Cornell
Stanford	Ohio State	Indiana
Purdue	Chicago	University of Washington
University ofCalifornia, Los Angeles	Massachusetts	Penn State
Cal Tech	Johns Hopkins	Michigan State
Penn	Brown	Minnesota
Colorado	Columbia	Duke
Iowa State	Oregon	Kansas
Lehigh	Rutgers State	Washington
Case Western	Dartmouth	Iowa
Rochester	North Carolina	Pittsburgh
Virginia	Arizona	Northwestern
Syracuse	Texas	

NOTE: There were a total of 1,385 doctoral degrees conferred by the indicated institutions. Each institution contributed at least eight doctoral degrees. The range was 68 (Harvard) to 8 (Texas).

to many years of postdoctoral experience prior to joining the faculty ranks. Although the rate of scientific publication for these scholars-teachers is less than that of their colleagues in major research universities, publication in the literature is a prominent feature in the careers of these scientists as well.

TRAINING FOR NEW NUTRITION SCIENTIST

Crafting an education for nutrition scholars of the twenty-first century is a challenge. While the Sputnik era presented the United States with an immediately recognized educational need, particularly in the chemistry, physics, and engineering arenas, at no other time in U.S. history has there been a greater need to have the best and brightest minds turned to understanding, unraveling, and interpreting the complexity of problems being approached by biological scientists. The field of nutrition science is one increasingly important emergent area that draws the attention of many modern biological scholars. On a weekly basis, new genes are being cloned, new insights into neural mechanisms are reported, chronic diseases are associated with new cofactors or modes of genetic regulation, and behavioral concomitant factors of disease are identified. Nutrition scientists are engaged in such investigations in significant numbers. In addition to the information being provided by the use of new technologies, their impact for individuals and for human societies and cultures is being hotly debated. It is both a time of feast for the scientific intellect and a time for profoundly probing the nature and meaning of human existence. Debate and study about the relationship of nutrients to disease and health figures prominently in the literature being written. The knowledge, tools, and technologies that now reside in the collective consciousness of biological scholars as we move into the next century hold serious implications for human society. Thus, our nation requires from our colleges not only technically sophisticated graduates who will continue to add to this knowledge base but also individuals trained to interpret this new knowledge for a citizenry that is generally scientifically illiterate, some of whom will become our legislators and policymakers, and all of whom will be called upon to voice their opinions and cast their votes on complex issues that are based on biotechnology or complex biobehavioral interactions.

The faculty in our research colleges is committed to the proposition that one critical approach to educating students for these challenges is to educate them to understand the interactive nature of the biological sciences. It is necessary to teach the necessity of drawing upon cognate fields and to imbue students with spirited curiosity and the confidence to address the hard questions. Perhaps most importantly in this age of scientific illiteracy and "math fear," undergraduate teachers must systematically and firmly dispel any lack of confidence in ability to master the hard sciences that students often have upon arrival at a college or university. To accomplish these ends, the infrastructure of the curriculum and departmental and collegial interactions must be such that, for example, students experience not only the individual pleasures and rigors of subdisciplinary study but also gain an appreciation of the overall intellectual network of ideas and the need for the constant communication among scholars that informs and shapes developing minds to be able to make creative leaps and connections. One of the great challenges of undergraduate science education, especially in the liberal arts setting, is to provide opportunity for detailed hands on state-of-the-art instrumental work, which is, by design, particular and subdisciplinarily specific, while at the same time encouraging students to keep minds open to ever-increasing opportunities for scholarship in emergent inter- and multidisciplinary fields. As nutrition becomes both more didactically specific and more multidisciplinary in its applications, the need to attract young scholars with vision and finely attuned skills at hypothesis testing will become ever more acute. The best of our research colleges have a special opportunity to provide this stimulation.

SOME DIFFERENCES IN EMPHASIS BETWEEN COLLEGES AND UNIVERSITIES

Our great universities place considerable emphasis on scientific specialization and productivity measured by a variety of standards such as publication rate, amount and duration of extramural funding, and national rankings. This atmosphere has certainly led to many superb accomplishments in nutrition science as well as in other subdisciplines of biological science, but the university model is not without its problems, particularly at the undergraduate level. In attempts to meet requirements for national and international success, departments may become insular, and individual investigators may feel that they do not have time to step outside their subdisciplinary area. Because of their size alone, university departments may not interact extensively with any but the most closely allied departments or with those with which they share equipment. In addition, the best and most experienced scholars are infrequently in extended contact with substantial numbers of undergraduate students.

In contrast, in the research colleges, departments are small, necessitating curricular and collegial interaction between science departments. While the need to produce recognized scholarship is also felt strongly at these institutions, the primary product for evaluation is the number of well-educated and inquisitive young scientists who are graduated. In these colleges, it is the mature scholars trained at the best research universities in the world who themselves serve at the bench with their students. They design the laboratory experimental work, they read and grade the papers and reports, they listen to the first (and subsequent) oral presentations attempted by students, and they make substantial contributions to the scientific literature with their own scholarly endeavors. This vital link in the scientific pipeline of the future must not only be preserved but it also must be strengthened.

THE PAST RECORD OF RESEARCH COLLEGES

Over the past several decades the research colleges, including Vassar College, have consistently contributed to maintenance of the scientific pipeline by proportionately outproducing the research universities in training science undergraduates. A 1951 Carnegie Foundation report examining the productivity of institutions whose graduates went on to obtain doctoral degrees in the sciences noted that small liberal arts colleges were prominently and disproportionately represented among the top 50 most productive institutions (Knapp and Goodrich, 1951). This early study concentrated primarily on the baccalaureate origin of males, but a more recent report confirmed that although the actual institutions from which women who subsequently go on to obtain doctorates differ from the male pattern, the small liberal arts colleges are most productive of female as well as male scientists (Tidball, 1986; Tidball and Kistiakowsky, 1976).

This argument is now detailed in the report entitled "Maintaining America's Scientific Productivity: The Necessity of the Liberal Arts Colleges" (Carrier and Davis-Van Atta, 1987). This study, released in March 1987, provides data from 49 colleges chosen because of their previous history of sending graduates for further professional scientific training. The study shows that these colleges, including Vassar, contribute over 40% of all baccalaureate degrees awarded in the basic sciences in this country. Even more impressive is the evidence that while the number of baccalaureate degrees in basic sciences produced by the research universities fell by 15% over the past decade, the number produced by these colleges has remained constant over the same period. Furthermore, the percentage of science graduates is greater in the research colleges that it is in the universities, and this percentage has remained constant for over a decade (Figure 1). In fact, the actual number of baccalaureate degrees may have increased since 1983.

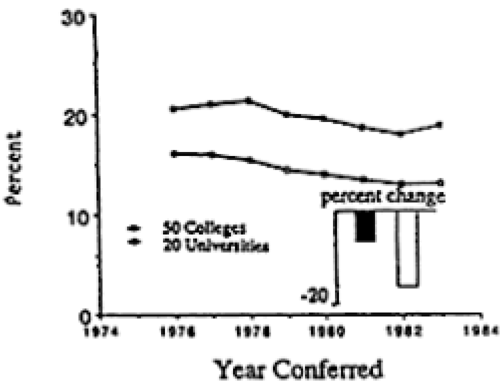

Figure 1 Percentage of baccalaureate degrees awarded to basic science majors. The overall percentage is highest in the colleges listed in Table 1 and has decreased less than that of the university group.
SOURCE: Data from Carrier and Davis-Van Atta (1987).

Of those students who graduate, a large proportion enter into postgraduate training. For example, of the students from the class of 1980 whose postgraduate fate was known, approximately 80% of biology majors and chemistry majors had entered professional training (primarily medical school) and nearly 50% of math majors had enrolled in postgraduate work (Figure 2). In addition, these graduates of the research colleges are prominently represented in measures of recognized scholarly contributions. For example, when the baccalaureate origins of members of the National Academy of Sciences were examined, 15 of the research colleges were represented in the top 25 institutions from which members obtained baccalaureate degrees. Furthermore, among the 1,000 most cited authors indicated in the I.S.I. Citation Index, again, the baccalaureate origins

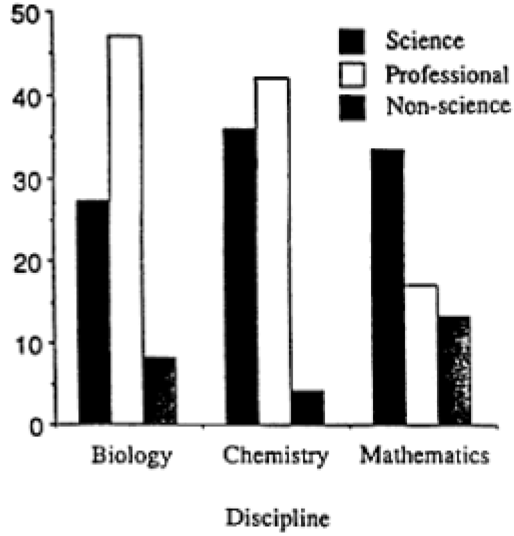

Figure 2 Patterns of graduate school attendance of the class of 1980 after 5-6 years. Nearly 80% of the biology and chemistry graduates, whose decisions were known, have entered graduate or professional schools. SOURCE: Data from Carrier and Davis-Van Atta (1987).

included 15 research colleges in the top 25 institutions and 5 among the top 10 institutions.

The future predictions of a continuing pool of new scientists from these institutions are also encouraging since, in these 49 research colleges, nearly 30% of entering freshmen intend to major in the sciences.

Furthermore, the representation of groups currently underpresented in science may be growing at these schools, and thus, the potential expansion of the overall pool may be possible in this setting. This current enrollment trend is in significant contrast to national trends at the highly selective top 20 research universities, where the percentage of freshmen intending to major in science is approximately 15% and is in stark contrast to overall national trends, for which the estimate is 5% (Figure 3). Thus, the major conclusion of

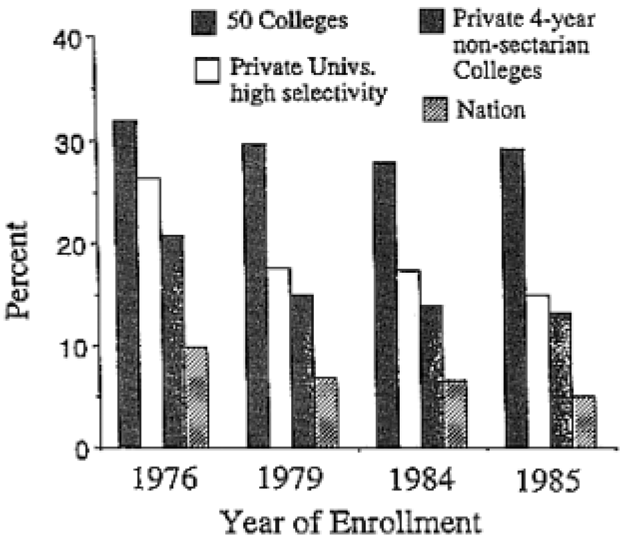

Figure 3 Freshmen intent to major in basic sciences is higher in the 50 college group than in any of the other comparison groups and is not declining significantly. SOURCE: Data from Carrier and Davis-Van Atta (1987).

the Oberlin College study (Carrier and Davis-Van Atta, 1987) is that the selective liberal arts colleges are an indispensable national resource for maintaining scientific manpower in the United States.

The success of these colleges in training fine scientists may lie at least partly in their historic traditions. In virtually all these colleges, classes are small and the faculty are dedicated to educating students in the process of science, rather than in its products alone. Thus, all those who major in the sciences have extensive laboratory experience. This tradition is particularly strong in the biological sciences, where most courses in the major include integral laboratories from the introductory to the senior level. In many of these colleges, upper-division courses feature project-oriented laboratories in which students first learn new basic methodologies, which they apply in the design, conduct, data analyses, and reporting of experimental projects.

In addition to course-related laboratory learning, the biological sciences curriculum frequently offers students the opportunity to earn credit in independent study with faculty members. When this is coupled with opportunities for summer research either at the home institution or at a university, considerable sophistication is evidenced. Thus, many biological science majors are able to engage in sustained experimental work that results in publishable contributions to the scientific literature. Indeed, nearly one-third of the publication emanating from these colleges are coauthored with undergraduate colleagues. Thus, for many undergraduates the opportunities provided in the research colleges are apparently important in maintaining and creating a sustained interest in science. This is a pool of talent that must be tapped with more frequency as we search to identify the next generation of nutrition scientists.

SUMMARY AND DIRECTIONS FOR THE FUTURE

The education of the nutrition scientists of the future requires the same basic education at the undergraduate level that is required of any prospective scientific scholar. There is considerable evidence that the nation's research colleges are an especially excellent source of such scientists. The new nutrition science will require that the best scientific minds be attracted into the field. The increasing need for scientists in many disciplines will be competing for an ever-shrinking traditional pool of potential scientists for all fields of science in the future (National Science Board Task Force, 1986). Thus, new mechanisms to expose students in these colleges to the excitement and opportunities in nutritionally related sciences must be found if we are to expect students to select careers in nutrition science.

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Commentary

Joan Gussow

I would like to begin this paper with an anecdote, since I believe in the value of example in communication. Last week a student of mine took his doctoral oral examination. His study looked at the beliefs and behaviors of professional nutritionists regarding the safety and nutritiousness of the food supply. He found that the nutritionists he interviewed--most of whom were involved to some extent in pubic education--generally believed that the U.S. food supply is nutritious but were somewhat less certain about its safety. They also believed that ordinary people might have a very hard time selecting safe and nutritious foods without knowing a great deal more than they do now; in other words, the public needed nutrition education.

The nutritionists themselves, however, turned out to be not very well informed about a number of consumer issues--food irradiation and aspartame, for example--that the public often wanted and perhaps needed to be educated about. In other words, these university-trained nutritionists felt that the food supply had reached such a level of complexity, and contained so many potentially unhealthy foods, that it was not at all easy for ordinary people to make the right food choices from it (or for practicing nutritionists to keep up with issues relevant to its safety and nutritiousness). Furthermore, these nutritionists believed that in the future the food supply would probably get worse, that is, would contain increasing numbers of unhealthy and questionably safe foods, but they felt that there wasn't very much they could do about this.

The dissertation was very carefully and objectively written, and as a good educator, its author concluded that everyone, including nutritionists, needed to become knowledgeable about the sources, the handling, and the ultimate quality of the food supply in order to make wise choices in the marketplace. One of the outside readers of the dissertation, however, an early childhood education specialist who chaired the oral exam, was obviously upset that the student had failed to sufficiently emphasize what the examiner took to be the obvious conclusion lurking in his results: that these nutritionists were caught in an ideological trap. They were, he pointed out, articulating the value of education, of individual knowledge, yet they could not adequately keep themselves informed about the changes in the food supply.

Obviously, this observer said, these nutritionists are aware that information is economically and politically driven; they are aware that powerful disinforming forces are acting in the domain they are concerned about, yet few of them had ever written a letter to a legislator about their supply concerns, and none of them has testified or taken other direct political action. They were suffering, he said, from a severe case of personalism, clinging to their faith that more knowledge alone can change things.

We nutrition educators have seen ourselves as a relatively powerless voice shouting into the wind of information that sells products, papers, magazines, and/or reputations--information that may or may not have consequences for eaters' nutritional status. Yet, these words of an observer outside the nutrition profession are a damning criticism of what it is nutrition educators think they are about. But to look at the food marketplace objectively is to be forced to acknowledge their truth. The politically and economically driven disinformation my colleague referred to comes, to begin with, from the food supply itself. Products with the life span of fruit flies (but whose ancestry is much less well studied) come and go from grocers' shelves; restaurants offer, on the one hand, spa cuisines for the already lean, while ordinarily hefty Americans are given the choice of full-fat toppings like bacon and cheese (or both) on already greasy hamburgers or are urged to partake of ham and cheese sandwiches on the once classy (and still greasy) croissant.

In 1987, 25 new dinners appeared in grocers' freezer cabinets each month. A total of 1,031 new products--a majority of them food products--came onto the market in the month of May alone. Hundreds of these food products, as one observer wrote recently, ". . . boast of being sugar-free, caffeine-free, low in cholesterol, low in salt, low in preservatives and additives, high in carbohydrates, high in fiber, nutrients, vitamins and minerals" (Gayle, 1987). Compound the confusion with products engineered to conform to the very latest laboratory findings on the possibly desirable composition of the food supply: edible oils, for example, first made high in polyunsaturates, then made high in monounsaturates, and finally made high in omega-3 fatty acids; fats and carbohydrates manipulated to be nonabsorbable; and other substances still referred to as "foods" whose strongest selling point is that they have no nutritional value at all but taste "wild."

Add to the confusion of commerce the confusion of science. Regular stories appear in the press, for example, reporting that prestigious researchers have decided fat is or is not implicated in breast cancer, or that less than one alcoholic beverage a week may increase a woman's risk of breast cancer although seven times as much may reduce a man's risk of heart disease. Readers must take with a grain of something other than salt the news that the dolphins dying on New Jersey shores have nothing to do with the safety of the fish caught in the waters off those same shores, or that the safety of the poultry supply has nothing to do with the pictures of someone's poultry floating in a soup of its own feces on the television program "60 Minutes." Put all this together and you have a recipe for a public that is truly dazed by food-related information that may or may not have health consequences.

As a missionary from one of the two cultures to the other, I assert that while we in education have, admittedly, not produced the science of teaching that our predecessors promised, we do know how to impart knowledge; and sometimes, under the right circumstances, we even know how to produce behavior change through education. I further assert that this general capacity can be applied to nutrition education, under the right circumstances. I am merely questioning here whether anything nutrition educators are supposed to do is likely to produce the right circumstances.

Having said that, I suggest that those who wish to know where nutrition education research is going should look at the American Dietetic Association's September 1987 journal supplement "The Leading Edge in Nutrition Education: Research Enhancing Practice." There is very poor funding for nutrition education research, and the profession has embarked on a desperate struggle to quantify in order to justify funding. Even though it is generally agreed that much of what we need to know requires qualitative methods--in-depth interviews, participant-observer approaches- -it is recognized that such studies do not get funded. There is beginning to be funding for community intervention studies, but since nutrition educators have had little to no opportunity to develop a track record in such projects, they are seldom even in the running to be project directors.

As for the education of nutrition educators, a document entitled "The Academic Preparation of the Nutrition Education Specialist" has been generated by a committee made up of representatives from the Society for Nutrition Education, the American Home Economics Association, the American Dietetic Association, and the Faculties of Graduate Programs in Public Health Nutrition. The document describes the competencies of those who consider themselves specialists in nutrition education (it is available from the Society for Nutrition Education, Oakland, California).

To learn who has been training such people, a questionnaire was sent out to the institutions who had helped generate the list of competencies. They were asked whether they, in fact, trained people who met these criteria. A rather wide range of programs were surveyed: nutrition and nutrition science, public health nutrition, foods and nutrition, home economics, animal science, and human development. The response was excellent, and 16 institutions said they provided such training.

Although professionals trained to mastery in the identified competencies would have both the scientific knowledge and the process skills needed to transmit nutrition knowledge to the public, in an educative environment, the listed knowledge and skills may not be sufficient, as I suggested earlier, to enable nutrition educators to operate effectively in the present disinformative milieu.

Therefore, I would like to suggest some of the other things that nutrition educators need to know and do if they are to have the remotest chance of being effective. This should by no means be looked upon as a complete list.

First, nutrition educators need to know much more than they do now about why people spontaneously change their eating habits when they are not subjecting themselves to intentional nutrition education. Mostly we study how effective we are with people who, in a sense, volunteer to get educated. We need to collect data that will allow us to understand how and why free-living individuals, floating in the tide of information and misinformation that floods their environment, start to eat better.

Second, nutrition educators must be trained to be politically as well as scientifically sophisticated. Recently, Barth Eide and I defined a nutrition educator as "one who helps people of whatever social, economic, political circumstance to meet their need for nutritious food," with the implication that at least part of the training of nutrition educators must teach them to seek out the real causes of poverty and hunger around the world and to act effectively against causes rather than ineffectually against consequences.

Third, nutrition educators need to be taught how to conceptualize, to make connections, and to understand the differences between facts and judgments. They must learn to be capable of dealing with ambiguities, to accept that for some issues there are no simple right answers but only choices that are often best made within a context wider than that commonly subsumed under the term nutrition. Such breadth of vision will make them vividly aware that all education is inevitably value-laden and cannot possibly be otherwise, because it is impossible to teach everything about a topic and decisions about what to leave in and what to leave out reflect the educators' values.

Should a nutrition lesson about a winter strawberry teach that it contains only 5 calories without teaching that 435 calories are expended flying it from California to New York? Should we consider as successful weight loss programs in which pounds are shed because clients are compliant, even though the world outside those programs demands noncompliance--the self-esteem and stubbornness to fight off the culture's blandishments to eat? Nutrition educators are always teaching more than they intend to, and they must be trained to become conscious of the broadest implications of what they do.

Finally, nutrition educators must learn to cope with scientists, and vice versa. I have said elsewhere that I wish we could get scientists to forcefully remind reporters of the modesty of their own results; but since that seems unlikely, I wish that, at a minimum, researchers would get in touch with a nutrition educator who is not tied to their particular vision of reality before they go public with their results and let that educator place their results in a context that will make sense to the average eater. Campbell pointed out in a recent paper that the unwarranted explicitness of dietary recommendations has helped create marketplace confusion (Campbell and O'Connor, 1988). The facts are not good enough to permit us to quibble honestly over 5 percentage points of fat calories or 5 grams of fiber. Nor will such distinctions matter to the eating public. The public needs to be told that nutritionists agree about the need for a lower fat and higher fiber diet containing an abundance of fruits, vegetables, and whole grains.

What are educators supposed to do about interviews like the one on the "MacNeil/Lehrer News Hour" in late 1987 in which a well-known scientist was quoted as saying that contaminated water from Silicon Valley wells was safer than broccoli, potatoes, or tomatoes. Unless such remarks are very carefully put into context, they are not helpful to those trying to teach people to eat more fruits and vegetables. Nutrition educators should not have to expend time and energy combatting misinterpretations or overgeneralizations that forethought could have avoided.

References

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