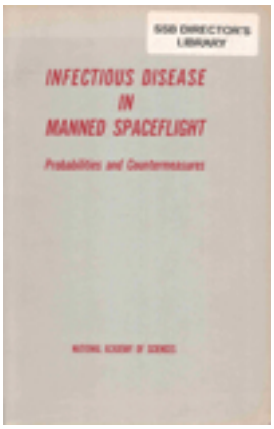

Infectious Disease in Manned Spaceflight: Probabilities and Countermeasures

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INFECTIOUS DISEASE IN MANNED SPACEFLIGHT

Probabilities and Countermeasures

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PREFACE

At the request of the Office of Advanced Research and Technology, National Aeronautics and Space Administration, the Space Science Board of the National Academy of Sciences convened a study to consider the problem of infectious disease on manned space missions and the effects of the space environment on man's resistance to disease.

The study was conducted at Woods Hole, Massachusetts, during the period June 30 to July 12, 1969, by the Panel on Microbiological Problems of Manned Space Flight under the chairmanship of John Spizizen. The six panel members were assisted by twelve consultants selected on the basis of their specialized knowledge of fields identified as possible areas of concern.

The contributions of all who participated in this study are gratefully acknowledged. The review of literature on infection in spaceflight (Appendix A) by Elliot Goldstein and the compilation and evaluation of microbiological studies on man in closed environmental systems (Appendix B) by Andrew J. Vargosko, Francis B. Gordon, and Judd R. Wilkins were of value as reference material during the study and in the preparation of this report. Chapter 6 draws heavily on a paper on cutaneous microbiology prepared by Gerbert Rebell of the University of Miami.

The Board acknowledges with appreciation the support of the National Aeronautics and Space Administration.

Roman Smoluchowski, *Chairman*
Division of Physical Sciences
National Research Council

CONTENTS

Chapter 1

SUMMARY AND RECOMMENDATIONS

The prevention and control of infectious diseases are key elements in the safety and success of manned spaceflights. Many of the special conditions characteristic of manned spaceflight are conducive to the development and spread of infection and, in the absence of satisfactory countermeasures, could pose a serious threat to the health of crew members and the successful completion of missions. That this is not idle speculation is borne out by the frequency and potential severity of illnesses in manned spaceflights to date. Just how serious is the threat and what countermeasures can be satisfactorily employed are the questions that the Space Science Board's Panel on Microbiological Problems in Manned Space Flight were asked to appraise. This is the report of their findings.

At first glance, it would seem that the problems of spaceflight are far removed from everyday problems of disease on earth. When we look more closely, however, we see startling similarities between the closed environment and crowded living conditions of astronauts in flight and those of our cities, schools, offices, mass transportation, theaters, and even homes. The central and menacing problems of our times--overpopulation, pollution, urban ghettos, poverty, and war--all have as a by-product the greatly increased probability of infectious disease. Too little is known about the different ways in which microorganisms spread, even less about the variety of ways in which defensive mechanisms operate to confer resistance, and very little indeed is known about the specific conditions that alter the normal relationships between man and microbe. The understandings we achieve and the countermeasures we devise with respect to infection in spaceflight have direct bearing on our ability to prevent and control communicable disease on earth.

The spacecraft environment has special features that may favor the incidence and transmission of disease (Chapter 2). Foremost is confinement in a small, enclosed volume for extended periods with special problems of waste disposal and limited opportunity for personal hygiene. Transmission from one crew member to another of body microflora (microorganisms that normally inhabit the surface and interior of the body as well as

infectious agents) will increase greatly, and virtually complete interchange of flora is possible. As life-support systems progressively close in more advanced spacecraft by recycling of water, wastes, and air, the likelihood of contamination by feces, in particular, increases. The absence of gravity may profoundly affect the pattern of spread of disease by allowing particles, including infectious agents, to remain suspended indefinitely in the air, available for inhalation and contamination. The high oxygen content (90 to 95 percent) of the atmosphere in present space cabins could increase microbial mutations and adversely affect host defense mechanisms. These factors underline the critical importance of effective systems for environmental control and purification and waste management. Engineering designs indicate that, barring malfunction or accident, a satisfactory degree of control of environmental microbes is possible.

If, as we anticipate, microorganisms are effectively cleared from the spacecraft environment, a converse problem is posed: whether long exposure to reduced numbers and types of microorganisms in an isolated environment will result in reduction in the normal microflora. Since the microflora are believed to have a significant role in maintaining host defenses against disease, a reduction could compromise health during prolonged flight and result in dangerous susceptibility, or "microbial shock," on return to earth.

The most important and efficient protectors that man has against disease are his own defense mechanisms and immune systems (Chapter 3). They are numerous and varied--nonspecific and specific, systemic, and local--and act to reject, clear, engulf, neutralize, or kill invading infectious agents. Our knowledge of these defenses is not sufficient to allow us to predict how the conditions and stresses of spaceflight may affect them. We consider research on these topics to be of major importance: clearly the most effective way to deal with infection in spaceflight is to prevent it.

Except during the early stages of a flight, whether disease develops will depend more on environmental conditions in the spacecraft and the state of the astronauts' defenses than on the availability of potentially pathogenic microorganisms. Moreover, as body defenses decline, susceptibility to normal microflora increases. If crew members' defenses are inadequate or impaired, illness will probably result.

Respiratory infections (Chapter 4) will probably be the most common, particularly during the earlier periods of flight, because they are the most common type of illness and disability in adults on earth. Treatment is limited because in most cases

fewer than half of the causative agents are known and vaccines are available for only three of them. The most effective way to control inflight infections is to allow time prior to flight for incubating illnesses to develop and run their course, for exchange of normal and pathogenic flora among crew members, and to prevent the introduction of new infections during the preflight period.

Acute gastrointestinal diseases (Chapter 5) will also be common. In the context of spaceflight, they are significant primarily because of their ability to incapacitate the host, making him unable to carry out essential tasks, and to lower his defenses through inadequate nutrition. Most acute gastrointestinal upsets are nonbacterial in origin and are noninfectious. Those that are infectious can be controlled best by the preflight regime outlined above together with vaccines when available. Of utmost importance is avoidance of the indiscriminate use of broad-spectrum antibiotics for any illness whatever. These drugs have a devastating effect on the gastrointestinal flora that is so essential to host defenses and well-being, and the repopulation that takes place rapidly under normal circumstances may be delayed or altered adversely under spaceflight conditions.

Infections of the skin (Chapter 6) are not expected to be a serious concern, provided a reasonable schedule of skin cleansing is followed. There is some speculation that spacecraft conditions, particularly the high-oxygen, low-pressure atmosphere, may alter the microflora or physiology of the skin and decrease its effectiveness as a barrier to pathogenic microorganisms.

Latent infections (Chapter 7) could conceivably pose a major threat in very-long-duration spaceflights. Some infectious agents, notably certain viruses, can persist undetected in the body for long periods--even years--without inducing overt disease; if the diseases do develop, they tend to be severe. These infections and the factors that cause them to erupt are numerous and poorly understood. If the spacecraft environment should favor or accelerate their activation, the consequences could be very serious indeed. Preventive measures consist primarily of medical examination of prospective crew members to detect carrier states and marked susceptibilities and consideration of these conditions in determining the composition of crews.

Microbial mutations (Chapter 8) may increase under the special conditions of spaceflight. New mutants might be virulent and have altered antigenic properties, greater resistance to antibiotics, or selective advantages over the normal micro-

flora that would adversely alter the microbial ecology. While the risk of infection from such mutants would be modest in short-term flights (< 30 days), increased mutations, if they occur, could be dangerous on extended missions.

In dealing with the problem of infection in spaceflight, the emphasis must be laid heavily on prevention rather than therapy (Chapter 9). Therapy under these conditions is necessarily limited and conventional and relies on treatment of symptoms. Prevention begins when astronaut candidates are first screened and continues through preparation for the flight, during flight, and well afterward, in a rational, paced program. Of all preventive measures, an effective preflight isolation period is the most important.

PRINCIPAL UNANSWERED QUESTIONS

Each chapter in this report identifies a number of major questions the answers to which are important in assuring the effective prevention and control of infectious diseases in manned spaceflight. Ten of these questions are presented here as both representative and particularly significant.

1. What methods or systems of waste disposal and personal hygiene during prolonged spaceflight will meet normal sanitary standards? This is a recurring, practical problem of special importance, and one that has been particularly stubborn.

2. What is the effect of zero gravity on the physical stability and rate of dissemination of microbial aerosols? What happens in the space-cabin environment to aerosolized particles of different sizes, and what is the likelihood that the normal pattern of penetration and lodgment in the human respiratory tract will be altered?

3. Will long exposure to reduced numbers and types of microorganisms in the environment, in the presence of a relatively few persons, result in reduction in the normal microflora of man?

4. Will long absence from normal contact with pathogens, as occurs in larger populations, result in reduction in specific immunity to these strains and perhaps truly dangerous levels of susceptibility, allowing the possibility of "microbial shock" on re-entry?

5. Assuming that the bacterial flora of the body may change from that of the individual to that of the group in

closed environments, how effectively will the altered and more restricted flora carry on the protective functions of the normal flora?

6. How can host defenses of astronauts be bolstered against invasive organisms and be maintained against potential disease caused by overgrowth of microflora?

7. What is the influence of dietary factors on microflora?

8. What diseases caused by a reactivated latent virus or by a "slow" virus might be expected to appear in astronauts?

9. How can the emergence of latent infections and carrier states and the impairment of host-immune systems be anticipated and prevented?

10. Are there special conditions in prolonged space travel that may significantly influence microbial-mutation rates? Are selective forces modified in the altered environment so that virulent agents could proliferate?

MAJOR RECOMMENDATIONS

The following major recommendations of this Study are drawn from individual chapters of this report. They are of two kinds: recommendations on operational procedures and recommendations for research. Both are essential.

1. We recommend, as highest priority, that a preflight quarantine or isolation period be instituted to (a) permit acute disease to express itself, (b) prevent contact and infection of the astronauts by the general population, (c) permit cross-contact of flora and exchange of microorganisms among the prospective spacecraft crew. This period of isolation should be a graduated program of increasing protection for the astronaut, starting one month prior to flight time. It should be regarded as an essential, ground-phase portion of the flight mission itself. During the last two weeks, the astronauts' contacts should be limited entirely to essential technical crew who should also be held under the same isolation regulations. No direct physical contact should be permitted with anyone else during this critical period. Social, voice, and visual contact with persons outside may be permitted under rigidly controlled conditions which isolate the astronauts behind a glass-enclosed panel in a separately ventilated and air-conditioned room. The concept of preflight isolation has

been firmly and repeatedly advocated by all specialists in infectious disease who have been consulted on the problem. If not carried out adequately, serious consequences to the astronauts and the mission may result.

2. We recommend that the following operational procedures be initiated:

(a) Screening of astronauts and astronaut candidates by means of a battery of immunological tests for viral and bacterial infections to delineate those at risk.

(b) Microbiological surveillance of the astronauts, their close technical associates, and their families beginning one to two months prior to flight time and continuing one to two months postmission. This program should include throat cultures on a routine weekly basis for group A hemolytic streptococcus and meningococcus and efforts to identify the causative agent of any illness by appropriate bacterial, viral-isolation, and serological studies.

(c) Exclusion from a mission of any astronaut who has an acute infectious disease. This includes even minor respiratory infections, because they may result in greatly accelerated clinical responses under space-cabin conditions if transmitted to other astronauts.

(d) Establishment of a serum and material bank of biological samples derived from the surveillance program. Samples of serum, leucocytes, and platelets from the astronauts should be systematically collected for immunological study, and throat washings and stool should be collected for both immunological and microbiological study. The materials should be divided into aliquots and stored at -70°C or in liquid nitrogen with appropriate descriptive data. Since many of the problems of spaceflight cannot be foreseen now or perhaps in the next several years, preflight and postflight materials from current missions must be available to permit later study.

3. We recommend that the following research projects be undertaken on a priority basis. In a number of cases, these projects could be carried out as extensions of ongoing medical and university research, and several of them are of direct relevance to problems of disease on earth.

(a) Determination of the viability and behavior of representative infectious aerosols in atmospheres of altered gas content and pressure. These studies should include not only the atmospheres planned for spaceflight but also further digressions from normal in order to detect effects that are potentially more significant and that would not be clearly apparent in less extreme conditions.

(b) Determination of the longevity of microorganisms in various sizes of aerosolized particles under weightless conditions in various atmospheres. Initial studies can utilize simulated zero-gravity chambers, e.g., a revolving torus; definitive experiments should be performed in spaceflight under actual weightlessness.

(c) Performance of epidemiological experiments, in simulated and actual flight, on the transmission of respiratory agents in relation to (i) number of persons or animals in the space chamber, (ii) their state of susceptibility or resistance, (iii) degree of confinement, i.e., space per unit animal or man, (iv) number of microorganisms released into the environment by the infected persons, (v) type of aerosol produced, and (vi) enhancing effect of sneezing, coughing, talking.

(d) Determination of the course of response, in chamber tests or in flight, to a live or inactivated vaccine with which the recipient has had no previous experience, e.g., Brucella, tularemia, or cholera vaccines or live adenovirus type 4 oral vaccine.

(e) Determination of the long-term effects of spacecraft environmental factors (particularly weightlessness, altered atmospheres, stress, and noxious substances) on local host defense mechanisms. Particular attention should be given to mucociliary function, phagocytic clearance of organisms from the lungs, lysozyme content of secretions and blood, drainage of nasal sinuses, secretion of immune globulin A (IGA) into respiratory and gastrointestinal tracts, and peristalsis.

(f) Investigation of the effects of prolonged spaceflight on specific immune mechanisms. Studies should emphasize processing of antigens by macrophages, response of lymphocytes to invading pathogens, function of the thymus, transformation of lymphocytes to antibody-producing cells, and synthesis of immune globulin.

(g) Development of means to repopulate the gastrointestinal flora in the event that broad-spectrum chemotherapy becomes necessary on long-duration spaceflights.

(h) Examination of the effects of the spaceflight environment on latent and slow virus infections experimentally induced in animals.

(i) Identification of the host factors that keep latent infections dormant and determination of the factors that may alter host defenses and thereby result in activation of a latent infection.

(j) Investigation of the changes that may occur in microbial flora, particularly as they relate to selection of viru-

lent agents, under conditions of long-term spaceflight, utilizing experimental animals.

(k) Studies, both animal and human, of the effects of isolation on susceptibility to infection, particularly as related to the re-entry problem and microbial shock.

(l) Development of techniques for early detection of infectious diseases and of changes in microbial flora, with emphasis on rapid, automated procedures.

Chapter 2

SPACECRAFT ENVIRONMENT

The environment of astronauts during space journeys differs from that of men under normal conditions on the surface of the earth, especially with respect to the atmosphere in which they live and the absence of gravity. The spacecraft is a small, closed habitation, in which components of the environment are recycled and in which special problems of waste disposal and personal hygiene exist. Without the possibility of reducing adverse or potentially dangerous elements in the atmosphere through the normal processes of diffusion and sedimentation, it is clear that particular attention must be directed toward preventing accumulation of microorganisms in the environment as aerosols or on interior surfaces where they could become aerosolized or otherwise contaminate crew, food, or water. It is assumed that the buildup of microbial populations in the spacecraft environment could result in threats to health in the form of infection of the respiratory tract, the skin, or the gastrointestinal tract or induction of allergic reactions. The analysis of this problem involves the existing and planned engineering designs for spaceflight. It will be seen below that present evidence allows the prediction of a very satisfactory degree of control of bacterial incidence in the closed atmosphere.

SOURCES OF ENVIRONMENTAL MICROFLORA

The principal source of microorganisms entering the closed environment of the spacecraft is the skin of the astronauts. Bits of the stratum corneum are constantly shed from the skin in surprisingly large numbers--up to 10,000 per minute--and carry varying numbers of viable bacteria. Sneezing and coughing are another major source: coughs can produce comparable numbers of organisms, and sneezes produce up to 20 million infectious droplets. Merely talking can expel 1000 infectious nuclei per minute into the air.

Properly functioning waste disposal and regenerative systems should not be a source of environmental contamination. In the case of malfunction, however, the reverse is true, and a grave threat to the health of the crew would result. The possibility of fecal microorganisms entering the environment is very real and depends to a great extent on the success of the methods that will be employed for collection and disposal of feces.

Another possible source of difficulty may be represented by the growth of bacteria or fungi in or on materials that become damp. Presumably dampness will not occur so long as the relative humidity of the space-cabin atmosphere remains at the levels planned.

CONFINEMENT

Because many infections are transmitted by direct contact, and because the risk of infection is inversely related to distance, the close confinement of men for prolonged periods in a fixed environment enormously increases the likelihood of transmission of infectious agents. A virtually complete interchange of skin, nasal, oral, and gastrointestinal organisms is possible.

Among the respiratory pathogens, Mycobacterium tuberculosis and fungi such as Histoplasma capsulatum would be most likely to survive at relatively high concentrations for prolonged periods of time. In men isolated in Antarctica, Staphylococcus aureus and Staphylococcus albus persisted in the noses, and alpha hemolytic streptococci persisted in the throats, throughout the almost year-long study periods. Beta hemolytic streptococci seemed to disappear from the throats during the isolation period, suggesting that this pathogen may not survive in a closed community. Studies of men confined in submarines for months have pointed out the risk of epidemic spread: epidemics of respiratory illness occur regularly, although most of these can be traced to exposure of crew members prior to voyage.

ZERO GRAVITY

One of the unique features of the environment in a space vehicle is the lack of gravity. This physical condition may profoundly affect the pattern of spread of airborne infection

as it is understood from studies on earth. Without gravity, the atmosphere can support an enormously increased burden of airborne particulates. The increase will consist of larger particles (a few to several hundred micrometers in diameter), which in an earth environment would sediment rapidly. Small particles (approximately 1 μm in diameter) would not be appreciably affected, because they remain suspended almost indefinitely in the earth's atmosphere. Given the tendency of both large and small particles to remain suspended in space, the limits for concentration of particles in the air of a spacecraft are set by the availability of particles and the space available for them in the atmosphere.

With the large reservoirs of bacteria, fungi, and to a lesser extent, viruses that are variously resident on mucous membranes, on skin, and in the gastrointestinal tract, and under the conditions of poor personal hygiene imposed by space travel, large numbers of microorganisms will be shed into the environment and become airborne.

One major effect imposed by the lack of gravity will be an altered pattern of deposition of particles in the respiratory tract. There may be a marked reduction in the number of inhaled small particles that are retained in the periphery of the lung. Studies have shown that inhaled particles greater than a few micrometers in diameter are efficiently removed in the upper respiratory tract, principally by inertial impaction. The extent to which gravity sedimentation takes place here is not known, but is considered to be small. Particles having diameters greater than approximately 1 μm that penetrate to the peripheral areas of the lung are almost completely removed. An important mechanism for their removal, increasing in significance with diminishing size of particles, is sedimentation by gravity. The percentage of deposition due to the effect of gravity is being investigated. It is this presently unknown fraction of small particles, removed by sedimentation by gravity in the peripheral lung areas, that might remain airborne and be exhaled from the lung of an astronaut in space together with whatever large particles are ordinarily sedimented in the upper respiratory tract by gravity. Thus, while the peripheral lung areas might be protected to a considerable extent from contamination during spaceflight, the upper respiratory tract would be a potential site for the contamination with large particles noted above.

Nevertheless, nature has provided man with excellent defenses against large-particle contamination by means of the mucociliary blanket and other mechanisms, so that large particles, unless they were extremely infectious, sensitizing, or

chemically irritating, could probably be rapidly cleared even though their numbers were large. Prolonged exposure might lead to some increased mucous secretions and deterioration in function of the clearing mechanisms and hence to increased susceptibility.

The chief hazard, however, might be the inadvertent inclusion on a space trip of an astronaut who is incubating or is nondetectably infected with such agents as influenza virus, adenovirus, meningococcus, Streptococcus, or tubercle bacillus. While some agents are more infectious when implanted into the lung (e.g., adenovirus and influenza virus), most of the foregoing would probably initiate infection if the dose to the upper respiratory tract were large enough.

An investigation of airborne infection in an orbiting laboratory would be of great interest, not only because of its relevance to spaceflight but also to help develop perspectives on earthly problems of airborne transmission of infection. There would be great interest in sampling the air of a spacecraft for the number and size of airborne particles and the amount and kind of microbial contamination and in studying the patterns of sedimentation of particles in the respiratory tracts of astronauts.

It is possible that weightlessness may enhance the growth rate and mutation rate of microorganisms; this is suggested by experiments performed on Biosatellite 2 and elsewhere. The studies are too preliminary, however, to derive firm conclusions. Certainly the ability of viruses, bacteria, and fungi to multiply in a weightless environment has been demonstrated.

ATMOSPHERE OF ALTERED CONTENT AND PRESSURE

Although many physical and microbiological studies have been made of the behavior of infectious aerosols in air at normal pressure, only a few such observations have been made, except on water vapor, on the effects of abnormal pressures or of alteration in ratios of normal gases of the atmosphere. It has been shown, however, that oxygen tensions have a definite influence on the viability of microorganisms in aerosols, their persistence being greater in an atmosphere containing an appreciable percentage of nitrogen. It is probable that a 90+% atmosphere of O_2 at 5 psia, as currently obtains in the Apollo spacecraft, adversely affects aerosolized bacteria. Whether

an atmosphere of 70% O_2-30% N_2 at 5 psia, for example, will significantly affect the viability of suspended bacteria remains to be determined. No differences are apparent in the results of the confined chamber tests performed in air at 1 atm in simulated-altitude and space-cabin atmospheres. Information concerning persistence of microorganisms on surfaces in altered atmospheres is also minimal.

Hyperoxia at ambient or at abnormal pressures is deleterious to all types of cells, including bacterial and mammalian. In host-parasite relationships the total effect is influenced by the type of microorganism and probably by the site of the infection. For example, hyperoxia will render one type of experimental viral pneumonia more severe but will protect an experimental animal from chlamydial pneumonia. An adverse effect of hyperoxia on local defense mechanisms such as the mucociliary stream has been observed. Nevertheless, it should be noted that at 90% O_2 and 5 psia, the alveolar and blood oxygen tensions approximate normal for the astronaut.

Cabin temperature and humidity should be maintained within normal limits (65-76°F; <55%) and, barring malfunction or accident, should, therefore, not be a significant factor.

OTHER FACTORS OF SPACE-CABIN ENVIRONMENT

The problem of chemical pollutants and toxic gases entering the environment from material outgassing or as systems by-products, although serious, lies outside the scope of this report. The reader is referred to the 1968 report of the Space Science Board's Panel on Air Standards for Manned Space Flight, Atmospheric Contaminants in Spacecraft (available from the Space Science Board), which identifies some 200 possible contaminants and sets provisional allowable limits of concentration. Possible microbiological effects of a few pollutants are discussed in Appendix A.

The fiber-glass material which is used in the astronauts' suits may have to be considered a possible atmospheric pollutant. The suit fiber-glass is composed of particles 1 to 3 μm in diameter, and during a recent Apollo mission some of the fiber glass fragmented, contaminating the atmosphere. While the fiber glass is believed to be biologically inert, particles of this size should deposit distal to the mucociliary stream and in large quantities may be capable of inducing a host response or synergistically activating a latent infection.

On the basis of present information, the fluxes of ionizing radiation ordinarily encountered in space will not be a significant factor in the microbiology of the environment.

LIFE-SUPPORT SYSTEMS AND ATMOSPHERE CONTROL

Because the control of environmental microflora depends so directly on the life-support systems, including treatment of the atmosphere, a fairly detailed discussion of this topic seems warranted.

The Mercury, Gemini, and Apollo manned spacecraft have had expendable life-support systems because of their short mission durations. Future extended missions will require varying degrees of "closed-loop" life-support systems which are maintainable and capable of operating indefinitely with minimum penalties in terms of expendables, power, and fixed weight. Research in support of the more advanced missions includes development of advanced techniques for atmosphere supply and control, regenerative atmosphere purification, oxygen recovery, water recovery, thermal control, humidity control, and waste management. A primary objective in the development is to achieve lower weight, size, and power requirements and to increase reliability, maintainability, and simplicity.

Because each of these systems is capable of contaminating the atmosphere, considerable research and development will be required to prevent such occurrences during spaceflight. For example, current planning for an advanced integrated life-support system calls for the use of steam for desorbing the carbon dioxide concentrator. This steam will also be used periodically to sterilize key subsystems such as water recovery and waste management. In addition, these subsystems will be continuously monitored by bacterial sensors having a response time of only a few minutes. Thus, if contamination does occur, an alarm will be generated and immediate corrective action applied. For future space missions every effort will be made to "engineer out" any potential sources of contamination that could arise from the basic life-support subsystems.

This philosophy also applies to the control of the atmosphere. In a typical advanced design the gas inside the spacecraft will encounter three basic systems for removal of airborne contaminants. The first is a catalytic burner or oxidizer for removing chemical contaminants which operates at a temperature of 700°F and through which the cabin air passes

at a flow rate of 3 to 6 $ft^3\ min^{-1}$. Dwell-time of the air inside this unit is approximately 1 sec. This system is preceded by a copper sulfate-coated sorbent and a postsorber of lithium carbonate, both of which will reduce the airborne count. The cabin temperature, humidity control, and air circulation are managed by fans having air-to-water heat exchangers, by supplementary ventilation fans, and by bacterial control fans. The total airflow in each of two compartments is 12,500 $ft^3\ min^{-1}$. At any one local area, the air movement is 50 $ft^3\ min^{-1}$. The bacterial control fans each move 750 $ft^3\ min^{-1}$ of air. Two are located in the crew compartment and one is located in the equipment compartment. The bacterial control fans are equipped with a "roughing out" filter of 50-μm pore size and a HEPA filter with 0.3-μm efficiency. These latter filters have an operational capacity of approximately 50 days, after which they are sterilized at 350°F and stored. This bacterial control system has been designed against a requirement of no more than 20 viable particles per cubic foot of air. This figure was based on an average shedding rate of 3000 bacteria per man per minute with the system having a 95% removal efficiency. In all probability, this type of proposed system will remove almost all viable particulates, and the final count will be less than one particle per cubic foot of air. Finally, every effort will be made to provide an even flow and exchange of air inside the space cabin. Although the proposed system does not include installed redundancy, key items such as fans can be carried as spares and replaced in flight if failure occurs.

Experience in Closed Environmental Systems

In attempting predictions concerning microbes in the space-cabin environments of the future, existing information from simulated and actual spaceflights is extremely useful. These data are reviewed and compared in Appendix B and are summarized here.

Four types of atmospheric environments were employed in these studies: air at ambient pressure in a simulated spacecraft; a two-gas system with increased percentage of oxygen but lowered pressure, simulating atmospheres of spacecraft; normal ambient air at approximately 1-atm pressure flowing through the chamber; and the hyperbaric pressure of experimental diving. In the last mentioned, there was no direct study of microflora of the environment, only of water in the

wet chamber, and comparison with the other studies is therefore not possible. Furthermore, in only one experiment was it possible to compare directly the effect of the simulated spacecraft atmosphere with ambient atmosphere holding other variables constant, and comparison of one study with another with respect to this variable is therefore not feasible. Any direct effect that the atmosphere would have on atmospheric microflora would probably not be striking and would require a careful and sophisticated kind of experiment to detect. Therefore, the effect of the spacecraft environment on microorganisms in or in contact with the spacecraft atmosphere, as compared with ambient atmosphere, has not been completely ascertained. No record was found of an experiment designed to assess the influence of zero gravity on, for example, microbial aerosols.

The data on atmospheric microflora available in these studies (see Appendix B, Table 9) indicate that other, perhaps identifiable, factors affect the level of atmospheric bacteria under the conditions tested. The simulated spaceflights coded in the Appendix as B1, B2, B3, and B4 consisted of unmanned tests primarily of life-support subsystems. They included recycling of the atmosphere at 900 ft^3 min^{-1} through a bacterial filter (CBR) and through a catalytic burner at approximately 700°F. Low bacterial counts of the atmosphere (air at 1-atm pressure) were recorded in the two instances in which such observations were made: B1 showed 3 to 4 bacteria ft^{-3} and B4 showed removal, within 1 min, of 90 to 99% of injected aerosols. In study C1 (a 30-day manned test in air at 1-atm pressure with filtration and recycling), the air was relatively bacteria-free for the duration of the test. The same general result was observed in C2 (conducted in an altered, recycled atmosphere at simulated altitude for 60 days) and in C3 (a 28-day test in air at ambient pressure), where 8 to 10 bacteria ft^{-3} were found. All other studies for which data are available indicate a fairly steady increase in numbers of bacteria in the air.

Examples of this steady increase in bacteria count in closed systems are shown in the results of tests performed at Wright-Patterson Air Force Base (coded in Appendix B as A1, A2, A3, A4, A5, and A6). These were manned tests, in air at 1 atm and were conducted in semiclosed or closed chambers in which no special provision was made for removal of bacteria from the atmosphere. The air was circulated at 400 to 500 ft^3 min^{-1} within the chamber through a nonbacterial filter and a CO_2-absorber consisting of barium hydroxide. Air conditioning maintained a comfortable temperature (70 to 78°F) and relative humidity (50 to 55%). An unsatisfactory level of

personal hygiene was deliberately imposed with no baths and few or no changes of clothes. Under these conditions, definite increases in numbers of bacteria on the skin and in the atmosphere occurred (A1, A5). Numbers of bacteria on plates exposed a week or more after the beginning of the tests were approximately 50 times greater than those encountered immediately after entry into the chamber. Similar results were observed in A9, which was conducted at simulated altitude and in which hygiene was minimal because spacesuits were worn by the personnel involved.

Confirmation of the effectiveness of atmosphere-control systems in closed environmental systems with respect to reducing microorganisms in the air is seen in data from studies on nuclear submarines. These studies were conducted in air at 1-atm pressure, and much larger groups of men were involved, of course, than in any simulated spaceflight tests. Atmospheric bacteria counts were reported to be low at all times except when venting the sanitary tanks, at which time an aerosol was generated.

It thus appears that present designs of air conditioning and recycling in space vehicles provide an atmosphere remarkably free of demonstrable microorganisms. This was demonstrated in study C1 despite some aerosolization of bacteria from the waste-disposal system. The low atmosphere counts should not be surprising in view of the filtration and heating involved in the atmospheric recycling process employed in the study. It may be assumed that the results with aerobic cultures are indicative of what was happening to airborne anaerobes and viral particles.

Microflora of Surfaces Microbiological observations on surfaces within the space cabin as yet provide no clear picture. In spite of the low atmospheric bacteria counts in C1 and C3, noted above, surface counts were regarded as high and in the latter test were said to increase during the period of the test (28 days). In unmanned tests B1 and B4, bacterial assays of surfaces were not remarkable. Insufficient data were recorded to determine to what extent the surface contaminants observed in C1 and C3 represent normal skin flora. Nevertheless, the tentative conclusion is warranted that a principal source of surface contamination in such systems is the personnel, who contribute microorganisms mainly from their skin.

When inadequate facilities for personal cleanliness exist, as in A9 where the subjects wore spacesuits, the feces represent a source of environmental contamination. In this study,

all surfaces tested were reported to be markedly contaminated with coliform bacteria.

Waste Disposal and Reclamation Systems Analysis of the observations made in B1, B2, B3, B4, C1, C2, and C3 indicate that much progress has been made in development of systems for provision of potable water and safe disposal of wastes, for example. There are also instances demonstrating clearly that malfunction or improper use creates microbiological hazards to the astronaut.

TRANSMISSION OF INFECTIOUS AGENTS TO PERSONNEL

The mechanisms of transmission of infectious agents will be much the same in spacecraft as under ordinary conditions on earth. From the standpoint of the physical environment, the factors already discussed will determine the extent to which these avenues will be greater or less in spacecraft, i.e., the increase or decrease in concentration or persistence of infectious aerosols, the contamination of the environment with microbes from the respiratory and gastrointestinal tracts or skin, and the integrity of water and food supply systems. Observations in these areas with attention to nonpathogenic bacteria will allow predictions concerning the extent of exposure to pathogens.

POSSIBLE ADVERSE EFFECTS OF REDUCED ENVIRONMENTAL MICROFLORA

As reported in studies C1 and C2 (Appendix B), which involved four men each and lasted 30 and 60 days, respectively, low levels of atmospheric microorganisms were found to be associated with decreases in total numbers of bacteria on the skin (C2) and in the oral cavity and pharynx. It has been postulated that prolonged isolation of minimal numbers of persons in a closed environment with sterile air, food, and water and a loss of immunogenic contact with the microorganisms of great numbers of people will result in decreases in numbers and simplification of types of organisms in normal microflora. Inas-

much as the normal microflora of the skin and of the gut are regarded as significant factors in maintenance of normal resistance against invading pathogens, a decrease in microflora brought about by isolation could represent a health hazard during flight and the possibility of "microbial shock" when normal contacts are re-established after return to earth. This latter problem has been compared with the gnotobiotic phenomenon whereby exposure of germ-free animals to the general laboratory environment results in fatal infectious diseases. There is in fact, however, a vast difference between the problems of gnotobiotic animals and those of returning space voyagers. In the case of gnotobiotic animals, there is a rigid isolation of the animal from birth in which the animal is protected from all external antigens and infectious agents. The situation of the space travelers, however, is different in that they have all experienced infectious agents and antigenic stimuli for many years prior to departure on the spaceflight. The loss of immunological memory is unlikely. Defense mechanisms against many diseases such as diphtheria, measles, mumps, and smallpox are relatively durable even without periodic renewal of contact with the agent. It is conceivable that new strains of microorganisms, such as influenza viruses, might emerge during the astronauts' absence from the earth's environment, and re-exposure could result in acute infectious disease. This problem, however, is more analogous to isolated communities than to the problem of gnotobiotic animals. As such this is a re-entry problem rather than a problem of true microbial shock. It would be of great importance to identify new infectious agents that occurred in the general population during the astronauts' absence and to immunize or vaccinate the astronauts against such agents on their return. For this purpose, a period of postflight isolation with gradual reintroduction to the earth environment would seem to have potential value.

The need for such a re-entry procedure and the techniques that should be used require definition and would appear to be an important area for laboratory and clinical investigation under experimental circumstances and under conditions of a simulated closed ecosystem. It does not, however, appear to be an immediate problem for relatively short spaceflights. Extremely long flights are not likely to occur until some fairly distant time in the future, which should allow sufficient time to examine this problem experimentally.

MAJOR UNANSWERED QUESTIONS

1. What is the effect of zero gravity on the physical stability and rate of dissemination of microbial aerosols? We need to know especially the fate of aerosolized particles of various sizes and their ability to penetrate the human respiratory tract.

2. What is the effect of atmospheres altered in content and in pressure on microbial aerosols and on contaminated surfaces.

3. What methods are satisfactory for decontamination or sterilization of the spacecraft atmosphere, materials, and surfaces, the water and food, and anything else with which the astronauts are likely to come in contact, in case of accident or of inadequate performance of life-support and waste-disposal systems?

4. Will long exposure to reduced numbers and types of microorganisms in the environment, in the presence of a relatively few persons, result in reduction in the normal microflora of man? Similarly, will long absence from normal contact with pathogens, as occurs in larger populations, result in reduction in specific immunity to these strains and perhaps truly dangerous levels of susceptibility?

RECOMMENDATIONS

1. Determine the viability and behavior of representative infectious aerosols, e.g., of bacteria and viruses, in atmospheres of altered gas content and pressure. These studies should include not only the atmospheres planned for spaceflight but also further digressions from normal in order to detect effects that are potentially more significant and that would not be clearly apparent in less extreme conditions.

2. Determine the longevity of microorganisms in various sizes of aerosolized particles under weightless conditions and in various atmospheres. Initial studies can utilize simulated zero-gravity chambers, e.g., a revolving torus; definitive experiments should be performed in spaceflight under actual weightlessness.

3. As a sanitary-engineering problem, develop satisfactory means of decontaminating or sterilizing the spacecraft atmo-

sphere, materials, and surfaces, the food and water, and anything else with which the astronauts are likely to come in contact, in case of accident or malfunction of the various waste-disposal, regenerative, and life-support systems.

4. Conduct a simulated manned spaceflight, which reproduces as nearly as possible all the elements of an actual flight, with all life-support systems closed. Attention should be directed particularly to careful quantitative assay of microorganisms of the atmosphere.

5. Carry out long-term, ground-based observations on experimental animals, preferably primates, held in a relatively microorganism-free environment, with detailed observations on the numbers and types of microflora of the body and assessment of the potentiality of the immune response of the animal.

6. Investigate the potential re-entry problem of increased susceptibility due to long-term isolation from the general environment, with research projects using animal and man.

Chapter 3

HOST DEFENSES AND IMMUNE SYSTEMS

In many respects, consideration of the mechanisms of host defenses against infectious agents, other than specific immunological factors, resembles discussion of the weather: there is considerable talk, but little can be done to alter the defenses in favor of the host. It is likely that astronauts will be exposed to infectious agents on prolonged missions in space. Insight into the mechanisms of the body's defense is therefore mandatory to circumvent these possible hazards. Unquestionably, a parasite's genetic capacity for virulence is essential to produce disease; nevertheless the host's defenses serve as the major force in determining whether clinical disease results from the encounter between man and invading microorganisms. Knowledge of the host's protection against invasive organisms is still somewhat superficial, and relatively few hard facts are yet available concerning the effects of spaceflight on his defense mechanisms.

Nature has evolved both nonspecific mechanisms and specific immune systems to protect the body against invasion. These will be dealt with in turn, and the means by which they function in various organ systems will be considered.

NONSPECIFIC HOST DEFENSES

Anatomical integrity of the skin and of the linings of cavities furnishes the first major defense against invaders. Disruption of the ectodermal or epithelial surfaces permits entry and often growth of otherwise harmless microorganisms--particularly if an unusually large accumulation of a unique flora of infectious agents develops, as the conditions during space travel may permit. Cilia, mucus secretions, and movement of secretions on the surfaces by peristalsis or respirations continually wash out particulate matter. In a similar manner, the constant flow of urine from the kidneys through the bladder continually removes organisms that are cleared from the blood by the kidneys. Stasis, which interrupts this

constant flow, is frequently followed by overt infection. If the parenchyma of the lung, which is customarily sterile, should be invaded by microorganisms, alveolar macrophages under ordinary circumstances phagocytose and remove them. Macrophages of the reticuloendothelial system and polymorphonuclear leucocytes in the spleen, liver, and lungs effectively engulf and clear the blood stream of bacteria which sporadically enter.

Unique serum proteins may also effectively serve in the body's defense. Complement, for example, appears essential for effective bacteriolysis of some bacteria, particularly of gram-negative organisms, and interferon probably serves an important role in prevention of and recovery from a large number of viral infections. The probable role of interferon is sufficiently important to warrant further discussion.

Interferon is a protein said to vary in molecular weight from 17 x 10^3 to 100 x 10^3 daltons. (Purification of interferons, however, has not been accomplished, and the wide range in sizes reported could be due to impurities complexed with interferon rather than numerous types of interferons.) Interferon does not act directly as an antiviral agent but instead induces the synthesis of another host protein which appears to selectively inhibit translation of viral proteins; the exact molecular mechanisms of inhibition are not yet clear. It is striking that interferons effectively induce resistance to a wide variety of viruses and even to some nonviral agents such as trachoma and intracellular protozoa. If exogenous interferon is employed to prevent viral infections, the interferon must be derived from a homologous or closely related animal species, i.e., mouse interferon will protect mice but not chickens or monkeys and vice versa. Existing evidence also suggests that interferon plays a critical role in an animal's recovery from viral infections. However, additional data are essential before this concept can be accepted without question.

The manner in which local mechanisms may serve in defense of the host can be exemplified best by examination of their function in specific organ systems. Defense mechanisms of the mouth and throat are treated below; those of the respiratory tract and the gastrointestinal tract are discussed in Chapters 4 and 5, respectively.

Oropharyngeal Defense Systems

The local defense mechanisms of the oropharynx are the anatomic and physiological barriers of the mucous membranes, the antibacterial properties of saliva, lysozymes, immune

globulins, low pH, deglutition, and the presence of an indigenous flora. Although information concerning the quantitative role that each of these systems performs is meager, it appears that the more important mechanisms are an intact mucous membrane and the indigenous flora. Local infections are most often associated with traumatic disruption of the epithelial cell lining and secondary bacterial infection. Systemic disease such as endocarditis may also follow physical disruption of the mucous membranes with consequent entry into the blood of such organisms as Streptococcus viridans.

Maintenance of the indigenous flora prevents overgrowth of any one strain and resultant superinfection. The specific mechanisms responsible for maintaining this remarkable ecological balance are poorly understood. Nutritional requirements probably limit individual bacterial growth. The pH of the oropharynx also determines the bacterial constituents, as a low pH favors the growth of certain organisms (lactobacilli), whereas a more neutral pH prevents their growth. Some oropharyngeal bacteria (Streptococcus salivarius) secrete substances that are bactericidal for pneumococci. Last, in some nonspecific manner, the oropharyngeal bacteria must inhibit fungal growth, because treatment with broad-spectrum antibiotics is often associated with candidal overgrowth.

The antibacterial properties of saliva, lysozymes, immune globulins, and deglutition also maintain the indigenous flora. Saliva performs three protective functions: it washes bacteria into the esophagus, it contains lysozymes, and it protects the mucous membranes from drying. The washing action of saliva appears to be a significant factor in preventing new bacteria from establishing themselves in the oropharynx. Organisms native to the mouth and capable of surviving in vitro in saliva rapidly disappear from the mouth following inoculation or aerosolization, presumably due to the flushing action of saliva. Salivary lysozymes are bactericidal for many bacteria. Immune globulins, especially immune globulin A (IGA), have been clearly shown to correlate with antiviral immunity to respiratory viruses. The antibacterial importance of these proteins probably relates both to systemic and local protection.

The effect of the above defense mechanisms is to regulate for each individual the species and numbers of the pharyngeal microbiota. It is of interest that the significance of local phagocytosis as well as of the large amount of pharyngeal lymphoid tissue is unknown.

SPECIFIC HOST DEFENSES

The impressive success of numerous vaccines in the prevention of bacterial and viral diseases testifies to the value of specific antibodies in protecting the host against invading organisms. The repeated bacterial infections experienced by persons who have little or no gamma globulin (agammaglobulinemia and hypogammaglobulinemia) reinforce this point. The synthesis of immune gamma globulins by lymphocytes in response to antigen challenge thus serves as a major line of specific defense.

Lymphocytes, derived ultimately from the bone marrow, seed the thymus and peripheral lymphoid tissues. Those that go to the peripheral lymphoid tissues are found in the spleen and in the germinal centers of the lymph nodes. These are a short-lived variety with a life span on the order of four or five days. Those that go to the thymus undergo some phase of immunological maturation, and they in turn are seeded out into the circulating lymphocyte pool. This circulating lymphocyte pool consists of a group of cells whose life span is very long, perhaps years in man; the cells constantly circulate from blood to lymph and back.

Macrophages engulf and process antigens introduced into the body. The altered antigen is then handed on to one or more of the lymphocyte types mentioned above. The involved lymphocytes are in turn transformed into plasma cells which synthesize the immune globulins that can react with homologous antigens in serum and secretions. Secretory IGA is effective in the latter material, i.e., in respiratory and gastrointestinal secretions.

Given adequate data on the physiological effects of prolonged space travel, one should be able to predict where, in the sequence of the cellular response and antibody synthesis, stress might adversely affect the immune mechanisms. For example, one of the acute effects of stress is to stimulate the adrenal cortex and the release of adrenocorticosteroids. There are several consequences: (1) cortisone inhibits biosynthesis of antibody without particularly changing already existing antibody levels; (2) corticosteroids affect phagocytosis, which in turn alters the rate of immune elimination (this may occur indirectly, by altering circulation dynamics and thus the numbers of macrophages available, or directly, by changing the activity of the available macrophages); and (3) corticosteroids affect lymphocytes by directly inhibiting their formation and by outright lympholysis. Indirectly, the

transformation of lymphocytes to plasma cells--the efficient antibody producers--is inhibited. Short-term stress does not seem to impair the human immune response mechanisms, but prolonged stress may result in an immunologically compromised host. The effect of prolonged stress on thymus function merits particular study: the thymus is the source of the long-lived cells that are responsible for immunological recognition as well as for a postulated hormone necessary to the immunological maturation of lymphoid cells.

MAJOR UNANSWERED QUESTIONS

1. How can host defenses of astronauts be bolstered against invasive organisms?
2. What is the long-term effect of spacecraft environmental factors on a human's local defenses, such as mucociliary action in the respiratory tract, mucus secretions, and protective enzymes (e.g., lysozyme)?
3. What are the consequences of space exploration on interferon induction and function, on the synthesis and persistence of complement components, and on the function of specific immune systems?
4. Assuming that the bacterial flora of the body may change from that of the individual to that of the group in closed environments, how effectively will the altered and more restricted flora carry on the protective functions of the normal flora?

RECOMMENDATIONS

1. Study the effects of spacecraft environmental factors (particularly weightlessness, altered atmosphere, stress, and noxious substances) for prolonged periods on local defense mechanisms: mucociliary function; phagocytic clearance of organisms from lungs; lysozyme content of secretions and blood; drainage of nasal sinuses; secretion of immune globulin A into respiratory and gastrointestinal tracts; and peristalsis.
2. Investigate the effects of prolonged spaceflight on specific immune mechanisms: processing of antigens by macro-

phages; response of lymphocytes; function of thymus; transformation of lymphocytes to antibody-producing cells; and synthesis of immune globulin.

3. Investigate the role of the changing microflora of skin, upper respiratory tract, and gastrointestinal tract in protecting the system and in local defense against parasitic invasion.

4. Study the effects of prolonged space missions on interferon induction and action; levels of components of complement; and induction, if any, of abnormal serum globulins.

5. Determine the half-life of passively administered immune globulins.

Chapter 4

ACUTE INFECTIONS OF THE RESPIRATORY TRACT

As acute respiratory diseases represent the most common type of infection and disability in adults on earth, they may be expected to be the most common type of illness on manned space missions, especially during the earlier periods of the flights. Indeed, this has proved to be the case on the Apollo 7, 8, and 9 flights. Contributing to the importance of the problems are the potentially enhanced transmission to the other crew members that may occur in the special environment of the space cabin and the possibility that more severe clinical illness may result as a consequence of altered host-parasite relationships under these circumstances.

Several potential sources of in-flight respiratory infection can be identified. The most likely sources are preflight contacts. In increasing order of importance these include the general public, the technical staff, intimate associates, including other astronauts, and family members. Because children are known particularly to originate respiratory illness, especially within the family circle, the group with whom the astronaut is most desirous of having social contact, especially just prior to the mission, is at the same time the most likely source of respiratory as well as other infections. Fellow astronauts would be another source of infection.

During flight, infection may be transmitted by another crew member, perhaps through an aerosol that could reach unusual sites for infection, persist longer in the air without gravity, and travel further. Disease could also result from buildup of microbial populations in a closed ecological system. This hazard would be important if the space-cabin environment favored the accumulation or persistence of viable viruses, bacteria, or fungi, so that a human infective dose would be achieved. If the air filter and recirculation system are functioning properly, this should not occur. Finally, a mechanical carrier state, or a latent state, can convert to one of active infection. The frequency of carriers of group A hemolytic streptococcus, Staphylococcus aureus, meningococcus, and pneumococcus make these the most likely pathogens in

spaceflight. Latent or carrier states for viruses pose a similar problem. Herpes simplex might be a special problem, especially if recrudescence occurs in the presence of another crew member who is totally susceptible. The question of latent infection is discussed in more detail in Chapter 7.

Our general concept of respiratory infection in the earth environment can be summarized as follows:

1. A single respiratory pathogen can result in a wide range of clinical syndromes, or none at all, depending on a variety of factors.

2. The reverse of 1: a single clinical syndrome can be produced by any one of a number of pathogens and sometimes from dual infections.

3. Certain factors are important in the type and severity of the clinical response and include age, pre-existing antibody levels, number of pathogens to which the person is exposed, duration and intimacy of the exposure, certain factors affecting the host state (e.g., stress and physical condition at time of exposure), and the integrity of the host immune system. In addition, individual and familial susceptibility affect not only the frequency of clinical illness but also the pattern of the clinical response. Some persons have many respiratory illnesses, and they may be severe, disabling, lower respiratory infections. Others have few, or only mild, upper respiratory illnesses.

Causes, or etiological agents, can be identified in only about 50 percent of all respiratory illnesses. The remainder are of unknown etiology and are presumably viruses that are not detectable in our currently available tissue-culture and bacterial-isolation media.

5. Of those specific agents that are identifiable, commercial vaccine is available for only one--the influenza group. Even here the degree of protection is limited and depends on the inclusion in the vaccine of the influenza-virus strain that is prevalent at that moment.

6. The pattern of bacterial infection of the lower respiratory tract has altered markedly over the past 25 years due, principally, to the introduction of effective antibiotic and chemotherapeutic agents. There has been a sharp reduction in morbidity and mortality from classical pneumonia caused by pneumococci and other bacterial pathogens. Pneumonia is no longer a serious disease in the healthy young adult although it continues to be a major cause, or a contributing cause, of death in elderly patients or those with chronic diseases. The

TABLE 1 Common Etiological Agents of Respiratory Disease of Possible Importance to Astronauts

Agent(s)	Common Types	Clinical Syndromes	Estimated Frequency in Astronaut	Estimated Severity in Astronaut	Immunity	Prevention	Communicability to Other Astronauts	Therapy
1. Rhinovirus	85 or more distinct antigenic types	Common cold; mild upper respriatory infection	Probably high and most common type of expected illness. Causes up to 25% of common colds. Most active in autumn	Ususally mild and not disabling. Plugging of Eustacian canal may cause pain or rupture of ear drum with pressure changes	Probably good and of long duration to the same strain	No vaccine available and little prospect for one in man of the multiplicity of distinct antigenic strains	High and perhaps certain to susceptible companions within 2-3 day period	Decongestants to relieve stuffiness and reduce plugging of Eustacian canal
2. Influenza	A, A', A2, B, and C	Acute febrile upper respiratory infection. Common cold to severe and fatal viral or viral/bacterial pneumonia	High risk in epidemic periods. Most common cause of moderate to severe illness at any time--about 12% of ARD that is hospitalized and about 80% of ARD in epidemic periods	The severity of the aching, the cough, and the fever may result in a disabling illness in which the astronaut could be ineffective 1-3 days. In terms of frequency and severity, most important viral pathogen	If both humoral and local antibody are present, the immunity to that specific strain is good. No cross protection between A, B, C	Commercial vaccine available. Must incorporate the current strains, i.e., the ones to which the astronaut may be exposed. With proper strain, the protection against clinical illness should be 50% or higher. Vaccinate yearly and during outbreaks	High to susceptible crew within 3-10 days	None specific. Aspirin or Darvon for aching and fever. Codeine for cough. Amantadine moderately effective against A2 strain
3. M. pneumoniae	One only	Primary atypical pneumonia syndrome of cold agglutium positive type. Mild upper respiratory illness	Unlikely infection unless (a) in epidemic year, (b) in the astronaut's family. Causes 25-50% of atypical pneumonia, higher in epidemic years (seem to be 4-5 year swings in epidemicity)	The potential severity of illness gives this agent importance. Severe, distressing, and protracted cough may be disabling	Good	No commercial vaccine. An experimental, killed vaccine (Merck) has given 50% protection against clinical illness. May "hypersensitize" in later natural exposure	Probably high to antibody negative crew members given close and prolonged contact. Estimated secondary incubation period 2-3 weeks	Erythromycin or a tetracycline (Declomycin). Improves clinical state but does not eliminate the organism (i.e, still communicable)
4. Group A hemolytic streptococcus	Many types with separate antigens	Acute tonsillitis and pharyngitis (exudative and nonexudative)	High, especially if exposed to young children and in Jan.-April season. Carrier state in 10-15% causes 15-25% of all severe acute tonsillitis/pharyngitis; highest in Jan.-April	Shaking, chills, high fever, and severe sore throat may make astronaut uncomfortable and perhaps render him operationally ineffective	Probably good to same type but too many types to make immunity of practical importance	No vaccine available. Penicillin prophylaxsis may be effective but its effect on other microflora may make its use undesirable	Probably high from clinically ill astronaut. Low to moderate from carrier dependent on number of colonies, frequency of sneezing or coughing, and duration of exposure	Oral and parentral penicillin in sufficient doses to maintain blood levels over 10 days. Erythromycin over 10 days useful in penicillin-sensitive persons. Eradication of group A carrier state with penicillin (or erythromycin) should be considered in the quarantine period

5. Parainfluenza	1, 2, 3	Acute upper respiratory infection. Rarely viral pneumonia	About 10% of all ARD in young adults. No clearcut seasonal or yearly pattern	Probably mild because illness in adult often represents reinfection. Importance moderate to low	Poor. Reinfection occurs in the presence of humoral antibody, but illness is milder	No available vaccine, and potential reinfection may limit usefulness	Probably relatively low depending on the antibody level of the exposed astronauts	None specific. Symptomatic only
6. Adenovirus	Over 30 types. Types 3, 4, 7, 21 most important	1, Acute upper respiratory; 2, viral pneumonia; 3, pharyngeal-conjunctival fever	Probably uncommon in astronauts--3-5% of severe respiratory illness due to this	Type 4 adenovirus pneumonitis could be incapacitating. Types 3, 7, and other types will probably not result in disabling illness	Good and durable to the specific type	A live, type 4 enteric-coated vaccine available from the armed forces should be used in those lacking type 4 antibody. A type 7 or 4-7 combination may become available. Inactivated vaccine is effective but not now available	Probably low because of slow spread, likelihood of immunity in fellow astronauts. But adenovirus may remain viable for long periods	No specific therapy available
7. Respiratory syncytial virus	One or two	Acute mild upper respiratory illness (croup and bronchitis in infants)	Rare	Mild, as illness would almost always be reinfection	Poor, Reinfection is common in the presence of antibody	No available vaccine	Probably low	No specific therapy. None likely to be needed
8. Epstein-Barr virus (herpes-like virus)	One	Infectious mononucleosis	Very low--probably only 15-20% susceptible. Very common in 15-25 year age group (rates 500-2000/100,000)	May be disabling	Probably good	None known. Determine susceptibility by EBV immunofluorescent test	Low as most others are immune. Incubation period 3-6 weeks. Virus persists in leucocytes for years: reactivation conceivable but not validated	None specific
9. Hemophilic influenza		Unusual source of acute respiratory illness in young adults	Low, but changes in this prevalent organism could cause upper or lower respiratory illness or ear infection especially in astronauts with chronic bronchitis	Occurs when resistance is reduced, and may induce pneumonia	Good except when individual has chronic bronchitis	Proper rest, etc. Long spaceflight may reduce intrapulmonary resistance and allow pathogens to multiply, initiating pneumonia	Low	None specific

pattern of bacterial infection of the lower respiratory tract has shifted from acute pneumonia to intercurrent bronchitis and bronchopneumonia. Low-grade bacterial infection of the lower respiratory tract persists as an important cause of illness and absenteeism even in young, apparently healthy individuals. These infections appear to be associated with a lowered state of host resistance and are significantly more frequent in smokers. There are multiple causes of such depressed host resistance, but tobacco smoking appears to be by far the most important one in the general population.

Bacterial infection of the lower respiratory tract in otherwise healthy astronauts in spacecraft environment is likely to be present as a manifestation of altered host defense mechanisms. The etiologic agent is likely to arise from the astronauts' endogenous flora rather than by transmission from one individual to another. Because of this, the hazards of bacterial infections of the lower respiratory tract will be related to those factors of the spacecraft environment that are likely to depress the host defense mechanisms of the respiratory tree. By the same token, it should be possible to control lower respiratory infections by careful attention and environmental control of the spacecraft cabin.

SPECIFIC INFECTIOUS AGENTS

Table 1 lists the common respiratory agents, the clinical syndromes with which they are usually associated, and the estimated probability and severity of infection in the astronaut. The importance of specific respiratory agents to the astronaut might be formulated as follows:

$$\text{Importance} = \frac{\text{Probability of infection} \times \text{Severity of illness}}{\text{Availability of effective vaccine, control measures, or antibiotic therapy}}.$$

CLINICAL SYNDROMES AND THEIR CAUSES

Common Cold

About 15 to 25 percent of common colds are due to rhinoviruses and perhaps 10 to 20 percent (based on preliminary

data) to an infectious bronchitis-like agent, a virus cultivated only in organ culture such as trachea or nasal epithelium. Influenza and parainfluenza cause 5 to 10 percent, and the remainder are of unknown cause.

Acute Pharyngitis and Tonsillitis

About 40 percent of college students admitted to infirmaries with sore throats have infectious mononucleosis. Of the remainder, about one third are due to group A hemolytic streptococcus, one third to an assortment of viruses among which herpes simplex is important, and the remaining third are of unknown cause, presumably viruses that cannot be isolated with current tissue-culture techniques. Hemophilus influenzae is also capable of producing acute sore throats in young adults. Hemolytic streptococcus or an unknown viral agent would be the most likely cause in astronauts.

Acute Upper Respiratory Disease

This is the most common respiratory syndrome in young adults. It is termed ARD in the armed forces and acute URI in civilian circles. Acute upper respiratory diseases are due to a variety of causes among which influenza is the most important--accounting, on the average, for about one third. Parainfluenza is important, and occasionally adenovirus plays a role--a very important role in military recruits. The causes of about 50 percent of this syndrome have not been identified.

Acute Lower Respiratory Tract Illnesses

The primary atypical pneumonia syndrome is mainly important in young adults. Mycoplasma pneumoniae is the most common identifiable pathogen and accounts for at least 25-50 percent of this syndrome, depending on whether it is a year of high or low frequency for this agent, and is almost solely responsible for pneumonia with positive cold agglutinins. Adenoviruses, influenza, and parainfluenza viruses can also cause this syndrome; less commonly, Q fever and histoplasmosis may be responsible. Most astronauts are probably immune to M. pneumoniae; nevertheless, immunity should be determined by

antibody tests. This illness might be incapacitating during flight.

Lower Respiratory Tract Bacterial Illnesses

The advent of effective antimicrobial agents has altered the emphasis of the diagnostic approach in dealing with bacterial respiratory infections. At the present time, diagnostic efforts are directed toward identification of the likely causative agent of the infection as rapidly as possible so that effective antimicrobial therapy may begin without delay. It is therapeutically more important to group the causative organisms by their sensitivity to antibiotics than to identify the individual species or strain.

Bacterial infections of the lower respiratory tract follow four major clinical patterns: acute, subacute, chronic, and latent. Each of these patterns has potential relevance to problems of infection in prolonged spaceflights.

Acute Bacterial Infection In the adult, the principal form of acute lower respiratory tract bacterial infection is a localized pneumonitis. Symptoms begin with a cough and may progress in a matter of hours to pleuritic pain, chills, fever, trachypnea, sputum production, and prostration. Such infections may be caused by pneumococcus, streptococcus, occasionally staphylococcus, and, uncommonly in the adult, H. influenzae. Klebsiella pneumoniae may also produce these symptoms, and, under special conditions of depressed host resistance, other gram-negative rods may also produce pneumonitis. The gram-stained sputum smear is the best single guide to an immediate selection of antibiotic therapy. A second group of acute pneumonitides may also be caused by the spread of gram-negative organisms and, on occasion, by anaerobic organisms from other regions of the body, particularly the gut, urinary tract, female genital tract, or wounds. Under these circumstances, the infection is likely to commence secondarily to symptoms of septicemia. Sputum may be scant and diagnosis is difficult. Causative organisms consist largely of the bowel flora, such as Escherichia coli, bacteroides, and anaerobic streptococci. The third form of acute bacterial infection may follow aspiration of oropharyngeal material and is characterized by chills and fever and the development of a pulmonary abscess. This lesion is usually associated with anaerobic organisms of the mouth and responds best to penicillin therapy.

Subacute Bacterial Infection The most common form of subacute infection of the lower respiratory tract is the prolonged bronchitis that follows simple upper respiratory tract infections in certain individuals. Symptomatology is minimal and consists of a chronic cough and sputum production with some fatigue and occasional wheezing, characteristically following an otherwise unremarkable respiratory tract infection. Organisms associated with this type of infection are pneumococcus, Hemophilus, and other members of the normal throat flora. This type of infection is of importance because of its potential to progress to pneumonia under the appropriate circumstances, particularly where there is some alteration of host resistance mechanisms in the lung. Pulmonary abscess may also assume a subacute form, which is characterized by nonspecific symptoms of cough, sputum production, and generalized fatigue. It is important also to note that certain chronic infections of the lung may assume subacute form in a reactivated state and give rise to symptoms of cough, night sweats and daily fevers, weakness, and weight loss. Tuberculosis is the classical example, but other fungal infections such as histoplasmosis and coccidioidomycosis may also produce these symptoms.

Chronic Bacterial Infection The most common chronic infection of the lower respiratory tract is chronic bronchitis. This illness is characterized by chronic cough and sputum production and is sometimes associated with nocturnal wheezing. This illness is most commonly associated with cigarette smoking. Although it is less likely to be found in healthy astronauts, it is a potential hazard on spaceflights of long duration where alterations in host-resistance mechanisms may permit symptoms of bronchial infection to arise. The most common causative organisms are pneumococcus, Hemophilus, and occasionally staphylococci and other gram-negative forms, such as *E. coli* and *Klebsiella aerobacter*. Whether this form of infection will appear on spaceflights is likely to depend almost entirely on the effects of long-term spaceflights on host resistance mechanisms of the lung. In similar fashion, it is well documented that tuberculosis may assume a chronic active form due to reactivation in individuals who have been previously exposed to this bacillus. Histoplasmosis, coccidioidomycosis, and similar fungal infections may also become activated under conditions of prolonged stress and lowered host resistance.

Latent Bacterial Infection In the category of people with latent infections would be placed the individual who has had

previous exposure to organisms such as the tubercle bacillus, Histoplasma capsulatum, and Coccicidioides immitis, as manifested by positive reactions to intradermal testing. Any such individual may harbor the causative organisms in a latent state, and reactivated disease may occur under conditions of prolonged stress, nutritional changes, or depressed host resistance mechanisms. In the reactivated form, these organisms could be distributed to other crew members in whom acute infections might subsequently develop. This is particularly true of tuberculosis. Finally, an abundance of other organisms may be carried in a latent state in the lower respiratory tract to produce disease under conditions of severely depressed host resistance. This category includes organisms such as atypical mycobacteria, Pneumocystis carinii, and a variety of ordinarily nonpathogenic fungi like Candida albicans, Aspergillus, and Nocardia. The likelihood of this type of infection is admittedly slight as long as host defense mechanisms are maintained.

TRANSMISSION

The prolonged and close contact of the space cabin will produce circumstances highly favorable to spread of infection, enhanced, perhaps, by environmental conditions such as weightlessness and hyperoxia. The number of crew, the degree of intimacy of their living area, the number and types of microorganisms they bring with them on the flight, the opportunity they may have had for reaching a microbiological and immunological equilibrium with each other prior to departure, the level of personal hygiene--all these factors will affect the transmission of respiratory infections during flight.

Acute respiratory infections are transmitted through droplet nuclei and personal contact. As noted before, sneezing and coughing produce large numbers of infectious particles: in one experiment in which volunteers were inoculated with Coxsackie A 21 virus, a single sneeze produced an up to 15,000 tissue-culture dose of virus (TCID 50), while coughs resulted in an up to 9000 TCID 50 per sample.

Animal models have also yielded pertinent data. For several years Jerome L. Schulman of Cornell University Medical College has been working with an experimental model of transmission of influenza virus infection in mice. In this model, transmission is mediated by small airborne droplet nuclei, and

the spread of infection is not influenced by separation of infectors and contacts but is inversely related to the ventilation rate. Transmission was also found to be influenced profoundly by relative humidity and occurred in much greater frequency at lower relative humidity. Because of these considerations, investigation was made of the performance of a commercial chamber designed to control temperature and humidity at very low ventilation rates. When infected and contact animals were placed together in this chamber for 24 hours, no transmission of influenza virus infection occurred. Subsequently, it became evident that the rapid recycling of air through compression heating and humidification phases was effectively removing any airborne influenza virus. It is possible that the ventilating equipment on spacecraft efficiently and rapidly removes airborne microorganisms also. However, the performance of this equipment must be tested in flight as well as under ground conditions to ensure its adequacy under weightlessness. Furthermore, equipment capable of maintaining a low mean level of airborne microorganisms might not be able to prevent transitory accumulations following a cough, sneeze, or other activities that may release bursts of organisms into the air.

HOST DEFENSES OF THE BRONCHOPNEUMONARY TRACT

Man's lungs are normally sterile. Numerous studies have shown that, despite continuous exposure to environmental bacteria, the region from the primary bronchus downward is free of bacteria. The defense mechanisms responsible for the sterile state (see Table 2) are primarily phagocytosis by pulmonary macrophages and physical removal of invading bacteria via the mucociliary stream. Phagocytosis is dependent primarily on the efficiency of alveolar macrophages whose function, in turn, is governed by metabolic and immunologic factors, many of which are unique to these cells. It should be stressed that the potential threat of lower respiratory tract bacterial infections, at least, is more likely to depend on proper functioning of these defense mechanisms than on the effectiveness of the air filtration mechanisms in the space-cabin environment.

Data concerning the relative significance of each of the defense mechanisms in man is meager. Techniques for determining intrapulmonary bactericidal activity in the human have

TABLE 2 Host Defenses of the Bronchopneumonary Tract

Normal flora
Transport mechanisms
Mucociliary
Mucus
Respiratory tract fluid
Lymph fluid
Phagocytosis
Immunity
Salivary and resistance transfer factor secretory globulin
Serum immune globulin A (IGA), immune gamma globulin (IGG), immune globulin, M factor (IGM)
Lymphocyte transformation
Chemical and physiochemical action
Resistance transfer factor bactericidal activity
Surfactant

not been developed. Similarly, studies of human alveolar macrophage function are few and concern anatomic descriptions of the cell. More recently, radioisotope techniques have been developed which allow study of the mucociliary stream. These studies show transport rates between 10 and 20 mm min^{-1} and clearance of more than 90 percent of material deposited on the mucosa in less than one hour. Studies performed in patients with chronic lung disease have demonstrated impaired mucociliary clearance, presumably due to alterations in ciliary activity. The pathogenic significance of this impairment, however, is uncertain, because coughing results in rapid movement of large amounts of radioactive material and may compensate for the reduced rate of mucociliary flow.

In contrast with the limited amount of human data, there is a large body of experimental evidence from animals on host resistance to pulmonary infection. Experiments using murine models have demonstrated that in both mice and rats intrapulmonary phagocytosis is the primary defense against inhaled organisms. In these experiments, radiolabeled bacteria were killed within the lungs at a much more rapid rate than they were removed. By the use of fluorescent-labeled bacteria the macrophage was shown ingesting the inhaled organisms. Similar inhalation experiments have demonstrated that this remarkable defense system is sensitive to parasite and host factors.

Different bacteria are killed at different rates, and these differences in bactericidal susceptibility in part account for variations in virulence. As an example, Proteus mirabilis is killed at a much slower rate than is Staph. aureus, and in instances where intrapulmonary bactericidal activity is impaired, simultaneous aerosolization of Proteus and staphylococcal organisms results in multiplication of the Proteus but continued inactivation of the staphylococci.

In addition to being affected by parasite differences, the intrapulmonary bactericidal system is altered by host abnormalities that are associated clinically with increased susceptibility to pulmonary infection. Hypoxia, starvation, acute renal failure, metabolic acidosis, viral infection, or alcoholism inhibit bactericidal function. The pulmonary defense mechanism responds to physiological derangement but is relatively resistant to anatomic injury such as is produced by silica. This impairment due to physiological derangement is probably the mechanism for the enhancement of murine susceptibility to inhaled bacteria that is observed in hyperoxic conditions. Together these data suggest that impaired pulmonary bacterial resistance may occur among the astronauts, especially during prolonged spaceflight with hyperoxic conditions.

Physical removal of inhaled bacteria and small particle pollutants is accomplished by the mucociliary stream, cough reflex, and, to a much lesser extent, the lymphatic system. The mucociliary stream can be divided into ciliary and mucus components. The cilia, by moving in a coordinated manner, rapidly propel the overlying mucus from the lung. The mucus layer is principally derived from nonciliated goblet cells and is composed of mucopolysaccharides, lysozymes, and immune globulins. Inhaled particles adhere to the mucus and are carried from the lungs. Although it is reasonable to assume that the removal of noxious inanimate particles, such as silica, asbestos, and smoke, is important in pulmonary defense, it does not appear as certain that bacterial removal is as beneficial. In fact, the evidence for enhanced bacterial susceptibility in instances of mucociliary dysfunction is minimal. While the mucociliary stream may play a role in pulmonary bacterial defense, its importance appears to be considerably less than the intrapulmonary bactericidal activity of the lung. Many environmental factors, such as drying, cooling, sulfur dioxide, ozone, cigarette smoke, nitrogen dioxide, and inanition, affect mucociliary function adversely. Experimental influenza virus infections destroy tracheobronchial mucosa. These deleterious actions may enhance susceptibility to

bacterial infection, but few bacterial studies have been performed, and these do not show an increased risk in instances of mucociliary stream impairment due to such pollutants as sulfur dioxide.

With the exception of the possible presence of toxic gases and other chemical pollutants, spacecraft conditions should preclude mucociliary injury from the other known adverse factors, i.e., cooling, drying, inanition, and cigarette smoke. The effects of several pollutants on pulmonary defense function are discussed in Appendix A.

FACTORS OF CLOSED ECOLOGICAL SYSTEMS RELEVANT TO RESPIRATORY ILLNESSES

A number of studies of volunteers in large test chambers simulating some aspects of spaceflight have been made. To date, none has been of long enough duration, sufficiently closed, or with adequate simulation of the space environment to give meaningful perspectives on the effect on acute respiratory infections. Tests meeting some of these objectives are planned in the near future, but weightlessness and radiation and altered biological rhythms may be hard to simulate.

In Chapter 2 are reviewed the environmental factors expected to increase the likelihood of infections in spaceflight; these are naturally relevant to respiratory infections as well. Pertinent submarine and flight data are summarized below.

Submarine (Polaris) Experiments

Knowledge of respiratory infections in closed ecologic systems is derived principally from studies on nuclear submarines and is at best fragmentary. The major points result from studies largely carried out at Naval Biological Laboratory in fifteen nuclear (Polaris) cruises. Each cruise involved 110 to 140 men living in a closed system for up to eight weeks. Each submarine has two crews, the Blue and the Gold. The Blue crew makes the first extended patrol en route to its permanent overseas base. The Gold crew is flown to the overseas base in Holy Loch, Scotland, and is housed in a tender. On arrival of the submarine the two crews intermingle, after which the Blue crew goes home. The Gold crew then takes over, living on the

submarine for several days with continued contact with the tender personnel. Thus the Blue crew brings potential pathogens from the United States, circulates them among their own crew en route, then on arrival in Scotland mixes with the Gold crew, which, in turn, carries the "Scottish" pathogens that they have in the meanwhile acquired.

Three patterns of respiratory disease have been seen. In the first, the incidence of acute respiratory disease, usually mild, rises from 25 percent at the beginning of the cruise to a peak of 60 percent involvement of personnel by the tenth day at sea; this then declines to a low of roughly 10 percent from the third or fourth week onward. The second pattern is a delayed second wave occurring in about 1 in 20 or 25 patrols and is termed the "midpatrol" syndrome. Here, a late and more severe wave of respiratory infection occurs at about the third week and may involve 25 percent or so of the crew over the following two or three weeks. In only one instance--an outbreak of M. pneumoniae involving 11.2 percent of the crew--could an etiological agent be identified for this more severe disease. A third pattern of respiratory infection was seen when the refit period in Scotland was extended from two to three to four weeks. Under these circumstances, most infections occurred in the harbor, prior to departure. This prior intermingling and early pattern of disease prior to departure may be equivalent to quarantine or "microbiological equilibrium" periods for astronauts prior to departure.

Attempts to isolate viruses from over 5000 gargles or swabs taken from crew members having respiratory disease on patrol by inoculation into tissue cultures including diploid strains have yielded very few viruses. In only one instance has an isolate been made after two weeks at sea--a rhinovirus. Direct inoculation of tissue cultures at sea resulted in isolation of two respiratory syncytial viruses, one rhinovirus, an adenovirus, and some herpes viruses. The rhinovirus isolates were checked using sera obtained from the on-going patrol and from a previous patrol; no diagnostic increases were found, but many already had a 1:64 titer. In other studies, serological tests of paired sera from ill or healthy crew members for M. pneumoniae and ten respiratory viruses showed no rises. Environmental air sampling for bacteria and viruses showed no evidence of a buildup.

Spaceflight Data

Microbiological problems of acute respiratory disease on actual or simulated spaceflights have been subject to little study thus far. In a Gemini flight, bacterial sampling prior to and after flight revealed a simplification of the indigenous microflora and transfer of organisms between crew members. In studies by Soviet investigators, increased neutrophil activity and a tenfold increase in throat microorganisms were noted; they also found that dogs exposed to spaceflight conditions exhibited wavelike fluctuation of the phagocytic index. E. coli was also found in the oral cavity.

Crew members of recent Apollo flights have experienced common respiratory disease.

Apollo 7 (Schirra, Eisele, Cunningham, October 11, 1968. Duration: 260:09 hr): At least two crew members had symptoms of upper respiratory infection during the four days prior to flight. All three had symptoms during flight. All three were asymptomatic at recovery, but one (Cunningham) had serous fluid level in the left middle ear. Cunningham developed typical influenza syndrome during the first week post recovery. His preflight A_2-Asian "Hong Kong" titer was <1:10. Titer during third week postflight was 1:160. A_2 serologies on other crew members were not performed, but frozen sera (preflight and postflight samples) are available for later analysis. No crewmen were vaccinated with monovalent A_2-"Hong Kong" prior to flight or during immediate postflight period.

In the Apollo 7 backup crew, a rhinovirus was isolated from throat gargle but was not specifically typed. No rhinovirus was isolated from any crew member of Apollo 7. Serologies on the crew were negative for principal rhinovirus types and for influenza (complement fixation, CF) and common adenoviruses (CF) as well.

Apollo 8 (Borman, Lovell, Anders, December 21, 1968. Duration: 147:01 hr): No viral isolations from crew or backup crew. Diplococcus pneumoniae was identified: rough and nonencapsulated. No respiratory illnesses occurred, but Borman developed gastroenteritis with vomiting and diarrhea during early phase of the flight which was not transmitted to other crew members during the mission.

Apollo 9 (McDivitt, Scott, Schweickart, March 3, 1969. Duration: 241:01 hr): Only flight in which launch was postponed

because of crew preflight illness. Three days before launch, McDivitt developed malaise, nasal discharge, and stuffiness--not present (asymptomatic) on F-4 physical examination. Two days before original launch date, McDivitt and Schweickart developed upper respiratory infection and were treated symptomatically. All were well after a three-day postponement of launch. At 45 hours after launch, Schweickart developed nausea and vomited twice during intravehicular transfer into the lunar module. Symptoms were aggravated by his motion. Afebrile. After 24 hours, Schweickart was sufficiently recovered to perform modified extravehicular activities. Diagnosis was motion sickness.

Influenza B virus was isolated from postflight specimens from Schweickart (March 17) and McDivitt (March 21). Schweickart's children had clinical influenza and probably were the source of his illness; McDivitt's children contracted the disease from their father. The acute and convalescent sera were stored. Results on Scott were negative.

Apollo 10 (Stafford, Young, Cernan, May 18, 1969. Duration: 192:03 hr): No preflight, inflight, or postflight illness.

Apollo 11 (Armstrong, Collins, Aldrin, July 16, 1969. Duration: 195:18 hr): A squirrel monkey belonging to Aldrin died June 15, 1969. Postmortem revealed a streptococcal fulminating septicemia with probably antecedent pulmonary viral disease. Consultant made tissue diagnosis of toxoplasmosis.

Two crew members had oral polio booster on June 12, 1969; the third at a later date. Scheduled cultures on June 16, 1969, yielded polio virus, especially type II, in stools of all three.

PREVENTION AND THERAPY

The problem of acute respiratory disease should be limited largely to the immediate preflight period and to the first few days in flight. After that, the acute illnesses should have run their course, and the supply of susceptible persons should be exhausted. New infections cannot be introduced subsequently from outside, so that sources of illness would then arise mainly through activation of latent or carrier microorganisms due to alterations in host resistance. This aspect is dis-

cussed in Chapter 7. Preventive and therapeutic measures are summarized in Table 1 and discussed in Chapter 9.

Here it is important to emphasize that the specific control of acute respiratory disease is limited by the fact that 50 percent of the causes of the disease are unknown and that, of the known causes, commercial vaccine is available only for influenza and experimental vaccines only for type 4 adenoviruses and for M. pneumoniae. Thus prevention is dependent on allowing time prior to flight for the incubating illnesses to develop, prevention of new introductions of infection, and the preflight exchange of normal and pathogenic flora among the crew members. Selection of astronauts from the microbiological standpoint and identification of specific susceptibilities by an immunologic profile are also discussed in Chapter 9.

Specific Preventive Measures

The principal, specific preventive measures are identification of latent infection by tubercle bacilli or certain fungae such as Histoplasma and Coccidioides using the conventional intradermal skin tests. The question might be raised as to whether an individual with a positive tuberculin skin test represents a significant threat on prolonged spaceflight. In the absence of data, it is difficult to answer this question with certainty. The use of chemotherapeutic prophylaxis with isoniazid in space travelers having a positive tuberculin test should be given serious consideration.

Therapy

In general, therapy of lower respiratory tract bacterial infections centers on the use of antibiotic drugs that are effective against the causative species. The difficulty in spaceflight will be to identify the causative species bacteriologically so that suitable antimicrobial therapy can be initiated. Under these circumstances, two courses of action are open: to treat empirically for all respiratory tract infections with drugs such as penicillin, ampicillin, or tetracycline or to develop a simple laboratory kit for the presumptive diagnosis of the causative agent. In respiratory tract infections the most meaningful simple laboratory test is the gram-stain smear of the sputum. This test can determine whether bacterial infection is present and can tentatively

identify the causative species. It would seem quite feasible to develop a small kit specifically for spaceflight use; the kit would have particular significance in the diagnosis and treatment of respiratory infections and would also be of considerable value in the general field of microbiology. The gram-stain smear of the sputum permits a fairly accurate selection of appropriate chemotherapeutic agents, based on the four characteristic presentations of respiratory infection on the gram smear: (1) the pattern of mixed gram-positive flora, treatable with penicillin; (2) the pattern of mixed gram-positive and gram-negative flora, generally treatable with ampicillin or tetracycline; (3) the pattern of predominant staphylococcal organisms, readily identifiable morphologically and treatable with one of the semisynthetic penicillins like methicillin or naphicillin; and (4) the pattern of predominant gram-negative organisms, treatable with one of the broad-spectrum antibiotics like kanamycin. Tuberculosis could probably be controlled with isoniazid alone. Therapy of fungal infections is rather unsatisfactory at this time.

MAJOR UNANSWERED QUESTIONS

1. What is the effect of the space environment, including weightlessness, on transmission of infection, on primary and secondary immune mechanisms, and on host-parasite interaction?
2. To what extent can latent infections and carrier states reactivate under prolonged spaceflights?
3. In re-entry, is there a possibility of "microbial shock?"
4. Can the space environment so affect host immune mechanism as to permit microbial agents considered as nonpathogenic, or normal flora, to produce illness?

RECOMMENDATIONS

Research

1. Examine host-parasite relationships and the host immune responses to microbial challenge with respiratory pathogens in experimental models and under actual flight conditions. Uni-

versities and other research institutions should be encouraged to examine these questions as extensions of their basic research programs on similar phenomena on earth.

2. Determine in flight or in chamber tests the course of response to a live or inactivated vaccine to which the recipient has not had previous experience--Brucella or tularemia or cholera bacterial vaccines and live adenovirus type 4 oral vaccine are some examples. Determine immunoglobulin and other defense responses.

3. Perform epidemiological experiments, in simulated and actual flight, on the transmission of respiratory agents in relation to (a) number of persons or animals in the space chamber, (b) their state of susceptibility and resistance, (c) degree of confinement, i.e., space per unit animal or man, (d) number of microorganisms eliminated by the infected person, (e) type of aerosol produced, (f) enhancing effect of sneezing, coughing, talking. In doing this, mouse influenza might serve as an animal model, and the human volunteer studies of Knight, Jackson, and others might serve as approaches to the human model.

Operational

Operational recommendations concerning respiratory illness are given in Chapter 9.

Chapter 5

GASTROINTESTINAL DISEASES

The state of health of the gastrointestinal (GI) tract plays a governing role in utilization of diet, maintenance of adequate nutrition, and preservation of physical well-being. Deterioration in general performance commonly accompanies acute gastrointestinal dysfunction. Chronic gastrointestinal disease leads to undernutrition, decrease in stamina, and enhanced susceptibility to acute infection. Host defenses against disease depend fundamentally on adequate nutrition to provide the basic essentials for metabolism. Although much is known about diet, nutrition, and metabolism, relatively little is known about those microbiological factors of the GI tract that govern assimilation of nutrients and establishment of adequate mechanisms of defense. Even less is known about the potential liabilities of the conditions of prolonged spaceflight to preservation of optimal microbial balance and proper function of the GI tract. The reasons for ignorance are largely attributable to the complexities of microbial ecology in the gut and to the lack of adequate tools for investigation. The impressive advances of civilization in sanitary engineering, knowledge of dietary and nutritional requirements, and methods of food production and modification have so drastically diminished the great problems of classical GI infections that the impetus for study has waned. The fundamental questions of microbial ecology and host defense mechanisms remain unanswered. It is these more subtle problems that have relevance for prolonged spaceflight and that require the studies and investigations to be discussed and recommended in this report.

The GI tract is unique among body organs in its content of an extraordinary diversity and abundance of bacterial microorganisms (gastrointestinal flora). These organisms are found throughout the length of the GI tract but increase in numbers and in kinds as the contents move through the bowel. The numbers of bacteria increase from 10^3 to 10^6 bacteria per gram of contents in the anterior small intestine to numbers as high as 10^{10} and 10^{11} viable and active bacteria per gram of contents in the large intestine. There may be from 100 to 200 species of bacteria at any one time in the GI tract.

The intestinal tract normally carries pathogenic bacteria and potentially pathogenic bacteria. Clostridia, enterococci, Bacteroides, and even Escherichia coli are but a few of the species of normal intestinal flora which under appropriate conditions are found in human infections. Thus astronauts will take aboard the space capsule an abundance of potential pathogens in the flora of their own GI tracts. Whether disease develops will depend more, therefore, on environmental conditions in the spacecraft and the state of host defenses of the astronaut than on the availability of potentially pathogenic species. These organisms may be looked upon as a microbiological time-bomb that awaits only deterioration or alteration of host defense mechanisms or an upset of the environmental or ecological balance to exert their full pathogenic potential.

The normal microflora appears to exert a powerful inhibiting activity against the introduction of new organisms, whether they be pathogens or nonpathogens. For example, it requires the ingestion of 10^7 to 10^8 typhoid bacilli before these organisms--which are intestinal pathogens--can be cultivated from the feces. Larger inocula are necessary to produce symptoms.

Another function of the microflora is the alteration of metabolites. Such alterations may produce either desirable or undesirable effects in the host. Vitamin K in newborn infants and many of the B vitamins are synthesized by microorganisms of the normal gut flora with benefit to the host. Other transformations, such as aromatization of certain organic compounds, may be harmful. It is possible that metabolites which are nontoxic in the general earth environment may become toxic in altered environments either because of increased or altered production in the gut or because the receptor of the pharmacologic action within the host may be altered by the unique space environment. Such alterations of microbial metabolism may produce chemical materials which when absorbed or liberated into the atmosphere might produce secondary effects on other organ systems, most notably the skin and respiratory tract. Some normal by-products of microbial metabolism in the gut may also be undesirable in a closed space; hydrogen sulfide, methane, and indol are possible examples, and appreciable amounts of methane have already been measured in previous spaceflights. In prolonged spaceflights, accumulation of these substances could be substantial.

Symptoms of GI infection can be induced by noninfectious causes such as changes of diet, antibiotic therapy, or psychologically generated stimuli. The introduction of a new flora associated with dietary changes is often associated with brief episodes of diarrhea, and accommodation to new flora may take

up to two weeks. Although previous experience indicates that there is some exchange of flora among inhabitants of a confined space environment, it has not been demonstrated that this exchange has any deleterious effect on the microecology of the GI tract or the normal function of microorganisms.

Since gastrointestinal disorders have already occurred in spaceflights or in simulated chamber studies, we cannot assume that future space missions will be free of this problem. On the Apollo 7 flight, GI symptoms were limited to motion sickness. On Apollo 8, one crew member suffered nausea, vomiting, and diarrhea, with accompanying disability. The causative organism was not determined, because the nature of waste disposal on the spacecraft prevented adequate viral or bacteriological culture. While acute GI infections will always be a hazard, these infections are generally self-limited and without prolonged consequences. It is not unlikely, however, that because of the difficulty of distinguishing infectious and noninfectious causes of gastroenteric symptoms, such symptoms will be treated someday with broad-spectrum antibiotics--with devastating effect on the gastrointestinal flora. There is no information at present whether under spaceflight conditions normal GI flora will be restored. If not, impairment of host defenses and nutritional deficiencies may be anticipated.

Clearly the problems of gastrointestinal microbiology are far broader than those involving specific acute infections.

SPECIFIC INFECTIOUS AGENTS

The gastrointestinal tract is susceptible to many infectious and noninfectious agents which act to disturb the organ functionally. Agents of infectious origin include the well-known organisms, Salmonella, Shigella, enteropathogenic E. coli, Staphylococcus, Proteus, Pseudomonas, Streptococcus fecalis, Vibrio comma, noncholera Vibrios, and Clostridium welchii. Less commonly encountered bacterial pathogens include Edwardsiella tarda, Aeromonas hydrophilia, Aeromonas shigelloides, and Yersinia enterocolitica. In addition, mycobateria and other fungi (including Histoplasma, Candida, and Actinomyces) are also documented as infectious pathogens of the GI tract. Viral agents are known to account for certain gastroentertides and are probably responsible for many more symptomatic episodes in which they are uncultivable. Such

agents include enterovirus, adenovirus, measles, viral hepatitis, and lymphogranuloma.

Host-pathogen interactions are governed by variable pathogenetic factors. The work of R. B. Hornick, University of Maryland School of Medicine, shows that a dose-response relationship is evident in bacterial gastrointestinal infection. In clinical studies of typhoid infection, as many as 10^3 organisms were noninfective for the 14 individuals exposed; 10^5 organisms fed to 116 individuals infected only 32, whereas 10^7 organisms infected only 50 percent of 32 persons. When the inoculum was raised to 10^8 and 10^9, more than 90 percent of those so inoculated became infected. The astonishing ability of the GI tract to protect itself against such large numbers of virulent microorganisms documents the power of the normal microbial flora of the gut and emphasizes the importance of maintaining the normal flora. When the normal flora is eliminated by broad-spectrum antimicrobial therapy, as few as 100 organisms introduced in the same manner are capable of infecting the intestinal tract. Vibrio comma, the organism responsible for cholera, follows similar principles of quantitative infection. More than 10^8 organisms are required to establish symptomatic infection. These quantitative data indicate that protection need not be absolute in terms of environmental control in order to prevent acute gastrointestinal infection.

By contrast, Shigella is capable of infecting the GI tract with relatively few organisms. Therefore, methods of sanitation which might be adequate to control typhoid or cholera might not be adequate in cases in which only a few organisms are required for infection.

Since most infectious agents involved in human enteric disease are highly host-specific, it is difficult to set up animal models of gastrointestinal infections using the infectious agents that are pathogenic for man. However, a great deal of pathogenetic information has been obtained in man which is useful in understanding bowel infections.

Four pathogenic mechanisms of injury in the bowel commonly result in diarrhea. The first is the exotoxin pattern characteristically produced by cholera. The infecting organisms lie next to the epithelial cells or the gut and excrete exotoxin, which induces some type of cellular paralysis whereby extensive amounts of fluid are lost into the lumen of the gut. The organisms do not penetrate the cells and do not penetrate the gut wall. The toxic disease produced by staphylococcal food poisoning has similar mechanisms, as does the infection of Giardia lamblia. Staphylococcal enterotoxin affects mitochondria without invasion of the cells by the bacteria.

The second mechanism is partial penetration of the intestinal epithelial lining. This mechanism is involved in intestinal spirochetal disease in animals and is not significant in man.

The third mechanism is invasion of the superficial epithelial cells by the infecting bacteria. This mechanism is characteristic of bacillary dysentery. The organisms do not enter the submucosa, so there is no systemic spread. There is, however, extensive production of mucus, ulcer formation, and, in the healing process, Crypt abscesses. The inflammatory reaction is limited to the diseased bowel wall.

In the fourth mechanism, characteristic of salmonellosis, bacteria invade the gut wall without damaging the epithelial cells. The organisms pass between the epithelial cells and do not multiply in the cells. A leukocyte response rapidly eliminates the organism. In typhoid fever, a monocytic response occurs, presumably related to different chemotactic factors produced by that organism.

The carrier state which frequently follows Salmonella infection and, in some cases, Shigella infection is a special consideration involving unknown pathogenic mechanisms. In the carrier state, organisms persist in some location in the bowel from which they may excrete sufficient numbers of organisms to be cultivable in the stool or, more commonly, may remain entirely undetectable within the GI tract. Autopsy studies of apparently uninfected individuals have demonstrated that the bowel may carry and be culture-positive for Salmonella and Shigella where there had been no evidence of such a carrier state during life. The mechanism of this particular host-parasite relationship is unknown but represents a fairly considerable hazard for long-term space travel in which alterations of host-defense mechanisms may liberate and reactivate latent Salmonella or Shigella infection.

The morphologic response of the host to invasion by pathogenic microorganisms is influenced by three principal factors: (1) The general condition of the host and the capacity of host tissues to react to the invading organism. A major mechanism of defense of the host involves rapid cell turnover. In conditions of poor nutrition and cell depletion, this host-defense mechanism may be incapable of effectively defending the host. (2) The nature of the injurious agent and the intensity of the stimulus. Specifically, the genetically determined presence of the Vi antigen is associated with increased pathogenicity of the invading microorganism. (3) The anatomical location of the invasion and organization of tissue at the invasion

site. Motility of the bowel, tonus, the secretory apparatus, and capacity for cell turnover and renewal are determined in part by the anatomical location and tissue organization at a given level of the small bowel.

The small bowel responds in four major morphologic ways to injury of the microbial type: (1) Increased turnover and shedding of epithelial cells. This serves to carry infected cells into the gut lumen and away from the wall of the intestine. (2) Discharge of mucus and altered goblet-cell function. (3) Degenerative changes of intestinal chief cells, affecting both absorption and secretion during acute infections. (4) Inflammatory cellular and vascular reactions of the lamina propria. This may result in the secretion of secretory globulins into the gut lumen as part of the host's defense mechanism.

It is of interest that involvement of the intestinal tract with microorganisms is not necessarily equated with disease. Subclinical infection and inflammation of the bowel wall may be found in the absence of symptoms of active infection. In addition, defensive mechanisms themselves may be harmful to the host. Rapid cell turnover results in the appearance of immature cells at the surface of the gut lumen which may adversely affect absorption of various toxic and metabolic products from the gut lumen into the systemic circulation. Altered mucus production may affect the protective mechanisms of the epithelial lining and also alter absorption. Finally, the inflammatory and cellular responses of acute inflammation may lead to immunologic damage. Enteritis gangrenosa in typhoid fever is an example of an immunologic Schwartzman phenomenon whereby fibrin precipitated in the reaction serves to immobilize bacterial pathogens involving the lamina propria but may also result in thrombosis of vessels in the bowel wall, leading to subsequent tissue necrosis.

In addition to morphologic and cellular responses to acute infection, the bowel also manifests microbiological responses to acute infection. Studies utilizing a triple-lumen tube introduced into the small bowel show that symptoms of GI infections may be due to the displacement of normal flora found in the lower GI tract to a position high in the jejunum. This type of symptomatology may be suppressed by antibiotic therapy, which eliminates the normal flora in the upper GI tract. Similarily, when Shigella organisms are introduced distally in the small intestine, the E. coli move into areas of the bowel in which they are not normally found, and symptoms result. In human Shigella infections, there is a decrease in short-chain fatty acids, and, at the same time,

a replacement of E. coli is found. The effect is relevant to aerobic flora but not to anaerobic flora. However, it is of interest that the E. coli return to the infected area of bowel before the Shigella disappear. These data illustrate that despite the apparent complexity of damage to intestinal microbial ecology, it is possible to uncover a precise mechanism and to make predictions when phenomena are carefully isolated and diligently investigated.

CLINICAL SYNDROMES

The clinical characteristics of acute GI infections are well documented in the medical literature and will be summarized here very briefly. Infection of the GI tract expresses itself in one of five general patterns of disease.

1. The first pattern is acute gastroenteritis of abrupt onset with nausea, vomiting, intestinal cramps, and diarrhea but without preceding fever due to upper respiratory infection, excessive fluid loss, prostration, or constitutional symptoms. It is a common malady associated with viral infections, changes of diet, stress, other environmental factors, and mild food poisonings due to enterotoxins or to Salmonella or other organisms of low virulence. The most common variety, which appears to be infectious and occurs at all ages and in families worldwide, is highly contagious and has an incubation period of 1 to 5 days with an average of 3 days. Symptoms last 1 or 2 days. Although this disease is felt to be often of viral origin such as by the Marcy agent virus, documentation by stool culture is usually unrewarded. This illness is generally self-limited and of little consequence, but it does reduce function and may severely hamper effective performance of complex duties. On occasion, a serious underlying chronic illness such as ulcerative colitis may be activated by otherwise apparently mild GI infection of this nature.

Although this type of disease is usually caused by viruses or by changes in normal microflora due to diet changes, it is not infrequently caused by bacterial infection. Bacterial infection takes two forms: (a) Enterotoxicity produced by an exotoxin such as in staphylococcal food poisoning. This infection has an incubation period of minutes to 6 to 12 hours, and is characterized by nausea, vomiting, sometimes violent abdominal cramps, and diarrhea but is without fever

or prostration. Bacterial cultures may be unrewarding because the toxin is elaborated outside the body, usually in food products. (b) Salmonella infection, usually distinguished from (a) on the basis of incubation time and culture results. In general, Salmonella infection incubates for 12 to 24 hours, and sometimes as long as 36 hours, before the onset of nausea, vomiting, and diarrhea. On careful culture the offending organism may be recovered. Again, this illness is associated with discomfort but is usually without serious effects. Similar symptoms of nausea, vomiting, and diarrhea may be produced by severe alterations of bowel microflora due to administration of broad-spectrum antibiotics.

2. The second type of clinical disease is similar to the first in that it involves the characteristic GI symptoms of nausea, vomiting, and diarrhea, but the symptoms, especially the diarrhea, tend to be far more extensive, involve extensive fluid loss, and may, if not treated, result in severe prostration. These are diseases such as bacillary dysentery and cholera caused by organisms which show no penetration, or only slight penetration, into the bowel mucosa. Chills may result after extensive fluid loss, and fever may result from dehydration or absorption of intestinal endotoxins. Generally these illnesses can be managed very well by fluid replacement.

3. The third type of GI disease is that in which the route of invasion is the GI tract, but the symptoms are more of systemic nature than related to the bowel. Nausea, vomiting, and diarrhea are minimal, and, in fact, constipation is more characteristic. Abdominal pain, fever, and constitutional symptoms are marked. This general type of response is found in some enterovirus and adenovirus diseases and, in more severe form, in typhoid fever. The viral form incubates for 1 to 2 days and symptoms persist for 1 to 2 days. It is less contagious than the diarrheal form of viral infection and was reproduced by William S. Jordan and co-workers at Western Reserve University in 1953 by feeding fecal supernates from patients with diarrhea (the F. S. agent virus). In typhoid fever, the illness is characterized by systemic multiplication and spread of the Salmonella organisms and progressive elevation of fever. During this time, blood cultures may be positive, although the stools may be negative. During the second week, there is a secondary invasion of the bowel resulting in GI symptoms and the beginning of positive stool cultures. Resolution is by lysis. Symptomatology and fever can be suppressed by antibiotics, but the carrier state is not affected, even though stool cultures may turn negative temporarily. A major public-

health hazard and potential hazard on spacecraft regarding Salmonella infection is the establishment of this carrier state (see item 5).

4. A fourth pattern of GI infection is characterized by chronic infectious states of the small bowel. Symptoms are of chronic bowel dysfunction characterized by steatorrhea, specific deficiency states, and chronic malnutrition.

5. Finally, an important pattern of bowel infection is the carrier state whereby organisms such as Salmonella or Shigella may be carried in the GI tract as a latent infection. This form of infection is probably the most dangerous from the point of view of long-term space travel because it may be undetectable preflight and, if reactivated in flight, could induce significant disease in the carrier and potential spread to other members of the crew. To date, there is little evidence that this form of infection is any appreciable threat, but our knowledge of the carrier-state mechanism indicates that a bacterial carrier runs considerably greater risk of infection in long-term space travel.

TRANSMISSION

Much has been learned in the past century about the origin and transmission of GI infections. Much of the reduction of severe GI disease can be attributed to the recognition of the communicability of infectious organisms through drinking water and the establishment of extensive public-health measures to protect water supply. The importance of the waterborne route of transmission is emphasized when sanitary precautions break down and fecal contamination of drinking water occurs. This is usually accidental but almost always accompanied sooner or later by outbreaks of GI infection, most usually of bacillary dysentery or typhoid fever. In civilian life then, water is undoubtedly the most important means of transmission of GI infection. It is to be anticipated that under spacecraft conditions, water would again be the major vehicle of transmission, and this would be particularly likely in a closed ecological system in which water is regenerated from body waste materials. Even in the absence of such cycling procedures, ample opportunity might exist for contamination of drinking water supplies either by direct fecal inoculation of drinking water or through the deposition of fecal material

suspended in aerosols or transmitted to drinking water by the hands or utensils of the astronauts. Similar contamination of food is possible but less likely as long as food continues to be dispensed in sealed and sterilized containers. As diets become liberalized on spacecraft, the usual measures for food preservation and sanitation practiced on earth must be followed on spaceflights. The prolonged close contact among the astronauts increases the likelihood of transmission, so that if an infection is brought on board either in an incubating or in a carrier state, it is quite apt to be transmitted to one or more of the remaining crew.

Transmission of GI infections is usually fecal-oral, hand-to-mouth, but, under spacecraft conditions, may be enhanced by aerosols. Moreover, although the evidence is scant, it is reasonable to postulate that GI infection could be transmitted by way of the respiratory tract whereby inhaled aerosolized material would find its way into the GI tract by way of the mucociliary escalator.

In general, the problems of transmission of GI infection are not felt to be so serious as those of the respiratory tract. However, the extensive fecal contamination of the interior of the spacecraft and of the hands of the astronauts that was demonstrated by culture in one of the Apollo missions is evidence of the importance of this mode of transmission and of the potential hazard on future space missions. Likewise, the finding of beta hemolytic streptococci, apparently of bowel origin, and its spread during an early Apollo flight, again indicate that control of fecal contamination is of importance to prevent the transmission of bowel-grown organisms from one space crew member to another. In general, such transmission, except in the case of a virulent intestinal pathogen, would result in no disease in the healthy crew member. However, the preservation of adequate host defenses on long-term spaceflights has not yet been demonstrated, and, until this has been done, there should be increased efforts to interrupt the chain of infection and transmission within the spacecraft.

HOST DEFENSE MECHANISMS

One of the major concerns about long-term space travel is the maintenance of the adequacy of host defense mechanisms under

the abnormal conditions of the spacecraft environment. Before considering what alterations might occur, it would be of value to review briefly the host defense mechanisms of the GI tract. The mechanism by which the upper GI tract is kept clear of facultative organisms (those which can be conventionally cultured in the clinical laboratory) appears to be primarily by mechanical transport. Studies have demonstrated that radio isotope-labeled bacteria deposited in the upper GI tract are rapidly moved caudad without concurrent reduction in the viability of the organisms. Although these studies demonstrate the fate of facultative organisms, it is difficult to explain the persistence of anaerobic organisms in considerable numbers in the upper intestinal tract, because one would expect that they would likewise be carried downstream by the motive forces of the upper GI tract. The mechanical cleansing of the upper GI tract is apparently produced by peristaltic action, by mucus secretion, and by the flow of the succus entericus through the lumen of the small bowel. The notion that motility is the major mechanism of defense in the small bowel is supported by the reports of enhanced susceptibility to infection in the small bowel under conditions where motility is suppressed.

The second major defense of the GI tract against invasion by outside microorganisms is the normal host flora. The operative mechanism is not well understood, but current formulations indicate that the invading organisms are suppressed by competition for nutrients and oxygen and by the acids produced by the anaerobic flora of the gut. Perhaps the best proof of the prime importance of the normal flora in inhibiting or suppressing infection evolves from experience with broad-spectrum antibiotics in which elimination of the normal host flora results in multiplication of species such as staphylococci or yeast organisms, with resultant symptoms of gastroenteritis.

Other defense mechanisms in the bowel may involve rapid epithelial cell turnover with shedding of infected cells into the gut lumen, phagocytosis by surface phagocytes or epithial cells, and bactericidal action of surface enzymes such as lysozyme. Evidence for bactericidal mechanisms is questionable in the light of radiotracer studies, and definitive evidence is needed that secretory immunoglobulin (or immune globulin albumin) is active in the GI tract, as it appears to be in the respiratory tract. Indeed, the experiments using radio isotope-labeled bacteria in the GI lumen would suggest that little bactericidal activity occurs in the upper GI tract, but the experiments have been done with very few species.

It should be emphasized that much of the evidence on host defenses in the GI tract is rudimentary, and there is a serious lack of basic information. Recent impetus has come from the field of immunology, where it has been shown that in lower forms of animals, particularly in the chicken, lymphoid follicles lining the GI tract serve a major role in the development of immunological competence and particularly in the genesis of immunoglobulin-producing lymphocytes. Although this system remains undefined in man, the lymphoid structures of the appendix and possibly of the jejunum might serve similar functions in monitoring and regulating immunity to external and endogenous antigens.

It is generally felt that GI microflora are important to the defense of the entire body. This is partly due to experience with gnotobiotic (germ-free) animals in which alterations in host defense mechanisms and susceptibility to common, normally harmless microbial species have been amply demonstrated. However, there is, in fact, little parallel between the conditions of the spacecraft and the highly defined, specialized conditions of the gnotobiotic phenomenon. The extreme experiments of gnotobiotic animals demonstrate that although normal flora may decrease the absorption of nutritional materials and possibly even decrease the growth or weight of the host species, these disadvantages are far outweighted by the host defense role of the gut flora and by the conventional animal's superior ability to cope with the microbic environment of the external world.

FACTORS OF CLOSED ECOLOGICAL SYSTEMS RELEVANT TO PROBLEMS OF GASTROINTESTINAL INFECTION

Closed Ecological System

The major significant factor of closed ecological systems is the potential for fecal contamination of water and food supplies. The closed, confined space of the space vehicle with limited opportunity for diffusion away of organisms will present an ideal epidemiological setting for the spread of fecal organisms. The potential for cross-contamination and infection will depend greatly on the effectiveness of air filtration systems, sanitary engineering, and personal hygiene. The hazard to the health of the astronaut will depend in large

part on what species of microorganisms accumulate and on whether contamination is predominant in the air, in the water, or in the food. This is an area in which sanitary engineering should provide the answers, because the means and ways of preventing cross-contamination are well known. Only by inventive and imaginative developments in sanitation facilities and waste disposal, however, is this problem likely to be circumvented.

Whether the closed environment will have a deleterious effect on the maintenance of normal GI flora is a second major factor to be considered. Data from early spaceflights suggested that there was simplification of flora as to species, although later experiments, particularly the 56-day simulation studies of J. T. Cordaro (Brooks Air Force Base), showed relatively little change in the normal flora, with the single exception of a decreased number of enterococci. It is possible, however, that experiments which are completely closed in terms of contact with the external environment will show greater alterations of microbial flora. Little is known about the effects of single agents on the normal flora or on altering susceptibility to acute GI infection.

Diet has an important influence on content of bowel microflora, and many of the changes in flora which have been reported under various experimental conditions may, in fact, be attributed to dietary factors.

L. S. Gall, P. E. Rielly, and associates at Republic Aviation Corporation have studied the effects of freeze-dried diets on groups of subjects confined in space-cabin simulators. In some cases, a shift in types of organisms has been noted. In one of the reports, the shift was said to have resulted in the flora having a reduced capacity for synthesis of certain B vitamins. In no case, however, was there any clinical evidence of disease or reduced resistance to infection. The conclusion seemed warranted that prolonged use of space rations will not have deleterious effect on resistance to infection. Although there is no really hard evidence to contradict that conclusion, the importance of diet in regulating bowel flora would seem to warrant further study. It can be anticipated that the more nearly a diet simulates what is consumed on earth, the less likely there are to be unfavorable dietary influences on GI microbial flora.

Sterile air, food, and water have been postulated by T. D. Luckey (University of Missouri School of Medicine) to be a potential threat to the maintenance of adequate antigenic stimulation and of adequate bowel flora. Studies to date in simulated space-cabin environments do not seem to support that

hypothesis. A more serious outcome might be anticipated if the diet were sufficiently incomplete to result in undernutrition or in caloric or other specific insufficiency. Under these circumstances bowel flora might be altered. However, Maxwell Finland of Boston City Hospital reported that although starvation results in a change in flora, there was no evidence that that change per se resulted in disease.

A major question in the closed environment is the long-term effect on the bowel flora in the event that antibiotic therapy becomes necessary for other purposes. Under normal circumstances, the extensive alteration of the flora which occurs subsequent to antibiotic treatment reverts readily to normality on cessation of antibiotics. However, on space missions where there is a specialized diet and a decreased opportunity to ingest normal flora, the possibility exists that repopulation of the bowel will be delayed or that agents more deleterious to the host, e.g., yeasts or fungi, may repopulate it. This question is of considerable importance and should be readily amenable to laboratory investigation in animals and clinical investigation in simulated space environments.

Radiation

The GI tract is one of the early organs to be affected by radiation because of the high rate of turnover of the epithelial cells, and symptoms attributable to the GI tract are among the earliest to develop in radiation toxicity. Since mutation of bacterial species is a frequency-dependent phenomenon, one would expect that in areas of high concentration of bacteria the emergence of pathogenic mutants might be a prominent problem. Increased susceptibility to infection is a common complication following exposure to radiation and relates not only to pathogenic bacterial, viral, fungal, and protozoan agents but also to ordinarily harmless, common inhabitants of the GI tract. Presumably the increased susceptibility and sometimes fatal infections that ensue are due primarily to depressed host resistance mechanisms, but the possibility of pathogenic mutations must also be kept in mind. Radiation has many effects including reduction of the white cells and suppression of the bone marrow as well as inhibition of antibody production. Such effects might have considerable relevance for the GI tract because of the sensitivity of the epithelial cells and the abundance of microorganisms.

From the dosimetry readings on manned spaceflights to date, it would appear that radiation exposure is likely to be low and that protection will be adequate. Whether this will hold true for longer-term, more distant space missions where the hazard of solar flares and primary cosmic rays is greater is undetermined at this time. In addition, synergistic or additive effects of radiation combined with other stresses such as cabin environment, weightlessness, hypoxia, or hyperoxia might lower the threshold of response to otherwise tolerable doses of radiation. These combinations have not yet received adequate study.

Weightlessness

In view of the efficiency of propulsive mechanisms throughout the GI tract and the extensive bacterial multiplication that proceeds under normal circumstances, it seems doubtful that lack of gravity will have significant influence on the microbial flora of the gut. Weightlessness is much more likely to have an influence on aerosolized particles. Any aerosolized material driven into the atmosphere during the process of handling waste materials would likely remain suspended in the atmosphere, leading to a much higher opportunity for transmission to other crew members. Without adequate precautions or without excellent filtration devices, considerable fecal flora could build up in the air as well as on the surface of the space cabin.

Effect of Atmosphere

Changes in atmospheric pressure and composition have been reported to affect a wide variety of bacterial species and a variety of host defense mechanisms, but little specific information exists for the GI tract. Altitude effects on intestinal flora of animals have been reported and consist of minor quantitative changes or simplification of species. Similar studies in man have been reported, but the effects of altitude are difficult to separate from other variables being tested such as diet. Future experiments should make efforts to pair-feed animals so that the variables of such factors as altitude, hyperoxia, and hypoxia could be separated from the effects of reduced food intake.

PREVENTION AND THERAPY

General Control Measures

General control measures of gastrointestinal infection include: (1) general control of sanitary facilities, (2) control of food and water, (3) appropriate personal hygiene, and (4) the reduction or elimination of preflight contacts of potentially infectious nature, particularly likely to occur within families.

Diet, food, water, and waste disposal are at the moment reasonably well controlled. The basic sanitary facilities and opportunities for attending to personal hygiene, however, are not yet satisfactory on the spacecraft. Control of fecal contamination of the space-cabin surfaces, of the astronauts' hands, and of the air is the most important general control measure. It may become even more imperative when regenerative cycles are instituted. On the other hand, with appropriate treatment of waste material in the recycling procedure, the risk of fecal contamination could actually be less than at present. Air filtration and water filtration should be efficient. These requirements apply equally to the spacesuit. Finally, proper rest and regularity of habits are important in maintaining host defenses and in reducing the liability and susceptibility to infection.

Specific Preventive Measures

1. Astronauts' case histories should be used in determining susceptibility to GI infection during the training period as well as for detection of early GI infections during the preflight and in-flight period.

2. Gastrointestinal tract cultures should be made during the training and preflight periods to rule out the possibility of a carrier state for typhoid, Salmonella, and Shigella. At the moment, stool culture is the principal method used for bacteriologically assessing the GI tract. Some thought might be given to the procedure of aspirating upper intestinal contents with a triple-lumen tube to determine more satisfactorily the microbiology of the upper GI tract and thereby to increase the likelihood of detection of the carrier state. The validity of the latter possibility must be further verified.

3. Acute GI disease ought to be permitted to express itself during the preflight period in a quarantine situation.

4. Likewise, opportunity for exchange of fecal flora among the space crew should be provided preflight during the quarantine period.

5. Immunization is planned against typhoid, tetanus, and polio. The possibility of specific immunization against adenovirus and enteroviruses should be explored, although no definite recommendation is made for the use of such therapy at this time.

6. Improved methods of early detection of infection, such as amino acid analysis of the serum, should be developed to provide techniques for distinguishing infectious from noninfectious illness.

7. A most important, specific preventive measure is a strong caution against the indiscriminate use, particularly for minimal symptomatology, of pharmocologic agents and hemotherapeutic drugs which might seriously alter the microflora of the GI tract. Other than avoiding excessive use of broad-spectrum antibiotics, there is no specific preventive measure to prevent the changing of the microbial flora of the GI tract.

Therapy

It is desirable to treat a moderate illness, particularly in spaceflight conditions, empirically and symptomatically with fluids and appropriate diet. Most acute GI upsets are nonbacterial in origin and noninfectious. Antibiotic therapy has a questionable benefit for most GI infections. For these reasons, antibiotic therapy should be reserved for serious GI infections or for illnesses in which significant systemic effects are apparent.

MAJOR UNANSWERED QUESTIONS

1. What sanitary methods and systems are adequate for prolonged spaceflight? This is a recurring, practical problem of particular importance, and one that has been particularly stubborn.

2. What is the effect of prolonged confinement in an artificial, isolated environment on the bowel microflora,

host defenses, and nutrition; and what are the limits within which alterations can occur without serious consequences?

3. What are the causes of alterations in susceptibility to acute GI infections? What are the specific factors of microflora responsible for its potency as a host defense mechanism?

4. What is the role of viruses in GI disease? Here the principal difficulty is the lack of adequate methods of cultivating and sampling GI secretions.

5. What detection methods can be employed to detect GI infections in their early states, carrier states, infectious as opposed to noninfectious illnesses, and differences in the microflora of the small and large intestines? Here, again, inadequate techniques are the main stumbling block.

6. What is the influence of dietary factors on microflora?

7. Will normal bowel flora be restored on prolonged spaceflights in the event that antibiotic therapy is necessary for other purposes? If so, by what mechanisms? These questions are of primary importance and should be readily amenable to laboratory investigation in animals and clinical investigation in simulated space environments.

RECOMMENDATIONS

Research

1. Continue efforts to improve waste-disposal systems and facilities for personal hygiene.

2. Initiate broad-based and extensive research programs on the effects of prolonged environmental alterations and isolations on gut microflora, host defenses, and nutrition. Direct microscopic examination should be done on all bacterial samples to ensure adequate cultural procedures.

3. Establish practical research projects to explore ways of repopulating bowel flora in the event that broad-spectrum chemotherapy becomes necessary on spaceflights of long duration. Such means might be achieved through dietary manipulation or through the actual feeding of bacteria carried along in stored form for such an eventuality.

4. Develop improved methods for sampling bowel flora, for detecting carrier states, and for distinguishing between

infectious and noninfectious symptomatic disease of the gastrointestinal tract.

5. Determine the role of virus infection in gastrointestinal disease and explore the possibility of immunization or prophylaxis against the common or more serious varieties of gastrointestinal viral pathogens.

Operational

6. Institute a preflight period or program of controlled, progressive, preventive diagnostic isolation (i.e., quarantine) to: (a) permit acute disease to express itself, (b) prevent contact and infection of the astronauts by the general population, (c) permit cross-contact of flora and exchange of microorganisms among the prospective spacecraft crew. This period of isolation should be a minimum of 3 to 5 days for viral infections and 10 to 14 days for the prophylaxis of typhoid fever.

7. Administer an adequate dosage of gamma globulin preflight as a prophylaxis against infectious hepatitis.

8. Prohibit the arbitrary use on space missions of antibiotics, particularly the broad-spectrum antibiotics, because of the disastrous effects of these agents on the bowel microflora.

Chapter 6

CUTANEOUS INFECTIONS

The skin is a special organ of the body with a characteristic microflora and is subject to its own types of disease, including infections peculiar to it alone. Because its outer layer, at least, is exposed to the ambient environment, radical changes in the environment threaten the physiological homeostatis of the skin. A marked change, such as a vacation at the seashore, may result in a complete change in the staphylococcal microflora of the skin. It is therefore important to examine the potential effects of prolonged exposure to altered atmospheric conditions and of other factors in the space environment on the microbiology of the skin and its susceptibility to cutaneous infections. This problem area, as well as prophylaxis or treatment, is discussed in this chapter. Infection of wounds of the skin is not considered.

A healthy condition of the human skin involves constant growth of epithelial cells in the germinal layer and shedding of cornified cells from the outer layer of the epidermis. This process can be thought of as being in equilibrium with adverse influences at the surface, such as mechanical trauma resulting in abrasions, contact with chemically harmful substances, and growth of microorganisms on or within the skin. Although the large population of microorganisms which normally reside on the skin may not be harmful and, in fact, may be beneficial, their numbers and types at any one time are the product of a dynamic process, for the most part in equilibrium. The cutaneous bacteria have been quite properly called an ecological system, subject to the many factors that influence any ecosystem of single or mixed species.

Such a biological equilibrium is subject to shifts, sometimes as the result of very minor or unrecognized factors. The space-cabin environment, being abnormal to man, may contain factors that will influence this ecosystem, at significant consequence to the health of the astronaut. The ecosystem we are considering, being on the surface of the body, would be expected to be stabilized less by host factors than would an internal system such as the microflora of the gut. Because the normal microflora of the skin is a key factor in

our discussion, considerable background information is given in the following section.

MICROFLORA OF THE SKIN

The normal human skin harbors relatively few types of microorganisms, although they differ greatly in ratios and in total numbers from one area of the skin to another. Microorganisms are found primarily on the surface of the stratum corneum and in the pilosebaceous orifices. The largest numbers of bacteria are found on oily, hairy, moist, and dirty skin. Aerobic and anaerobic types of Corynebacterium and coagulase-negative micrococci constitute the principal bacteria types regarded as normal. C. minutissimum (aerobic), C. acnes (anaerobic), and Staphylococcus epidermidis are the foremost defined species. The lipid-requiring, yeast-like fungus, Pityrosporum ovale, and several of the ringworm fungi are also considered normal inhabitants. Bacteria of the genera Mima and Herellea are reported on the normal skin of 30 percent of people. The predominant factors known to control the incidence of these microorganisms are humidity and the presence of sebaceous secretions. Lipophilic types such as C. minutissimum are found in increased numbers in intertrigenous areas such as the axilla; smaller numbers of a more evenly distributed population are present in dry glabrous areas such as the skin of the back. When skin areas are unnaturally in contact or occluded, e.g., under adhesive tape, the microflora population tends to become more like that of naturally intertrigenous surfaces.

As in the intestinal tract, the microbial flora of the skin of any one individual at any one time consists of a hierarchy of bacterial clones. Barring any disturbance tending to upset the ecological balance achieved, this hierarchy remains stable from week to week for long periods of time. The cocci, primarily Staph. epidermidis, are particularly prone to mutation, apparently giving rise in this way to the numerous clonal types found on the skin. The skin of some individuals regularly supports heavy populations of microorganisms and that of others, relatively light populations. The large populations appear to be made up of fewer clonal types and are more stable. These are associated with what is popularly called dark, oily, or sweating complexions, as

contrasted with dry-skin types, the difference presumably related to the output of sebum. (Very little has been done to translate these subjective lay terms into scientifically objective and measurable descriptions.) Superimposed on this relationship between skin types in the adult and the bacterial flora is the effect of personal cleanliness. Infrequent bathing enormously increases the number of microorganisms on the skin and tends to favor the addition of microorganisms which are not truly native to the skin.

Dispersion of Bacteria from the Skin

The horny layer of the skin is constantly being replaced from below, and the cells of the surface layer of the stratum corneum are constantly being shed into the environment, carrying with them any microorganisms that are present on them. The skin thus would appear to be potentially a significant source of bacterial dispersion. It has been shown that hospital personnel disperse more Staph. aureus from the skin below the belt than they do from the nose, and that following a bath this dispersal is temporarily and paradoxically increased. We have no data about the influence of various factors, such as bathing, on the rate of shedding of the epidermal cells.

Until recently the nose was thought to be the principal site in which coagulase-positive staphylococci were carried in normal persons. However, we know now that these staphylococci are frequently carried in the perineal region. These may or may not be a different group of Staph. aureus phage types than those found in the nose. The evidence is not conclusive. We would like to know, too, if the presence of Staph. aureus on the perineal skin is dependent on its presence in the bowel. An important point, however, is that once on the skin, it is effectively dispersed into the environment. The efficiency of bacterial dispersal from the skin is probably due to the buoyancy of the dry, flat, cornified cells of the skin surface. This may not be an especially greater problem under weightless conditions than it is on earth, although the effect of gravity on this dispersal is largely unknown.

Normal Skin Flora and the External Environment

The constant shedding of the cornified epidermis disperses the cutaneous flora widely in man's environment. Staph. epi-

dermidis and other forms may be isolated from many sources in the environment. It is not known to what extent the environmental micrococci and staphylococci, such as those that are particularly abundant in dairy products, are the same as those present in the normal skin. A similar cutaneous flora of micrococci is present on the skin of dogs and other animals. Isolates of the organisms from external environments are not, however, expected to be representative of the populations on the human skin. In particular, the coagulase-negative staphylococci, such as Staph. epidermidis from wounds and internal lesions, may not be typical of the skin flora. The important point, however, is that the major transport of bacteria is from the skin to the external environment in normal, healthy individuals rather than from the external environment to the skin.

SPECIFIC INFECTIOUS AGENTS

Opportunists which may sometimes be found on normal skin, but which do not ordinarily infect, are Staph. aureus, beta-hemolytic streptococci, Pseudomonas, Candida albicans, and the fungal dermatophytes. These can cause infections of varying types and severity, as can C. minutissimum and Staph. epidermidis when normal conditions are disturbed and they proliferate greatly. Pseudomonas is especially likely to infect the skin of the external auditory canal under humid conditions. Among the potentially pathogenic bacteria which are rather commonly encountered on the skin are gram-negative bacteria of the Mima and Herellea groups. These do not appear to produce lesions on the skin but are commonly present in intertrigenous sites. They may cause infections of the urinary tract and may produce septicemia if introduced into the blood stream. Their presence on the skin is therefore somewhat disconcerting.

Staph. aureus and other bacteria, principally gram-negative rods and streptococci, are the characteristic flora of skin lesions in which the stratum corneum has been denuded. Of these bacteria, group A hemolytic streptococci are the most significant. Recent studies suggest that they may be the only components of the flora of simple skin lesions that are capable of increasing the severity of the initial lesion and converting it into a true bacterial infection. It is rather surprising to realize that there is very little information, perhaps no defin-

itive information, that implicates Staph. aureus as a cause of skin infections in the adult other than boils and abscesses. This common pus-forming coccus nevertheless is virtually ubiquitous in sores on the skin. Current evidence is more and more tending to deprecate its significance in denuded lesions of the skin, although it can be a serious pathogen in deeper tissues of the body.

DEFENSE MECHANISMS

The balance between health and infectious disease in the skin is the result of the constant battle between host defense mechanisms and environmental factors that permit invasion of normally avirulent bacteria. Host defense mechanisms include: the mechanical barrier of the keratinous protein in the superficial layers of epithelium; maintenance of optimal balance between excessive dryness and moisture; shedding of superficial epithelia cells; periodic aqueous cleansing; the normal host microflora; appropriate pH; and certain surface lipids and fatty acids that favor the growth of normal flora to the detriment of potential pathogens.

Factors in the environment that tend to break down host defenses include: abrasion; excessive moisture caused by sweating or lack of ventilation, which leads to maceration; confinement, which limits convection currents and thus the disposal of moisture and of shed epithelial cells; lack of aqueous cleansing; alterations in pH; and destruction or alteration of surface lipids. Some of these mechanisms are discussed below.

Acid pH of Skin Surface

The skin surface maintains an acid pH of about 5.5 which has been thought, but without adequate experimental proof, to confer antibacterial defense against most potentially pathogenic bacteria. It is true that certain important bacteria, such as hemolytic streptococci, may be sensitive to this amount of acidity or perhaps more specifically to fatty acids. However, it probably is also a desirable pH for maintaining the undenatured, insoluble form of the keratinous proteins of the stratum corneum. The sources of the pH control are unknown,

but there are reasons to suspect that it is produced by the normal bacterial flora of the skin which are capable of producing fatty acids by lipolytic and fermentative activities on the skin. Changes toward the alkaline in the pH of the skin surface, particularly in intertrigenous areas, are frequently associated with the presence of gram-negative bacteria, yeasts, and other foreign microflora. It was once though that the presence of these organisms was a result of the breakdown of the "acid mantle" of the skin. It appears more likely, however, that the alkaline changes are a consequence of the displacement of the normal bacterial flora by other bacteria.

Role of Surface Lipids

Many of the microorganisms that reside on the skin are lipid-dependent, and most of them hydrolyse fats. None of the bacteria except the erythrasma diphtheroid, which seems to invade the horny-layer cells, and a strange new bacterium which causes pitting keratolysis of the soles of the feet, have given evidence of keratolytic properties. It seems probable, therefore, that the sebaceous secretions and lipid components of the stratum corneum have a major influence in determining the ecology of the skin surface. Electron micrographs support the notion that the normal bacteria grow in a thin layer of lipids and constantly evaporating water, with some additional dissolved nutrients, on the relatively impervious surface of the stratum corneum.

Moisture and Maceration

One of the common causes of a change in skin integrity is the collection of sweat under clothing where it can no longer perform its primary role of thermoregulation by evaporation but collects instead as a culture medium for many bacteria. With alkaline changes and hydration, the compact structure of the cornified barrier of the skin is probably disturbed by loosening of the molecular structure and actual solution of keratinous proteins. These conditions lead to the clinical condition of maceration of the stratum corneum, which renders the skin susceptible to infection, contact dermatitis, and chemical and physical damage. Pseudomonas, when it is present, may produce a potent keratolytic protease which further macerates the stratum corneum. Maceration

due to retention of sweat in skin folds is particularly troublesome in obese persons. A similar situation, resulting in diaper rash, is seen in infants constantly wet with urine. Defects in the performance of spacesuits with respect to control of sweat or to elimination of excreta could create similar problems. Bolstering the natural defensive properties of the human skin is a constant preoccupation of the cosmetic and soap industries. While, in spite of claims, no signal success has been achieved, the idea probably has merit. The normal adult skin is a relatively dry and water-repelling surface. Gram-negative bacteria such as E. coli lose viability within a few minutes on its surface. This seems to be due mainly to desiccation and matches the effect when these bacteria are placed on other dry surfaces. Under conditions of high environmental humidity and temperature, with profuse sweating, E. coli cells remain viable in small numbers. It has been found that ambient temperature and ambient humidity both affect the persistance of such bacteria on the skin. Under tropical conditions, some microorganisms susceptible to desiccation are usually present on the skin. There are thus a variety of factors that render the skin unsuitable for easy colonization by foreign bacteria.

Importance of Normal Flora

The possibility that the normal skin bacteria may have an active role in the defense of the skin against other bacteria is an intriguing concept that is largely unexplored, although interest is quickening among workers in the field. As we have noted, bacterial counts are especially high in areas rich in sebaceous secretion and in intertrigenous skin folds. In the former site, however, a healthy population of Staph. epidermidis and lipid-requiring diphtheroids is the rule, whereas the latter site is prone to harbor the multiplication of bacteria foreign to the skin. Specific antibiotic substances or bacteriocins may be produced by the resident flora. There is minimal but strongly suggestive evidence for this. Many clones of Staph. epidermidis produce surface-active hemolysin, so-called delta hemolysin, which has a lytic effect on cell membranes. The antibacterial action of peroxidases in leukocytes, saliva, and, most interestingly, in milk is currently under study. Hydrogen peroxide- and catalase-producing bacteria have been shown to contribute to or influence this antibacterial effect. Because milk is produced by modified skin

glands, it would seem worthwhile to investigate other skin-gland secretions for similar activity. Lysozyme is also a possible factor in the natural control of skin microorganisms.

SPACECRAFT FACTORS RELEVANT TO CUTANEOUS INFECTION

The possibly significant factors of the space-cabin environment, with respect to cutaneous disease, include: (1) changes in humidity, particularly markedly increased humidity inside spacesuits; (2) changes in habits and methods of personal hygiene; (3) increased exposure of skin to bacteria due to greater numbers of bacteria accumulating in the spacecraft environment; and (4) altered content and pressure of the spacecraft atmosphere. Before discussing these further it will be useful to consider the observations made on personnel in the various tests performed in closed environmental systems.

Experimental Data

This section summarizes the rather considerable work that has been done on the microbiology of skin of subjects confined in altitude chambers, or comparably restricted environments, for varying periods of time. These are tabulated and abstracted in Appendix B. In a few of the studies, daily skin care was carried out. In most, however, it was not. The limited hygiene was therefore additive with confinement and close contact. The degree of crowding in altitude chambers did not as a rule match that of actual spacecraft. Periods of observation ranged from 14 to 60 days.

In nine of the studies, samples were taken from the skin areas to determine an incidence of general bacterial types. In four of these (A8, D2, F1, and H2), the data can be interpreted as indicating a steady state with no significant change. This was true also of A3 and A4, concerned only with micrococci. In four studies (A1, A5, A9, and H1), a definite increase in incidence was recorded, but in the case of H1, this followed immersion of divers into contaminated water and is not comparable with the others. The other three were tests in which the bacterial count in the atmosphere increased and in which a very poor level of personal hygiene prevailed.

In the McDonnell Douglas 60-day test (C2), full daily sponge baths were permitted. The bacterial incidence in the

air was low, and in this test the skin flora appears to decrease in numbers throughout the test.

A definite correlation is thus indicated between the incidence of bacteria on the skin and the numbers in the air. Conclusions from other studies indicate that bacteria from the skin are a usual source of bacteria in the air, and in the present tests poor personal hygiene evidently resulted in a higher bacterial count in the air by increasing the numbers of bacteria on the skin.

Other evidence indicates that persons vary in the degree to which skin bacteria are shed. It was observed in study C3 that microbial counts of the air samples increased when one of the four operators who worked on shifts was present in the chamber.

Rielly (A5) commented on the buildup of skin microorganisms and noted that the feet became uncomfortable in some subjects, and persons with histories of athlete's foot tended to have recurrence. Borchardt et al. (D1) reported that groins and axilae were reservoirs for potentially pathogenic Enterobacteriaceae. Kellett et al. (A9) reported on the wearing of pressure suits for 20 days. One subject showed some flaking of the skin, and another had two small pustules over the coccyx. Otherwise there were no skin problems. In the McDonnell Douglas study, there was some desquamation of the feet, concurrent with a buildup of micrococci. Rack and Loudon included preliminary scrubbing with hexachlorophene soap on one side of the body before subjects entered the experiment. In one individual, skin lesions developed on the feet, on the side that had not previously been scrubbed with hexachlorophene soap. Thus, although some skin lesions were observed, no serious disease occurred in spite of very poor hygienic conditions in some experiments.

Potential Effects of the Spacecraft Environment

The possibly significant factors of the space-cabin environment, enumerated at the beginning of this section, can now be considered.

Changes in Humidity The undesirable effects of increased humidity observed in the tests summarized above were brought about by prolonged wearing of spacesuits and were accompanied by restrictions on skin cleansing. In situations where this kind of regime will be necessary in spaceflight, some difficulty

could be anticipated. However, it is understood that in the foreseeable future spacesuits will be worn only for relatively short periods at critical times. Increased humidity of the skin environment should therefore not be a significant problem.

Changes in Habits of Personal Hygiene For the reasons given immediately above, it is assumed that a reasonable schedule of skin cleansing by some form of aqueous ablution will be feasible, and no problem is expected from accumulation of dirt on the skin.

Hazard of Skin Infection from Increased Numbers of Bacteria in Spacecraft Environment The possible buildup of microflora in the spacecraft environment is considered at length in Chapter 2. The conclusion is made that this is not expected to become a problem except in the case of breakdown of waste-disposal and life-support systems. Development of sensors to detect such events is recommended, as well as methods for disinfecting the environment in such an emergency. This potential hazard to health of the skin is therefore controlled best by removal of the source of infections.

Difference in Content and Pressure of Atmosphere Bacteria on the skin of astronauts will presumably be subjected to an altered atmosphere characterized by reduced pressure, altered ratios of O_2 to N_2, and, to some extent, an absolute partial pressure of O_2 higher than normal. These differences might be expected to provide pressures within the bacterial ecosystem favoring selection of other types of microorganisms than those normally found. This effect has not been observed, although optimal quantitative and qualitative techniques have probably not been applied. Further, the fairly steady state of the skin microflora (as determined at the species level) suggests that mechanisms exist by which the skin microflora are protected to considerable extent from external influences. It may be postulated, therefore, that the spacecraft atmosphere *per se* will not have a significant *direct* effect on the skin microflora, but further observations are indicated before this can be established.

CONTROL OF SKIN INFECTION IN ASTRONAUTS

Prevention

The primary preventive measure against skin disease during spaceflights is the maintenance of normal environmental conditions for the skin through the maintenance of a normal range of humidity, regular changes of clothing, and maintenance of cleanliness by a reasonable but not excessive schedule of skin cleansing.

Before flight, the personnel should be carefully examined by case history and inspection for any skin disorders, and every effort made to correct abnormalities.

The question might be asked whether an attempt should be made to remove potentially pathogenic microorganisms that might be identified on the skin before flight. We have no tried and proved method of getting rid of the undesirable transients on the skin surface. Various scrub-up preparations used in surgery, based on hexachlorophene and related compounds, selectively reduce the gram-positive normal flora of the skin. Such preparations may actually become contaminated with viable gram-negative bacteria such as Pseudomonas. The desirability of killing off the normal microflora of the skin with preparations which may at the same time inoculate the skin with Pseudomonas or encourage their growth is, to say the least, questionable. All local antiseptics are based more on tradition and faith than on objective evaluation. The normal skin cocci tolerate ordinary soap quite well, and a few vigorous scrubbing baths just prior to spaceflight might prove to be as effective as any measure to remove nonresident bacteria from the skin.

The effect of selectively suppressing the gram-positive microflora with antibacterial agents, such as neomycin and hexachlorophene, has been studied in intertrigenous areas as well as under dressings on nonintertrigenous skin. These measures are followed by the appearance of potentially deleterious gram-negative bacteria, such as Aerobacter, Pseudomonas, and E. coli, which are not primary residents of the normal skin surface. The native gram-positive microflora of the skin seems to prevent colonization of the skin by gram-negative bacteria.

Treatment

No need for special treatment of skin disorders is visualized. Standard methods are expected to be satisfactory, with the proviso that therapeutic agents be in the form of ointments or creams for easy handling and application, avoiding fluids and powders.

With respect to diagnosis of skin disorders in space, it should be remembered that dermatology is one area of medicine in which many diagnoses can be made by inspection alone. It is therefore conceivable that, with color television available, diagnosis can be facilitated through long-range observation by a qualified dermatologist on earth. The feasibility of this method rests primarily on the quality of the television pictures.

MAJOR UNANSWERED QUESTIONS

1. Will prolonged exposure to the abnormal atmosphere of spaceflight (increased O_2 ratios, decreased pressure) induce a change in the normal microflora of the skin, either by direct effects or indirectly through alteration in the microenvironment? Such changes could result in lowering of normal defense processes and the development of the skin disorders.

2. Correlated with the above, will the spacecraft environment alter the normal physiology of the skin? Changes in humidity will, of course, change the microenvironment of skin bacteria significantly, but in normal relative humidity, changes in oxygen tension with reduced pressure might affect the skin in more subtle ways to alter its effectiveness as a barrier to pathogenic microorganisms.

RECOMMENDATIONS

Research

1. Determine the effects, if any, of the spaceflight environment on the normal microflora and physiology of the skin. Experimental models for this purpose will be of no real value because of the unique characters of human skin disorders. For this reason, it does not appear feasible to set up experimental systems to assess this hazard other than those in which man is

used. An opportunity should be provided to perform repeated quantitative and qualitative tests with the best techniques available to determine what happens to the skin microflora during actual or simulated spaceflights.

Operational

2. As a secondary objective, especially if alterations in cutaneous microflora are demonstrated, examine the physiological state of the skin during prolonged, simulated or actual, space-cabin exposure. The amount and analysis of sebaceous secretions, acidity, and presence of enzymes are among the factors that should be observed. The reason for this recommendation is that a significant change in cutaneous microflora, if it occurs during exposure to the space-cabin environment, will likely be associated with, or be the result of, physiological changes in the skin.

Chapter 7

LATENT INFECTIONS

Man being basically egocentric, it is understandable that he has been concerned principally with infections that cause his own discomfort. It is becoming increasingly evident, however, that certain infectious agents produce latent infections in which the infectious agent persists in the tissues for long periods, even years, without inducing overt disease. With some agents, such as herpes simplex virus, the agent may be periodically activated producing a self-limited disease, after which the agent once more becomes occult. Infectious agents, particularly viruses, may also exist in a latent state for a greatly extended incubation period preceding overt disease; this situation is found notably in rabies and hepatitis and occasionally in diseases induced by agents such as Rickettsia and Chlamydia. Exaggerated forms of this type of latency are diseases in which the incubation period may be a year or longer; these are termed "slow" virus infections.

Latent infections have been identified in widely varied host species, including vertebrate and invertebrate animals, plants, and bacteria. Moreover, many orders of infectious agents seem capable of inducing this somewhat protective type of host-parasite relationship. Because latent infections are, in fact, so pervasive in nature, and because some chronic diseases of man may be the result of previously unrecognized slow virus infections, successful prolonged space exploration requires identification of any factors that may upset these precisely balanced interactions between parasite and host.

Numerous bacteria and other infectious agents may induce a carrier state in their natural hosts; among the most prominent of those that infect man are mycobacteria, Salmonella, Brucella, Treponema pallidum, streptococci, meningococci, and pneumococci. Those nonviral agents which might present potential dangers for astronauts are considered in other chapters, and although the carrier state or latent infection may be upset by prolonged space travel, the factors involved are probably similar to those implicated in viral infections and therefore will not be considered separately in this chapter.

TABLE 3 Examples of Latent and Slow Virus Infections

Virus	Host	Type Infection	Tissues Affected or Associated Disease
Herpes simplex	Man	Latent	Primary: Epithelial surfaces, eye, brain Recurrent: Skin, eye
Varicella, herpes zoster	Man	Latent	Primary: Skin Recurrent: Peripheral nerves
Cytomegalovirus	Man	Latent	Primary: Brain, lungs, kidneys Transfer: Infectious mononucleosis-like
Epstein-Barr virus	Man	Latent	Infectious mononucleosis (?)
Hepatitis	Man	Latent	Liver
Lymphocytic chorio-meningitis	Mouse	Latent, slow	Central nervous system, lungs, kidneys
Pneumonia virus	Mouse	Latent	Pneumonia
Kuru	Man	Slow	Brain
Scrapie	Sheep	Slow	Brain
Aleutian mink	Mink	Slow	Kidneys, hyperglobulinemia
Rabies	Man, dog, etc.	Slow	Central nervous system
Simian virus 40	Rhesus monkey	Latent	Sarcomas
Mammary tumor	Mouse	Latent, slow	Carcinoma of breast

RELEVANCE OF LATENCY AND SLOW VIRAL INFECTIONS TO SPACE EXPLORATION

Realization of the ubiquitous nature of latent (see Table 3) viral infections in man forces our attention toward events that may activate an occult virus or hasten the course of a slow virus infection. Certainly, prolonged travel in space may induce deleterious alterations in man's host defenses and hence substitute a serious disease for a seemingly harmless and hidden viral infection.

Although there exist few hard facts to prove that space travel may alter the relationship between virus and host in favor of the virus, one need look at only a few examples listed in Table 3 to realize the potential problems.

Infection with herpes simplex virus represents the most thoroughly studied example of prolonged viral latency in man and, therefore, will be discussed as a prototype. The initial infection most commonly occurs during infancy, and it generally produces a mild respiratory illness or subclinical infection; occasionally severe stomatitis, generalized dermatitis, or encephalitis will ensue. The rare primary infections in adults tend to be severe and generalized. Repeated recurrences of localized lesions--most commonly manifest in the form of painful blisters on the lips, i.e., herpes labialis--are relatively common in those having experienced a primary infection with herpes simplex virus. The specific mechanisms mediating these recurrences are unknown. The recurrences are triggered by a variety of provocative conditions; most commonly fever and exposure to ultraviolet irradiations are responsible, but such diverse events as ovulation, physical trauma, and emotional distress may activate the virus. Recurrences do not appear to be related to changes in levels of viral neutralizing antibody which are generally high before, during, and after each clinical episode. Individually or in concert, changes in interferon levels, membrane permeability, cellular physiology, or hormone levels may be responsible. Space travel conceivably could induce these alterations.

Primary herpes simplex infections are generally acquired by contact of an immunologically naive individual with a person experiencing a recurrent infection. Hence, it would clearly be unwise to send an uninfected astronaut on a long mission with colleagues who have recurrent herpes simplex infections. It might further be inadvisable to employ on prolonged spaceflights persons who frequently have recurrent herpes, since

it suggests that the balance between virus and the host's defenses is easily shifted in favor of the parasite.

Table 3 undoubtedly lists only a minimal number of latent infections known to occur in man, because additional examples of latent viral infections in man are uncovered with each new technique that permits more sophisticated examination of the biology of cells and the nature of viruses. The significance of the phenomenon becomes horrifying if one considers the implications of the notion that space travel might hasten the inexorable course of a slow virus infection which produces severe neurological or oncological disease. This unpleasant consequence would follow if changes in host responses resulted in accelerated viral replication or reduced the body's capacity to retard viral propagation or restrict viral spread.

MAJOR UNANSWERED QUESTIONS

1. What effects, if any, will the space environment have on reactivation of latent infections or acceleration of slow virus infections? This question is of vital importance to safe missions in space and must be answered before one can guarantee the level of safety desired. The relevant factors of host defense are discussed in Chapter 3, and they are obviously of basic significance to the problems and dangers concerned with latency and slow viruses.
2. What properties of some viruses make these agents susceptible to assume the latent state or to have an extremely prolonged incubation period?
3. Is latency, at least of some viruses, similar to lysogeny in bacteria?
4. What diseases in man are due to a reactivated latent virus or to a slow virus?

RECOMMENDATIONS

Research

1. Examine the effect of prolonged closed chamber tests on known latent infections in animals and in man.

2. Examine the effect of prolonged spaceflights on latent and slow virus infections experimentally induced in animals.

3. Initiate research to identify host defenses that keep latent infections dormant and to determine the factors that may alter host defenses and thereby activate a latent infection.

Operational

4. Determine astronaut's antibody status for herpes simplex virus.

5. Obtain detailed history on astronaut concerning primary and recurrent herpes infections.

6. Do not send on a mission an astronaut who has frequent and severe recurrent herpes simplex infections.

7. Do not send an astronaut who is deficient in neutralizing antibodies for herpes simplex virus on a mission with a colleague who has recurrent though mild episodes of herpes simplex.

Chapter 8

MICROBIAL MUTATIONS

The possibility that the special conditions of long-duration space missions may give rise to microbial mutants must be carefully considered. Microbial mutants having increased virulence or greater selective advantages would be a serious hazard to astronauts.

A number of conditions exist in the space environment which could potentially increase mutation rates of microorganisms. Increased oxygen levels and radiation are known to increase mutation rates; synergistic effects of these factors with other environmental conditions are possible. Whether other potential mutagenic agents exist in the confines of the space capsule is at present unknown. Chemical contaminants are a possibility. Conditions such as lowered gravity states, which affect dispersion of microbial cells, could affect the capacity of mutants to establish themselves. These would be of particular significance in the case of mutants having altered antigenic components. The possibility cannot be ruled out that unique mutations of bacteria, viruses, fungi, and other microbial forms leading to virulent agents may occur.

The densities of microbial populations in the gastrointestinal tract are statistically adequate for the presence of significant numbers of spontaneous mutants. Of even greater significance from the point of view of genetic alterations in microbial flora is the likelihood of population changes. Selective forces may favor proliferation of mutant types having altered antigenic properties and greater virulence, as well as increased resistance to antibiotics. It is well known that increased oxygen availability can have a marked effect on population changes involving bacterial mutants of increased virulence; and changes in diet or environment, not to mention broad-spectrum antibiotics, can induce overwhelming alterations in population content and size. In addition, changes in gravity may influence population changes by affecting dispersion of bacterial cells and permitting mutants to establish themselves. It would thus be of great value to investigate the influence of environmental factors associated with spaceflight on population changes. Mixed bacterial populations containing various

proportions of virulent and avirulent types of staphylococci, streptococci, and Escherichia coli, for example, could be evaluated under a variety of conditions including various oxygen levels, gravity conditions, and radiation levels. Assays of the proportion of virulent to avirulent types would involve determination by plating of colonial morphology characteristic of virulent states or antigenic types. Similar tests with antibiotic-resistant mutants could also be made. In vivo studies with seeded populations would be of great value. In this way, some understanding of the importance of selective forces in man could be achieved.

Consideration should also be given to temporary phenotypic modification (nongenetic) in microbial characteristics under certain environmental conditions. Some avirulent mutants of Salmonella may become potential pathogens under certain conditions of cultivation, for example, in media containing polysaccharides not synthesized by the mutant. Phenotypically "rough" Salmonella types can be produced in sera containing enzymes capable of destroying the terminal O-antigen groupings, thus rendering genetically "smooth" pathogenic types susceptible to phagocytosis. There are other examples of potential host-modifying conditions, such as those leading to wall-defective "L" forms of bacteria, which may permit survival of pathogenic microorganisms as well as influence their virulence.

On balance, the risk of infection of astronauts by new mutants arising in space appears to be modest in short-duration (<30 days) missions. The possible effect of population changes due to modified selective forces, nevertheless, is not known and deserves careful experimental investigation in preparation for long-duration missions in order to forestall surprises.

MAJOR UNANSWERED QUESTIONS

1. Are there special conditions in prolonged space travel that may significantly influence mutation rates?
2. Would normally present or new mutants become established in a manner that would alter the existing normal flora ecology?
3. Are selective forces modified in the altered environment so that virulent agents could proliferate?

RECOMMENDATIONS

1. Investigate the effect of spacecraft conditions on the rate of mutations in different microorganisms, including viruses, in cell culture.

2. Investigate the effects of oxygen, lowered gravity conditions, and other factors potentially encountered in space on mixed populations of virulent and avirulent microorganisms to determine the possibilities of selection of potential pathogens. The influence of antibiotics on selection in such mixed cultures both *in vitro* and in animal hosts should be studied.

3. Investigate the changes that may occur in microbial flora, particularly as they relate to selection of virulent agents, under conditions of long-term spaceflight. These studies should utilize experimental animals, preferably in actual flight.

Chapter 9

PREVENTION AND THERAPY

Susceptibility and exposure are the major determinants of the occurrence of infectious diseases on earth. Infection results when a susceptible individual comes into contact with an infected person or with a pathogen carried in the environment--by air, water, milk, food, insect, or animal. The basic concepts of prevention are based on interrupting this chain of events by immunizing the human host if he is susceptible, by enhancing his nonspecific defense mechanisms, by eliminating the environmental factors that transmit the infection, and by controlling the sources of infection that are introducing the pathogen into the environment. In the space capsule, there are no insect or animal sources of infection, and the environment itself has been designed to eliminate pathogens or to keep their number below the usually infectious level. This involves an air filtration system, which effectively cleanses the atmosphere of microbiological contaminants; specially prepared and preserved food, which is free of enteric pathogens and toxic substances; and a safe and palatable water supply. As a consequence, the astronauts themselves should be the sole sources of in-flight infection.

Infection might be expected to arise in one or more of three ways. First, disease could be caused by exposure to a pathogen prior to flight or carried by a fellow crew member. The adequacy of this latter exposure to induce disease, given susceptibility, seems inevitable in a prolonged mission. Second, illness could occur when the basic defense mechanisms are so altered that susceptibility to one's own normal flora results. Third, a new pathogen to which the astronaut is susceptible might emerge from his own resident flora by the process of selection or by mutation. For these reasons, preventive measures must be directed primarily toward the astronaut himself, toward enhancing his specific and nonspecific defenses, and toward keeping to the barest possible minimum the number of pathogens he brings on board.

CRITERIA OF PREVENTION

The major focus of prevention should be on the astronauts themselves. It is of primary concern to eliminate the two factors of susceptibility and exposure at the critical period of takeoff, so that important pathogens will not be taken aboard in their incubation period. It should be emphasized that a minor infection for one astronaut may become a much more serious infection if transmitted to another.

Because the possible effects of prolonged spaceflight on infection have never been studied under closely simulated or actual conditions, the specific problems that may require preventive action are largely speculative. After an initial period of a spaceflight in which acute diseases in the incubation period have evolved, been transmitted to others, and burned out for lack of susceptibles, one can only be guided in identifying trouble areas by the consequences of an altered environment as we now know them: (1) any change producing mutation or selection of the microbial flora will probably be in the direction of greater pathogenicity; (2) any effect on host defense mechanisms and host-parasite relationships will probably be detrimental and clinical illness enhanced. These concepts stress the need for preserving normal flora and normal host-parasite relationships--what might be called microbiological homeostasis--by maintaining conditions as close as possible to those of earth for which we are adapted.

The elements of prevention include proper selection of astronauts; identification by immunological tests of those astronauts especially susceptible to infection; correction of such immunological defects where possible; microbiological surveillance of astronauts and of those with whom they are in close contact; and, finally, utilization of a quarantine or preflight isolation period. Each of these elements is of importance and will be discussed separately, but the institution of an effective preflight isolation period is the most essential of all.

SELECTION AND SCREENING

The purpose of selection and screening procedures is to identify those astronaut candidates most susceptible to infection, to correct defects where correctable, to eliminate

TABLE 4 Immunological Profiles as a Basis for Prevention

Agent	Types to Be Tested	Test Methods	Incubation Period of the Agent (days)	Protective Measure for Susceptible Person	Comment
Respiratory					
1. Adenovirus	3, 4, 7, 14, 21	Neutralization test	3-8	Oral type 4 live vaccine, possibly specially prepared vaccines for other types	Inactivated 3, 4, 7 vaccine effective but now not commercially available. Oral type 4 from Armed Forces
2. Epstein-Barr virus	One	Indirect immunofluorescent test	14-45	None available	Done at Yale (Evans), Philadlphia (Henle), CDC, Baylor (Melnick)
3. Herpes hominis	One	Neutralization test		None	Exclude persons with recurrent herpes or without antibody
4. Histoplasmosis	One	Skin test		None	Reactivation uncommon on earth, might pose problem on long flight
5. Influenza	A2, B	Hemagglutination inhibition	3-7	Vaccination with most recent strain	In epidemic times protection may require special measures
6. Mumps	1	Neutralization test		Live mumps vaccine if no antibody	80% of persons 25 and over probably have antibody
7. Parainfluenza	Types 1, 2, 3	Hemagglutination inhibition	3-7	None	Experimental vaccine under test
8. Mycoplasma pneumoniae	One	Metabolic-inhibition test	Up to 3 weeks	None	Broad-spectrum antibiotics for therapy. Experimental vaccine under test
9. Rhinovirus	3 or 4 types current in preflight period	Neutralization test	1-5	None except possible exposure to live virus	Surveillance of associates and families needed
10. Streptococcus	Group A hemolytic	Throat cultures weekly in last month before flight	2-5	Penicillin for 10 days for group A carrier or infection	Erythromycin substituted in face of sensitivity
11. Tuberculosis	Mycobacterium hominis	Skin test		May be inadvisable to send astronauts on long mission if skin test is positive	Susceptible crew members might be given BCG vaccine before. Isoniazid should be taken along
Central Nervous System					
1. Polio virus	1, 2, 3	Neutralization test	5-15	Oral polio vaccine	Probably all are immune
2. Meningococcus	A, C	Nose and throat cultures	3-5	Eradicate carrier state with penicillin	
Exanthema					
1. Measles	1	Hemagglutination inhibition	7-14	Measles vaccine	95% probably already immune
2. Rubella	1	Hemagglutination inhibition	7-14	Rubella vaccine	80+% probably immune
Gastrointestinal					
1. Hepatitis	Infectious	No test	15-45	Give gamma globulin 0.06-0.1 cc/lb in divided doses 7 and 14 days preflight	Unlikely possibility but serious if it occurs
2. Hepatitis	Serum	Australia antigen serum measurable in blood by agar gel test	40-180	None. May be inadvisable to send Australia antigen carrier on long mission	Test done at Yale (McCollum)

astronauts from missions where the risk is significant and uncorrectable, and, where the defect is not a major one or the skills of that astronaut are essential for the mission, to anticipate the problems that may arise.

Selection

The choice of astronauts for training and for specific missions obviously depends on a wide range of intellectual, psychological, physical, biological, and experience factors. For microbiological purposes, as well as for other reasons, persons should be selected who show normal responses to stress and a good adaptive mechanism. Specifically, one should avoid persons who show (1) exaggerated physiologic or allergic responses to common drugs or to common infections or other marked hypersensitivity reactions (even a strong family history of hyperresponsiveness might weigh against selection because of the clearly higher risk in certain families to drug reactions, allergic disease, paralytic poliomyelitis, rheumatic fever, and the like); (2) evidence of repeated episodes of common illnesses, especially lower respiratory illness or severe diarrhea, in the candidate or his family because such episodes may indicate a basic pattern of hypersusceptibility; (3) a history of recurrent latent or carrier infections, especially herpes simplex or staphylococcal skin infections.

Screening

The purpose of screening is to identify by immunological tests those pathogens to which the astronaut is immune, those to which he is susceptible, and those with which he has had prior experience but which might reactivate or recur in prolonged space travel.

Table 4 summarizes the microorganisms for which screening is desirable, suggests tests to determine antibody status or hypersensitivity, and outlines the corrective measures to be taken if antibody is absent. The next section will elaborate on this last aspect. The purpose of these profiles is to delineate risk factors. Some of these hazards are remote, but they could have unfortunate consequences if infection occurred. Rubella, for example, has probably been experienced by most astronauts, but if the 10 to 20 percent who are susceptible should be exposed to children (as in their families) who are

infected, rubella's two-week incubation period might permit infection in space to result. Rubella can be incapacitating in adults.

As there are some 85 separate antigenic types of rhinovirus, it is clearly impossible to screen for all, but if the few types prevalent near flight-time are known, it would be useful to test for them.

Finally, aliquots of serum should be taken preflight and postflight for later study of agents not included in the screening tests. This is most important.

SURVEILLANCE

This term designates an ongoing, planned, and sequential microbiological evaluation of the astronauts, their associates, and their families. Its objective is to provide up-to-date information on the infectious agents to which the astronauts have been exposed before flight. This surveillance should be continued during space missions and for 1 to 2 months subsequently as a basis for control comparison of possible illnesses encountered during the mission and as a baseline to evaluate claims that a "space microbe" has been brought back to earth and escaped detection in the quarantine period in the Lunar Receiving Laboratory.

The elements of surveillance include (a) daily, "calendar"-type illness records; (b) weekly collections of blood, throat washings, nasal swabs, and stool samples, part for testing and part for storage for later reference; and (c) examination by a physician at time of illness.

The suggested protocol is:

Time Daily illness records; weekly blood and material collections.

Surveillance Period Start at least 30, preferably 60, days prior to flight time and continue 30 to 60 days postflight.

Persons Studied The astronauts and their backup alternates, all family members of above, all close contacts of astronauts. This last includes, especially, the 30 or so technical personnel who will be in intimate contact with the

astronauts in the final 2 or 3 weeks prior to flight time.

Tests To Be Done (a) Bacterial culture of the throat weekly for group A hemolytic streptococci and meningococci; (b) other bacterial and viral examinations to identify illness episodes. This should include efforts to isolate the agent in appropriate bacterial media and in tissue culture (monkey kidney, WI 38, Hep-2 cells) and appropriate serologic tests; (c) the rest of sera, stool, and throat washings which have been collected should be divided into aliquots and stored for reference at -70°C or in liquid nitrogen.

Personnel A physician-epidemiologist, one or two public-health nurses for weekly visits, and a technician for the serum and material bank.

QUARANTINE OR PREFLIGHT ISOLATION PERIOD

The need for a period of preflight isolation of the astronauts and for the backup crew has been clearly and urgently recommended by all members of the present Committee, by all their consultants, and by several previous studies.* This period should be regarded as an essential part of the mission and a designation indicative of its importance given, such as "ground-based phase of flight mission," or "critical microbiological equilibrium period."

The basic objectives for this period are: (1) To allow infectious agents encountered by the astronauts just prior to flight time to become manifest and for recovery to ensue. The time must be adequate for possible secondary spread to other astronauts. (2) To permit exchange of microflora among astronauts so that a state of microbiological equilibrium is established. (3) To protect the astronauts against exposure to new infectious agents.

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* Space Science Board, Physiology in the Space Environment, Volume II, Respiration (NAS-NRC, Washington, D.C., 1967), p. 16 and Chapter 17

Directorate of Medical Research and Operations, NASA, A Biomedical Program for Extended Space Missions (NASA, Washington D.C., May 1969), Microbiology Section, p. 5, A1.

TABLE 5 Outline of Preflight Isolation Period--The Ground-Based Phase of an Extended Space Mission

Persons	Days before Mission	Type of Action		Nature of Isolation		Throat Culture[a]	Protective Action
		Surveillance	Isolation	Persons	Space		
Astronauts Backup crew Essential technical persons	-60	x x x	x x x	None	None	+	Review immunization status; give influenza vaccine (0.5 ml)
	-30	x	x	Contacts mostly limited to persons on base	Most operations limited to base	+	5-ml dose of gamma globulin for astronauts. Booster dose of influenza vaccine to be given (0.5 ml)
	-21	x	x	All direct contacts with children to stop	Limited to base quarters and operational areas	+	All contacts outside of technical personnel to be made through glass
	-14 to flight time	x	x	Direct contacts limited to technical personnel	Limited to base quarters and operational areas	+	5-ml dose of gamma globulin to treat streptococcus group A and meningococcal carriers; wear air control helmets

[a]Indicates a throat culture for Staphylococcus and meningococcus should be done.

Our inability to protect astronauts against many of the common infectious diseases, especially respiratory and gastrointestinal, is clearly indicated by two facts. The causes of only one half of the acute respiratory and a much smaller percentage of acute gastroenteric infections can be identified; of the known agents, vaccines are available only for influenza (commercially) and for type 4 adenovirus and Mycoplasma pneumoniae (experimentally), and none of these vaccines is fully protective: effective therapy is limited to antibiotic therapy of acute streptococcal infections. This means that the only way to guard against the development of infectious diseases in space is to allow adequate time in the preflight period for diseases to develop and for recovery to ensue and to protect astronauts against contact with new infections in that period. The duration of this isolation period or ground-based phase of the mission is therefore dependent on the incubation period of the particular agent. Table 4 gives many of these. A minimum period of two weeks permits the emergence of most common infections except M. pneumoniae, infectious mononucleosis, and infectious hepatitis. The presence or absence of immunity to the first two can be ascertained, and the likelihood is high that most astronauts are immune. For infectious hepatitis, administration of gamma globulin is recommended.

The isolation period can be graduated in terms of space and time as shown in Table 5. Adoption of the procedural elements of this table are strongly recommended. If an adequate and effective quarantine period of this type is not followed, serious consequences may result.

The preflight preparatory program should start one month prior to flight time. Astronauts should be mostly restricted to base (Houston or Cape Kennedy) and all direct contact with the public and press should be minimized. Special rooms should be established for contact with the public, and interviews with the press in which a glass-walled section of a conference room is set up with separate air filter and ventilation systems for the astronauts alone. For the last two to three weeks prior to flight time, all contacts, especially with the children of the astronauts, should be carried out through such a glass barrier.

The last two weeks of this ground phase of the mission is a critical period and must be carried out under carefully supervised conditions:

1. Personal contacts of the astronauts must be limited solely to the technical staff needed for direct assistance (e.g., in donning the spacesuit).

2. Astronauts and technicians included in the "count-down circle" should all wear light, plastic helmets with a positive-flow air system. The avoidance of respiratory exposure is of great importance in this period, and design of a comfortable, effective, transparent helmet is well within simple technology if not already adaptable from the spacesuit helmet. The helmet is to be worn at all times during contact with the technical staff but not during the time the astronauts are by themselves in their own quarters.

3. The astronauts and essential technical personnel should be restricted to special isolation living quarters adjacent to the operational area, to essential operational areas, and to the special conference room. The facilities for the astronauts should be separate, both physically and in terms of air-control systems, from that of the technical staff. The astronauts should be housed together and without helmets. No other persons should be permitted in these areas when the astronauts are present. The objective of this final phase is to provide maximal opportunity for the exchange of microflora and pathogens among the astronauts and minimal or no opportunity for exposure to outside organisms or infected persons. Food should be introduced through a two-step isolation passway with ultraviolet light or prestocked in the quarters. Final physical examination should be conducted under strict isolation techniques.

Facilities that meet these requirements appear to be available at the Lunar Receiving Laboratory and should be constructed at Cape Kennedy.

SPECIFIC PREVENTIVE MEASURES

Vaccination

Astronauts should receive vaccinations as follows:

Influenza Annually, with most currently available product, and 60 and 30 days prior to mission. In the face of an epidemic in which vaccine has been prepared for epidemic strain, give monovalent vaccine in two spaced doses. If no such vaccine is available and the risk of infection is high, consider exposure to live virus under controlled circumstances.

If epidemic is of A2 type, consider use of Amantadine in last two weeks only but do not give during flight because of central nervous system reactions.

Type 4 Adenovirus Oral, live, for astronauts lacking this neutralizing antibody, given at time of selection for a mission or preparation of purified antigen to types 3, 4, 7, 14, and 21 for parenteral administration.

Oral Polio Virus Given at time of selection for a mission.

Chemoprophylaxis

Antibacterial The main reason for inclusion here is to condemn the indiscriminate use of antibiotics such as tetracyclines, chloromycetin, or any other prophylactic antibiotic during flight. These drugs would upset the normal ecologic balance whose preservation is so strongly urged by all consultants.

Antiviral Drugs With the possible exception of Amantadine, no other compound has relevance to space infection.

Amantadine has a quite well established prophylactic effect against the A2 strain of influenza and, perhaps, produces a slight modification in the course of clinical illness if given early enough. It has no effect on other influenza strains or on other respiratory viruses. Its only conceivable use would be in the preflight isolation period when exposure of astronauts was known to have occurred and a specific launch time was critical. The drug is capable of affecting the central nervous system, and tasks requiring high coordination and concentration would be adversely affected. It should therefore, never be used during actual flight.

Nonspecific Stimulators of Host Defense The use of interferon inducers has not reached the point of applicability, but deserves further research (see Chapter 3).

THERAPY

Therapeutic problems would be referred to a ground-based physician for advice. Acute respiratory diseases are largely

of viral origin for which only symptomatic therapy can be given. Antibiotic treatment would be required only for (1) group A hemolytic streptococcal infection, in which penicillin or erythromycin would be used; (2) M. pneumoniae, in which erythromycin or tetracyclines are employed; and (3) other bacterial pneumonia, possibly due to gram-negative organisms. The only gastrointestinal infections likely to occur are nonbacterial, and only symptomatic treatment can be given (paregoric or Lo-motil).

If the recommendations for an adequate and effective preflight isolation period are followed, the probability of acute respiratory and gastrointestinal infections should be very low.

Review of the Apollo medical kit reveals it to be adequate, with these suggested changes: substitution of crystalline penicillin for ampicillin and of tetracycline for achromycin. If an astronaut has known sensitivity to penicillin, then erythromycin should be carried for hemolytic streptococcal infections. A potent gram-negative antibiotic might be included for possible pneumonia or septicemia of this type.

EARLY DETECTION OF CLINICAL INFECTIOUS DISEASE

It is essential to detect the presence of certain pathogenic organisms during prequarantine and quarantine periods. Such organisms include beta hemolytic streptococci, meningococcus, M. pneumoniae, Salmonella, and other enteric pathogens. These organisms should be eliminated preflight by appropriate therapeutic means. In-flight detection of pathogenic agents, particularly in missions of long duration, is also of great importance. Activation of latent infections or selective proliferation of microorganisms could be serious hazards, and the ability to identify the agents would be valuable for therapy. It is therefore of great importance to design microbial isolation and detection devices suitable for ground-based and in-flight use.

A number of studies have been initiated by NASA to develop an on-board microbiology laboratory (Integrated Medical and Behavioral Laboratory Measurement System, Microbiological Ecology Measurement System, Microbial Load Monitor), capable of semiautomated or automated detection of microorganisms. Under these studies, devices are being developed for sample collection, culture and isolation of colonies, and identification. Specific identification procedures include precipitation tests, fluores-

cent antibody reaction on filters, agglutination of specifically sensitized polystyrene beads, and gas-chromatographic methods. Techniques could also be developed inolving preliminary agglutination or precipitation followed by very sensitive methods for detection of adenosine triphosphate (ATP). Some of these techniques for microbial detection have been under study by the Department of Defense. These procedures would be relevant also for determining the microbiological safety of water in the reclamation system and the buildup of microorganisms on spacecraft surfaces.

A particularly promising system for microbial detection is under development by Donald Glaser and co-workers at the University of California, Berkeley. A flying spot scanner is used to scan large populations, and the organisms may be identified by profile scanning as programmed by computers. Antibiotic sensitivities and other genetic traits can be determined rapidly. This device may be valuable in recognizing microbial flora changes and could be automated to determine the microbiological safety of water in reclamation systems.

Infectious disease may also be detected in its early stages by determination of antigens released by certain pathogens or by early immune responses. Sensitive immunological procedures for such determinations could be developed. Equally important are studies reported by William R. Beisel (Fort Detrick, Maryland) of protein and amino acid changes that occur early in certain infections. Thus, pneumococcal infections appear to induce the enzyme tryptophan pyrrolase. Other changes, such as turnover of ribonucleic acid and other macromolecules, may also be detected.

UNANSWERED QUESTIONS

1. What is the most desirable duration and degree of a preflight isolation period?
2. How can the emergence of latent infections, of carrier states, and of impairment of host-immune systems be anticipated and prevented?
3. Can special vaccine preparations be developed for astronauts for those conditions to which they may lack immunity--adenovirus 3, 7, 14, 21; parainfluenza 1, 2, 3; M. pneumoniae; certain rhinovirus types?
4. What potential hazards do the normal flora of the

respiratory tract and gastrointestinal tract pose in flights of long duration, and how can these be prevented or treated?

5. Can nonspecific defense measures like interferon producers be developed for practical use?

RECOMMENDATIONS

Research

The types of studies most needed for prevention and therapy include those outlined in other chapters.

1. Determine the effect of spaceflight on all elements of the host defense system and on the effectiveness and nature of host responses to specific antigens, especially the immunoglobulin system. This question urgently needs study in actual and simulated conditions.

2. Determine the effect of prolonged exposure to low levels of a limited number of microorganisms or toxins (carried on board the mission).

3. Ascertain the consequences on host immunity of removal of pathogens present in the earth environment. Such pathogens may be required to sustain the level or the efficiency of antibody-forming or defense mechanisms.

4. Investigate, as an item of high priority, the possible enhancement in the spread of infections in the spacecraft environment.

5. Evaluate the potentially adverse influence of the space-cabin environment, of the absence of the usual antigenic stimuli, and of close confinement, acting in concert, on chronic and latent host-parasite balance. Specifically, antibody levels to latent agents such as herpes simplex, Epstein-Barr virus, and cytomegalic virus should be studied preflight, during flight, and postflight, and the possible reappearance of these agents in the throat, blood, and urine should be determined.

6. Develop reliable procedures for the isolation, specific identification, and enumeration of microflora, which are applicable onboard. Semiautomatic or fully automatic equipment such as the flying spot scanner would be highly desirable. An astronaut trained in the techniques would be desirable, since decisions relative to such procedures as sampling are involved.

7. Develop procedures for monitoring the microbial content of reclaimed drinking water and microbial buildup on surfaces.

8. Develop techniques for early detection of disease. Sensitive immunological procedures and biochemical markers should be studied.

9. Undertake long-range research programs to determine feasible methods for determining microbial flora profiles for man. The use of automated procedures, such as the flying spot scanner, should be examined.

Operational

10. Select and screen all astronaut candidates to avoid those showing (a) exaggerated responses to usual drugs and infections, (b) known allergies or hypersensitivities, (c) repeated attacks of herpes simplex or staphylococcal skin infections, and (d) repeated episodes of lower respiratory infection.

11. Screen astronauts and astronaut candidates by a battery of immunological tests for viral and bacterial infections to delineate those at risk.

12. Establish a microbiological surveillance of the astronauts, their close technical associates, and their families one to two months prior to flight time and continue one to two months postmission. This program should include throat cultures on a routine weekly basis for group A hemolytic streptococcus and meningococcus, and efforts to identify the causative agent of any illness by appropriate bacterial, viral-isolation, and serological studies.

13. Establish a serum and material bank of samples (throat washing, stool, and the like) derived from the surveillance program and stored for later reference. Material should be divided into aliquots, properly labeled, and kept at -70°C or in liquid nitrogen. The material should be collected and stored in a uniform, planned, and conscientious manner. An individual with sole responsibility for its maintenance should be appointed.

14. Impose a preflight quarantine or isolation period, as a measure of highest priority. A graduated program of increasing protection for the astronaut should be instituted starting one month prior to flight time. It should be regarded as an essential, ground-phase portion of the flight mission itself. During the last two weeks, the astronaut's contacts should be limited entirely to essential technical crew, who

should also be held under the same isolation regulations. No direct physical contact should be permitted with anyone else during this critical period, not even the astronaut's family or high officials. Social, voice, and visual contact with the latter can be permitted under rigidly controlled conditions which isolate the astronauts alone behind a glass-enclosed panel in a separately ventilated and air-conditioned room. The concept of preflight isolation has been firmly and repeatedly advocated by all consultants in infectious disease who have considered the problem. If not carried out adequately, serious consequences to the astronauts and the mission may result.

15. Do not send on a mission any astronaut who has an acute infectious disease. This includes even minor respiratory infections, because they may result in greatly accelerated clinical responses under space-cabin conditions if transmitted to other astronauts.

Appendix A: Review of the Literature Pertaining to Infection within a Spacecraft

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The pathogenesis of infection in a spacecraft environment poses a number of biomedical problems which heretofore have received inadequate research attention. These problems center in two major areas: the effect of unique alterations from terrestrial environmental factors on parasitic virulence and host resistance and the significance of an intimate and closed ecology on the type and transmission of infection. The first of these problems is illustrated in dramatic fashion by the environmental change to weightlessness. Will this marked physiological alteration enhance, impair, or not affect bacterial growth, and, conversely, will significant alterations in human metabolism leading to changes in host resistance occur now that the human system is freed from gravity?

The significance of an intimate and closed ecology on the spread of infectious disease also requires elucidation. A large body of information exists for various viral and bacterial diseases. However, these studies uniformly presuppose environmental dilution. In spacecraft, the environment might become saturated with microorganisms, with potential change in host-parasite interaction. As an example, a small mycobacterial inoculum usually produces primary pulmonary tuberculosis. Will the same response occur to a much greater and continuing mycobacterial exposure?

This report reviews present knowledge concerning the effect on host-parasite relationships of the changed environment of spacecraft.

THE SPACE ENVIRONMENT

The conditions of space which differ most from terrestrial environments are weightlessness, cosmic radiation, absolute temperature determined by radiation effect alone, and high vacuum. Of these, weightlessness is perhaps the most significant.

Weightlessness

The biological significance of weightlessness is virtually unknown. Except for minimal periods of free flight, weightlessness cannot be achieved in the earth's environment, and it is by no means certain that experimental simulation duplicates its effects. The few U.S. experiments performed in zero gravity have suggested that increased bacterial growth rate may occur (1). These experiments have established the ability of many forms of life (viruses, bacteria, fungi, etc.) to multiply in a weightless environment. The authors also noted an antagonism to radiation-induced lysogeny in studies of Neurospora crassa (orange bread mold). These studies are too preliminary, however, to derive firm conclusions concerning the interrelationship of radiation and weightlessness.

Radiation

In space, radiobiological effects may be produced by ultraviolet, x-ray, gamma-ray, and particulate (or ionizing) radiation. Ordinarily, these radiations do not penetrate the earth's atmosphere in quantities sufficient to cause damage, but in space exposure may become significant unless adequate shielding is provided. The available evidence indicates that the spacecraft provides satisfactory shielding from ultraviolet radiation, most forms of ionizing radiation, and protons with energies less than 60 MeV (2, 3). However, protection may not be adequate against very high-energy particles, particularly those emitted during solar flares, nor against low-level secondary radiation produced when high-energy primary radiation strikes the shielding. Two aspects of the exposure are of direct relevance to infectious disease: the bactericidal effect of the radiation and the probability of mutation. Indirectly, the debilitating effects of radiation would make crew members more susceptible to disease. Because both frequency of mutation and bactericidal effect increase with exposure to radiation, the possibility of virulent mutations exists. Experimental data concerning irradiation-induced mutations during spaceflight are meager. Reynolds and Sanders, reporting the Biosatellite results on N. crassa, noted no increased mutation rate under weightless and hyperoxic conditions during the two-day flight (1).

External Temperature and High Vacuum

Neither of these environmental conditions applies to the intact space-cabin environment.

ENDOGENOUS ENVIRONMENTAL FACTORS

Endogenous environmental factors which may affect host-bacteria interrelationships are: chemical contamination, hyperoxia, reduced atmospheric pressure, temperature, humidity, and the ecological considerations of a closed system. Each of these factors is to a certain extent amenable to engineering control.

Chemical Contamination

Environmental pollution of the space cabin has been studied by a number of investigators (4, 5). In a 14-day, four-man test designed to simulate space-capsule conditions, Conkle (4) found potentially significant increases in methane (20.9 mg/m^3 to 84.6 mg/m^3) and carbon monoxide (4.8 mg/m^3 to 23.7 mg/m^3). Increases of questionable biological significance were noted for many trace pollutants. NASA similarly reported elevated levels of atmospheric methane and hydrogen during an eight-day simulated space-capsule experiment (5). Carbon monoxide levels increased to 28 ppm, verifying the Conkle data. The NASA experiment demonstrated satisfactory control of carbon dioxide, acetone, and ethanol pollution. Fourteen unidentified compounds, one of which reached a concentration of 350 ppm, were detected in the gas sampling lines. Further information on this experiment was not available at the time of this report. Contaminants of potential biological significance for which few spaceflight data are available are ozone, sulfur dioxide, and nitrogen dioxide. Data on further relevant compounds may be found in "Atmospheric Contaminants in Spacecraft," a 1968 report of the Space Science Board.

Hyperoxia

Space-cabin atmospheres have ranged from 100% oxygen to 70% oxygen and 30% nitrogen at 5 psia (6). Hyperoxia either at ambient or hypobaric pressures is deleterious to host and bacteria (7-14). In host-parasite interrelationships the impairment is more pronounced in the host, resulting in enhanced bacterial virulence. Ehrlich and Mieszkuc (7) aerosolized Klebsiella pneumoniae into mice which had been exposed to a simulated space-cabin environment and noted significantly increased mortality throughout the 30-day test period. The impairment in bacterial resistance occurred in instances of prior infection, infection during parabaric conditions, and infection induced immediately after return to ambient conditions. Schmidt et al. (8) have demonstrated that staphylococcal skin infections are adversely influenced by spacecraft conditions. The impairment in bacterial resistance is apparently time-related, because in vivo experiments with shorter oxygen exposures have not shown differences in treated and control mice (9). An adverse effect of hyperoxia on local defense mechanisms such as the mucociliary stream has also been observed (15).

Although only a few studies have been reported, hyperoxia appears to influence adversely viral infection (7, 16). These investigations have demonstrated increased susceptibility to murine influenza and meningovirus infections. Alteration in susceptibility to viral challenge appears less uniform than for bacterial infection, with resistance to some viruses not being depressed (17) and depression of resistance being conditional with others (16). These variations in host response may relate to differences in parabaric effect on interferon production. Huang and Gordon (18) have shown that hyperoxia per se does not adversely affect murine interferon levels, but change in pressure does.

The bacteriostatic effect of increased oxygen tensions on both aerobic and anaerobic growth is well documented (9, 12-14). Although quantitative variations occur, a number of human pathogens, e.g., Staphylococcus typhimurium, Diplococcus pneumoniae, Staphylococcus aureus (9, 12), and Mycobacterium tuberculosis (13) grow poorly under hyperoxic conditions. From the previously cited in vivo data, it would appear that that this in vitro inhibition of bacterial growth is not of practical significance. A cellular basis for the in vivo findings may be postulated from the studies showing enzyme inhibition (19, 20) and chromosome breakage (21) following exposure to increased oxygen tensions.

Temperature and Humidity

These conditions are usually maintained within normal limits in the space capsule. Temperature (65-76°F); humidity less than 55%.

Light

The loss of the daily diurnal cycle may result in increased exposure to visible light. Since light is bactericidal for certain nonpigmented organisms (22), possibly due to production of endogenous photosensitizers (23, 24), atmospheric survival and hence transmission of infection may be influenced by the ability of the organism to withstand this sterilizing effect. An interesting but at present controversial area concerns the possibility that visible light produces mutations (25, 26). Leff and Krinsky (25) reported a mutagenic effect of visible light in Euglena gracilis, but other scientists have not agreed with their interpretation of the data (26).

Ecologic Conditions of a Closed System

The close confinement of men for prolonged periods in a fixed environment without means of microbial filtration could represent a serious threat to their health. Up to the present time few simulated studies have been performed to allow accurate assessment of this risk. Contamination by sneezing, coughing, and touch can be expected on every spacecraft surface. Since it is well established that transmission of a number of infections is by direct contact (27, 28), and that the risk of infection is inversely related to distance (29), virtually complete interchange of skin, nasal, oral, and gastrointestinal organisms is possible. The only parameters that might impede bacterial transmission are extreme environmental susceptibility and host resistance. The bacterial concentration will depend on the immigration of new organisms from the infecting host and the emigration either by death or by egress via outgassing. Sneezing should lead to the highest bacterial concentrations by expelling large numbers of organisms which at zero gravity will remain suspended as an aerosol. Coughing and direct contact will probably produce lower concentrations. Since bacterial loss via spacecraft leak is

small and the survival time of most pathogens is measured in days if not weeks, immigration will determine maximum concentrations. Among the respiratory pathogens, Myco. tuberculosis and fungi such as Histoplasma capsulatum would be most likely to survive at relatively high concentrations for prolonged periods of time.

Sladen studied groups of men isolated in Antarctica for prolonged periods of time (30). He noted that Staph. aureus and Staph. albus persisted in the noses and alpha hemolytic streptococci in the throats of men throughout the almost year-long study periods. The men kept their own strains (by phage type) of Staph. aureus. Beta hemolytic streptococci seemed to disappear from the throats during the isolation period, suggesting that this pathogen may not survive in a closed community. Data concerning transmission of organisms were not given in this study.

Studies of men confined in submarines for long periods have pointed out the risk of epidemic spread (31). Epidemics of respiratory illness occur regularly, although most of these can be traced to exposure of crew members prior to voyage.

Investigations in which healthy volunteers were confined in various types of enclosures have shown marked shedding of organisms into the surrounding environment (32-34). This shedding is continual and reaches rates of 10^4 organisms per minute.

Studies involving simulated and actual spacecraft conditions will be discussed in a later section, but a conclusion which is pertinent at this time is that transfer of organisms occurs rapidly among personnel in a closed environment.

OROPHARYNGEAL INFECTION

Oropharyngeal Flora

The normal flora of the oropharynx shows marked individual variation. However, the flora of each individual remains relatively constant (35, 36). The most commonly found organisms are aerobic and anaerobic streptococci, hemolytic and nonhemolytic staphylococci, Neisseria species, Fusobacterium, lactobacilli, coliforms, corynebacteria, and Candida species. Quantitative studies of the orophryngeal flora, which at best present rough estimates, indicate that streptococci and lacto-

bacilli occur in the highest numbers (37, 38). From the above list of most commonly found organisms it is apparent that only a few oropharyngeal bacteria have pathogenic properties, and unless the environmental changes of space induce virulence or greatly reduce resistance, these bacteria would not be expected to cause significant disease. Before discussing the pathogenic potential of the more virulent members of the oropharyngeal flora, the local host mechanisms responsible for the ecological balance will be described.

Oropharyngeal Defense System

The local defense mechanisms of the oropharynx are the anatomic and physiological barriers of the mucous membranes, the antibacterial properties of saliva, lysozymes, immune globulins, low pH, deglutition, and the presence of an indigenous flora. Although information concerning the quantitative role that each of these systems performs is meager, it appears that the more important mechanisms are an intact mucous membrane and the indigenous flora. Local infections are most often associated with traumatic disruption of the epithelial cell lining and secondary bacterial infection (38, 39). Examples of this pathogenesis are anaerobic cellulitis following dental extractions (39) and lingual infections resulting from prior trauma (40). Systemic disease such as endocarditis may also follow physical disruption of the mucous membranes with consequent entry into the blood of organisms such as Streptococcus viridans (41, 42).

Maintenance of the indigenous flora prevents overgrowth of any one strain and resultant superinfection. The specific mechanisms responsible for maintaining this remarkable ecological balance are not well understood at this time. Nutritional requirements probably limit individual bacterial growth. The pH of the oropharynx also determines the bacterial constituents, as a low pH favors the growth of certain organisms (lactobacilli), whereas a more neutral pH prevents their growth (38). Some oropharyngeal bacteria (Streptococcus salivarius) secrete substances that are bactericidal for pneumococci (43). In some nonspecific manner, the oropharyngeal bacteria must inhibit fungal growth, because treatment with broad-spectrum antibiotics is often associated with candidal overgrowth (38, 44).

The antibacterial properties of saliva, lysozymes, immune globulins, and deglutition also maintain the indigenous flora.

Saliva performs three protective functions. It washes bacteria into the esophagus, it contains lysozymes, and it protects the mucous membranes from drying. The washing action of saliva appears to be a significant factor in preventing new bacteria from establishing themselves in the oropharynx (35, 45). Organisms native to the mouth and capable of surviving in vitro in saliva rapidly disappear from the mouth following inoculation or aerosolization, presumably due to the flushing action of saliva. Salivary lysozymes are bactericidal for many bacteria (38, 46). How important this effect is cannot be determined at present, but because lysozymes are considered a major component of the antibody-complement reaction (47), it is likely that lysozymes act in the immune reactions that prevent multiplication of invading pathogens. Immune globulins, especially IGA, have been clearly shown to correlate with antiviral immunity to respiratory viruses (48). The antibacterial importance of these proteins probably relates both to systemic and local protection. Deglutitions approximate 600 per day and aid salivary washing (49).

The effect of the above defense mechanisms is to regulate for each individual the species and numbers of the pharyngeal microbiota. It is of interest that the significance of local phagocytosis as well as of the large amount of pharyngeal lymphoid tissue is unknown.

Oropharyngeal Pathogens

The oropharyngeal bacteria of significant virulence are Neisseria meningitidis, beta hemolytic streptococci, Staph. aureus, D. pneumoniae, and Corynebacterium diphtheriae. With the exception of C. diphtheriae, each of these organisms is often part of the normal oropharyngeal flora. However, as the data to be cited will show, the susceptible individuals are the newly infected; carriers are generally resistant.

Neisseria meningitidis

Carrier rates vary with population geographics and density. Civilian carrier rates approximate 15 percent (50, 51). During epidemics, especially in military camps, the carrier rate may reach 40 percent (52). Transmission is person to person via droplet spread. The organism is metabolically too fragile to survive the external environment for significant

periods, and contamination is not an epidemiological problem. The carrier state may persist for months in an asymptomatic individual. It is generally agreed that a bacteremic episode follows acquisition of the organism, and, at this time, meningococcemia or meningitis develops (53).

The available evidence suggests that susceptibility to disseminated disease is more dependent on host defense than on bacterial virulence (53). Both during and between epidemics, large numbers of people become colonized by potentially virulent meningococci, but only an occasional person develops significant disease. The exact nature of the factors responsible for preventing disseminated disease in the vast majority of infected individuals is unknown. Antibodies of the agglutinating and complement-fixation types can be demonstrated in diseased as well as nondiseased newly infected individuals. Recent studies have suggested that antibody to group-specific A and C capsular antigens does correlate with immunity (54). These studies, although admittedly in an early stage, offer the possibility of vaccination.

Since the carrier is not the susceptible person, the significance of local defense mechanisms is minimal in this disease. This is borne out in studies in recruits which show that most, if not all, of the subjects acquire the epidemic strain in a short time (55).

Effect of Environmental Factors on the Meningococcus The effect of ultraviolet light on various meningococcal species has been extensively studied by Jyssum and Lie (56-58). These authors have demonstrated with auxotrophs that ultraviolet irradiation is lethal to meningococci. A single "hit" inactivates the cell and its diplococcal partner without causing an increase in mutation. Ninety-nine percent of cells are killed by ultraviolet irradiation at a wavelength of 2537 A, the wavelength that would be expected to be most mutagenic (58).

Prophylaxis Because of the metabolic fragility of meningococcus, its susceptibility to ultraviolet irradiation, its possible susceptibility to hyperoxia, and its mechanism of infection, the risk of meningococcal disease within the space capsule does not appear to be greater than normal. However, the number of individuals harboring meningococci makes it possible that an astronaut may be a carrier and that droplet transmission could ensue. Should this happen, meningococcal typing and determination of the noncarrier antibody levels ought to be performed. The decision to eradicate the menin-

gococcus with penicillin can then be considered, with the understanding that evidence supporting this type of prophylaxis is far from conclusive and that the efficacy of prophylaxis is therefore speculative. Should vaccines become available, they would be the prophylactic method of choice.

Beta Hemolytic Streptococci

Approximately 10 percent of individuals harbor hemolytic streptococci in their throats (59). The carrier rate increases to 25 percent among populations where predisposing environmental conditions of crowding and viral infections are present (60). Unlike the meningococcus, the streptococcus is capable of surviving for several weeks outside the body (61). However, while the organism survives the external environment, it rapidly loses its infectivity (62). Transmission is primarily via intimate contact with infected individuals (63-65) and less frequently by droplet spread (29, 63, 66). In selected instances, contact with contaminated materials such as bedding may induce infection (29, 66, 67). The many excellent studies of streptococcal epidemiology have clearly shown that the nasal carrier, by dispensing hundreds of thousands of streptococci into the environment, is the significant transmitter, whereas the pharyngeal carrier is relatively harmless because this group expels few organisms (68, 69). Because of the importance of intimate contact, infection is a function of distance from the nearest carrier, and decreasing acquisitions occur up to 30 feet (29). Individual streptococcal properties, as well as local host defense mechanisms, affect streptococcal communicability. Loosli et al. (70) have shown that differences in invasiveness occur among streptococcal strains. Protection is limited because solid immunity to the more virulent group A strains depends on previous infection with the homologous M-type (62). Because of the many M-protein types and the specificity of immunity, streptococcal reinfection is frequent.

Effect of Environmental Factors on the Streptococcus

Ravin and Mishra (71) have demonstrated that ultraviolet irradiation will readily induce streptomycin-resistant mutants. Reflecting the dual effect of radiation, the mutation rate is maximal (2000-10,000-fold increase) from a dose that kills 99 percent of the colony-forming units.

The bacteriostatic effect of hyperoxia varies with the streptococcal species. Strep. pyogenes is very susceptible,

Strep. viridans less susceptible, and Strep. faecalis is resistant to the inhibitory effect of oxygen at 1.0 atm pressure (11).

Ozone is more deleterious to host resistance than to bacterial growth, and levels as low as 0.08 ppm enhance streptococcal infectivity (72). Carbon monoxide at the low levels (25 ppm) that might occur in spaceflight has also been shown to depress murine resistance to streptococcal aerosol (73). The risk from both of these pollutants may increase in the Apollo Application Program, because the orbiting laboratory may contain fuel-burning machinery capable of producing carbon monoxide and ozone.

Prophylaxis The above data suggest that streptococcal disease may be a significant risk in future space operations. Because of the high rate of communicability via droplet or contact transmission, nasal carriers should be treated prior to the mission. Pharyngeal carriers are less dangerous, and the decision in these cases is not clear-cut. Elimination of even these carrier states may be wise because of the increased susceptibility associated with prior viral illness (74) and the possibility of exposure to increased carbon monoxide concentrations.

Staphylococcus aureus

Staphylococci, both coagulase-positive and coagulase-negative, are found in the nasopharyngeal passages of a large percentage of the population. Leedom et al. (75) recorded a nasal carrier rate of 22 percent for coagulase-positive staphylococci and 62 percent for coagulase-negative. The carrier state may be transient, intermittent, or permanent (76). The organism is particularly hardy and survives for considerable periods of time in the air or surrounding environment. Ultraviolet irradiation is lethal for staphylococci at doses that do not significantly affect man (77), and this effect is utilized during surgery (77, 78). Mutation data for ionizing irradiation were not found. Staphylococcal growth in vitro is inhibited by hyperoxia (9, 11). In vivo studies have given conflicting results, with some investigators reporting a beneficial effect of hyperoxia in experimental staphylococcal infection (79), others no effect (9), and some a deleterious effect (80). These differences may be due to differences in host (guinea pigs and mice) and methods of infection.

While the evidence presented is crude, the consensus of those in the field is that hyperoxia decreases staphylococcal infectivity in humans (81).

Transmission of staphylococcal infection is person to person or via contact with contaminated sites. Numerous studies have shown that the strain of staphylococcus in a relatively closed ecological system, such as a hospital, will within a short time be implanted in a newcomer's nasopharyngeal flora (76, 82, 83). If the newcomer receives an antibiotic to which the environmental staphylococcal strain is resistant, the chance for colonization increases markedly. These studies, together with spacecraft data from NASA (84, 85), indicate that staphylococcal spread will invariably occur within the space capsule. However, since serious staphylococcal disease usually requires an individual with altered host resistance (76), it is doubtful that the acquisition of staphylococci will be clinically significant except under special circumstances.

Diplococcus pneumoniae

The pneumococcus is not a significant cause of local pharyngeal infection. Twenty-five to fifty percent of the population carry virulent pneumococci in their nasopharyngeal regions (86). These asymptomatic carriers continually lose old types and acquire new pneumococcal types. Pneumococcal virulence is related to its capsular polysaccharides which prevent phagocytosis (87). Nasopharyngeal colonization is specifically affected by the local flora. Organisms such as Strep. salivarius prevent colonization by secreting antipneumococcal substances. However, the clinical importance of these bactericidal substances is unclear because studies have failed to demonstrate an inverse association of pneumococcal disease to concentration of Strep. salivarius (43). Host factors play an important role in pneumococcal disease (88). Previous viral infections, alcoholism, and immunologic deficiency states are predisposing conditions. Aspiration following anesthesia or alcoholic debauch is also associated with pneumococcal disease, presumably due to tracheobronchial inoculation. Impairment in intrapulmonary bactericidal function may also reduce host resistance and result in pulmonary infection. Person-to-person transmission does not appear to be an important factor.

Effect of Environmental Factors on the Pneumococcus
Ravin and Mishra (71) were unsuccessful in attempts to induce streptomycin-resistant mutants of pneumococcus with ultraviolet irradiation. This resistance to the mutagenic effect of ultraviolet radiation did not carry over to its lethal effect, because 90-99 percent of colony-forming units were susceptible to standard dosages.

Pneumococcal multiplication is susceptible to hyperoxia (9). Experiments using 100 percent oxygen at 2 atm pressure have shown marked *in vitro* inhibition. As with staphylococci, *in vivo* experiments have produced conflicting results. Ross and McAllister (89) injected mice under hyperoxic conditions intraperitoneally with *D. pneumoniae* and concluded that therapy prolonged life. Kaye (9) exposed mice to hyperoxic conditions for 30-90 min following intravenous injection of *D. pneumoniae* and did not note a protective effect.

Prophylaxis Pneumococcal disease, especially pneumonia, is always a possibility. However, the incidence in the astronaut age group is low, and there is no reason to suspect an increase due to spacecraft conditions. Except for a prior viral illness, the usual predisposing factors are unlikely in an astronaut population. Therefore, although pneumococcal transmission via a nasal carrier may be anticipated, the recipient can be expected to be asymptomatic. Treatment of the pneumococcal carrier is unnecessary.

Aerospace Data

Since the aerospace era is in its infancy, few studies concerning transmission of infection within a spacecraft have been reported. One of the earliest studies, by Moyer and Lewis in 1964 (85), demonstrated constancy of the individual oropharyngeal flora during a 14- to 30-day simulated flight of two men in a space capsule. Oxygen concentrations from ambient to 100 percent and altitudes from sea level to 33,500 ft were experienced without alterations in the flora of test pilots. Interchange of organisms (*Staph. aureus*) between pilots occurred in one of four experiments. Moyer subsequently reported a more extensive study of four volunteers exposed for 56 days to an oxygen-helium atmosphere in a simulated spaceflight (84). The subjects harbored the usual aerobic oropharyngeal flora (alpha hemolytic streptococci, Neisseria, and staphylococci). Beta hemolytic streptococci were not found.

Transfer of Staph. aureus from one volunteer to another appeared to occur in one instance. Phage typing was used to substantiate the identity of the transferred organism. Staphylococci with phage types identical to those present in the volunteers were recovered from the spacecraft atmosphere. Quantitative studies, although crudely performed by open agar plate sampling, failed to demonstrate a cumulative increase in aerobic organisms. The maintenance of bacterial contamination rate was attributed to the effectiveness of the microbiological filtration apparatus.

Lotter et al. (90) studied volunteers confined for six weeks under simulated aerospace conditions. Selected body areas (ear, nose, throat, and skin) were sampled for bacteriological flora by means of cotton swabs, and environmental areas such as the bed, table, and floor were sampled by swabbing and exposing media to the air. Culture identification was performed for staphylococci and micrococci. These authors also did not find significant change in volunteer or environmental flora. They concluded that confinement, even under minimal hygienic conditions, did not cause a buildup of pathogenic organisms or lowered resistance to infection.

NASA, in a much more detailed study of an eight-day space capsule test, found that Staph. aureus and alpha streptococci were transmitted by nasal carriers to other crew members (5). This report also noted the appearance and possible pharyngeal transfer of D. pneumoniae. The majority of nasal and pharyngeal organisms cultured prior to the space simulation test were present in similar concentrations post-test. Data describing the environmental bacterial populations within the spacecraft were not presented.

Bacteriological study of space missions began with Apollo 7. The following data from the Apollo 7-9 missions were kindly supplied for this report by J. K. Ferguson and G. T. Taylor from their as yet unpublished studies at the Manned Spacecraft Center in Houston. These findings are preliminary. Cultures were taken 30 days before flight, immediately preflight, and immediately postflight from the axilla, umbilicus, inguinal, hand, throat, scalp, nose, and toe regions. Stool and urine specimens were also cultured. Samples were placed in trypticase soy broth for aerobic organisms and vermillion-inhibiting broth for anaerobic organisms. Quantitative estimations were performed by serial dilution techniques, and qualitative isolations were attempted for all bacteria and fungi.

Apollo 7 Beta hemolytic streptococci were isolated from the skin of all three astronauts at the 30-day and immediately

preflight examinations. The organism was not present in nasal or throat cultures at these times. Postflight throat gargles grew large numbers of beta hemolytic streptococci (10^5/ml) from each of the astronauts. Streptococci were also present in several cultures of skin and stool. In this study oropharyngeal colonization from direct contact appears to have occurred during spaceflight.

Staph. aureus (not typed) was isolated from the skin, scalp, nares, and throats of the three astronauts at each of the culture periods. Postflight cultures did not show an increased incidence of staphylococci. Transmission of the organism cannot be evaluated from these data. D. pneumoniae was not isolated from any of the astronauts. Pseudomonas aeruginosa and Mima polymorpha were inconstantly found. Herellea species were not cultured prior to spaceflight but were present in large numbers at eight sites in two crew members postflight.

Candida albicans, as would be expected, was cultured from each of the astronauts at the three time periods studied. Aspergillus fumigatus was present in one astronaut throughout the study, in one before and after the spaceflight, and one astronaut may have become contaminated during the spaceflight. These data are too fragmentary to derive any conclusions from them.

Apollo 8 A profile of the same organisms gave markedly different results from Apollo 7. Oropharyngeal colonization by beta hemolytic streptococci during the mission was not demonstrated. Staph. aureus and D. pneumoniae were irregularly cultured from the three astronauts. Ps. aeruginosa was not found preflight but was present in two astronauts postflight (site not specified). M. polymorpha, Herellea, and Proteus showed changes in one instance each. Candida and Aspergillus were more frequently isolated preflight than postflight. The overall effect appears to be a minor and probably insignificant individual floral change.

Apollo 9 Similar results were obtained for this flight as the previous Apollo 8 mission. Beta hemolytic streptococci were isolated from one crew member throughout the study, from the second in preflight specimens only, and were never present in the third crew member.

PULMONARY INFECTION

Aerosols

Pulmonary deposition of bacteria is primarily the result of exposure to aerosols. A number of factors determine the significance of this exposure. The inhaled particles must be approximately 4.0 μm or less if they are to traverse the mucociliary stream and reach the deeper recesses of the lung (91). The particles must be in an environment that allows bacterial survival. Low relative humidity and temperature cause death of airborne cells (92-94). Rapid changes in relative humidity also cause death for certain species (95). Visible light and hyperoxia which have been previously discussed decrease airborne survival. Although unstudied at present, the zero gravity state may affect survival. It probably will affect infectivity by increasing particle volume and by changing rates of deposition. Of the above factors, hyperoxia, visible light, and zero gravity are the ones that apply to the spacecraft environment. Temperature and relative humidity are fixed in ranges which, while not optimal, should allow bacterial survival. The significance of the other factors awaits environmental investigations that can be performed during spaceflight.

Pulmonary Defense System

Man's lungs are normally sterile (96-99). Numerous studies have shown that despite continuous exposure to environmental bacteria, the region from the primary bronchus downward is free of bacteria. Experimental evidence which will be discussed later indicates that the defense mechanisms responsible for the sterile state are phagocytosis by the pulmonary macrophage system (97, 99) and physical removal of invading bacteria via the mucociliary stream (100, 101). Data concerning the relative significance of each of these mechanisms in man is meager. Techniques for determining intrapulmonary bactericidal activity in the human have not been developed. Similarly, studies of human alveolar macrophage function are few and concern anatomic descriptions of the cell (102, 103). More recently, radioisotope techniques have been developed which allow study of the mucociliary stream (104-107). These studies show transport rates between 10 and 20 mm/min and clearance of more than 90 percent of material deposited on the mucosa

in less than 1 h. Studies performed in patients with chronic lung disease have demonstrated impaired mucociliary clearance, presumably due to alterations in ciliary activity. The pathogenic significance of this impairment, however, is uncertain because cough results in rapid movement of large amounts of radioactive material and may compensate for the reduced rate of mucociliary flow (108).

In contrast with the limited amount of human data, there is a large body of experimental evidence on host resistance to pulmonary infection. Experiments using murine models have demonstrated that in both mice and rats intrapulmonary phagocytosis is the primary defense against inhaled organisms (99, 109). In these experiments, radiolabeled bacteria were killed within the lungs at a much more rapid rate than they were removed. By the use of fluorescent-labeled bacteria, the macrophage was shown ingesting the inhaled organisms (99). Similar inhalation experiments have demonstrated that this remarkable defense system is sensitive to parasite and host factors. Different bacteria are killed at different rates (110), and these differences in bactericidal susceptibility in part account for variations in virulence. As an example, Proteus mirabilis is killed at a much slower rate than is Staph. aureus, and in instances where intrapulmonary bactericidal activity is impaired, simultaneous aerosolization of Proteus and staphylococcal organisms results in multiplication of the Proteus but continued inactivation of the staphylococci (111).

In addition to being affected by parasite differences, the intrapulmonary bactericidal system is altered by host abnormalities that are associated clinically with increased susceptibility to pulmonary infection. The experimental induction of hypoxia (112), starvation (112), acute renal failure (113, 114), metabolic acidosis (109), viral infection (115, 116), or alcoholism (112) cause inhibition in bactericidal function. The pulmonary defense mechanism responds to physiological derangement but is relatively resistant to anatomic injury such as is produced by silica (117). This impairment due to physiological derangement is probably the mechanism for the enhancement of murine susceptibility to inhaled bacteria that is observed in hyperoxic conditions. Together these data suggest that impaired pulmonary bacterial resistance should be suspected among the astronauts, especially during prolonged spaceflight with hyperoxic conditions.

Physical Removal Mechanisms

Physical removal of inhaled bacteria and small-particle pollutants is accomplished by the mucociliary stream, cough reflex, and, to a much lesser extent, the lymphatic system. The mucociliary stream can be divided into ciliary and mucus components. The cilia, by moving in a coordinated manner, rapidly propel the overlying mucus from the lung. The mucus layer is principally derived from nonciliated goblet cells and is composed of mucopolysaccharides, neuraminic acid, lysozymes, and immune globulins. Inhaled particles adhere to the mucus and are carried from the lungs. Although it is reasonable to assume that the removal of noxious inanimate particles, such as silica, asbestos, and smoke, is important in pulmonary defense, it does not appear as certain that bacterial removal is as beneficial. In fact, the evidence for enhanced bacterial susceptibility in instances of mucociliary dysfunction is minimal (100, 101, 118, 119, 120). While the mucociliary stream may play a role in pulmonary bacterial defense, its importance appears to be considerably less than the intrapulmonary bactericidal activity of the lung (99). Many environmental factors such as drying (121), cooling (121, 122), sulfur dioxide (123, 124), ozone (125), cigarette smoke (127, 128), nitrogen dioxide (121, 126), and inanition (129) affect mucociliary function adversely. Experimental viral infections destroy tracheobronchial mucosa (101). These deleterious actions may enhance susceptibility to bacterial infection, but few bacterial studies have been performed, and these do not show an increased risk in instances of mucociliary stream impairment due to such pollutants as sulfur dioxide (120).

With the exception of the possible presence of toxic gases (ozone, sulfur dioxide, nitrogen dioxide) and other chemical pollutants, spacecraft conditions should preclude mucociliary injury due to the other known adverse factors, i.e., cooling, drying, and inanition.

Effect of Pollutants

The chemical pollutants most likely to alter pulmonary defense function are ozone, nitrogen dioxide, sulfur dioxide, and carbon monoxide. Since measurements during spaceflight of ozone, sulfur dioxide, and nitrogen dioxide were not made in early spaceflights, the risk from these noxious gases is not well known.

Ozone Ozone is one of the most toxic pollutants known. It has been found in airplane cabins at altitudes above 30,000 ft, presumably related to the high ozone concentrations that are present in the upper atmosphere (130). Exposure to levels as low as 5-20 ppm for 1 h or more can cause pulmonary edema, hemorrhage, and death (106). Ozone is toxic for all components of the pulmonary defense system. It impairs the alveolar macrophage (132) and mucociliary function (125) and inactivates bronchial mucous lysozyme (133). Exposure to ozone increases murine susceptibility to inhaled pathogens (Klepsiella pneumoniae) (131). These studies indicate that astronauts exposed to elevated ozone levels for prolonged periods may have an increased risk of infection.

Sulfur Dioxide Sulfur dioxide enters the atmosphere from combustion of coal or fuel oil. Since neither of these energy sources is presently used in the space capsule, it is unlikely that sulfur dioxide will be an important pollutant. Investigations with volunteers have demonstrated that the effects of sulfur dioxide are more symptomatic than permanently deleterious. Thus while the gas causes coughing and posterior pharyngeal and substernal discomfort, it is almost entirely absorbed within the nasopharynx and, as such, probably does not affect pulmonary bacterial resistance (134). More detailed experiments with dogs have substantiated the localized absorption of sulfur dioxide within the upper airways (135). These studies using radiolabeled sulfur-35 did show, however, that a small amount of sulfur dioxide is expelled from the pulmonary capillary bed and in this manner reaches the alveoli. The significance, if any, of these small concentrations within the pulmonary airway system could not be ascertained from these experiments. Should significant amounts of sulfur dioxide reach the tracheobronchial mucosa, impairment in mucociliary function would be expected due to reduction in ciliary activity (121) and hypersecretion of mucus (120).

Nitrogen Dioxide Nitrogen dioxide enters the atmosphere as a by-product of natural gas combustion, following explosions, and in industrial processes requiring the handling of nitric acid (136). Acute exposures cause pulmonary edema, cyanosis, and dyspnea and may eventuate in bronchopneumonia. Occasionally, bronchiolitis obliterans occurs and may result in death (137). Prolonged exposure to relatively low concentrations of nitrogen dioxide (4.0 ppm) does not cause either pulmonary pathology or decreased respiratory function in animals (138, 139). Ehrlich

(136), however, has demonstrated increased susceptibility to pulmonary infection in mice exposed to very low concentrations of nitrogen dioxide (0.5 ppm) for three months. These studies indicate, as had the previously cited studies of Green and Kass (97, 110), that pulmonary resistance to inhaled bacteria is a delicate physiological mechanism which can be inhibited by small environmental change.

Carbon Monoxide While there are many studies of carbon monoxide toxicity (140-143), few relate to infection (142, 143). Those that do usually include carbon monoxide as a component of automobile exhaust fumes. In experimental studies, carbon monoxide in concentrations of 25 ppm (this level is reached in space cabins) depresses murine resistance to streptococci (73). Although superficially these data suggest significance, further study is necessary to determine if these data can be extrapolated to human situations.

Methane The increased concentrations of methane within the space capsule are produced by the astronauts' intestinal flora. The gas has not increased to toxic levels in simulated spaceflights (personal communication from Dr. E. S. Harris).

Fiber Glass The fiber-glass material that is used in the astronauts' suits is a potential hazard peculiar to spaceflight. The suit fiber glass is composed of molecules 1-3 μm in diameter. During recent Apollo missions, some of the fiber glass has fragmented, contaminating the atmosphere (personal communication from Dr. E. S. Harris). While the fiber glass is believed to be biologically inert, particles of this size should deposit distal to the mucociliary stream and in large quantities may be capable of inducing a host response or synergistically activating a previously present disease process.

Conditions that Increase Pulmonary Susceptibility to Infection

Viral Infection Viral infections are a well-established predisposing cause of bacterial illness (74, 144-146). Clinical studies have shown increased susceptibility to *Staph. aureus* (144, 145), *D. pneumoniae* (146), and *Hemophilus influenzae* (147) following viral infection. The pathophysiological basis for this association was supplied by Green and colleagues who demonstrated in mice impaired pulmonary resistance to in-

haled bacteria during the 7-10 day period following challenge, with either a benign (116) or virulent virus (115). These observations are pertinent to spacecraft missions because the long subclinical period in viral infections makes it a certainty that some astronauts will develop illness during the mission. If bacterial virulence is enhanced in the space environment due to any of the previously mentioned mechanisms, severe respiratory illness may result.

Immunity The importance of cellular and humoral immunity in preventing bacterial illness does not need substantiation. Both genetic and acquired host deficiencies increase susceptibility to infection. A very few studies have been performed concerning the effect of either simulated or actual space missions on immune mechanisms. These are only preliminary (148-150). Glenn and Becker (148), in primate studies under aerospace conditions, state that "the bacterio-immunological balance for oral bacteria seemed to favor the parasite during the 19 days of simulated flight." Harris, in studying a six-day simulated spaceflight with 100 percent oxygen at 5 psia atmosphere, reported an unchanged total protein, albumin, and serum electrophoresis (149). Berry summarized data from Apollo 7 and 8 and noted that significant change did not occur in serum protein functions, lymphocyte response, or RNA and DNA synthesis (150).

Significant Pulmonary Pathogens

The large number of potential pulmonary pathogens necessitates discussion of a representative few. The pneumococcus, Staphylococcus, and Streptococcus have been considered in the oropharyngeal section. This section will discuss Mycobacterium tuberculosis as an example of a virulent organism with potentially increased pathogenicity due to space environment, and Hemophilus influenzae as a minimally pathogenic bacterium with increased disease potential if host resistance decreases.

Mycobacterium Tuberculosis Increased risk of tuberculosis will occur within the spacecraft due to the close contact of astronauts, the elevated atmospheric concentrations of bacteria, and the probable increase in reactivation potential. The close contact makes transmission of this highly infectious agent likely. The closed environment will significantly increase mycobacterial concentrations because the organism is very hardy and can survive for months as an aerosol. Although hyperoxia

may diminish the number of viable aerosolized organisms (12, 13), it is doubtful that this inhibitory effect will overcome the increase due to a closed environment, especially since the organisms will be in the resting rather than in the growth phase, and it is the multiplication phase that is most susceptible to hyperoxia. Since severity of disease is a function of inhaled dose (151, 152), severe disease might develop.

Because of the stringent medical requirements, it is unlikely that an astronaut with active tuberculosis will be involved in spaceflights. However, the widespread prevalence of inactive tuberculosis presents the possibility that some personnel having inactive tuberculosis will eventually be part of a crew. On a theoretical basis, these astronauts may have an increased risk of reactivating their disease. Viable organisms may be present in "inactive" lesions. High pulmonary oxygen tensions favor growth of tuberculous lesions, and, in experiments with monkeys, the shunting of arteriolized blood through a tuberculoma causes rapid spread of disease. Hence, the hyperoxic conditions of spaceflight may possibly increase the reactivation potential of "inactive" tuberculomas.

The potential risk from the above factors cannot be quantitatively evaluated with present data. It would appear worthwhile to obtain these data, and, in the meanwhile, to administer a tuberculin skin test to astronauts prior to flight and to consider isoniazid prophylaxis for those who have positive reactions.

Hemophilus influenzae In patients with chronic bronchitis, H. influenzae is one of the most frequently found lower respiratory pathogens (153, 154). The organism is of low virulence and induces bronchitis or pneumonia as an opportunistic pathogen, especially in patients with defective immune mechanisms (155, 156). Since chronic bronchitis is often overlooked, it is conceivable that astronauts with low-grade pulmonary infection could be selected for space missions. Prolonged spaceflight might reduce their intrapulmonary resistance to infection and allow this opportunistic pathogen to multiply, initiating pneumonia. Since H. influenzae is representative of a large number of indigenous pulmonary pathogens, the potential magnitude of this problem requires that studies of the effect of prolonged space exposure on intrapulmonary antibacterial function be performed.

SUGGESTIONS FOR FUTURE INVESTIGATIONS

This review demonstrates the need for studies of "normal" and "environmental" flora during prolonged spaceflight and subsequent study of the effect of the unique environmental conditions on various host-parasite interrelationships. The space environment is sufficiently unique to predict that variations from terrestrial normal may be found. However, present knowledge is insufficient to predict the medical significance of the new "normal." In order to define the new bacterial ecology, investigations such as those being performed by NASA ought to be enlarged during the Apollo Application Program to include more frequent sampling of the various body and environmental sites. After establishing the host bacterial response to space exposure, an admittedly difficult task, indicator organisms, such as uncommon mutants or radiolabeled bacteria, could be used to determine rates of bacterial implantation and clearance. Similar studies of the environment would establish atmospheric concentrations of benign and pathogenic bacteria. As an example, an avirulent tubercle bacillus (H 37 Ra) could be used to follow mycobacterial contamination and host infection. Transmission of bacteria could be studied in a similar manner with enzymatic mutants of indigenous organisms. A biochemically discernible nonencapsulated pneumococcal mutant might be implanted in an astronaut's oral flora and its course followed.

Since all simulated experiments preclude a weightless condition, the important pathophysiological experiments of Ehrlich, Gordon, Mieszkuc, and others should be repeated in space conditions to determine the significance of the individual environmental parameters (hyperoxia and ozone, for example) in enhancing bacterial virulence. Studies of the effect of the space environment on phagocytosis, antibody production, complement, and other immune factors will be necessary to understand which diseases will occur.

In summary, the environmental changes of prolonged exposure to space conditions will cause alterations in host-parasite relationships that in all probability will result in variations from terrestrial pathophysiology. Whether these variations will be minor and amenable to present concepts of therapy or major and require radical therapeutic change, cannot be determined at this time. However, much of the available evidence suggests that increased bacterial disease potential will occur, necessitating therapeutic adaptation.

REFERENCES

1. Reynolds, O.E., and Saunders, J.F. Biosatellite II. Preliminary scientific observations. Currents in Modern Biology 2:147-157, 1968.
2. Thede, A.L., and Radke, G.E. Correlation of dose rate and spectral measurements in the inner Van Allen belt. Life Sciences and Space Research VI:59-68, 1968.
3. NASA. A biomedical program for extended space missions. Ionizing Radiation, pp. 1-35, May 1969.
4. Conkle, J.P. USAF School of Aerospace Medicine, SAM-TR-67-16, pp. 1-142, March 1967.
5. NASA Medical Research and Operations Directorate. The 2TV-1 Test Medical Report, June 16-24, 1968.
6. Gordon, F.B. Position Paper: Alteration in severity of disease because of altered host factors induced by parabaric environments. March 1969.
7. Ehrlich, R., and Mieszkuc, B.J. Resistance to experimental bacterial pneumonia and influenza infection in space cabin environment. Aerospace Med. 40:176-179, 1969.
8. Schmidt, S.P., Cordura, J.T., and Ball, R.J. Effect of environment on staphylococcal lesions in mice. Appl. Microbiol. 15:1465-1467, 1967.
9. Kaye, D. Effect of hyperbaric oxygen on aerobic bacteria *in vitro* and *in vivo*. Proc. Soc. 124:1090-1093, 1967.
10. Ehrlich, R., and Mieskzkuc, B.J. Effects of space cabin environment on resistance to infection. 1. Effect of 18,000 foot altitude on resistance to respiratory infection. J. Infect. Dis. 110:278-281, 1962.
11. McAllister, T.A., Stark, J.M., Norman, J.N., and Ross, R.M. Inhibitory effects of hyperbaric oxygen on bacteria and fungi. Lancet 2:1040-1042, 1963.
12. Hopkinson, W.I., and Towers, A.G. Effects of hyperbaric oxygen on some common pathogenic bacteria. Lancet 2: 1361-1362, 1963.
13. Gottlieb, S.F., Rose, N.R., Maurizi, J., and Lanphier, E.H. Oxygen inhibition of growth of Mycobacterium tuberculosis. J. Bact. 87:838-843, 1964.
14. Gottlieb, S.F. Bacterial nutritional approach to mechanisms of oxygen toxicity. J. Bact. 92:1021-1028, 1966.
15. Laurenzi, G.A., Yin, S., and Guarheri, J. Adverse effects of oxygen on tracheal mucus flow. New Eng. J. Med. 279: 333-339, 1968.

16. Giron, J.D., Pindak, F.F., and Schmidt, J.P. Effect of a space cabin environment on viral infection. Aerospace Med. 38:832-834, 1967.
17. Erhlich, R., and Miller, S. Effect of high altitude on resistance to inhalation. VEE virus infection. Arch. Environ. Hlth. 16:469-471, 1968.
18. Huang, K.Y., and Gordon, F.B. Production of interferon in mice: effect of altered gaseous environments. Appl. Microbiol. 16:1551-1556, 1968.
19. Chance, B., Jamieson, D., and Coles, H. Energy-linked pyridine nucleotide reduction: inhibitory effects of hyperbaric oxygen in vitro and in vivo. Nature 206: 257-263, 1965.
20. Gottlieb, S.F. Hyperbaric oxygenation. Adv. Clin. Chem. 8:69-139, 1965.
21. Conger, A.D., and Fairchild, L.M. Breakage of chromosomes by oxygen. Proc. Nat. Acad. Sci. 38:289-299, 1952.
22. Harrison, A.P., Jr. Survival of bacteria. Ann. Rev. Microbiol. 21:143-156, 1967.
23. Sistrom, W.R., Griffiths, M., and Stanier, R.Y. The biology of a photosynthetic bacterium which lacks colored carotenoids. J. Cell. Comp. Physiol. 48:473-515, 1956.
24. Mathews, M.M., and Sistrom, W. R. Function of carotenoid pigments in non-photosynthetic bacteria. Nature 184: 1892-1893, 1959.
25. Leff, J., and Krinsky, N.I. A mutagenic effect of visible light mediated by endogenous pigments in Euglena gracilis. Science 158:1332-1334, 1967.
26. Margulis, L. Visible light: mutagen or killer? Science 160:1255-1256, 1968.
27. Colebrook, L. Infection acquired in hospital. Lancet 2:885-890, 1955.
28. Mortimer, E.A., Lipsitz, P.J., Wolinsky, E., Gonzaga, A.S., and Rammelkamp, C.H., Jr. Transmission of staphylococci between newborns: importance of the hands of personnel. Amer. J. Dis. Child. 104:289-295, 1962.
29. Rammelkamp, C.H., Jr., Mortimer, E.A., Jr., and Wolinsky, E. Transmission of streptococcal and staphylococcal infections. Ann. Intern. Med. 60:753-758, 1964.
30. Sladen, W.J.L. Staphylococci in noses and streptococci in throats of isolated and semi-isolated antarctic communities. J. Hyg. 63:105-116, 1963.

31. Sawyer, R., and Sommerville, R.G. An outbreak of Mycoplasma pneumoniae infection in a nuclear submarine. JAMA 195:958-959, 1966.
32. Sciple, G.W., Remensnider, K., and Schleyer, C.A.S. Recovery of microorganisms shed by humans into a sterilized environment. Appl. Microbiol. 15:1388-1392, 1967.
33. Duquid, J.P., and Wallace, A.T. Air infection with dust liberated from clothing. Lancet 2:845-849, 1948.
34. Noble, W.C., and Davies, R.R. Studies on the dispersal of staphylococci. J. Clin. Path. 18:16-19, 1965.
35. Bartels, H.A., and Bleehman, H. The rapid clearance from the oral cavity of introduced streptomycin dependent and resistant strains of lactobacilli. J. Oral Med. 21:111-114, 1966.
36. Kraus, P.W., and Gaston, C. Individual constancy of numbers among the oral flora. J. Bact. 71:703-707, 1965.
37. Calloway, N.O., and Kujak, R.S. Pharyngeal flora of aged persons: effect of a penicillin (sodium nafcillin) administered orally. J. Amer. Geriat. Soc. 14:1261-1264, 1966.
38. Nolte, W.A. Oral Microbiology. C. V. Mosby Co., St. Louis, 1968. pp. 20-56.
39. Goldsend, G., and Braude, A.I. Anaerobic infections. Disease-A-Month 1-62, 1966.
40. Agarnal, K.K., Chhangani, D.L., and Bhattacharyya, S. Lingual abscess--aetiopathogenesis. J. Laryng. 80:1038-1040, 1966.
41. Hobson, F.G., and Juel-Jensen, B.E. Teeth, Streptococcus viridans and subacute bacterial endocarditis. Brit. Med. J. 2:1501-1505, 1956.
42. Lerner, P.I., and Weinstein, L. Infective endocarditis in the antibiotic era. New Eng. J. Med. 274:199-206, 1966.
43. Johanson, W.G., Sanford, J.P., Pierce, A.K., and Blackstock, R. Bacterial antagonism: viridans streptococci versus the pneumococcus. Clin. Res. 17:369, 1969.
44. Words, J.W., Manning, I.H., and Patterson, C.N. Monilial infections complicating the therapeutic use of antibiotics. JAMA 145:207-211, 1951.
45. Ostrom, C.A., Wolochow, H., and James, H. Studies on the experimental epidemiology of respiratory disease. IX. The recovery of airborne bacteria from the oral cavity of humans: the effect of dosage on recovery. J. Infect. Dis. 102:251, 1958.

46. Nemes, J.L., and Wheatcroft, M.G. Action of salivary lysozyme on Micrococcus lysodeikticus. Oral Surg. 5: 653-658, 1952.
47. Austin, K.F., and Cohn, Z.A. Contribution of serum and cellular factors in host defense reactions. I. Serum factors in host resistance. New Eng. J. Med. 268:933-938, 1963.
48. Cates, T.R., Rossen, R.D., Douglas, R.G., Jr., Butler, W.T., and Couch, R.B. The role of nasal secretion and serum antibody in the rhinovirus common cold. Amer. J. Epidem. 84:352-363, 1966.
49. Lear, C., Flanagan, J.B., and Moorees, C.F. The frequency of deglutitions in man. Arch. Oral Biol. 10:83, 1965.
50. Eickhoff, T.C. Current status of meningococcal infections in the United States. Read before the Conference of State and Territorial Epidemiologists. May 10-14, 1965.
51. Farrell, D.G., and Dahl, E.V. Nasopharyngeal carriers of Neisseria meningitidis: Studies among Air Force recruits. JAMA 198:1189-1192, 1966.
52. Aycocki, W.L., and Mueller, J.H. Meningococcus carrier rates and meningitis incidence. Bact. Rev. 14:115-160, 1950.
53. Feldman, H.A. Recent developments in the theory and control of meningococcal infections. Disease-A-Month 5-31, Feb. 1966.
54. Roberts, R.B. Opsonins after immunization of man with meningococcal capsular polysaccharides. Amer. Soc. Clin. Invest., 61st Annual Meeting, May 5, 1969, p. 69a.
55. Gould, J.R., Nitz, R.E., Hunter, D.H., Rush, J.H., and Gould, R.L. Epidemiology of meningococcal meningitis at Fort Ord. Amer. J. Epidem. 82:56-72, 1965.
56. Jyssum, K. Mutator factor in Neisseria meningitidis associated with increased sensitivity to ultraviolet light and defective transformation. J. Bact. 95:165-172, 1968.
57. Jyssum, K., and Jyssum, S. A genetic locus responsible for high mutability in Neisseria meningitidis. Acta Path. Microbiol. Scand. Suppl. 187:52-64, 1967.
58. Lie, S. The inactivating and mutagenic effect of ultraviolet irradiation on Neisseria meningitidis. Acta Path. Microbiol. Scand. 63:456-468, 1965.
59. Dingle, J.H. The role of Lancefield groups of beta hemolytic streptococci in respiratory infections. New Eng. J. Med. 236:157-166, 1947.

60. Dingle, J.H. The clinical pattern of streptococcal infection in man. In McCarty, M. (ed.), Streptococcal Infections. Columbia Univ. Press, New York, 1954. pp. 120-129.
61. Zinsser, H.S., ed. Microbiology, 13th ed., Appleton-Century-Crofts, New York, 1965. p. 418.
62. Stollerman, G.H., and Pearce, E.A. The changing epidemiology of rheumatic fever and acute glomerulonephritis. Advances Intern. Med. 14:201-239, 1968.
63. Hamburger, M., Jr. Studies on the transmission of hemolytic streptococcus infection. I. Cross infections in army hospital wards. J. Infect. Dis. 75:71-78, 1944.
64. Kuttner, A.G., and Krumwiede, E. Observations on the epidemiology of streptococcal pharyngitis and relation of streptococcal carriers to the occurrence of outbreaks. J. Clin. Invest. 23:139-150, 1944.
65. Wannamaker, L.W. The epidemiology of streptococcal infections. In McCarty, M. (ed.), Streptococcal Infections, Columbia Univ. Press, New York, 1954. pp. 157-175.
66. Lemon, H.M., Loosli, C.G., and Hamburger, M., Jr. Studies on the transmission and control of respiratory disease within army barracks. II. Spread of streptococcal infections among enlisted personnel. J. Infect. Dis. 82: 72-85, 1948.
67. Perry, W.D., Siegel, A.G., Rammelkamp, C.H., Jr., Wannamaker, L.W., Chamovitz, R., and Marple, E.L. Transmission of group A streptococci: I. The role of contaminated bedding. Amer. J. Hyg. 66:85-101, 1957.
68. Loosli, C.G., Lemon, H.M., Wise, H., and Robertson, D.H. Studies on the transmission and control of respiratory disease within army barracks. I. Hemolytic streptococcal contamination of the environment. J. Infect. Dis. 82:59-71, 1948.
69. Hamburger, M., Jr., Green, M.J., and Hamburger, V.G. The problem of the "dangerous carrier" of hemolytic streptococci. I. Number of hemolytic streptococci expelled by carriers with positive and negative nose cultures. J. Infect. Dis. 77:68-81, 1945.
70. Loosli, C.G. The transmission of hemolytic streptococcal infections in infant wards with special reference to skin dispersers. J. Lab. Clin. Med. 36:342-359, 1950.
71. Ravin, A., and Mishra, A. Relative frequencies of different kinds of spontaneous and induced mutants of pneumococci and streptococci capable of growth in the presence of streptomycin. J. Bact. 90:1161-1173, 1965.

72. Sharp, D.C. Lethal action of short ultraviolet rays on several common pathogenic bacteria. J. Bact. 37:447-460, 1939.
73. Coffin, D.L., and Blommer, E.S. Acute toxicity of irradiated auto exhaust indicated by enhancement of mortality from streptococcal pneumonia. Arch. Environ. Hlth. 15:36-38, 1967.
74. Nichol, K.P., and Cherry, J.D. Bacterial-viral interrelationships in respiratory infections of children. New Eng. J. Med. 277:667-672, 1967.
75. Leedom, J.M., Kennedy, R.P., Lepper, M.H., Jackson, G.G., and Dowling, H.F. Observations of the staphylococcal nasal carrier state. Ann. N.Y. Acad. Sci. 128:381-403, 1965.
76. Koenig, M.G. Staphylococcal infections treatment and control. Disease-A-Month 1-36, April 1968.
77. Hart, D., and Nicks, J. Ultraviolet radiation in the operating room. Arch. Surg. 82:449-465, 1961.
78. Hart, D., Postlethwaite, R.W., Brown, I.W., Smith, W.W., and Johnson, P.A. Postoperative wound infections. A further report on ultraviolet irradiation with comments on the recent (1964) National Research Council Cooperative Study Report. Ann. Surg. 167:728-743, 1968.
79. Irvin, T.T., Norman, J.N., Suwanagul, A., and Smith, G. Hyperbaric oxygen in the treatment of infections by aerobic microorganisms. Lancet 1:342-394, 1966.
80. Grogan, J.B. Lethal effect of hyperbaric oxygen on experimental staphylococcal infections. Surg. Forum 16: 81-82, 1965.
81. Behnke, A.R., and Saltzman, H.A. Hyperbaric oxygenation. New Eng. J. Med. 276:1478, 1967.
82. Lepper, M.H., Tillman, P., and Devetsky, R. Patterns of transmission of staphylococci. Ann. N. Y. Acad. Sci. 128:404-427, 1965.
83. Fekety, F.R., Jr. The epidemiology and prevention of staphylococcal infection. Medicine 43:593-613, 1964.
84. Moyer, J.E., Farrell, D.C., Lamb, W.L., and Mitchell, S.L. Study of man during a 56 day exposure to an oxygen-helium atmosphere at 258 mm Hg total pressure. XI. Oral, cutaneous, and aerosol bacteriologic evaluation. Aerospace Med. 37:597-600, 1966.
85. Moyer, J.E., and Lewis, Y.Z. Microbiologic studies of the two man space cabin simulator. Interchange of oral and intestinal flora. USAF School of Aerospace Medicine. SAM-TDR-64-3, March 1964.

86. Finland, M. Recent advances in the epidemiology of pneumococcal infections. Medicine 21:307-344, 1942.
87. Smith, D.T., Conant, N.F., and Overman, J.R. The pneumococcus and pneumonia. In Zinsser, H.S. (ed.), Microbiology, 13th ed., Appleton-Century-Crofts, New York, 1965. pp. 407-415.
88. Austrian, R., and Gold, J. Pneumococcal bacteremia with especial reference to bacteremic pneumococcal pneumonia. Ann. Intern. Med. 60:759-776, 1964.
89. Ross, R.M., and McAllister, T.A. Protective action of hyperbaric oxygen in mice with pneumococcal septicaemia. Lancet 1:579-581, 1965.
90. Lotter, L.P., Meyer, B.S., Horstman, M., and Rehg, U. Distribution of staphylococcal and micrococci among humans and their physical environment during simulated aerospace confinement. Amer. J. Clin. Path. 49:414-423, 1968.
91. Hatch, T. Respiratory dust retention and elimination. Proceedings of the Pneumoconiosis Conference, Johannesburg, 1959. J. and A. Churchill, Ltd., London. pp. 113-132.
92. Webb, S. Factors affecting the viability of airborne bacteria. I. Bacteria aerosolized from distilled water. Canad. J. Microbiol. 5:649-669, 1959.
93. Webb, S.J. The effect of relative humidity and light on air-dried organisms. J. Appl. Bact. 26:307-313, 1963.
94. Wells, W.F., and Riley, E.G. An investigation of the contamination of air of textile mills with special reference to the influence of artificial humidity. J. Ind. Hyg. Toxicol. 19:513-561, 1937.
95. Hatch, M.T., and Dimmick, R.L. Physiologic responses of airborne bacteria to shifts in relative humidity. Bact. Rev. 30:597-603, 1966.
96. Laurenzi, G.A., Potter, R.T., and Kass, E.H. Bacteriologic flora of the lower respiratory tract. New Eng. J. Med. 265:1273-1278, 1961.
97. Green, G.M., and Kass, E.H. Mechanisms of resistance to bacterial infection in the lung. Inhaled Particles and Vapours II, Pergamon Press, New York, 1966. pp. 229-241.
98. Pecora, D.V. A comparison of transtracheal aspiration with other methods of determining the bacterial flora of the lower respiratory tract. New Eng. J. Med. 269: 664-666, 1963.

99. Green, G.M., and Kass, E.H. The role of the alveolar macrophage in the clearance of bacteria from the lung. J. Exp. Med. 119:167-176, 1964.
100. Bang, F.B. Mucociliary function as protective mechanism in upper respiratory tract. Bact. Rev. 25:228-236, 1961.
101. Kilburne, K.H. Cilia and mucus transport as determinants of the response of lung to air pollutants. Arch. Environ. Hlth. 14:77-91, 1967.
102. Karrer, H.E. Electron microscopic study of the phagocytosis process in lung. J. Biophys. Biochem. Cytol. 7:357-366, 1960.
103. Myrvik, Q.N., Leake, E.S., and Fariss, B. Studies on pulmonary alveolar macrophages from the normal rabbit: A technique to procure them in a high state of purity. J. Immunol. 86:128-133, 1961.
104. Albert, R.E., Lippmann, M., Spiegelman, J., Liuzzi, A., and Nelson, N. The deposition and clearance of radioactive particles in the human lung. Arch. Environ. Hlth. 14:10-15, 1967.
105. Albert, R.E., and Arnett, L.C. Clearance of radioactive dust from the lung. Arch. Ind. Hlth. 12:99-106, 1955.
106. Morrow, P.E., and Gazioglu, K. The clearance of dust from the lower respiratory tract of man: An experimental study. In Davies, C.N. (ed.), Second International Symposium on Inhaled Particles and Vapours, Cambridge, England, 1966.
107. Luchsinger, P.C., Lagarde, B., and Kilfeather, J.E. Particle clearance from the human tracheobronchial tree. Amer. Rev. Resp. Dis. 97:1046-1050, 1968.
108. Green, G.M. Pulmonary clearance of infectious agents. Ann. Rev. Med. 19:315-336, 1968.
109. Goldstein, E., Green, G.M., and Seamans, C.S. The effect of metabolic acidosis on pulmonary bactericidal function in the rat (in preparation).
110. Green, G.M., and Kass, E.H. The influence of bacterial species on pulmonary resistance to infection in mice subjected to hypoxia, cold stress, and ethanolic intoxication. Brit. J. Exp. Path. 46:360-366, 1965.
111. Green, L., and Green, G.M. Differential suppression of pulmonary antibacterial activity as the mechanism of selection of a pathogen in mixed bacterial infection of the lung. Am. Rev. Resp. Dis. 98:819-824, 1968.
112. Green, G.M., and Kass, E.H. Factors influencing the clearance of bacteria by the lung. J. Clin. Invest. 43:769-776, 1964.

113. Goldstein, E., and Green, G.M. The effect of acute renal failure on the bacterial clearance mechanisms of the lung. J. Lab. Clin. Med. 68:531-542, 1966.
114. Goldstein, E., and Green, G.M. Alteration of the pathogenicity of Pasteurella pneumotropica for the murine lung caused by changes in pulmonary antibacterial activity. J. Bact. 93:1651-1656, 1967.
115. Green, G.M. Patterns of bacterial clearance in murine influenza. In Antimicrobial Agents and Chemotherapy, American Society for Microbiology, Washington, D. C., 1965. pp. 26-29.
116. Klein, J.O., Green, G.M. Tilles, J.G., Kass, E.H., and Finland, M. Effect of intranasal reovirus infection on antibacterial activity of mouse lung. J. Infect. Dis. 119:43-50, 1969.
117. Goldstein, E., Green, G.M., and Seamans, C. The effect of silicosis on the antibacterial defense mechanisms of the murine lung. J. Infect. Dis. 120:210-216, 1969.
118. Laurenzi, G.A., Guarneri, J.J. Endriga, R.B., and Carey, J.P. Clearance of bacteria by the lower respiratory tract. Science 142:1572-1573, 1963.
119. Arnold, L., Ostrom, M.L., and Singer, C. Autosterilizing power of nasal mucous membrane. Proc. Soc. Exp. Biol. Med. 25:624-627, 1928.
120. Reid, L. Natural history of mucus in the bronchial tree. Arch. Environ. Hlth. 10:265-273, 1965.
121. Dalhamn, T. Mucous flow and ciliary activity in the trachea of healthy rats and rats exposed to respiratory irritant gases (SO_2, H_3N, HCHO)--a functional and morphologic (light microscopic and electron microscopic) study, with special reference to technique. Acta Physiol. Scand. 36 Suppl. 123:1-161, 1956.
122. Krajina, G.Z. Damage of the respiratory mucus membrane of rats exposed to cold. Acta Otolaryng. 57:342-351, 1964.
123. Dalhamn, T., and Rhodin, J. Mucous flow and ciliary activity in the atachea of rats exposed to pulmonary irritant gas. Brit. J. Ind. Med. 13:110-113, 1956.
124. Hilding, A.C. Ciliary streaming in the lower respiratory tract. Amer. J. Physiol. 191:404-410, 1957.
125. Sheel, L.D., Dobrogorski, O.J., Mountain, J.T., Svirbely, J.L., and Stokinger, H.E. Physiologic, biochemical, immunologic and pathologic changes following ozone exposure. J. Appl. Physiol. 14:67-80, 1959.

126. Kensler, C.J., and Battista, S.P. Chemical and physical factors affecting mammalian ciliary activity. Amer. Rev. Resp. Dis. 93:142-149, 1966.
127. Dalhamn, T. Studies on tracheal ciliary activity: Special reference to the effect of cigarette smoke in living animals. Amer. Rev. Resp. Dis. 89:870-877, 1964.
128. Ballenger, J.J. Experimental effect of cigarette smoke on human respiratory cilia. New Eng. J. Med. 263:832-835, 1960.
129. Taramin, A., Wannamaker, B., and Srubny, L.M. The effect of inanition on the submandibular salivary glands and exocriae pancreas of the rat. Ann. N.Y. Acad. Sci. 121: 609-624, 1965.
130. Clamann, H.G., and Bancroft, R.W. Toxicity of ozone in high altitude flight. Adv. Chem. Series No. 21, 352-359, 1959.
131. Miller, S., and Ehrlich, R. Susceptibility to respiratory infections of animals exposed to ozone. I. Susceptibility to Klebsiella pneumoniae. J. Infect. Dis. 103:145-149, 1958.
132. Coffin, D.L., Gardner, D.E., Holzman, R.S., and Wolock, F.J. Influence of ozone on pulmonary cells. Arch. Environ. Hlth. 16:633-636, 1968.
133. Holzman, R.S., Gardner, D.E., and Coffin, D.L. In vivo inactivation of lysozyme by ozone. J. Bact. 96:1562-1566, 1968.
134. Speizer, F.E., and Frank, N.R. A comparison of changes in pulmonary flow resistance in healthy volunteers acutely exposed to sulfur dioxide by mouth and nose. Brit. J. Ind. Hlth. 23:75-86, 1966.
135. Frank, N.R., and Speizer, F.E. Sulfur dioxide effects on the respiratory system in dogs. Changes in mechanical behaviour at different levels of the respiratory system during acute exposure to the gas. Arch. Environ. Hlth. 11:624-634, 1965.
136. Ehrlich, R. Effect of nitrogen dioxide on resistance to respiratory infection. Bact. Rev. 30:604-614, 1966.
137. Lowry, T., and Schuman, L.M. Silo fillers disease-- A syndrome caused by nitrogen dioxide. JAMA 162:153-160, 1956.
138. Gray, E.L., Patton, F.M., Goldberg, S.B., and Kaplan, E. Toxicity of the oxides of nitrogen. Arch. Ind. Hyg. 10:418-422, 1954.
139. Wagner, W.D., Duncan, B.R., Wright, P.G., and Stockinger, H.E. Experimental study of threshold limit of NO_2. Arch. Environ. Hlth. 10:455-466, 1965.

140. Roberts, W.C. Correlation of blood carbon monoxide level with symptoms. Ind. Med. Surg. 21:323-325, 1952.
141. Goldsmith, J.R., Terzaghi, J., and Hackney, J.D. Evaluation of fluctuating carbon monoxide exposures. Arch. Environ. Hlth. 7:647-663, 1963.
142. Rokaw, S.N., and Massey, E. Air pollution and chronic respiratory disease. Amer. Rev. Resp. Dis. 86:703-704, 1962.
143. Baetjer, A.M. Chronic exposures to air pollutants and acute infectious respiratory diseases. Arch. Ind. Hyg. Occupat. Med. 2:400-406, 1950.
144. Finland, M., Peterson, O.L., and Strauss, E. Staphylococcal pneumonia occurring during epidemic of influenza. Arch. Intern. Med. 70:183-205, 1942.
145. Miller, W.R., and Jay, A.R. Staphylococcal pneumonia in influenza: Five cases. Arch Intern. Med. 109:276-286, 1962.
146. MacLeod, C.M. Pneumococci. In Dubos, R.J., and Hirsh, J.G. (eds.), Bacterial and Mycotic Infections of Man. 4th ed. J.B. Lippincott Co., Philadelphia, Pa., 1965.
147. Webster, L.T., and Clow, A.D. Association of pneumococci, Hemophilus influenzae, and Streptococcus hemolyticus with coryza, pharyngitis and sinusitis in man. J. Exp. Med. 55:445-453, 1932.
148. Glenn, W.G., and Becker, R.E. Aerospace profiles and normal immunological balance. Biosciences Division, USAF School of Aerospace Medicine Research Activities summary 1968 (Dec.), pp. 20-21.
149. Harris, E.S. Bioassays of body fluids. Physiologic results of Apollo spacecraft 008 space environment simulation test. NASA MSC-IN-DB-40-67, Jan. 11, 1967.
150. Berry, C. A. Preliminary clinical report of the medical aspects of Apollos VII and VIII. Aerospace Med. 40:245-254, 1969.
151. Glover, R. E. Infection of mice with Mycobacterium tuberculosis by the respiratory route. Brit. J. Exp. Path. 25:141-149, 1944.
152. Davis, B.D., Dulbecco, R., Eisen, H.N., Ginsberg, H.S., and Wood, W.B., Jr. Microbiology, Hoebner Medical Division, New York, p. 850.
153. Lees, A.W., and McNaught, W. Bacteriology of lower respiratory tract secretions in "normals" and chronic bronchitics. Lancet 2:1112-1115, 1959.

154. Davis, A.L., Grobow, E.J., Tompsett, R., and McClement, J.H. Bacterial infection and some effects of chemoprophylaxis with intermittent tetracycline. I. Chemoprophylaxis with intermittent tetracycline. Amer. J. Med. 31:365-381, 1961.
155. Kaplan, N.M., and Braude, A.I. Hemophilus influenzae infection in adults. Arch. Intern. Med. 101:515-523, 1958.
156. Wechsler, H.F., and Wolf, M.S. Agammaglobulinemia. Report of a case. JAMA 161:526-528, 1956.

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Appendix B: Microbiological Studies on Man in Closed Environmental Systems--Summary and Interpretation of Reported Observations

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INTRODUCTION

Microorganisms are an inescapable part of man's environment. He carries his own indigenous microflora with him wherever he goes, and in all ordinary circumstances there is some degree of interaction and interchange of microflora with the environment, including transfer between persons. It is now known that ordinary bacteriological sampling of body surfaces, including the gut, demonstrates only a small and uncertain proportion of the microorganisms present. Nevertheless, the general conclusion from extensive observations of this type is that each individual has a more or less static indigenous microbial population. It may appear to vary widely under normal conditions, but to what extent this is real or is the result of inconstant sampling and culturing methods is not clear. Variations beyond those regarded as within normal limits are known, or assumed, to be effected by such factors as diet, climatic conditions, personal hygiene, and physiologic alterations such as stress.

When man is put into a closed artificial environment such as a spacecraft, the factors that ordinarily control the bodily and environmental microflora are possibly modified, some perhaps profoundly. Over extended periods of time this could result in marked changes in the indigenous microflora. Under some circumstances it is clear that quantitative or qualitative changes in the normal flora of the gut are accompanied by disturbances

TABLE B1 Studies Included in This Report with Ancillary Data

Study Code No.	Category	Title of Tests (Abbreviated)	Where Performed and by Whom	Date	Chamber or Facility Used: Full Name	Chamber or Facility Used: Facility Code	Table in Which Results are Described
A1	Simulator; manned	Indigenous microflora of men	Wright-Patterson AFB, and contractors	1964-65	Controlled Activity Facility Life Support Systems Evaluators (2 connected chambers)	W-P	2
A2	Simulator; manned	Hazard of micrococci(1)	As in A1	1964-65	As in A1	W-P	2
A3	Simulator; manned	Hazard of micrococci(2)	As in A1	1964-65	As in A1	W-P	2
A4	Simulator; manned	Hazard of micrococci(3)	As in A1	1964-65	As in A1	W-P	2
A5	Simulator; manned	Microflora of man under simulated space environment	As in A1	1965-66	As in A1	W-P	2
A6	Simulator; manned	Hazard of micrococci(GT7)	As in A1	1965-66	As in A1	W-P	2
A7	Simulator; manned	Microbiological problems, sealed cabin	Brooks AFB; School of Aerospace Medicine	1961-62	Altitude simulator	Brooks	2
A8	Simulator; manned	56-day exposure to O_2-He	As in A7	1961-62	Altitude simulator	Brooks	2
A9	Simulator; manned	20-20-34 days of confinement	Aerospace Crew Equipment Lab; NMRI, NASA contracts	1964-65	Altitude chamber; control chamber	ACEL	2
A10	Simulator; manned	Microflora of feces	Wright-Patterson AFB, and contractor	1964	Contolled Activity Facility	W-P	2
B1	Simulator; unmanned; recycling	7-day closed door	Langley Research Center and contractor	1967	Integrated Life Support Systems	ILSS	3
B2	Simulator; unmanned; recycling	3- and 4-day closed door	As in B1	1967	As in B1	ILSS	3

B3	Simulator; unmanned; recycling	28-day closed door	Langley Research Center and contractor	1968	Integrated Life Support Systems	ILSS	3
B4	Simulator; unmanned; recycling	17-day closed door	Boeing Co.	1964	High Altitude Chamber	Boeing	3
C1	Simulator; manned; recycling	MESA II (Boeing 30-day)	As in B4	1964	High Altitude Chamber	Boeing	4
C2	Simulator; manned; recycling	Douglas--60-day	McDonnell Douglas Co.	1968	Space cabin simulator	DOUG	4
C3	Simulator; manned; recycling	28-day closed door	Langley Research Center	1968	Integrated Life Support	ILSS	4
D1	Spacecraft; ground tests	Partial bacteriological profile, etc.	North Amer. Aviation Corp., Downey, Calif.	1966	Apollo spacecraft	Apollo	5
D2	Spacecraft; ground tests	2TV-1/CSM	Space Environment Simulation Lab.; NASA, Houston	1968	Apollo spacecraft	Apollo	5
E1	Spacecraft; flights	Gemini flight IX	Cape Kennedy; contractors	1966	Gemini spacecraft	Gemini	5
E2	Spacecraft; flights	Apollo flights VII and VIII	Medical Res. and Operations; NASA, Houston	1968	Apollo spacecraft	Apollo	5
F1	Submarines	Epidemiologic studies aboard Polaris subs	At sea; Naval Biological Laboratory	Several years	Polaris submarines	Sub	6
G1	Protective shelter	Protective Shelter. I. Winter trials	Natl.Nav.Med.Center, Bethesda; Navy and Army Laboratories	1962	Protective Shelter (blast, radioactive fallout, biological and chemical warfare)	Navy, PS	7
G2	Protective shelter	Protective Shelter. II. Summer trials	As in G1	1962	As in G1	Navy, PS	7
H1	Experimental dives	Microflora of divers	Experimental Diving Unit, U.S. Navy	1967	Diving chamber	Navy, EDU	8
H2	Experimental dives	Microflora of divers	As in H1	1968	As in H1	Navy, EDU	8

in health, e.g., during antibiotic therapy, and maintenance of a normal microflora of other parts of the body is regarded as a factor in preserving health. If closed environmental systems do indeed modify normal body and environmental microflora it is important to assess this potential hazard to the health of astronauts.

The artificial environment of a space vehicle, including the abnormal atmosphere, may also influence the transmission of pathogenic microorganisms among astronauts by aerosol or other means or between the astronaut and his environment. The need for microbiological studies in connection with space travel is clear and has been recognized.

Over the past years a number of microbiological observations have been made on human volunteers and their immediate surroundings in restricted or closed environments which, more or less closely, simulate the conditions found in space vehicles. In some instances the microbiological studies were made only incidentally during the course of experiments that had other primary objectives, and the methods and scope of such studies have varied widely. It has been difficult to interpret the results, including the significance of observed changes, and precise comparison of observations performed by different investigators has not been possible.

The objectives of this report may be described as follows:

1. To bring together in one document the available information on microbiological studies on man in closed environmental systems, including pertinent details on the physical state of the environment, the microbiological methods used, and the results obtained. Related data on morbidity from infectious disease are included.
2. To compare and evaluate data from various experiments and observations to determine if general or specific conclusions can be drawn as bases for predictions of possible microbiological hazards in actual space vehicles or other closed environmental systems.
3. To identify remaining areas of ignorance.

METHOD

Twenty-six studies have been thoroughly reviewed to form the basis of this report. They were given code numbers for easy identification and are listed in Table 1. Each was

abstracted for significant information on the physical environment used, including content and pressure of the atmosphere, the design and methods of the experiments, the results, conclusions, and recommendations recorded. The individual abstracts comprise the final section of this Appendix. In most of these studies, various areas of the body of the personnel in the chamber were cultured regularly, some extensively, using as many as eight skin sites plus nose, eye, oral cavity, pharynx, and stool. In several, the atmosphere was cultured quantitatively or semiquantitatively, and in others, cultures were taken from interior surfaces of the chamber.

From the abstracts and original reports, significant items relating to the microbiological observations were selected as entries in Tables 2-8, which present the studies by categories determined primarily by the types of physical environments used. These data are analyzed in the Discussion section, and major comparisons are tabulated in Table 9.

Some of the studies reviewed here, and given a single code designation, represent a series of similar experiments or observations, the results of which are reported as a whole. In the Wright-Patterson study (W-P), coded as A1, for example, five separate but essentially replicate experiments were performed and reported together. The Brooks Air Force Base study, A7, summarizes eleven separate runs with two men each. In contrast, studies A2, A3, and A4 report observations on micrococci and staphylococci only, made during the broader studies described under A1 but published separately. This information is recorded in the tables as well as in the abstracts.

DISCUSSION

In this section, an attempt is made to interpret and compare microbiological results from the various studies. Table 2 summarizes the results obtained in closed chambers that were manned and that simulated to various degrees actual or possible spacecraft (Code A). Variation in results is evident, which will be shown below to correlate mainly with levels of personal hygiene and with the design of atmospheric control. Tables 3 and 4 describe results of tests in chambers containing integrated life-support systems. Microbiological observations were made on these systems as well as on the environment and the subjects. Although included in the unmanned tests (Code B),

TABLE B2 Studies on Spaceflight Simulators--Manned

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Environment	Observations on Microflora: Skin	Observations on Microflora: Oral Cavity and Pharynx	Observations on Microflora: Feces
A1	W-P	4 (5X)	42	Air at ambient pressure. Subjects were first in a 20' x 20' chamber (CAF) for semi-isolation for 7 days, moved to closed 1100 cu ft chamber (LSSE) for 28 days, and returned to CAF for 7 days; diet of precooked, freeze-dried food	Subjects and chambers thoroughly cleaned and disinfected before initial entrance to chambers; personal hygiene minimal thereafter. Unpressurized MA-10 suits worn	Moderate buildup in air of staphylococci from 0 time, then leveling off; data on other types not recorded; surfaces cultured only for micrococci (see Codes A2, A3, A4)	Increase in total nos. to 3rd week and stable thereafter. Detailed data available on Corynebacterium and Staph.	No remarkable changes in usual microflora; large nos. of *Neisseria* in mouth in 2 subjects; sporadic recovery in others; transfer suspected	No recognized transfer of gut microflora. Changes noted attributed to diet
A2 Micrococci only	W-P	4 (2X)	42	As in A1	As in A1	No significant changes in micrococci noted	No significant changes in micrococci noted; no evidence for transmission	No evidence for transmission of micrococci; no evidence of change in biochemical types	No significant changes seen in micrococci
A3 Micrococci only	W-P	4	42	As in A1	As in A1, except for slightly improved hygiene	As in A2	As in A2	As in A2	As in A2
A4 Micrococci only	W-P	4 (2X)	42	As in A1, except diet of liquid food	Essentially as in A1	No significant changes; one phage type of micrococcus transferred from subject to environment	No evidence for interpersonal transfer of micrococci; evidence for transfer from person to environment; no significant quantitative changes	Same data as for skin	As in A2
A5	W-P	4 3 4	34 21 60	As in A1, but time intervals varied; ambient temp. 73°F, but 90°F (LSSE) for two 1-week periods; diet changed from fresh to various processed foods with time	Essentially same as A1	General increase in nos. of bacteria in environment (LSSE) to day 25, then a leveling off	Increase in microflora, including enterobacteria, in groin, axilla, and glans penis, Corynebacteria predominated over Staph.; evidence for transfer of Proteus from men to environment	Evidence for transfer of a Staph. from mouth and nose to environment; transfer of typable Staph. appeared to be temporary. Evidence for interpersonal transfer of Candida	Marked change in anaerobic flora toward proteolytic types; shift in E. coli to typable, potentially pathogenic strain

A6	W-P Micrococci only	4	42	As in A5	As in A1	No buildup of potentially pathogenic types	Nose and groin most likely sites to harbor potentially pathogenic Staph.	(See A5)	Not recorded
A7	Brooks	2 (11X)	14 to 30	Elliptical steel cylinder, 380 cu ft, sealed; sea level to 33,500-ft altitude, varying with test; ambient to 100% O_2; recirculated, 300 cu ft/min; environmental control and life support equipment inside; diet of precooked, dehydrated whole foods	No information	No evidence for sustained change; no significant differences between tests at different altitudes	Not examined	Evidence for interpersonal transfer of micrococcus	Evidence for interpersonal transfer of a Salmonella
A8	Brooks	4, test 2, control	68	40.2 cu m compartment; during altitude run (56 days), 70% O_2, 30% He, 258 mm Hg; 250 cu ft/min flow through fiberglass filter (aerosolve 95, Cambridge Filter Corp.); temp. and humidity controlled; experimental diet not described	Daily bath	Aerosol counts did not change significantly with time; content normal	No changes in normal flora; interpersonal transfer of a Staph. from nose	No change in normal flora	Enterococci decreased during period of experimental diet; no transfer detected
A9	NAV	6, test 2, control	34	Cylindrical chamber, 22' x 8.5'; 7 days prerun and postrun in air at sea level; 20 days at 27,000 ft, 100% O_2; full pressure suits worn; diet of freeze-dehydrated food	Men and chamber cleaned at start; zero gravity sink used 1st week only; wash cloths used and regarded as source of contamination, no baths	Increased in incidence of normal types; all surfaces markedly contaminated with coliforms	Skin irritated by constant wearing of suits; increase in normal microflora of skin, particularly where sweat accumulated, attributed to lack of personal hygiene	Increase of streptococci, micrococci, and others in throat and mouth	Evidence for interpersonal transfer of a Salmonella; shifts in types of anaerobes attributed to experimental diet
A10	W-P	4	42	Controlled Activity Facility; a 20' x 20' chamber; air at ambient pressure; dehydrated space-type diet, 2 subjects; fresh and canned diet, 2 subjects, alternated	Not recorded	Not tested	Not tested	Not tested	Space diet resulted in predominance of new type of proteolytic anaerobe, flatulence. Pathogenic *E. coli* serotypes and Shigella found; no referable clinical illness

TABLE B3 Studies in Spaceflight Simulators--Unmanned--with Integrated Life-Support Systems (Recycling)

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Microflora of Environment
B1	ILSS	0	7	Vertical cylinder, 18 ft in diameter and height. Volume 4150 cu ft, divided into levels consisting of work area and crew quarters. Ambient pressure with 21% oxygen and 79% nitrogen. Air partially filtered, temp. 65-70°F, RH 34-45%; life-support systems, recycling	Air bacteria counts decreased with time. Avg. 3-4 bacteria per cu ft of air. Portions of water-recovery system were supporting bacterial growth. System was initially contaminated with soil or water bacteria. No coliforms recovered. Bacteria recovered from all areas of the living quarters
B2	ILSS	0	3 4	As in B1; 4 men present, as operators, for each 8-h shift; this test preliminary to study C3	Bacterial count of H_2O reached 10^6/ml; count in air varied depending on crew composition and activity; no *E. coli* in air, water, surfaces, or hands
B3	ILSS	0	28	As in B1	Possible to produce water of no more than 10 microbes per ml. Proteus recovered from water supply when contamination occurred. No data on air or surfaces
B4	Boeing	0	17	2350 cu ft chamber, 10' x 22' x 8'; normal ambient air; life-support systems with recycling (air loop open; partial closure water loop)	*Serratia marcescens* and *Bacillus globigii* added to air; former removed quickly, latter persisted and recovered from surfaces; only normal atmospheric bacteria recovered otherwise

TABLE B4 Studies in Spaceflight Simulators--Manned-- with Integrated Life-Support Systems (Recycling)

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Observations on Microflora			
						Environment	Skin	Oral Cavity and Pharynx	Feces
C1	Boeing	4	30	2350 cu ft chamber 10' x 22' x 8'; normal ambient air; life-support systems with recycling; diet of prototype Gemini meals and simulator study menus	Facilities excellent	Air was relatively free throughout; surfaces had a high bacterial count	No satisfactory data obtained	Decline in microflora of nose and throat of all subjects; concomitant relative increase in potential pathogens	No remarkable changes during or after confinement
C2	Douglas	4	60	4100 cu ft chamber; O_2, 160 mm Hg; N_2; 19,000-ft altitude; RH, 30-70%; life-support systems with recycling; space-type diet, except a specially prepared sumptuous dinner provided 1X/week	Facilities good; Astrovac baths	Atmosphere contained only 1 bacterium per cu ft throughout; water recovery system met microbiol. standards	Axillary cultures of 3 subjects constant; generally a decrease with time	Microflora of throat (aerobic) remained relatively constant; shift in mouth flora from 50% anaerobes to 12% anaerobes on 58th day; moderate but steady decrease in total	Wide variation noted between subjects; no conclusions drawn
C3	ILSS	4	28	4150 cu ft chamber; normal ambient air; temperture 65-70°F; RH, 34-45%, life-support systems with recycling	Men in chamber on 8-h shifts to provide continuous occupancy	Atmospheric counts cyclic, 8-10 organisms per cu ft; buildup on surfaces. Water system contaminated but standards met			

TABLE B5 Studies in Spacecraft

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Observations on Microflora			
						Environment	Skin	Oral Cavity and Pharynx	Feces
D1	Apollo	3	14	Spacecraft on ground; 97% O_2, 3.75-5.0 psia, 88-90°F, RH high; Apollo diet	Hexachlorophene baths	Air not sampled; minimal contam. of surfaces; urinal highly contam. with Enterobacter	Groin and axilla revealed as reservoirs of Enterobacter and Strep. fecalis: interpersonal transmission of Enterobacter	Throat cultures normal, except Enterobacter in 2 on 13th day	No examinations
D2	Apollo	3	8	Essentially same as D1, but 65-76°F; max. RH 55%; preflight and postflight samples only	No data given	No adequate data on air; no evidence for increasing incidence of bacteria in environment; decrease in nos. of fungi	Aerobic microflora maintained throughout; decrease in nos. of fungi	Possible transfer of beta strep; pneumococcus found one time only	Anaerobic forms decreased in no.; no pathogens found; negative for parasites
E1	Gemini	2	3	Actual spaceflight; samples before and after flight of environment only	Tissues, towels, wet pads, toothbrushes, etc.	Expected contaminants found; no remarkable changes recorded			
E2	Apollo	3	11, 6	Actual spaceflights; samples from crew and environment before and after flights	Not noted	Only preliminary interpretations available: "A considerable amount of change does appear to be occurring in the bacterial and fungal flora. They vary greatly with the individual, but some general indications of an early nature appear to be evident. There are transfers of microorganisms from man to man within the isolated environment. There is enhancement of the growth of gram-positive organisms, such as Staphylococcus aureus and beta streptococci and there is inhibition of certain microorganisms or groups of microorganisms within the anaerobic flora. It does appear to be an environment producing some simplification of microflora and enables opportunist microorganisms to dominate the flora."			

TABLE B6 Studies Conducted on Submarines

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Observations on Microflora			
						Environment	Skin	Oral Cavity and Pharynx	Feces
F1	Sub (8 patrols)	100-140	Avg. 56	Polaris-type submarines; air at normal pressure; recycled and treated; normal diet	Good	10 bacteria or less per cu ft of air; low level of environmental contamination, except after venting of sanitary tanks	No remarkable data reported	Enteric bacteria found in throats after venting of sanitary tanks; occasional virus isolated; no remarkable changes in bacteria	No remarkable data reported

TABLE B7 Studies in Navy Blast Protective Shelter

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Observations on Microflora			
						Environment	Skin	Oral Cavity and Pharynx	Feces
G1	Navy PS	100	14	Underground quonset hut, 25' x 48' x 12'. Filtered air from exterior at ambient pressure; 73°F, RH 36%; test occurred in winter; no artificial heat	Adequate facilities, but crowded	Bacterial counts of air varied but considered normal; no apparent trend in time	Not examined	Normal flora encountered, except 12 instances of transient beta streptococci; no related illness	No Shigellas or Salmonellas found; pathogenic coliforms identified in 4 men; no transmission; no related illness
G2	Navy PS	100	14	As G1, but test took place in summer; average "effective" daily temp. 80-85°F	As in G1	Daily fluctuations in bacterial counts of air, but considered low. Bacterial count of water increased but met standards	Not examined	Only normal flora found	Pathogenic coliforms found repeatedly; no other pathogens; no related illness

TABLE B8 Studies on Navy Divers

Study Code No.	Facility	No. of Subjects	Duration, Days	Physical Environment	Hygienic Procedures	Observations on Microflora			
						Environment	Skin	Oral Cavity and Pharynx	Feces
H1	Navy EDU	4,5	9,4 (4 dives)	Pressure chambers, 1 dry, 1 with water. 2 dives at 450 ft, excursion to 600 ft in wet chamber; 2 dives at 200 ft, excursion to 300 ft in wet chamber; O_2 + He; wet suits for immersion	Not recorded	Evidence of heavy fecal contamination of water in wet chamber	Bacterial count increased after immersion; Ps. aeruginosa in an external ear with infection	Total counts constant; pneumococcus(?) in 2 subjects-transfer? E. coli in 2 subjects following immersion; potentially pathogenic staphylococci in 2 subjects	No pathogens; nothing remarkable
H2	Navy EDU	5	12	Dry pressure chamber; one dive to 600 ft; O_2 at 0.3 atm and He	Not recorded	Not tested	Great daily variation; increase in Klebsiella aerugenes in ear of 4 subjects	Potentially pathogenic types (pneumococci; beta strep., staphylococci) found in various patterns; no clinical illness	No pathogens; nothing remarkable

TABLE B9 Summary and Analysis

Code	Type of Chamber	Atmosphere and Pressure	No. Tests	No. Subjects	Duration, Days	Hygiene	Results of Culture: Atmosphere	Surfaces	Skin	Oral Cavity and Pharynx	Feces
A1,5	Life Support Systems Evaluator	Air; ambient	8	4	21-60	Poor	↑		↑	—	Ch
A2-6+	As in A1,5	Air; ambient	6	4	21-60	Poor		—	—	—	—
A10	As in A1,5										Ch
C1,3	Space Cabin Simulator	Air; ambient, recycled	2	5,(4)	30, 28	Good	— (low)	high		↓ Ch	
B1,4	Same, with life-support systems (unmanned)	Air; ambient, recycled	2	0	7, 17		↓	—			
A7	Space Cabin Simulator	Spacecraft, recycling	11	2	14-30	?	—		—	—	Ch
A8	Internal Environment Simulator	Spacecraft, recycling	1	6	68	Good	—		—	—	Ch
A9	Spacecraft Simulator	Spacecraft, not recycled	1	8	34	Poor	↑	— (high)	↑	↑	
C2	Space Cabin Simulator with life-support systems	Spacecraft, recycling	1	4	60		— (low)		—	— Ch	
D1,2	Apollo spacecraft, grounded	Spacecraft, recycling	2	3	8, 14	?		—		—	Ch
E1	Gemini IX	Spacecraft	1	2	3			—			
E2	Apollo, VII, VIII	Spacecraft	2	3	6, 11		"simplification of microflora"				
F1	Submarine patrol	Air, recycled	8	100+	Av=56	Good	(low)	(low)	—	—	—
G1,2 +	Underground shelter	Air	2	100	14	Minimal	—			—	—
H1,2	Exp. diving chamber	Hyperbaric O_2 - He	2	4, 5	4, 12	Minimal			↑#	—	—

+: Observations on micrococci only.
#: Related to contact with contaminated water.
↑↓: Increase or decrease in bacterial counts
—: Incidence steady; no significant variations.
Ch: Change in incidence of types.

Blank space: Not done or unknown

study B2 required the constant presence of operators who worked in shifts. They were not considered as part of the experiment, and no microbiological observations were made on them. Studies of Code C (Table 4) included observations on subjects in the same or similar chambers with integrated life-support systems. Table 5 records the data from spacecraft during experimental tests on the ground (Code D) or in connection with actual flights (Gemini IX, Apollo VII and VIII; Code E). A definitive report of results for the latter was not found. The tests reported in Tables 6, 7, and 8 were special types not directly related to the spacecraft environment.

In order to bring out significant comparisons in this series of tests, it was found useful to group the studies coded as A, B, and C in still another manner, as employed in Table 9. The basis for this grouping is primarily the type of atmosphere used. There were essentially four types of atmosphere employed in the studies summarized:

1. Studies in Air at Ambient Pressure The studies performed in one or another type of spacecraft simulator, in air at 1 atm pressure, are accumulated in the first section of Table 9. In the first two groups (Codes A1, 5; A2, 3, 4, 6, 10) air was supplied as required, and there was recycling through a CO_2 absorber and dehumidifier, but a microbial filter was not placed in the line. In Codes C1, 3 and B1, 2, 3, 4 the air was recycled through filters, CO_2 scrubber, dehumidifier, and other purifiers. This type of atmosphere is represented also in the submarine environment, Code F1.

2. Simulated Altitude The second type of atmosphere (Codes A7, A8, A9, C2) resembled the gas phase of a space cabin in which the pressure was that of 17,000 ft altitude or higher, and O_2 was supplied in a partial pressure equal to or some greater than that at sea level. Ordinarily the atmosphere was recycled for adsorption of carbon dioxide and was passed through filters. Study A9 was an exception in which a spacecraft atmosphere was maintained with only oxygen being introduced into the chamber and no recycling. The studies coded as D1, 2; E1 and E2, which were observations in actual spacecraft, grounded or in flight, also belong to this second category.

3. Air, Constant Flow-through Observations coded as G1, 2 were conducted in an underground shelter in which fresh outside air was filtered and pumped constantly through the shelter, at a pressure only slightly greater than ambient.

4. Hyperbarosis For the several studies coded as H1, 2 the experimental diving chamber was at simulated depths of 200-600 ft and the gas was a mixture of He with O_2 at approximately normal partial pressure.

Microflora of Atmospheres

Few tests were designed to provide direct comparisons between atmospheric microflora in normal and abnormal atmospheres, with other factors constant. In fact, any direct effect a spacecraft atmosphere has on microflora will be detected, it may be assumed, only by more sensitive types of observation than have yet been employed for this purpose. Studies A7, 9, however, give some basis for comparison, although detailed information is scanty. In A7, there were two subjects in each test, in a spaceflight simulator of 380 ft^3 capacity. Oxygen concentrations varied from ambient to 100 percent, depending on the pressure. Almost all counts were in the same general range (e.g., 20-100 colonies per plate exposed 90 min), although counts made at sea level were somewhat more irregular. There was no increase in atmospheric microflora over the period of the tests. Study A9 was performed with six subjects in a chamber at simulated altitude and two in a control chamber in air. The atmospheric count increased, as discussed below, but resembled A7 in the reported greater irregularity in counts made in the control atmosphere. These results suggest that the numbers of microorganisms in a chamber atmosphere are not significantly changed from "normal" levels in ambient air when only pressure and gaseous content are altered to resemble spaceflight.

Of the nine series of studies in which the atmosphere was examined, two of them (A1, 5; A9) showed marked increases in bacterial "load" in the atmosphere described as increasing from day 0 and later leveling off or dropping somewhat. The five experiments of A1, 5 were conducted in air at ambient pressure, which was recycled through a CO_2 absorber and an air conditioner but not through a microbial filter. The predominant type on the plates was recorded as staphylococci. The other study (A9), in which an increase occurred in the microflora of the atmosphere, was performed in a chamber at a simulated altitude of 27,000 ft, using 100% O_2 and in a control chamber with ambient air. Humidity and CO_2 were kept at desirable levels in the altitude chamber by a continuous flow-through of O_2 with no recycling. The atmospheric bacteria, found in increased

numbers during the course of the study, were described as "largely staphylococci or micrococci, gram negative rods and to a lesser extent, streptococci." In both of these studies an almost total absence of personal hygiene was achieved deliberately (no baths, restricted change in clothes, etc.), and it is not possible to evaluate the relative significance of this factor in comparison with lack of recycling with filtration in producing the increased level of microflora in the atmosphere. In contrast to these two reports, the atmospheric bacteria in seven other studies were reported as low or decreasing in four instances and as steady or moderate in three. In all but one (G1, 2) of these latter studies recycling of atmosphere was occurring through systems that included a microbial filter.

The two underground shelter experiments, coded as G1, 2, took place in a quonset hut that measured 48 ft x 25 ft on the floor, and in which, on two occasions, 100 men spent two weeks. Although facilities for personal hygiene were only minimal, no increase in atmospheric microflora was reported. This study used a flow-through type of ventilation using outside air and is in this way similar to study A9, in which the atmospheric flora increased. The recorded data are insufficient to compare rates of flow.

There is a very clear indication in these studies that filtration through microbial-type filters of the atmosphere in this type of confined environment will control any reasonable bacterial level. However, there is no direct answer to the question of whether recycling of the atmosphere will reduce the increased atmospheric bacterial level occasioned by poor personal hygiene such as that practiced deliberately in studies A1, 5 and A9. Nevertheless, satisfactory microbiological control of the atmosphere in spacecraft of the future seems to be a reasonable assumption providing there is no breakdown or malfunction of the various life-support systems. The effect of zero gravity on atmospheric microorganisms is yet to be determined.

Microflora of Surfaces

No clear relationship is evident between microfloral counts on chamber surfaces and data from other sources. On the basis of the reports from C1, 3 and B1, 4, it may be seen (Table 9) that discrepancies between atmospheric levels and surface levels can occur. Available data do not permit identi-

fication of the factors responsible for a high count in study A1, 3, although the reported high, but steady, level in A9 is perhaps related to a poor state of personnel hygiene and a high microbial count in the atmosphere. A potential source of microorganisms in confined spaces is represented by the growth of bacteria and fungi in or upon materials that become damp. Presumably dampness will not occur in spacecraft as long as relative humidities remain under control at the levels planned.

Microflora of Skin

A principal source of microorganisms in the close environments was, no doubt, from the skin of the personnel. Bacteria-laden particles are constantly being shed from the normal human skin at an estimated rate of many thousands per minute. Under the conditions of poor or absent skin hygiene in studies A1, 5 and A9, increases in skin microflora occurred, and presumably greater numbers were shed into the environment. This, with absence of recycling through a microbial filter, resulted in greater atmospheric counts, as discussed in the preceding section.

In study A5, the wearing of spacesuits coincided with culturing of enterobacteria from the axilla; when the suits were no longer worn no more enterobacteria were cultured from that site. Some degree of maceration of the skin of the feet, with increased numbers of bacteria cultivated from the feet has also been observed (C2).

Other evidence indicates that persons vary in the degree to which skin bacteria are shed. It was observed in study C3 that microbial counts of the air samples increased when one of the four operators who worked on shifts was present in the chamber.

The increase in skin count in experimental divers (H1, 2) was directly related to immersion in contaminated water and need not be considered further here.

In spite of poor hygiene and increased bacterial counts on the skin in some instances, no significant skin infections were observed. Lack of a significant change in numbers of bacteria cultivable from the skin occurred in those tests in which a reasonable degree of personal hygiene was possible. As we have seen already, these were mainly the tests in which bacteria were filtered out of the air.

Microflora of Oral Cavity and Pharynx

In most studies no remarkable changes were noted in numbers or types of microorganisms in the mouth and throat, except for intermittent presence of abnormal forms for which, in some cases, the cause was apparent. Enteric bacteria were found in the throats of submariners (F1) after venting of the sanitary tanks, at which time the incidence of such bacteria in the atmosphere was very high. The principal changes in microflora of throat and other sampling areas of the divers of study H1 appear to be the result of immersion in contaminated water. Escherichia coli was found in throat specimens of two divers.

In contrast to the usual stability observed in throat and mouth flora, in study A9 a definite increase in numbers of bacteria in these areas was recorded. Streptococci accounted for most of the total increase, with some due to increases in staphylococci or micrococci. In this experiment, two subjects were retained in a restricted environment in ambient air, for comparison with the six subjects who were at 5 psia in 100% O_2. No significant differences between the two groups were seen in the bacteriologic observations.

Study C1 records first a decrease in normal microflora of throat and nose followed by replacement, in some cases almost completely, with Staphylococcus aureus, during the 30-day test. The precise numbers were not reported. In the same study a marked increase was noted in numbers of bacteria referred to as organisms of Vincent's angina, as determined by direct smear of teeth, gingivae, and tonsillar areas. The increase was found in all subjects. In study C2 a shift in bacterial types was seen in mouth cultures.

Microflora of Feces

The changes observed in fecal flora can probably be related largely to changes in diet. Definite alterations in populations of microorganisms occurred, but there were often wide variations between subjects in the same experiment. In study A5, for example, in one subject there was a shift in the E. coli population during the course of the test from 100 percent nontypable strains to 50 percent of the isolates being a typable pathogenic type. This was attributed to an altered diet. It is not possible to detect effects on enteric flora of any of the other factors in the tests.

Interpersonal Transmission of Pathogens

In considering the transmission of pathogenic microorganisms in these restricted environments the two series in which more than a few subjects were involved (submarine studies, F1; underground shelter studies, G1, 2) will be excluded. In both the studies mentioned febrile respiratory disease occurred, which in some instances was due to interpersonal transmission within the environment under study. In the other experiments, in which there were never more than six subjects in the same chamber, little or no evidence for transmission of disease was seen--in fact, illness was never a problem. Considerable attention was paid, however, to evidence for transmission of potential pathogens, such as staphylococci or enterobacteria, among the subjects.

Study A7, performed in a spaceflight simulator, was specifically designed to determine the extent of transmission of potential pathogens. It consisted of 11 separate experiments lasting 14-30 days with two men each. They were confined in an elliptical cylinder of a total capacity of 380 ft^3. The environment varied from ambient pressure to that of 33,500 ft, and the O_2 concentration ranged from ambient to 100%. The results of cultures of the atmospheric microflora were discussed above. Observations were made on bacteriophage types of staphylococci in throat cultures, and of potential enteropathogens in fecal cultures, in order to detect transmission of these types between the two subjects. There were one or possibly two clear instances, in a total of five reports, of transfer of a staphylococcal type cultured from the throat. Among the enterobacteria used as tracers were Proteus mirabilis, Proteus morgani, Salmonella arizona, Providence group, Aerobacter aerogenes, and Alcaligenes. In only a few instances, in the total of 11 reports, was convincing evidence of transmission found. In one of the tests, one of the pair of experimental subjects was regarded as a true carrier of a member of the Providence group. His stools were positive at the beginning of the test, at frequent intervals throughout, and were still positive two months after termination. Members of his immediate family were harboring the same microorganism. This enterobacterial type was found in his experimental partner six days after they entered the chamber and repeatedly during the test but never after the termination of their residence together.

Perhaps of greater significance is the failure to detect transfers between two subjects living in such crowded conditions. In another pair of partners, a Providence type was found

repeatedly in cultures of one but not the other. Similarly, a specific phage type of Staph. aureus and A. aerogenes were found many times in the throat of one team member but were never observed in his partner. The authors of the report make the appropriate comment that other factors, in addition to exposure, determine whether a microorganism will establish itself as a part of a person's indigenous microflora. In another study (A2-6), on micrococci only, transfers of phage-typable staphylococci among subjects and environment were apparently temporary only. During the 60-day test (C2) involving four men, two of them entered the chamber with Staph. aureus in their noses. It was never cultured from the other two crew members. In none of the studies was there any clinical illness related to the carriage or the transmission of potentially pathogenic bacteria.

In attempting to summarize what has been learned from the reports reviewed here, it is desirable to recall that these studies show great heterogeneity in objectives, methods, and detail of information reported. It is not surprising, then, that seemingly conflicting results occurred and that definite conclusions are necessarily few. With a few exceptions, it may be said that really nothing of serious import did happen, as far as can be seen, to the microflora or to the host-parasite relationship, under the conditions used and within the time of observation. This is reassuring, but a series of negative results is not a safe base for extrapolation.

In a few of the studies summarized, a reduction in numbers of indigenous microorganisms, or a "simplification" of microflora, was reported. The evidence for these conclusions was not always provided, and in other seemingly similar experiments such changes were not observed. Evaluation of these findings must be deferred.

The conclusions derived from this summary of studies are tabulated below, but it is appropriate to emphasize here remaining areas of ignorance or uncertainty.

Data are inadequate on the contamination of interior surfaces of spacecraft under actual or simulated flight conditions.

The effects of zero gravity and abnormal atmospheres on aerosols, on contamination of surfaces, and on interpersonal transmission of microorganisms are largely unknown. Information in this area is needed before intelligent assessment can be made of airborne infection as a health hazard in spacecraft.

Longer-term observations of small crews under optimal hygienic conditions are needed to determine to what extent numbers and types of bacteria may be changed under such condi-

tions. If significant changes do occur, such as those reported in the pharynx in C1, their potential for adversely affecting the health of astronauts should be assessed.

It has been assumed that the data derived from observations in these studies, mainly on the readily cultivated bacteria of mouth, throat, and skin, for example, are representative of what is occurring with all other types of microorganisms at those sites. This is not necessarily true because it is possible that the anaerobic bacteria, Mycoplasma fungi, spirochetes, and viruses are affected differently at epithelial barriers by alterations in atmosphere and pressure. Study C2 reported a shift in numbers of anaerobic bacteria in the mouth; cultures for Mycoplasma and fungi were included in a few of the studies. Although the detection of such effects on the less easily studied microorganisms represents a formidable, if not impossible, task at present, the possibility exists of yet undetected effects of this kind.

CONCLUSIONS

The principal conclusions that can be drawn from the present summary of observations are as follows:

1. Recycling of the atmosphere through filters under the test conditions maintained the bacterial load of the atmosphere at a very low level. The bacterial incidence on environmental surfaces did not necessarily follow that of the atmosphere.
2. A positive correlation was seen between poor personal hygiene, high bacterial incidence on the skin, and increased bacterial load in the atmosphere. Present information (incomplete) does not indicate whether recycling of atmosphere through bacterial filters would have prevented the atmospheric buildup in these situations.
3. There is tentative evidence for a positive correlation between reduction of bacterial counts in the oropharynx, associated factors of good hygiene, and low bacterial counts from skin and air.
4. The changes seen in microflora of the gut are attributable to changes in diet.
5. Interpersonal transfer of bacterial pathogens occurred occasionally but did not result in clinical disease, except in the case of outbreaks of respiratory (viral?) disease in sub-

marine crews and in occupants of the underground shelter. In several instances transmission of respiratory and enteric bacteria of potential pathogenicity did not occur even under conditions of extreme crowdedness.

6. Although a few exceptions occurred which are difficult to evaluate, most of the results reviewed here suggest that the conditions of spaceflight, as simulated by these studies, and for the time intervals tested, will not significantly affect either the microorganisms of the human environment or their hosts to cause a shift in the normal host-parasite equilibrium.

7. Areas of ignorance or uncertainty remain; these were briefly described above in the Discussion.

CODE NO.
A1

TYPE
Spaceflight simulation; manned.

TITLE AND REFERENCE
Determination of the indigenous microflora of men in controlled environments, P. E. Rielly, D. Geib, and D. Shorenstein, AMRL-TR-66-33, April 1966; The potential hazard of staphylococci and micrococci to human subjects in a life support systems evaluator with elevated cabin temperature, L. P. Lotter and B. S. Horstman, AMRL-TR-67-43, September 1967.

WHERE DONE
Air Force Systems Command, Wright-Patterson Air Force Base, Ohio.

BY
Aerospace Medical Research Laboratories, Aerospace Medical Division, Wright-Patterson AFB, and Republic Aviation Division, Fairchild Hiller Corporation, Farmingdale, Long Island, New York.

CHAMBER DESIGN
Two connecting facilities. The Controlled Activity Facility (CAF), a 20 ft by 20 ft room with controlled temperature and humidity primarily for confinement. It contains beds, individual television, and essential accommodations. The Life Support Systems Evaluator (LSSE) is a 1100 cu ft, double-walled, 7-ft-diameter cylinder. The gas mixture, pressure, temperature, and humidity can be controlled. Minimum essential crew accommodations and facilities for constantly monitoring the subjects are installed. Air at ambient pressure.

EXPERIMENTAL DESIGN
Samples were collected from body areas, feces, and environment from men confined in either the CAF (approximately one week pretest and posttest) and LSSE (approximately one month) for a total of 6 weeks. In the 5 experiments spacesuit wear, confinement in the CAF and LSSE, temperature, personnal hygiene, environmental area sampled, and diet were varied slightly. The microbiological studies were divided between two contractors. One was

concerned only with staphylococci and micrococci. The effect of space-type diets on microorganisms was evaluated in a space environment. Benzalkonium chloride spray and scrub used to reduce residual bacterial count in chambers before experiments. Soap, pHisoHex, body wipes, edible dentifrice used during confinement but not in every experiment; sterile clothing donned before entry into LSSE.

CREW SIZE

4 men; 20 men studied in 5 different experiments.

TEST LENGTH

42 days.

TEST OBJECTIVES

(1) Collect under controlled simulated space environment microbiological data from 14 body areas of 20 subjects and their specialized environment; (2) evaluate data to establish biomedical criteria for personal hygiene and sanitation for space missions; (3) suggest indices to measure deterioration of closed ecosystem; (4) study effects of space-type diets on microbes of men.

METHOD

Swabs or samples from 14 areas of the body taken, diluted, plated, and incubated aerobically and anaerobically. Samples of the environment taken from areas having little and heavy usage by swabbing and sedimentation plates exposed 30 min to the environment. Specimens were transferred out of the chamber immediately upon being taken by crew members. Specimens in which Mycoplasma and fungi were searched for were inoculated into specialized medium. Standard procedures for inoculation, growth, and identification of microorganisms were followed.

RESULTS

Conclusions are based on results that occurred in a large number of the 50,000 primary cultures taken. These studies in general agree with earlier studies on normal microbial flora of man. The BAC treatment of the chamber was successful in holding pre-entry surface counts to less than 10 in every experiment. Few pathogens recovered from environment. Those recovered were from the vicinity of the personal hygiene area, but total counts on sedimentation plates (tables, floor, beds) rose to levels considered dangerous. Corynebacteria built up to significant

levels and was recovered more frequently than Staphylococcus from the skin. Distribution on the body areas varied among the men. Bacteria built up on the skin to the 3rd or 4th week, leveled off, and slightly decreased without causing any visible dermatological problems. The indicator area for bacterial growth of the body was determined to be the groin and glans penis. Bacterial growth on the skin of men wearing spacesuits was generally little different from those who were unsuited. Skin bacteria were only temporarily affected by sweating and washing. Problems occurred with men having history of athlete's foot with itching between toes and in groin areas. Enterobacteriaceae were sporadically recovered from several body areas. The effect of a particular diet may have been evident when a specific potential pathogenic Escherichia coli was recovered in high numbers. Normally these organisms are in a minority in the intestine. The relationship between the men and their anaerobes was not completely defined. The study confirms the predominance of anaerobic bacteria in fecal flora. A new working classification has been devised to describe the many newly recovered anaerobes based on morphological and physiological characteristics. Neisseria was recovered sporadically from the mouth and in two instances in great number. Data suggest transfer from subject to subject. No illness associated with PPLO recovery.

RECOMMENDATIONS AND CONCLUSIONS

Prior to confinement each man should be microbiologically screened for presence of potential pathogens as well as to detect carriers of troublesome microbes. Assess value of different antibacterial agents on skin microbes. Attempt pretreatment of skin with antibiological agents before chamber confinement. Evaluate fully the effect of intestinal anaerobic bacteria on Vitamin B group metabolism by man. Standardize designs, methods, and procedures of large-scale studies on man in closed ecosystems. Study strains of bacteria normally found on the skin and intestine of man for antibiotic properties against transient microbes so their presence and number can be specifically enhanced. Personal hygiene and food areas should be monitored frequently. The usual microbial interactions between the men and their environment was considered as being one of maintaining a delicate balance between highly unstable factors. Any event or procedure which contributes to the removal of large numbers of the normal flora may permit unusual or rare microorganisms to become predominant with unknown influence and consequences.

CODE NO.
A2

TYPE
Spaceflight simulation; manned.

TITLE AND REFERENCE
The potential hazard of staphylococci and micrococci to human subjects in a life-support-systems evaluator and on a diet of precooked, freeze-dehydrated foods. Study One, L. P. Lotter, B. S. Horstman, and J. V. Rack, AMRL-TR-67-18, September 1967.

WHERE DONE
Wright-Patterson Air Force Base, Ohio.

BY
Department of research of the Miami Valley Hospital, Dayton, Ohio, and the Biotechnology Branch, Life Support Division, Biomedical Laboratory, Aerospace Medical Research Laboratories.

CHAMBER DESIGN
Same as A1.

EXPERIMENTAL DESIGN
The subjects were in the CAF 7 days before and 7 days after LSSE confinement of 28 days. During LSSE confinement each man wore the MA-10 pressure suit with helmet, gloves, and boots for at least 8 h a day for 14 days. Men showered with soap before entering CAF. Wet wipes impregnated with sodium lauryl sulfate used to cleanse body before meals and after defecation. No bathing, hair grooming, nail maintenance, teeth brushing, or changing of clothes done while in test. CAF and LSSE sprayed and sponged before start of study. This experiment is part of larger study summarized in A1.

CREW SIZE
4 men.

TEST LENGTH
42 days, total.

TEST OBJECTIVES
Determine the distribution of staphylococci indigenous to

humans and their environment in a controlled ecological system. Determine if the biochemical markers associated with the microorganisms provide reliable criteria of pathogenicity.

METHOD

Samples taken from various body and environment areas with cotton swabs and placed in broth, diluted, plated, and incubated aerobically. Sites sampled included: eye, ear, nose, throat, axilla, umbilicus, groin, anus, scalp, glans penis, forearm, and toes; also seven environmental areas. Most body sites and environment sampled twice weekly. Staphylococci grouped according to following biochemical criteria: coagulase production, mannitol utilization, DNAse production, gelatinase production, hemolysis on 5% sheep blood agar.

RESULTS

No particular biochemical marker can be used as a reliable indicator of the potential pathogenicity of staphylococcal strains. No significant differences in frequency of occurrence of biochemical types among the subjects or among the environmental areas observed during the LSSE confinement. There was no buildup of biochemical types in the test areas. Nose and groin are most likely to harbor potential pathogens. 700 catalase-positive staphylococci strains isolated. Different biochemical types were isolated from selected body sites but were not associated with the time frame.

RECOMMENDATIONS AND CONCLUSIONS

If the role of stress in enhancing susceptibility to infection is to be evaluated, a more measurable situation must be created. In this study, confinement under simulated space-cabin conditions with minimal personal hygiene indicates that establishment of special biomedical criteria is not required. Phage-typing studies are suggested for future studies so that transmission of staphylococci among body areas on the same man, among men, and between men and their environment can be monitored.

CODE NO.
A3

TYPE
Spaceflight simulation; manned.

TITLE AND REFERENCE
The potential hazard of staphylococci and micrococci to human subjects in a life-support-systems evaluator and on a diet of precooked, freeze-dehydrated foods. Study Two, L. P. Lotter and B. S. Horstman, AMRL-TR-67-43, September 1967.

WHERE DONE
Wright-Patterson Air Force Base, Ohio.

BY
Department of Research of the Miami Valley Hospital, Dayton, Ohio, and the Biotechnology Branch, Life Support Division, Biomedical Laboratory, Aerospace Medical Research Laboratories.

CHAMBER DESIGN
Same as A1.

EXPERIMENTAL DESIGN
The subjects were in the CAF 7 days before and 7 days after LSSE confinement of 28 days. During LSSE confinement each man wore an unpressurized MA-10 pressure suit with helmet, gloves, and boots before entering CAF. At the beginning of CAF and LSSE periods, men washed all parts of their bodies with pHisoHex. Ear and nose areas cleaned with sterile cotton swabs. Started with sterile garments. Used five wipes per day saturated with sodium lauryl sulfate to cleanse body areas before meals and after defecation. Water used as dentifrice. Environment sponged and sprayed with benzalkonium chloride at beginning of study. This experiment is part of larger study summarized in A1.

CREW SIZE
4 men

TEST LENGTH
42 days

TEST OBJECTIVE

Determine the quantitative distribution of staphylococci indigenous to humans and their environment in a controlled ecological system. Determine if the biochemical markers associated with the microorganisms provide reliable criteria of pathogenicity.

METHOD

Specimens taken from selected body sites and environmental areas with cotton swabs streaked directly onto plates and incubated aerobically. Body sites sampled were: ear, nose, throat, mouth, axilla, groin, glans penis, scalp, eye, forearm, umbilicus, anus, and toes. Seven areas of the environment were sampled. The environment and most body sites were sampled twice weekly. Staphylococci grouped by following biochemical criteria: production of coagulase, gelatinase, and DNAse; hemolysis on 5% sheep blood agar; mannitol utilization.

RESULTS

Confinements even under minimal hygienic conditions did not cause any buildup of potentially pathogenic organisms nor lower resistance to infection. No particular biochemical marker can be used as the index of potential pathogenicity of staphylococcal strains. Nose and groin most likely to harbor potential pathogenic staphylococci. 1300 catalase-positive staphylococci strains isolated. Different biochemical types were isolated from different body areas but were not associated with the time frame.

RECOMMENDATIONS AND CONCLUSIONS

A more measurable situation must be created if the role of stress in enhancing susceptibility to infection is to be evaluated. Phage-typing studies are suggested so that transmission of staphylococci among body areas in the same man, among men, and between men and their environment can be followed.

CODE NO.

A4

TYPE

Spaceflight simulation; manned.

TITLE AND REFERENCE

The potential hazard of staphylococci and micrococci to human subjects in a life-support-systems evaluator and on a diet of liquid foods, L. P. Lotter, B. S. Horstman, and J. V. Rack, AMRL-TR-67-21, September 1967.

WHERE DONE

Wright-Patterson Air Force Base, Ohio

BY

Department of Research of the Miami Valley Hospital, Dayton, Ohio, and the Biotechnology Branch, Life Support Division, Biomedical Laboratory, Aerospace Medical Research Laboratories.

CHAMBER DESIGN

Same as A1.

EXPERIMENTAL DESIGN

The subjects were in the CAF 7 days before and 7 days after LSSE confinement of 28 days. MA-10 spacesuits, unpressurized, with boots, helmet, and gloves, were worn at two 8-h periods daily for 28 days by 2 men, and 2 men wore the torso and boots continually but the helmet and gloves part-time. Temperature in the simulator was kept at 70°F for 4 weeks and 90°F for 2 weeks. Only personnel wearing sterile clothing were permitted to enter the CAF, and only test subjects entered the LSSE. pHisoHex was used to cleanse body before entering CAF. Men donned sterile clothing for transfer to CAF and to LSSE. Used sodium lauryl sulfate and a quarternary amine saturated wipes for personal hygiene in first study and plain wipes in second study. Toothbrushing with water only in first study, and an edible dentifrice used in second study. This experiment is part of larger study summarized in A1.

CREW SIZE

4 men; 8 men in two tests.

TEST LENGTH

42 days.

TEST OBJECTIVES

For both studies an attempt was made to determine the distribution of staphylococci indigenous to humans and their environment in a controlled ecological system. Also

determine if specific biochemical markers provide reliable criteria of pathogenicity.

METHOD

Swabs of body areas taken by dry cotton swabs and streaked onto a plate which was incubated aerobically. Fecal material inoculated into broth, diluted, streaked, and incubated aerobically. Environmental areas sampled by exposing plates for 30 min at selected locations. Body areas tested: ear, nose, throat, mouth, axilla, groin, glans penis, scalp, eye, forearm, umbilicus, anus, and toes. These were sampled from 3 to 12 times. Seven environmental areas were sampled 13 times in one experiment and 11 times in the other experiment. Staphylococci grouped by following biochemical criteria: production of coagulase, gelatinase, and DNAse; hemolysis on 5% sheep blood agar; mannitol utilization.

RESULTS

No significant buildup or differences in the frequency of occurrence of biochemical types among men and environmental areas, but there were differences between individual sites on the men even under minimal hygienic conditions. Two phage types recovered: UC-18 and 79. Phage type UC-18 was transferred from subject to environment only. Ears and nose most likely to harbor staphylococci. Data indicate little danger in the transmission of potentially pathogenic staphylococci.

RECOMMENDATIONS AND CONCLUSIONS

No special biomedical criteria need be operable for men confined under simulated spacecraft conditions than guidelines presently operating.

CODE NO.

A5

TYPE

Spaceflight simulation; manned.

TITLE AND REFERENCE

Microbiological flora of human subjects under simulated space environments, P. E. Rielly and D. J. Shorenstein, AMRL-TR-66-171, October 1966; Distribution of staphylo-

cocci and micrococci among humans and their physical environment during simulated aerospace confinement, L. P. Lotter, B. S. Horstman, and V. Rehg, Amer. J. Clin. Pathol. 49: 414-423, 1968.

WHERE DONE

Wright-Patterson Air Force Base, Ohio.

BY

Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base; Republic Aviation Division of Fairchild Hiller Corporation; and Miami Valley Hospital, Dayton, Ohio.

CHAMBER DESIGN

Same as A1.

EXPERIMENTAL DESIGN

In test number one, the men were in CAF 14 days preconfinement and postconfinement in the LSSE. LSSE confinement was 20 days. In test number two, men were in CAF for an initial 3 days, for 15 days in LSSE, and an additional 3 days in the CAF. In test number three, the subjects were in CAF for an initial 45 days, for 10 days in LSSE, and an additional 5 days in the CAF. Spacesuits were worn in all studies. In test number one, 2 men wore MA-10 spacesuits in LSSE and final 14 days in CAF. In test number two, 3 men wore MA-10 spacesuits for just 7 days in LSSE. In test number three, one man wore an Apollo-type suit and one man wore a Gemini-type suit 10 days in LSSE. In CAF teeth brushed after every meal on days 1-15, no brushing thereafter. Teeth brushed once a day in LSSE.

CREW SIZE

Total of 11 men in three separate tests: 4 men in test one, 3 men in test two, and 4 men in test three.

TEST LENGTH

Test one, 34 days; test two, 21 days; and test three, 60 days.

TEST OBJECTIVES

To study the effect of diet on fecal flora. To determine the indigenous microflora of man. To establish personal hygiene protocols for safeguarding the well-being of men in a closed ecosystem. To evaluate microbial interactions

among men, between men and their environment, and within or upon man himself in a specific length of time.

METHOD

Samples were collected by swab from selected body sites of each man periodically: eye, groin, axilla, throat, mouth, glans penis, ear, nose, umbilicus, anal fold, toes, scalp, tongue, and gingiva. The feces were sampled a varied number of times in each of the 3 studies. Environmental areas (tables, bed, floor) were sampled by swabs and sedimentation plates which were exposed for 30 min. All samples were tested for aerobic and anaerobic bacteria. Quantitation of each specimen was attempted.

RESULTS

There was evidence of a small amount of microbe exchange. Proteus recovered from glans penis of one subject. Later found in environment, but no clinical illness observed. Escherichia coli shift from a nontypable to 0125:B15, probably due to diet change along with drastic change of nonsporing fecal anaerobes. Great variations in anaerobic bacteria occurred when diet altered. Diet was biggest single factor. There appears to be a quantitative rise in number of bacteria in the environment proportioned to time of chamber occupancy with the peak occurring at 25 days. There were great individual variations reflecting personal hygiene procedures and individual performance. Mycoplasma was recovered from only one subject by tongue and gingival sampling. Studies indicated that the groin, axilla, and glans penis are the most significant indicator areas of bacterial buildup and should be selected for microbial monitoring. Corynebacteria predominated on most body areas.

RECOMMENDATIONS AND CONCLUSIONS

(1) Men wash every 10 days to maintain their normal microlevels; (2) the environment cleaned at 10-day intervals with special attention directed at the personal hygiene area; (3) commonly used equipment should be cleaned frequently to prevent buildup of microbes on surfaces; (4) further work be done on changes in anaerobe bacteria populations related to diet change.

CODE NO.
A6

TYPE
Spaceflight simulation; manned.

TITLE AND REFERENCE
The potential hazard of staphylococci and micrococci to human subjects in a life-support-systems evaluator while on a simulated GT-7 mission, L. P. Lotter and B. S. Horstman, AMRL-TR-67-45, September 1967

WHERE DONE
Wright-Patterson Air Force Base

BY
Biotechnology Branch, Life Support Division, Biomedical Laboratory, Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio; and Department of Research of the Miami Valley Hospital, Dayton, Ohio.

CHAMBER DESIGN
Same as A1.

EXPERIMENTAL DESIGN
Subjects were in CAF for an initial 14 days, for 14 days in the LSSE, and an additional 14 days in the CAF. Contact with personnel outside chamber was minimized. Thorough cleansing of subjects before each 14-day period, but personal hygiene was minimal during each period. Subjects wore unpressurized MA-10 suits. Bacteriological sampling performed repeatedly on men and environment.

CREW SIZE
4 men.

TEST LENGTH
42 days, total.

TEST OBJECTIVES
Determine distribution of staphylococci indigenous to humans and their environment in a controlled ecological system and ascertain if the associated biochemical markers provide reliable indications for pathogenicity. This report concerns only observations on micrococci. Data on other microorganisms reported in Code No. A5.

METHOD

Selected body areas and the environment were sampled by dry cotton swabs and streaked upon plates during the three phases. Fecal samples were collected 11 times, as well as swabs from most designated body areas which are: throat, gingiva, axilla, groin, glans penis, anus, and toe. The scalp, eye, arm, and umbilicus sampled three times. The environment sampled 12 times. All plates incubated aerobically. Micrococci grouped by production of coagulase, gelatinase, and DNAse as well as hemolysis on 5% sheep blood agar and mannitol utilization.

RESULTS

No significant difference in frequency of occurrence or buildup of biochemical types of staphylococci among subjects and among environmental areas during test period. A phage type transferred from one man to the environment but not to other subjects. Nose and groin are body areas likely to harbor potentially pathogenic staphylococci.

RECOMMENDATIONS AND CONCLUSIONS

Nasal carriers of staphylococci should be detected and disinfected before association in a confined group.

CODE NO.

A7

TYPE

Spaceflight simulation; manned.

TITLE AND REFERENCE

Microbiologic studies of the two-man space cabin simulator; interchange of oral and intestinal bacteria, J. E. Moyer and Y. Z. Lewis, SAM-TDR-64-3, March 1964; Microbiological problems of sealed cabin environments, J. E. Moyer, Devel. Ind. Microbiol. 5:216-223, 1964.

WHERE DONE

U.S. Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas.

BY

Environmental Systems Branch, Bioastronautics Department, Biosystems Research Division, Brooks AFB, Texas.

CHAMBER DESIGN

Elliptical steel cylinder 12 ft long, 8 ft high, 5 ft wide; total volume 380 cu ft. Varied from sea level to simulated altitudes up to 33,500 ft. Oxygen concentration varied from ambient to 100%. Air was recirculated through cabin at 300 cu ft per min in all experiments. Chamber was hermetically sealed with environmental control and life-support equipment inside; power supply and heat exchanger outside.

EXPERIMENTAL DESIGN

Samples were taken from men and the environment. The men were confined within a two-man space cabin simulator for periods ranging from 14 to 30 days. Samples were also taken preconfinement and postconfinement. The diet was of dehydrated precooked whole food.

CREW SIZE

Two men, Air Force pilots 24-39 years old.

TEST LENGTH

Summary of 11 tests that varied in duration from 14 to 30 days (January 1961 to September 1962).

TEST OBJECTIVES

To study microbial interchanges under conditions of simulated spaceflight of close occupancy for extended times.

METHOD

Throat cultures and stool specimens collected prior to, during, and after confinement in the simulator. Prior to confinement, 4 samples generally obtained, 2 or 3 per week during confinement, and 2 or 3 following confinement. Similar procedures used for fecal samples. Plates exposed 90 min to cabin atmosphere at 5 locations to determine bacterial aerosol counts. Attention given to isolation and follow-up passages of marker organisms harbored by one subject.

RESULTS

No increase in aerosol counts noted. A Staphylococcus epidermidis was most frequently recovered which was coagulase negative and exhibited a phagolytic pattern. Several examples given of microbial transfer. A Providence-type Salmonella was transferred from one man to another, but infection was not prolonged once contact was broken from original host.

RECOMMENDATIONS AND CONCLUSIONS

No special microbiological precautionary measures required for astronauts other than preliminary screening necessary to eliminate pathogen carriers. Close personal contact in a prolonged ground training program will in all probability encourage microbial interchange among individuals selected for crew.

CODE NO.

A8

TYPE

Spaceflight simulation; manned.

TITLE AND REFERENCE

Study of man during a 56-day exposure to an oxygen-helium atmosphere at 258 mm Hg total pressure. (1) J. J. Hargreaves, W. G. Robertson, F. Ulvedal, H. J. Zeft, and B. E. Welch, I. Introduction and general experimental design, Aerospace Med. 37:552-555, 1966; (2) J. T. Cordaro, W. M. Sellers, R. J. Ball, and J. P. Schmidt, X. Enteric microbial flora, Aerospace Med. 37:594-596, 1966; (3) J. E. Moyer, D. G. Farrell, W. L. Lamb, and J. L. Mitchell, XI. Oral, cutaneous and aerosol bacteriologic evaluation, Aerospace Med. 37:597-600, 1966.

WHERE DONE

U.S. Air Force School of Aerospace Medicine, Brooks Air Force Base, Texas (internal environment simulator).

BY

Environmental Systems Branch, Aerospace Medical Research Division, Brooks AFB, Texas.

CHAMBER DESIGN

This simulator is double-walled with the inner chamber 6.1 m long and 2.4 m in diameter. It is divided into three areas: an air lock of 11.6 cu m, a transfer lock of 0.8 cu m, and the main test cell of 27.8 cu m. All were operated as one 40.2 cu m compartment. Main test cell was divided by panels into: (a) sleeping, storage, and physiological testing area; (b) galley, ECS, and hygiene area; (c) cockpit area. Oxygen and helium supplied from outside; CO_2 removed by lithium hydroxide, odors by

activated carbon, bath units replaced periodically, blowers and cooling coils for control of temperature and humidity.

EXPERIMENTAL DESIGN

Six men were confined for 56 days. Two were controls held at ground conditions throughout. Four were at ground level for 8 days, at altitude for 56 days, and at ground level for 4 days. The conditions for 56 days at 257.7 mm Hg total pressure atmosphere were 175.2 mm Hg pO_2 and 73.9 mm Hg pHe; pN_2 averaged 1.9 mm Hg (70% O_2 and 30% He); 250 cu ft/min flow through a fiber-glass filter (Aerosolve 95, Cambridge Filter Corp.).

CREW SIZE

4 men, 27-29 years old. 6 men started, 2 were used as ground controls.

TEST LENGTH

Total 68 days with 56 days of simulated space environment.

TEST OBJECTIVES

Evaluate the physiological suitability of this atmosphere in future manned spaceflights. Determine microbial change that might occur due to diet and environment change. Determine numbers and types of microorganisms in environment, in oral cavity, and on skin.

METHOD

Bacteriological samples collected twice a week during test and during pretest and posttest to establish baseline. Five aerosol sampling stations. Blood agar plates exposed to cabin environment for 1 h. 124 fecal, nasal, throat, and skin samples collected from each man prior to and during test to determine any significant alterations in the aerobic microflora.

ORGANISMS RECOVERED

Skin: Staphylococcus epidermidis, Staphylococcus aureus, a diphtheroid, various saprophytic fungi. Air: Predominant organism was Staph. epidermidis, also found were Staph. aureus, Bacillus sp., saprophytic fungi. Nose: Staph. aureus. Throat: Streptococci, Neisseria, Staph. epidermidis, Staph. aureus. Intestinal: Lactobacilli, Bacteroides, coliforms, enterococci.

RESULTS

No shift in normal oral or skin bacteria distribution noted. Staphylococci transfer among subjects occurred, but no illness reported. Staphylococcal phage types harbored by the men were isolated from the environment at least once during the period of confinement. There was not a significant buildup of organisms in the environment. No exchange of fecal microbes reported. Coliforms, lactobacilli, Bacteroides all stayed within normal limits. Enterococci, however, went below normal limits while men were on experimental space diet, down to 10^2 organisms per ml. Normal limits are considered to be between 10^4 to 10^8 enterococci per ml. As soon as the men returned to a normal diet after confinement, the organisms rose to normal range. The change in fecal microbes not considered clinically significant.

RECOMMENDATIONS AND CONCLUSIONS

Part of the air was passed through a lithium hydroxide-activated charcoal-filled cannister with a fiber-glass filter which appeared to act as a bacterial trap. From a microbiological view no objections are evident to the use of oxygen-helium atmosphere at 258 mm Hg total pressure. A daily sponge bath is considered sufficient to control skin microbes.

CODE NO.

A9

TYPE

Spaceflight simulation; closed-door; manned.

TITLE AND REFERENCE

A report of the physiological, psychological, and bacteriological aspects of 20 days in full pressure suits, 20 days at 27,000 ft on 100% oxygen, and 34 days of confinement, K. R. Coburn, NASA Contractor Rept CR-708, February 1967.

WHERE DONE

Aerospace Crew Equipment Laboratory, U.S. Naval Air Engineering Center, Philadelphia, Pennsylvania.

BY

NASA: U.S. Naval Aerospace Crew Equipment Laboratory; U. S. Naval Medical Research Institute; and Republic Aviation Division, Fairchild Hiller Corporation, Farmingdale, Long Island, New York

CHAMBER DESIGN

Two facilities were used. Control subjects were confined in a 8 ft x 8 ft x 16 ft plywood room furnished similarly to the test facility. The test chamber was a double-walled cylinder, 8½ ft in diameter and 22 ft long. The atmosphere was 100% oxygen at 258 mm Hg derived from liquid oxygen. It was fitted with a zero gravity sink and a toilet in a corner under an exhaust port.

EXPERIMENTAL DESIGN

Six experimental subjects and two controls were confined so that they used the same minimal personal hygiene procedures and had a similar diet of dehydrated foods. The controls lived at ambient atmospheric conditions. The test subjects were at 258 mm Hg under 100% oxygen (5 psia) for a total of 3 weeks and wore spacesuits during the final 2 weeks at altitude and the last week postaltitude. The controls wore spacesuits for the last 3 weeks of confinement. Samples for aerobic and anaerobic microbial assessment were taken throughout the confinement period. Men and chamber scrubbed prior to first sample.

CREW SIZE

6 men as test subjects and 2 men as controls.

TEST LENGTH

20 days at 27,000-ft altitude, 7 days prerun and postrun evaluations, total 34 days.

TEST OBJECTIVES

Determine effect of 100% oxygen environment on bacterial population, effect of wearing a full pressure suit, and personal hygiene evaluations. Studies on body function and psychological manifestation also done.

METHOD

Each man was taught the sampling techniques that had to be used for sampling their bodies, chamber walls, and air. Specimens were taken at the start of the test and at fre-

quent intervals during the test from the following body areas: throat, buccal area, axilla, groin, glans penis, and eye. Fecal samples taken twice a week. Fourteen samples from each of several environmental areas in both chamber and control facility by sedimentation plates or swabs. Also cultures taken from urine collection bottles, face cloths, and spacesuit.

RESULTS

Buildup of normal bacteria occurred in both environments. The fecal flora was affected by type of diet data. Anaerobes in feces outnumbered aerobes 1000:1. Diet encouraged gas-formers (anaerobes). A transfer of bacteria observed. Problem of cross-contamination present at two places: wash-water handles and neck of urinal. No clinical illness observed although the potential was present. Constant wearing of full pressure suits impaired adequate personal hygiene procedures. However, the 100% oxygen at 5 psia did not appear to influence the situation markedly. All surfaces became markedly contaminated with coliforms. Buildup of microbes occurred in areas where sweat is a factor. One apparent transfer of a microbe was observed, but it did not implant well as it was recovered only once from one of the men.

RECOMMENDATIONS AND CONCLUSIONS

Since the buildup of bacteria reached a plateau it is suggested that a longer confinement probably would not result in a much greater buildup of microorganisms. The results of this study confirm general findings from the literature in normal flora of adults. The confinement under the conditions provided was not harmful to the men. Future work should include a study to detect carriers of potentially pathogenic bacteria prior to confinement. Also suggest better personal hygiene methods for body and clothing.

CODE NO.

A10

TYPE

Spaceflight simulation; closed-door; manned.

TITLE AND REFERENCE

Determination of aerobic and anaerobic microflora of human feces, L. S. Gall and P. E. Rielly, AMRL-TR-64-107, October 1964.

WHERE DONE

Aerospace Medical Research Laboratories, Wright-Patterson Air Force Base, Ohio.

BY

Biotechnology Branch, Life Support Division, Biomedical Laboratory, Aerospace Medical Research Laboratories, and Paul Moore Research and Development Center of Republic Aviation Division, Fairchild Hiller Corporation, Farmingdale, Long Island, New York.

CHAMBER DESIGN

The Controlled Activity Facility (CAF), a 20 ft x 20 ft room with controlled temperature and humidity primarily for confinement. It contains beds, individual television, and essential accommodations.

EXPERIMENTAL DESIGN

From 4 men confined for 6 weeks, 13 fecal specimens were collected. Two men were maintained on an experimental freeze-dehydrated space-type diet, whereas the other 2 men had identical fresh and canned foods. Midway in the experiment the diets of the men were switched. Unpressurized spacesuits were worn during certain periods, but the torso and boots were worn continuously during the 16-day period. Gloves and helmet were worn for 4 h a day. Approximately 2 weeks into the test, gamma globulin was administered to the men who had been exposed to measles. The possible effect of this upon the results is unknown.

CREW SIZE

4 men.

TEST LENGTH

42 days total, but 28 days experimental period.

TEST OBJECTIVES

Determine the aerobic and anaerobic microflora of human feces and any changes that occur when men are maintained on a space-type diet.

METHOD

Fecal material was placed in broth, diluted, and inoculated onto and into appropriate media. Aerobic and anaerobic bacteria were looked for. Standard procedures were used throughout. The media selected for this study were chosen to recover the maximum number of intestinal bacteria. The 7 new "type cultures" isolated during the trial were studied in detail under anaerobic conditions. The predominating bacteria, those isolated in greater number than one million organisms per gram of sample, were studied for their physiological characteristics.

RESULTS

The aerobic intestinal flora differed slightly from that cited in the literature. Enteropathogenic type of Escherichia coli and Shigella were recovered more often than reported before. There is evidence of transfer of Candida among the men, although the data are not clear-cut. The possibility of a common source such as food was also considered feasible. Although anaerobic bacterial content of the feces remained relatively constant, a shift was found in the types of anaerobic organisms isolated. Diet appeared to influence this change in intestinal flora. However, anaerobes are the predominant fecal flora of the young adult male. The new types were classified into broad categories by differences in: gas production, formation of black slime, proteolysis in litmus milk, relative amount of lactic acid produced, gelatin liquification, and morphology. As the experiment proceeded and the men were in the test diets for an extended time, more "new types" of anaerobes, and fewer "normal" anaerobes (those the man brought with him into the chamber) were recovered. These "new types" increase threefold over the old original types. No marked differences observed in anaerobic fecal flora between subjects on the fresh and dehydrated diets or between the suited and nonsuited individuals. There did appear to be slight simplification of the bacterial flora toward the end of the experimental period.

RECOMMENDATIONS AND CONCLUSIONS

The space-type diet appeared to influence the shift of predominant anaerobic and aerobic flora from that observed in the early part of the study. Studies to test the influence of test conditions on anaerobic bacterial should continue for long enough periods of time to allow adequate

number of samples to be studied so that daily, transient fluctuations will not lead to misinterpretation of the data. Also future studies should include enough subjects to overcome individual variations, and control samples should be taken from subjects before confinement. There is a need to investigate the relationship between aerobic and anaerobic bacteria.

CODE NO.

B1

TYPE

Spaceflight simulation; unmanned, with integrated life-support systems (recycled).

TITLE AND REFERENCE

7-day, closed-door test of the Langley integrated life-support system: air, water, and surface bacteriologic investigations, J. R. Wilkins, Langley Working Paper, LWP-431, August 31, 1967.

WHERE DONE

Langley Research Center, Hampton, Virginia.

BY

Applied Materials and Physics Division, Langley Research Center.

CHAMBER DESIGN

Diameter, 18 ft, 2 in.; height, 18 ft; interior volume, 4150 cu ft divided into two levels consisting of a crew quarter and work area. Pressure, 1 atm, 21% oxygen and 79% nitrogen. 900 cu ft air movement per minute through two systems: (a) 300 cu ft per min (cfm) through a 0.3-μm particulate filter and 1 cfm through catalytic burner 69-75°F; (b) 600 cfm through heat exchanger, 65-70°F, relative humidity 34-45%. Water and waste systems treated with 50 ppm of benzalkonium chloride. Potable water tank maintained at 150°F. Water recovered from urine, humidity condensate, and wash water using a wick evaporator. Oxygen recovered by electrolysis with the hydrogen combining with oxygen to generate more water. Carbon dioxide is collected as solid carbon. Solid wastes are dried and stored.

EXPERIMENTAL DESIGN

To determine numbers, distribution, and types of microbes in the circulating atmosphere, water system, and surfaces of the chamber during one week in operation. No personnel testing was done. Water-management subsystem not cleaned or sterilized prior to use. Water from tap was 160°F.

CREW SIZE

Test was unmanned except insofar as systems operation and test procedures required man to be in the chamber. Designed for 4 men.

TEST LENGTH

7 days.

TEST OBJECTIVES

To develop a baseline on the types, distribution, and numbers of microorganisms present in the effluent from the water-management subsystem, in the circulating atmosphere, selected surfaces of the living quarters, and personal hygiene facilities.

METHOD

Air sampling: Andersen sieve samples at 1 cfm used before and after closing door from 5 min to 1 h sampling time at a specific hour. Plated and aerobically incubated.

Water sampling: Collected samples from water-management subsystem that processed humidity condensate, used wash water, and urine. Also water from hot and cold water of food-management subsystem. Plated and aerobically incubated.

Surface sampling: Rodac plates and sterile cotton swabs used on bed and exterior of food storage bin. Swabs of hygiene plunger, drip cup, urinal. Placed in saline and thioglycollate broth, plated, and incubated aerobically.

ORGANISMS RECOVERED

Air: Staphylococcus epidermidis, Achromobacter Sp., Corynebacterium sp.

Water: Pseudomonas sp., Achromobacter sp.

Surface: Not identified.

RESULTS

Air counts: Average counts of 3-4 bacteria per cu ft of air for lower and upper levels of chamber, respectively. Downward trend with time.

Water counts: A gradual increase of bacteria in the humidity condensate-wash water-urine unit from 10^4 bacteria per ml to 8 x 10^5 by the 7th day in the humidity condensate-wash water and from 5 x 10^4 to 5 x 10^6 bacteria per ml from the processed urine unit after 7 days. The cold water tap averaged 1 x 10^4 bacteria per ml for each sample. The water tap was sterile except for the first day when 10^3 organisms were recovered. No coliforms recovered.
Surface counts: Bacteria from beds recovered on Rodac plates ranged from 9-101 per plate with an average of 40. They appeared to be staphylococci. Food storage bins averaged 3 organisms per 25 cm^2. No growth found in urinal.

RECOMMENDATIONS AND CONCLUSIONS

(1) Clean and sterilize the water-management system. (2) Analyze all materials used in construction of water-management system, and identify sources of microbial contamination.

CODE NO.

B2

TYPE

Spaceflight simulation; unmanned, with integrated life-support systems (recycled).

TITLE AND REFERENCE

Microbiological studies on life support subsystems for manned space flight. Three and 4-day tests, J. R. Wilkins, presented at the American Industrial Hygiene Association, St. Louis, Missouri, May 13-17, 1968.

WHERE DONE

Langley Research Center, Hampton, Virginia.

BY

Applied Material and Physics Division, Langley Research Center.

CHAMBER DESIGN

Same as B1.

EXPERIMENTAL DESIGN

Microbiological studies to evaluate the systems and environment of the integrated life-support chamber. With the exception of crew members who used the waste-management system, no microbiological studies were made on personnel before, during, or after the two tests.

CREW SIZE

Both 3- and 4-day studies conducted with 4 men for each shift, alternating every 8 h to provide continuous occupancy.

TEST LENGTH

Two studies, one of 3 days and one of 4 days.

TEST OBJECTIVES

Perform microbiological studies supporting development and testing of water, waste, and personal hygiene systems.

METHOD

Water management: Specimens taken at various sites in the system by swab, plated, and incubated aerobically.
Waste management: Swab specimens taken from fecal collector and flush control lever. Rodac plates used to take samples from the floor, toilet seat, wall, crew's hands.
Air: Andersen sieve samples placed at sites about the chamber.

RESULTS

The product water did not meet recommended standards of a maximum of 10 microorganisms per ml: total plate counts averaged 10^6 bacteria per ml at end of both tests. No bacteria recovered from food-management hot-water tap, which operated at 160°F. Escherichia coli never recovered from air, waste-management subsystem, surrounding surfaces, or from hands of the crew. Depending on crew composition and activity, high or low counts of microorganisms found in air. Some individuals in crew were classified as heavy shedders. Urinal had a buildup of bacteria during 3-day test suggesting carelessness on part of a user to actuate flushing with benzalkonium chloride water solution.

RECOMMENDATIONS AND CONCLUSIONS

Assess role of "shedders" in the crew and the test personnel by determining numbers and types of microorganisms

recovered from each individual and from the air of closed environments. Extend surveillance of subsystems development by having microbiologist working closely with the engineers.

CODE NO.
B3

TYPE
Spaceflight simulation; unmanned, with integrated life-support systems (recycled).

TITLE AND REFERENCE
Microbiological studies on a water management subsystem for manned space flight, J. R. Wilkins and D. C. Grana, presented at the National Aeronautics and Space Engineering meeting, Los Angeles, California, October 7-11, 1968.

WHERE DONE
Langley Research Center, Hampton, Virginia.

BY
Applied Materials and Physics Division, Langley Research Center.

CHAMBER DESIGN
Same as B1.

EXPERIMENTAL DESIGN
Samples collected from waste system and water system while the chamber was charged with urine and feces but unmanned.

CREW SIZE
None.

TEST LENGTH
28 days.

TEST OBJECTIVES
Identify problem areas of the water-management subsystem.

METHOD
200 ml of water samples collected once each day, 7 h after processing units had been working. Each sample was tested

within 2 h of collection for bacteria. Samples collected for virus and pyrogen studies held at -70°C. Plating of aliquots was by millipore filter technique with incubation aerobically and anaerobically.

ORGANISMS RECOVERED

Proteus mirabilis, Pseudomonas sp., Aerobacter sp., Streptococcus sp., Alcaligenes sp., and Klebsiella

RESULTS

Of the 26 samples from the urine reclamation unit, 4 had counts that exceeded the recommended criterion of no more than 10 microorganisms per ml: 10^2-10^5 bacteria per ml. Of the 27 samples from the wash water, humidity condensate, and Sabatier water processing one sample exceeded the recommended standard, and it is believed that contamination occurred when sample was withdrawn rather than through equipment malfunction. The study demonstrated that it was possible to produce water meeting the recommended standards.

RECOMMENDATIONS AND CONCLUSIONS

(1) Steam sterilization procedures to be an integral part of the water-management subsystem. (2) Need for an on-line monitor to detect bacteria within a short period of time. (3) The goal of complete sterility for the water-management system is realistic and should be the end result for all future studies. (4) Early sterilization of urine. (5) Automatic monitoring and operation of the water-management subsystem.

CODE NO.

B4

TYPE

Spaceflight simulation with integrated life-systems support; unmanned.

TITLE AND REFERENCE

Manned Environmental System Assessment. NASA CR-134, November 1964.

WHERE DONE
The Boeing High Altitude Chamber.

BY
The Boeing Company.

CHAMBER DESIGN
The test chamber is rectangular, 8 ft high, 22 ft long, and 10 ft wide. Controlled access by a cylindrical air lock 8 ft in diameter and 16 ft in length. The 2350 cu ft of the rectangular chamber is organized into 3 functional units: sleeping, living, and work areas. A 6-in.-diameter air lock permitted small items necessary for testing to be passed in and out. A slight positive pressure over outside pressure was maintained in the chamber with oxygen 20% and nitrogen 80%. Although there was minimum change of chamber air due to leakage, contaminants generated remained in the chamber. The life-support systems consisted of: air controls, waste treatment, water treatment, trace contaminants, humidity underflow, air conditioning, personal hygiene, and food systems.

EXPERIMENTAL DESIGN
A 17-day chamber evaluation to conduct tests on integrated systems preceded the 30-day manned test (C1). The first 13 days were unmanned, and during the last 4 days 5 men were inside the chamber to operate the systems. The air loop was open but water loop partially closed.

CREW SIZE
None.

TEST LENGTH
17 days.

TEST OBJECTIVES
Complete an integrated systems chamber test to provide the necessary confidence and experience for a 30-day manned test with full crew.

METHOD
Bacteriological samples from water system were taken at various times during the trial. An Andersen six-stage sieve-type sampler outside the chamber sampled air. All the air sampled was pumped back into the chamber. Aerobic

bacteria and molds were looked for. In an aerosol test with two bacteria, Serratia marcescens and Bacillus globigii, the organisms were injected into the chamber. The air was sampled periodically. Rodac plates were used to sample 20 sq in. of surface each time. Samples were taken from designated ports located at sites in the waste system and evaluated for aerobic and anaerobic bacteria.

RESULTS

Both superoxide and Hopcalite systems appeared to remove S. marcescens from the air more efficiently than B. globigii. It was not determined if S. marcescens died quickly or was removed from the atmosphere by impacting on surfaces of the air-conditioning ducts. Recovery of S. marcescens from chamber surfaces was low, while recovery of B. globigii from surfaces was high. The external water holding tanks were not sterilized before use and contributed to bacterial count. No accurate data available on the water system because of procedural difficulties. However, the bacteria that were recovered were common airborne contaminants. During the 17-day test the waste system was vented overboard for the first 2 days so airflow necessary for aerobic bacteria could be adjusted. As expected, the viable bacteria found in the waste system were also found on exposed surfaces throughout the chamber.

RECOMMENDATIONS AND CONCLUSIONS

Overall, the systems were operating well with only a few microbiological problems. Some of the difficulties could be traced to improper preparations of the systems and were soon remedied. It was apparent from this test that an instrumented assay system must be developed which can rapidly assess the microbiological status of any system.

CODE NO.

C1

TYPE

Spaceflight simulation with integrated life-support systems.

TITLE AND REFERENCE

Manned Environmental System Assessment, NASA CR-134, November 1964.

WHERE DONE
The Boeing High Altitude Chamber

BY
The Boeing Company.

CHAMBER DESIGN
Same as B4.

EXPERIMENTAL DESIGN
The men were confined for 30 days. Samples from the men, air, and systems were taken periodically in the 30-day test by 2 of the subjects within the chamber. A microbiological baseline for each man and for the chamber was established before entry.

CREW SIZE
5 men.

TEST LENGTH
30 days.

HYGIENE
Excellent.

TEST OBJECTIVES
Investigate all aspects of a closed ecosystem that includes man.

METHOD
Bacterial sampling of the men included samples from the nose, throat, skin, and mouth by swabbing with cotton-tipped applicators. Stool samples were obtained only on the first specimen day. Remainder of the fecal samples were obtained by using rectal swabs. All swabs were put into nutrient medium before streaking. Direct smears on slides were prepared from nasal, throat, and mouth swabs and gram stained. Standard laboratory procedures for growth, isolation, and identification were used throughout for the aerobic bacteria. Andersen sieve-type samplers were used to test for the viable bacteria. Air was sampled from eight gas sample ports. The surfaces inside the chamber were sampled by the Rodac plate method. A total of 20 sq in. per surface was sampled. Water samples were withdrawn from selected sampling ports in the water

system and in the humidity underflow system for bacterial counts.

RESULTS

During confinement all men had a decline in number of normal nasal and throat flora and a concomitant increase in potential pathogenic bacteria. Staphylococcus aureus became the predominant organism. Gram strains from direct smears showed a decrease in bacteria from the nose and pharyngeal regions a few days after entry into the chamber. The predominant organisms of the throat were Streptococcus, Staphylococcus, Micrococcus, and Corynebacterium. Each man's mouth during the test had Vincent's angina organisms in concentrations higher than that considered normal. There were no remarkable changes in the fecal flora during or after confinement. Approximately 40% of all the processed water was rejected due to excessive amounts of bacteria. Contamination occurred after treatment. However, coliforms were never present in the water system or final water. Only common airborne bacteria were found. Coliforms were, however, present in the humidity underflow subsystem, probably due to maintenance procedures. Sampled air indicated that the cabin was relatively bacteria-free for the entire 30 days. The surfaces tested in the chamber had a high bacterial count.

RECOMMENDATIONS AND CONCLUSIONS

The air systems worked reasonably well. There was a decrease in microbes after passage through the superoxide beds and Hopcalite burner. The waste system was a biological activated sludge system with aerobic microbes which produced atmospheric contaminants which were chemically controlled. By continued monitoring of the amount of aeration and of exhaust gases, good performance was achieved. The filtration, catalytic oxidation, and ultraviolet sterilization worked well, but considerable maintenance was required. The personal hygiene procedures of shower and drying-air flow after shower appeared adequate, as did chewing gum, mouthwash, and toothpaste for oral hygiene. Future investigations should be made into the causes of the decline of the normal nasal-pharyngeal flora and subsequent increase in potential pathogens. Possible causes cited are conditions of temperature, humidity, bacteriologically clean air within the chamber, or trace quantities of an unknown chemical agent in the air. Con-

trol of bacterial contamination of the essential systems has not been fully accomplished. Stations for monitoring, rapid procedures for detection of contamination, and on-site sterilization must be developed.

CODE NO.
C2

TYPE
Spaceflight simulation with integrated life-support systems.

TITLE AND REFERENCE
60-day manned test of a regenerative life support system with oxygen and water recovery. II. Aerospace medicine and man-machine test results, DAC-62296, NASA CR-98500, December 1968; unpublished data from Dr. W. E. C. Moore, Professor, Bacteriology, Virginia Polytechnic Institute, Blacksburg, Virginia

BY
McDonnell Douglas Astronautics Company, Western Division, Santa Monica, California.

CHAMBER DESIGN
A horizontal cylinder 12 ft in diameter, 40 ft long, 4100 cu ft, divided into 5 areas: command, bunk, galley, exercise, and waste management. Total atmosphere pressure of 362 mm Hg (7 psia), and an oxygen partial pressure of 160 mm Hg (3 psia). Nitrogen was the other gas in the two-gas atmosphere. Relative humidity ranged from 30 to 70%, temperature 70-80°F. Carbon dioxide partial pressure ranged from 3 to 6 mm Hg. The closed-loop water-purification system consists of an evaporator unit, a charcoal filter, and a condenser which reclaims moisture directly from the crewmen and from air in the cabin. Oxygen was reclaimed through a process of mixing hydrogen and carbon dioxide and converting them to water and methane gas. Oxygen is recovered from the water by electrolysis, and the methane gas is expelled from the cabin.

EXPERIMENTAL DESIGN
The men were confined under simulated space-cabin environment for 60 days. Samples were taken from the men before,

during, and after confinement. Culture samples taken frequently from the water, waste, and air systems as well as from surfaces in the chamber. Intensive anaerobic studies were conducted on mouth, skin, and fecal microflora. Men periodically full-body sponge bathed (Astrovac) with an aqueous solution of benzalkonium chloride. Brushing and gum were used for oral hygiene. The major efforts were directed toward monitoring the changes that occurred.

CREW SIZE
4 men.

TEST LENGTH
60 days.

HYGIENE
Facilities good; Astrovac baths.

TEST OBJECTIVES
Test the life-support systems simulating earth-orbital flights of 1- or 2-year duration with resupply 60-90 days. Microbiological emphasis was placed on monitoring the potable water recovery system, chamber's environment, and microflora of the crew; providing new data on microbial characteristics of a closed ecological system; and determining any microbiological interference with the life-support-system components.

METHOD
Samples were taken almost daily from the water systems. Air samples were collected at 12-h intervals at both ends of the chamber with both Reynier (55 min) and Andersen (15 min) samplers operational at 1 cfm and also settling plates (55 min). Each man's dermal bacteria and fungi were assessed before, during, and after the test. Swabs were taken from the nose, pharynx, axilla, perineum, and toes. All were passed out of the chamber immediately, plated, and incubated aerobically and anaerobically. Specimens were taken at approximately weekly intervals with the last taken 40 days after test completion. Cultures for special anaerobic studies were obtained on the 24th and 58th day of confinement and 40 days after test completion.

RESULTS

The total atmospheric microbial count in the chamber, once stability was achieved, was one organism per cubic foot of air. Simplification of organisms came early in the test. Water stored at 150°F inhibited bacterial growth. The water recovery system produced water that met required microbiological standards. No quantitative changes of men's microflora could be correlated with significant clinical events. Generally body microflora decreased in number. Microflora of the throat remained relatively constant. Staphylococcus aureus did not colonize the two men who entered the chamber free of this organism. The axilla specimens from three of the men yielded equal numbers of gram-positive cocci and gram-negative rods. The coliform isolated most often from the perineum was Klebsiella. Shift of flora in the mouth from 50% predominantly anaerobic (Actinomyces and Veillonella) at 24 days to 88% predominantly alpha hemolytic gram-positive faculative anaerrobic cocci occurred. Most skin samples were superficial; however, those taken on the 24th and 58th day from behind the ear and tested anaerobically showed 10^5 Corynebacterium acnes. Predominant fecal flora varied from individual to individual and appears to be extremely complex. Bacteroides was most common anaerobe recovered but representatives from eight other genera were present. Anaerobes decreased during the test and emerged following confinement.

RECOMMENDATIONS AND CONCLUSIONS

The predominant intestinal microbes may vary from one individual to another even though the subjects have been on identical diets for some time. Future quantitative studies should compare cultural counts from samples with direct microscopic clumps for valid determinations of populations. Microbial standards for wash water recovery should be established and monitored. The men should be maintained for a sufficient time together before confinement to reach microbiological equilibrium. Future studies should have microbiological evaluations with a "specialist task group" of expert microbiologists who represent all the necessary disciplines. This type of team is not attainable within any one industrial organization. It should be organized by interested groups and charged with the responsibility of conducting all similar spacecraft-related studies, thereby reducing or precluding the errors of inexperience and maximizing information.

CODE NO.
C3

TYPE
Spaceflight simulation; manned, with integrated life-systems support (recycled).

TITLE AND REFERENCE
Integrated Life Support System, 28-day manned evaluations. Internal Langley Working Papers, 1968-1969.

WHERE DONE
Langley Research Center, Hampton, Virginia.

BY
Applied Materials and Physics Division, Langley Research Center, Hampton, Virginia.

CHAMBER DESIGN
Same as B1.

EXPERIMENTAL DESIGN
Three crews of 4 men each working under industrial standards; water not consumed, waste management used, door closed, maintained the chamber for 28 days. The influence the men exerted on the systems was studied.

CREW SIZE
4 men for each shift alternating every 8 h to provide continuous occupancy.

TEST LENGTH
28 days.

TEST OBJECTIVES
(1) To evaluate the water-recovery system and adjust it if necessary so that it can meet chemical and biological standards for potable water. (2) To assess the oxygen recycling system.

METHOD
Water recovery: Water samples were removed from selected ports after processing (wick evaporation and charcoal filtration). Samples removed daily and standard procedures used with aerobic and anaerobic incubation for bacteria and molds.

Oxygen recovery: Atmospheric samples were taken 3 times daily on both levels of the chamber by an Andersen sampler set within the chamber. The specimens were diluted, plated, and incubated aerobically.
Waste management: Selected sites were sampled from ports in the waste-management system. Buildup studied on floor and areas where constant usage caused coating of microbes.

ORGANISMS RECOVERED

Water system: Pseudomonas, Proteus, Alcaligenes, Chromobacter.
Air: Staphylococcus, diphtheroids, Neisseria, fungi, and yeasts.
Surface: Staphylococcus, fungi, yeasts, and bacillus.

RESULTS

Water: Standards were met for the duration of the test except for two periods of contamination. Proteus was the predominant organism.
Air: Counts were cyclic ranging from 8 to 10 organisms per cubic foot of air.
Surface: Bacteria built up on the surfaces of the chamber as the test progressed.

RECOMMENDATIONS AND CONCLUSIONS

No illnesses were observed. All systems generally met standards. There is a great need for on-line rapid detection of contamination in the water system.

CODE NO.

D1

TYPE

Spacecraft on ground.

TITLE AND REFERENCE

A partial bacteriological profile of test pilots and their Apollo spacecraft during a simulated fourteen-day lunar flight, K. A. Borchardt, J. M. Vogel, and C. R. Goucher. Aerospace Med. 39:166-171, 1968.

WHERE DONE

North American Aviation Corporation, Downey, California.

BY

Jointly conducted by members of the Pathology Service and the Research Service of the U.S. Public Health Service Hospital, San Francisco, California.

CHAMBER DESIGN

Apollo spacecraft. Cabin maintained at 97% oxygen, 3.75-5.00 psi. Temperature maintained at 88-90°F with high humidity. The vehicle was surrounded by a simulated atmosphere equivalent to an altitude of 245,000 ft. Although material was carried in and out of the vehicle through an air interlock system, no attempt was made to isolate the interior of the capsule and the chamber about it to prevent microbial exchange.

EXPERIMENTAL DESIGN

A full crew simulation lunar flight with personal hygiene routines to be followed as would be performed on an actual mission. Crew took hexachlorophene baths on day zero prior to suiting and daily hexachlorophene sponge baths during the study.

CREW SIZE

3 men.

TEST LENGTH

14 days.

TEST OBJECTIVES

Observe changes that occur in the bacterial population of the test pilot crew and vehicle.

METHOD

Specimens were taken at 2-day intervals by swabs moistened with saline. Body areas were: throat, groin, axilla, hands, and feet. 14 spacecraft areas were sampled. Air microbiology was not done. Each man took his own specimens. The same man sampled the spacecraft throughout the study. Tested for aerobic and anaerobic bacteria.

RESULTS

Enterobacter sp. recovered from urinal in high counts. The groin and axilla areas were reservoirs for Enterobacter. Most areas of the vehicle incurred minimal con-

tamination after 14 days of use. Simplification of microflora did not occur.

RECOMMENDATIONS AND CONCLUSIONS

The personal hygiene systems of the spacecraft performed adequately. Foci of possible crew contamination inside urine relief receptable should be eliminated.

CODE NO.

D2

TYPE

Spacecraft on ground.

TITLE AND REFERENCE

The 2TV-1/CSM Test. Medical Research and Operations Directorate. The 2TV-1/CSM Test Medical Report, Medical Operations Office, Manned Spacecraft Center, NASA, June 16-24, 1968.

WHERE DONE

Space Environment Simulation Laboratory, Manned Spacecraft Center, NASA, Houston, Texas.

BY

Medical Operations Office, Manned Spacecraft Center, Houston, Texas.

CHAMBER DESIGN

Apollo spacecraft. 365 cu ft. 99% oxygen, less than 1% nitrogen, and less than 1% carbon dioxide after 135 h of elapsed test time at 4-7 psia. Temperature 65-76°F, humidity 55% (max.).

EXPERIMENTAL DESIGN

Samples to be collected from the men and spacecraft that: verify functional performance of engineering changes, demonstrate integration of man and life-support systems, show development in time lines of the test procedures, and assess medical status of the crew and microbiology of the environment.

CREW SIZE

3 men.

TEST LENGTH

8 days.

TEST OBJECTIVES

(1) Determine microbial population of the spacecraft atmosphere during final phase of the chamber test and determine the effects of the spacecraft environment on two known species of microorganisms. (2) Identify problem areas and improve laboratory procedures so that a rapid microbiological analysis could be done under simulated flight conditions. (3) Establish normal baseline so that comparisons can be made later. (4) Detect possible untoward variations in microbial balance.

METHOD

Specimens obtained pretest and posttest from body surfaces, urines, throat, stools, and spacecraft hardware were examined for bacteria and molds. All specimens were immediately serially diluted and plated on various differential media for isolation and enumeration. Each isolate was identified.

RESULTS

There was a readjustment (loss or gain) of groups and of specific microorganisms by transfer from one crew member to another. Because sampling time was inadequate, no microorganisms were obtained from the capsule's atmosphere. No difference in number detected between the test and control microorganisms that would indicate contamination. No ova, cysts, or parasites detected.

RECOMMENDATIONS AND CONCLUSIONS

Data indicate a more rapid change of the microflora in the spacecraft than was previously believed. It is believed potential problem areas have been uncovered. Future fungal isolation attempts should be made at lower dilutions. Additional studies should be done to establish baseline of normal microflora for the spacecraft.

CODE NO.

E1

TYPE

Manned spaceflights.

TITLE AND REFERENCE

The microbiological flora of the Gemini IX Spacecraft before and after flight, J. Hotchen, P. Lorenz, A. Markusen, and S. Covert, NASA CR-972, December 1967.

WHERE DONE

Cape Kennedy, Florida.

BY

Division of Laboratories and Research of the New York State Department of Health; Dudley Observatory, State University of New York at Albany and Albany Medical College.

CHAMBER DESIGN

A Gemini capsule with 40 cu ft of cockpit. Spaceflight was at 100% oxygen at 5 psia. Personal hygiene items included the following: tissues, fabric towels, wet cleaning pads, toothbrushes, and chewing gum.

EXPERIMENTAL DESIGN

Three sets of samples were obtained: Preflight set #1, 16 May 1966; following GT-9A prescrub on 31 May 1966, Preflight set #2, 3 June 1966; Postflight swabs taken 6 June 1966. These were sent to three different laboratory groups: Group I, a biological research laboratory which attempted a quantitative assay with little identification; Group II, also a biological research group interested in long-term incubation periods with some diagnostic studies; and Group III, a hospital diagnostic laboratory.

CREW SIZE

2 men.

TEST LENGTH

Flight was 3 days. Two sets of preflight and one set of postflight samples taken.

TEST OBJECTIVES

To establish number and type of microorganisms in the Gemini IX spacecraft immediately before and after flight.

METHOD

Three locations representative of areas frequently touched (door handle), occasionally touched (above center panel),

and protected or dust collectors (behind seat) were sampled by swabbing with dry swab. Samples returned to N.Y. labs, loaded with dirt, squeezed out in 5 ml of thioglycollate broth, agitated, and distributed among three groups of investigators.

ORGANISMS RECOVERED

Micrococcus ureae, Bacillus arus, Bacillus megaterium, Bacillus subtilis, Bacillus coagulans, Bacillus pumiles, Penicillium sp., Aspergillus sp., Corynebacterium acnes, Flavobacterium breve, Streptococcus sp., Staphylococcus albus.

RESULTS

Bacteria and molds were observed before and after the flight. Each group found different organisms because of choice of methods. There was no indication of bacterial or mold buildup. Only microorganisms indigenous to man were recovered. There is a great variation in results by the three groups.

RECOMMENDATIONS AND CONCLUSIONS

This report shows that one finds only those microorganisms one is specifically prepared to look for. There is a need to sterilize spacecraft before space missions.

CODE NO.

E2

TYPE

Manned spaceflights.

TITLE AND REFERENCE

Preliminary clinical report of the medical aspects of Apollos VII and VIII, C. A. Berry, Aerospace Med. 40:245-254, 1969.

WHERE DONE

Manned Spacecraft Center, Houston, Texas.

BY

Medical Research and Operations, Manned Spacecraft Center, NASA.

CHAMBER DESIGN

Apollo spacecraft. 365 cu ft. Launched with 64% oxygen and 36% nitrogen; most of flight with 90-97% oxygen at 5 psi; cabin temperature approximately 70°F with variations between 63° and 80°F. A cross-connection between the potable water system and waste water system led to use of sodium hypochlorite with a buffer to be used routinely.

EXPERIMENTAL DESIGN

Samples were collected preflight and postflight from the men and the spacecraft.

CREW SIZE

3 men.

FLIGHT LENGTH

Apollo VII, 10 days and 20 h; Apollo VIII, 6 days and 4 h.

TEST OBJECTIVES

Assurance of good mission management, mission completion, and crew safety; prevention of back contamination of earth's biosphere; further study of the biomedical changes incident to manned spaceflights; provision of microbial baseline for later lunar quarantine operations.

METHOD

Serum samples were taken periodically from all men. Samples to test for viruses, bacteria, Mycoplasma, and molds were taken preflight and postflight from the men. The spacecraft was swabbed at selected sites before and after flight. Standard microbiological procedures were followed.

RESULTS

No viral agents recovered in preflight and postflight samples. A rhinovirus was isolated from the Apollo VII backup crew, but serologic studies on the prime crew did not implicate this particular virus in the illness. Results from Apollo VII and VIII missions appear to show a change in the bacterial and fungal flora. These vary greatly with the individual. There are transfers of microorganisms from man to man within the spaceship. It appears to be an environment that produces simplification of microflora and allows opportunistic gram-positive bacteria to dominate. There is an inhibition of certain anaerobes.

RECOMMENDATIONS AND CONCLUSIONS

A considerable amount of change does appear to be occurring in the microbial flora. Reduced contact with possible sources of infection imperative in preflight period to reduce the incidence of inflight illness.

CODE NO.

F1

TYPE

Submarines.

TITLE AND REFERENCE

Epidemiological studies aboard Polaris submarines, H. M. S. Watkins, M. A. Mazzarella, C. E. Meyers, T. R. Wilkinson, J. P. Hresko, W. E. Beam, A. Leibovitz, and collaborating submarine Medical Officers. Epidemiologic investigations in Polaris submarines, presented to the Armed Forces Epidemiological Board Commission on Acute Respiratory Diseases, March 27, 1967.

WHERE DONE

Aboard operational submarines.

BY

Naval Biological Laboratory, Naval Medical Research Unit No. 1, and the University of California School of Public Health.

CHAMBER DESIGN

Fleet Ballistic Missile Submarine.

EXPERIMENTAL DESIGN

The microbiological and epidemiological parameters of the crew and environment were investigated. Samples were collected from the environmental air and selected body sites, frozen, and shipped to a laboratory for evaluation. Respiratory disease investigations were emphasized. Some on-board virus studies were done in a miniaturized mobile virus laboratory which was part of a program to develop and test equipment and procedures for conducting diagnostic microbiology at sea.

CREW SIZE

Approximately 100 to 140 men depending on vessel and missions.

TEST LENGTH

Average length 56 days.

TEST OBJECTIVES

Determine types of infections that occur and the source of infections, and study spread throughout the crew. If bacteria and viruses survive in treated air, seek ways to control atmospheric microbial contamination.

METHOD

Samples collected were: environmental air, skin and nasal swabs, throat washings, saliva, and blood serum. Atmospheric samples were collected by air samplers run for 20 min 4 times a day at 8 locations. Immediately after the samples were taken they were divided into aliquots which were frozen except for nasal and saliva samples which were not divided because they were assayed for bacteria only. The crew was surveyed for upper respiratory illness approximately every 5 days. Samples were routinely sent to shore laboratories for analysis. Limited viral isolations were attempted by direct inoculation of cell cultures on some cruises.

RESULTS

Significant epidemiological results can be obtained from as few as 30 crewmen who could mirror respiratory symptoms of the entire crew. Three patterns of respiratory infection noted: peak reached by 10th day, peak reached before mission, and peak of respiratory illness reached at mid-mission. Airborne bacteria are removed by air processing system to 10 microorganisms or less per cubic foot of air. Approximately 50-60% of the crew may be infected at peak periods. Cross-infection has not been a major problem. No evidence of significant airborne bacteria buildup, but a low level of environmental contamination. No viruses recovered from air. Enteric bacteria found in oropharyngeal samples following venting of sanitary tanks.

RECOMMENDATIONS AND CONCLUSIONS

Air is recycled and treated by filtration, electrostatic precipitation, charcoal beds, carbon dioxide scrubbers,

and carbon monoxide burners which appear to remove microbes effectively from the air in all but unusual circumstances. There is a need for better methods of evaluation of contamination. Those crews with high carrier rates of meningococci and streptococci need further study.

CODE NO.
G1

TYPE
Navy blast-protective shelter.

TITLE AND REFERENCE
Studies of the Bureau of Yards and Docks Protective Shelter. I. Winter Trials, prepared cooperatively by U.S. Naval Research Laboratory, Bureau of Yards and Docks, Naval Medical Research Institute, U.S. Army Medical Research and Nutrition Laboratory, NRL Report 5882, December 31, 1962.

WHERE DONE
National Naval Medical Center, Bethesda, Maryland.

BY
Bureau of Yards and Docks, U.S. Naval Research Laboratory, and Naval Medical Research Institute.

CHAMBER DESIGN
A reinforced quonset hut 25 ft wide, 48 ft long, and 12 ft high. The floor is reinforced concrete. Air from the outside is drawn through an intake pipe and the filter unit by a blower having a maximum capacity of 600 ft per min. The air is circulated through the living quarters, through the drying, shower, and undressing rooms, and vented to the outside through a pipe in the trash room by a 300-cfm blower. The pressure in the shelter is kept higher than that outside to prevent inward leakage of contaminated air. Temperature averaged 73°F with relative humidity of 36%. Toilet facilities consist of six chemical units. Water for drinking and decontamination is supplied by an underground tank buried outside the shelter. There are two water outlets within the shelter.

EXPERIMENTAL DESIGN

In a shelter kept at a slight overpressure some microbiological and epidemiological aspects of confinement were studied. Of the 100 volunteers taking part in the shelter study under minimal hygiene conditions, 50 were selected for bacteriological surveillance. All were sampled 3 days prior to entering the shelter. The 50 men were divided into 2 groups and each group was sampled each 4 days. All samples were passed out of the shelter to a laboratory for immediate processing. Air was sampled periodically. No cultures were taken after the men left the shelter. Lectures on hygiene and sanitation were given to the group. There was routine disinfection of hands of food handlers and each man used alcohol-impregnated tissues before eating. Ill men were segregated behind blankets to provide a modicum of isolation from heavy traffic.

CREW SIZE

100 men. Recruits graduating from boot training.

TEST LENGTH

14 days.

TEST OBJECTIVES

The primary objective was to determine the effectiveness of the shelter from an engineering standpoint. Surveillance of the men bacteriologically was to determine what caused an illness if any occurred during the trial.

METHOD

Throughout the 2 weeks air samples for bacteriological studies were taken 15 min each day by an air sampler. Plate counts were done to get total number of organisms per cubic foot of air, and the predominant organisms were identified. Rectal and throat samples were taken each time the men were tested and immediately sent to the laboratory. All samples were plated. Standard isolation-identification procedures were used throughout. Water samples were taken daily.

RESULTS

Rectal: No pathogens such as Shigella or Salmonella recovered. An enteropathogenic coliform 0126:B16 was found in 4 men prior to entering the shelter. This organism was recovered periodically from the same 4 men, but no

spread to others was detected.
Throat: The predominating organisms found were, in descending order of predominance, nonhemolytic Streptococcus, Staphylococcus, Neisseria, diptheroids, beta-hemolytic Streptococcus. All considered normal except the latter, which was not recovered twice in succession from any subject. No clinical symptoms observed. There was noted a tendency toward a common flora.
Air sampling: The numbers of organisms varied somewhat from day to day. Counts were considered within a normal range throughout the study. Predominating organisms were Staphylococcus and Bacillus subtilis.

RECOMMENDATIONS AND CONCLUSIONS

Crowding and lack of facilities for personal hygiene are major factors that promote the spread of disease in a shelter environment. Preventive measures are better suited to control diarrheal diseases transmitted by feces, fingers, and food than upper respiratory and other contagious diseases spread by direct contact. Data indicate the possibility of spread if an upper-respiratory infection should get started during the period of confinement. There was a need for virological or serological backup for the bacteriological studies, since upper-respiratory infections were seen in the shelter that could not be explained bacteriologically.

CODE NO.

G2

TYPE

Navy blast-protective shelter.

TITLE AND REFERENCE

Studies of the Naval Facilities Engineering Command Protective Shelter. II. Summer Trials, prepared cooperatively by Naval Research Laboratory, Naval Facilities Engineering Command, Naval Medical Research Institute, U.S. Army Medical Research and Nutrition Laboratory, NRL Report 6656, March 29, 1968.

WHERE DONE

National Naval Medical Center, Bethesda, Maryland.

BY

Naval Facilities Engineering Command (formerly Bureau of Yards and Docks), U.S. Naval Research Laboratory, and Naval Medical Research Institute.

CHAMBER DESIGN

A reinforced quonset hut 25 ft wide, 48 ft long, and 12 ft high. The floor is reinforced concrete. Air from the outside is drawn through an intake pipe and the filter unit by a blower having a maximum capacity of 600 ft per min. The air is circulated through the living quarters, through the drying, shower, and undressing rooms and vented to the outside through a pipe in the trash room by a 300-cfm blower. The pressure in the shelter is kept higher than the outside to prevent leakage of contaminated air inward. Temperature was 85°F during the first week (average daily effective temperature) and 80°F during the second week. Toilet facilities consist of six chemical units. Water for drinking and decontamination is supplied by an underground tank buried outside the shelter. There are two water outlets within the shelter.

EXPERIMENTAL DESIGN

In a shelter kept at a slight overpressure some microbiological and epidemiological aspects of confinement were studied. Of the 100 volunteers taking part in the shelter study under minimal hygiene conditions, 50 were selected for bacteriological surveillance. All were sampled 3 days prior to entering the shelter. The 50 men were divded into 2 groups and each group was sampled each 4 days. All samples were passed out of the shelter to a laboratory for immediate processing. Air was sampled periodically. No cultures were taken after the men left the shelter. Lectures on hygiene and sanitation were given to the group. There was routine disinfection of hands of food handlers and each man used alcohol-impregnated tissues before eating. There was head-to-foot orientation for sleeping.

CREW SIZE

100 men.

TEST LENGTH

14 days.

TEST OBJECTIVES

The primary objective was to determine the effectiveness of the shelter from an engineering standpoint. Bacteriological studies done as backup for the medical and physiological studies: estimate the extent to which pathogens may be transmitted throughout a shelter. Test water used for drinking purposes.

METHOD

Throughout the 2 weeks air samples for bacteriological studies were taken 15 min each day by an air sampler. Plate counts were done to get total number of organisms per cubic foot of air, and the predominant organisms were identified. All samples were sent to the laboratory immediately from the shelter. 50 men were selected for surveillance from which rectal and throat cultures were taken prior to entry and every 4 days during the test. Blood samples taken in anticipation that a viral agent may cause an infection. Sera were a baseline. If infection occurred, a second serum would be used for diagnostic tests. Water samples were taken daily.

RESULTS

Rectal: No Shigella or Salmonella recovered. An enteropathogenic coliform isolation made prior to confinement. 31 enteropathogenic coliforms recovered during the test period.

Throat: The predominating organisms found from the throat cultures were, in descending order predominance, nonhemolytic Streptococcus, Staphylococcus, Neisseria, and diphtheroids, all normal flora.

Blood: The 4 cases of upper-respiratory infection (febrile) and the 11 cases of mild diarrhea did not justify testing of sera. Nothing further was done with the blood samples.

Air samples: No unusual bacteria recovered from the air. There were day-to-day fluctuations. Number of organisms was low: only on 4 days were counts higher than 50 organisms per ml of impinger fluid. Believe this low count due to high humidity within the shelter, low dust content, and low level of activity of the men.

Predominant organisms: Staphylococcus, Bacillus subtilis, and Streptococcus.

Water samples: The total number of organisms in the water increased substantially as the test progressed but remained

safe for drinking. Predominating organisms were: Staphylococcus, gram-positive rods, B. subtilis, gram-negative rods.

RECOMMENDATIONS AND CONCLUSIONS

Crowding, high temperature, and lack of personal hygiene facilities are the major factors contributing to medical disorders encountered due to infectious agents. The problem of communicable diseases was minimized in the trial because the men had lived in fairly close contact with each other for several months of recruit training immediately before the trial began and had thus acquired immunity from agents which may have been uniformly distributed throughout the group.

CODE NO.

H1

TYPE

Experimental dives (4 dives).

TITLE AND REFERENCE

Microflora of divers, personal communications from C. E. Meyers, J. D. Gillmore, and N. A. Schlamm, 1969.

WHERE DONE

Experimental Diving Unit, U.S. Navy, Washington, D. C.

BY

Personnel of Naval Medical Research Institute, Bethesda, Maryland.

CHAMBER DESIGN

Two interconnecting pressure chambers for providing simulated depths in ocean, one chamber dry and the other containing water for immersion. Two dives were made in dry chamber to 450 ft with an excursion in "wet suit" on 2nd day to 600 ft in wet chamber; 3 days required for decompression; total = 9 days. Two similar dives were made to 200 ft with excursion in "wet suit" on 2nd day to 300 ft in wet chamber; decompression required only 1 day; total = 4 days. Oxygen used at approximately normal partial pressure, with He.

EXPERIMENTAL DESIGN

Daily specimens taken by cotton swabs from nose, oropharynx, skin, ear, and rectum; transferred daily to exterior through a lock, frozen in skim milk, and dilutions later plated on differential media; water also sampled.

CREW SIZE

4 or 5 divers.

TEST LENGTH

9 days including decompression, 2 dives.
4 days including decompression, 2 dives.

TEST OBJECTIVES

To determine if alterations in normal body microflora occur under the conditions of the tests, to detect transfer of microorganisms among personnel, to detect alterations in resistance or exacerbation of any unknown chronic infection in divers, and to determine if incidence of microorganisms increased in the environment of the diving chamber.

METHOD

See experimental design.

RESULTS

Incidence of bacteria in skin and ear specimens increased sharply after excursion dive into wet chamber; predive levels attained near end of decompression period. Total aerobic and anaerobic counts of oropharynx and nasal samples remained fairly constant throughout; Pneumococcus (?) found in throats of 2 subjects; increase in one was coincident with upper-respiratory symptoms. Escherichia coli in throats of 2 divers following wet excursion dives; other possible fecal bacteria, including Pseudomonas aeruginosa in ear specimens and in nose of one diver. One subject developed external ear infection with Ps. aeruginosa. High levels of fecal microflora in water. Potentially pathogenic staphylococci were found in 2 divers and interpersonal transfer may have occurred.

CONCLUSIONS

Person-to-person transfer or person-to-habitat-to-person transfer of Staphylococcus, Pseudomonas, and E. coli may have occurred.

CODE NO.
H2

TYPE
Experimental dive.

TITLE AND REFERENCE
Microflora of divers, personal communications from C. E. Meyers, J. D. Gillmore, and N. A. Schlamm, 1969.

WHERE DONE
Experimental Diving Unit, U.S. Navy, Washington, D. C.

BY
Personnel of Naval Medical Research Institute, Bethesda, Maryland.

CHAMBER DESIGN
A pressure chamber for providing simulated depths in the ocean, but without immersion in water. One experimental dive was made to 600 ft; duration, 12 days, including decompression time. O_2-helium atmosphere with partial pressure of O_2 at 0.3 atm.

EXPERIMENTAL DESIGN
Daily specimens were taken by cotton swab from 5 men, from nose, ear, groin, and anal area; an oropharyngeal specimen was taken by gargling. After transfer to the exterior through a lock, specimens were stored frozen and later plated quantitatively on differential media. Identifications made to generic level.

CREW SIZE
5 divers.

TEST LENGTH
12 days, including decompression.

TEST OBJECTIVES
To detect shifts in normal human microflora and interchange of bacteria among personnel during exposure to experimental diving conditions.

METHOD
See experimental design.

RESULTS

Day-to-day variations in numbers of bacteria in samples from same sites reached as much as several orders of magnitude. Pneumococci found in nose of 2 subjects on day 7 and following; beta-hemolytic streptococci found intermittently in 4 subjects; coagulase-negative staphylococci also recovered, no clinical illness occurred. Increase in numbers of Klebsiella aerobacter species occurred in ear samples in 4 of 5 subjects.

CONCLUSIONS

Interchange of pneumococci may have occurred; other significant shifts in numbers of microflora or interchange among personnel did not occur.

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