

1. BIOSCIENCE EXPERIMENTS UNDER CONSIDERATION AND REVIEW FOR AES AND AAP

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BEEM: Now we are going to delve into the AAP concept a bit further. Our first paper is by Dr. Siegfried Gerathewohl, Manager, Life Sciences Projects, OSSA. He will be talking on "Bioscience Experiments Under Consideration and Review for AES and AAP."

GERATHEWOHL: It must have become clear to you from the previous presentations that NASA has a continuing effort underway to define experiments for the Apollo Applications Program. This is necessary to assure maximum utilization of the Apollo spacecraft when they become available, and to permit the planning of a program which is compatible with the technical and scientific requirements for doing research in space. About a year ago, a questionnaire was sent to a representative segment of the scientific community (including scientists at NASA field centers) to obtain their suggestions for experiments in Apollo spacecraft. In addition, advisory teams were set up in the various scientific disciplines for the review of these suggestions. I was appointed Chairman of the Manned Earth Orbital Technical Advisory Team on Bioscience. Dr. Walton Jones from OART was Cochairman. Other members of the team were Dr. Belleville, Dr. Fellows, and Dr. Saunders from NASA Headquarters; Mr. Lewyn and Dr. Soffen from JPL; Mr. MacLeod from Goddard Space Flight Center; and Dr. Winget from Ames. This group convened early in January of this year at the Washington office of the American Institute of Biological Sciences, and laid the groundwork for a report on Bioscience Experiments for a Manned Orbiting Laboratory. This report was then used by the individuals in charge of this exercise—Mr. Dennis and Mr. Garbarini—for their "Advanced Earth Orbital Mission Definition Document" (dated January 19, 1965), which contains "the preliminary description of the rationale, content, structure and proposed method of implementation of a comprehensive, cohesive manned Earth orbital experiment program."

Before I present a survey about the contributions of the biologists to this document, let me briefly report on earlier efforts on this same subject.

Nearly 2 years ago, Dr. Soffen was called to the newly created Manned Space Science Division at Headquarters, NASA, to prepare recommendations for a bioscience program to be conducted in a Manned Orbiting Research Laboratory. Dr. Soffen gathered a group of life scientists, mainly from the Washington area, and discussed the problem individually and during several sessions with this group. This work resulted in the "Preliminary Bioscience Recommendations for MORL Program," which describes the problem areas and possible biological investigations in very general terms. It was undoubtedly of value to the follow-on studies, which were undertaken by the Bioscience Team for the so-called Garbarini Exercise, which led to the "Advanced Earth Orbital Mission Definition Document," which is also the basis of the present Apollo Applications Program.

Some of the facts and some of the fancies of such an effort must be pointed out at this conjunction.

- (1) We are faced with the reality of big boosters and large spacecraft which will be manned and available for Earth-orbiting flights in the 1968-72 time period. We can now assume with a relatively high degree of certainty that astronauts—and eventually scientists—will be able to experiment in space.
- (2) We are aware that scientists of various disciplines are proposing experiments for manned spacecraft and that—for example, in the areas of space medicine, space technology, and the geological sciences—impressive programs are already under development.
- (3) We know of quite a number of biologists who are interested in the opportunities offered by manned space flight and want to participate in our program. As a matter of fact, that is the reason why you are here.
- (4) NASA and the National Academy of Sciences have already selected the first astronaut-scientists, and a curriculum for their training is being worked out at present.

On the other hand, there are all sorts of contingencies or limitations which confront the scientist who is planning to submit experiments. The major contingencies are listed as follows:

- (1) Availability of appropriate launch vehicles and spacecraft
- (2) Provision for adequate flight and mission profile
- (3) Requirement for manned inflight experimentation
- (4) Man's tolerance of spaceflight conditions
- (5) Capable and competent scientist-astronauts

First of all, the launch vehicles and the spacecraft to be used must be appropriate. I am not quite sure whether the LEM, which will be made available for accomodating experiments, will suffice as a laboratory facility. The nominal capabilities and characteristics of the spacecraft and launch vehicles include minimal modifications of Apollo hardware for Earth orbital missions. Moreover, it is not clear yet whether or not adequate flight and mission profiles can be provided because of the high acceleration loads during launch and reentry. Our present launch vehicles are "man rated" only in regard to the astronauts. If a strong case for scientific inflight experimentation can be built—and I intentionally use this terminology—flight and mission profiles will have to be adjusted to the scientific requirements. For example, the guidelines for our exercise specified that if particularly significant experiments require modifications, such experiments should be proposed with a qualitative indication of the required changes, as well as any additional spacecraft capability that may be needed.

At present, we have three sources which provide leads to the requirements for experimentation in manned spacecraft. The first one is the manned space-flight program by itself. Although 21 Russian and American astronauts were exposed to space-flight conditions with no lasting detrimental effects for periods up to 8 days, man's tolerance to long-term weightlessness and its interaction with other factors has not been established yet. The experiments, which were conducted in manned spacecraft, yielded interesting but inconclusive results. I am referring, for instance, to Dr. Mack's experiment on bone demineralization and Dr. Bender's experiment on radiation and weightlessness effects on human blood. These experiments therefore should be continued. The second source is the demand from the biological science community for doing research in space. So far, this demand was not very strong—partly, I think, because of lack of information about the opportunities, partly because of the biosatellite project, which is our third source of information. Until recently, the

biosatellite was the only projected source for obtaining data about basic biological phenomena in the U.S. space program. However, the first of the biosatellites will not be launched before the end of 1966, and results of the experiments in the last spacecraft of this series will not be available until perhaps 2 years later. If no provisions are being made for continuity now, there will be a lack of information essential to the planning of a comprehensive flight program.

As to man's tolerance of space-flight conditions, it is reasonable to adopt the Air Force standards. The MOL assumes stay times from 30 to 90 days. The experiences gained by the 8-day Gemini flight are very encouraging. In order to do inflight experiments by man, we need—at least for the next few years—the scientist-astronaut who will combine the qualifications of an experienced scientist with those of a capable astronaut. It is unfortunate that none of the biologists, who volunteered in this program, qualified; and this shows that the physical standards should be revised or that other measures must be taken to assure scientific competence in the manned bioscience flight program.

The opportunity to leave the surface of the Earth and to enter a foreign environment for long periods of time should be a challenge to biologists. The space environmental factors, which are accessible for study on terrestrial biology, are listed as follows:

- (1) Position above the atmosphere as a vantage point for observations
- (2) Subgravity and weightlessness
- (3) Ultrahigh vacuum
- (4) Van Allen, solar, and cosmic radiation
- (5) Lack of Earth magnetic field
- (6) Escape from terrestrial periodicity
- (7) Exposure to astrophysical factors
- (8) Synergistic effects of space parameters

They are so well known that I do not have to spend time on their discussion. They are shown here because they determined the scope of our effort. These areas, which were roughly outlined in the guidelines for the "Manned Earth Orbital Mission Definition Document," are as follows:

- (1) The role of environmental inputs for the establishment and maintenance of normal organization in the living system
- (2) Investigations about the effects of gravity on life forms, including the fundamentals of gravitation biology
- (3) Basic biological processes and forms of life as they may have developed under extraterrestrial conditions
- (4) Basic concepts of life and its generation and distribution in the planetary system

In essence, they cover the same subjects which form the basis of the biosatellite project, which shows an orderly progression of experiments commensurate with increasing scientific knowledge and technical experience.

As a matter of fact, the biosatellite project was one of the main sources of potential experiments considered by the Technical Advisory Team for the Garbarini Exercise. These were mostly proposals which could not be accommodated in the biosatellite for one reason or another. They had been turned over to Dr. Gill for consideration for the Mercury or Gemini flights. Other proposals were submitted in response to Dr. Gill's call for proposals in 1963, and the questionnaire which I mentioned earlier. When the Advisory Team convened in January 1965, we had a total of 76 proposals to evaluate. Some of them were quite old, rather sketchy, or did not comply with the guidelines. Some of them had been previously reviewed by the Bioscience program offices and the Bioscience Subcommittee and were turned down for various reasons.

The Technical Advisory Team reviewed a total of 76 experiments. They were grouped in four major experimental areas:

Environmental biology:	Psychobiology:
Genetics	Neurophysiology
Molecular and cellular biology	Ethology
Morphogenesis and growth	Exobiology (life in free space)
Biorhythms	
Ecology	
Physiology:	
Systemic physiology	
Pathophysiology	

The above also shows the major subgroups which were formed by the various proposals. I will now say a few words about the experiments which were selected for consideration for the AES program and why they were selected by the Technical Advisory Team.

In environmental biology, the dramatic changes of the developing organism are of immediate interest to the investigator. After fertilization, cell division and differentiation proceed at a high rate and are sensitive to environmental influences. On the other hand, the development and growth process follows a well-established plan.

It has been theorized that lack of gravity should affect vital biological processes such as fertilization, cell division, differentiation and metabolism, tissue and organ formation, and related functions. According to some calculations made by Pollard and Sagan, gravity is supposed to influence the behavior of cells which exceed 10 microns in diameter. Whether or not this is true, down to what magnitudes of mass and size the effect of the gravity vector can be verified, and how it operates to determine the physical form and the biochemical character of the organism, are major subjects of investigation in the Gemini, Apollo, and biosatellite programs. Experiments suggested for AES were:

A. GENETICS

- (1) The effects of weightlessness on the replication and recombination of DNA
- (2) The effect of the space environment on the feeding, survival, and production of Daphnia pulex
- (3) The independent and synergistic effects of 0 G and radiation upon growth rate and mutation rate of bacteria (transport of material across the cell membrane)

B. MOLECULAR AND CELLULAR BIOLOGY

This area contains experiments on basic life processes other than reproduction and early development. They concern changes in cytochemistry, cellular ultrastructure and cellular metabolism associated with exposure to weightlessness, radiation, and their synergistic actions. Photosynthesis was included as a special area of investigation because of its implications for the development of closed ecological systems in which OART is particularly interested. The experiments concern—

- (1) Development, testing, and use of a 0 G growth chamber
- (2) Morphological changes in cells exposed to prolonged weightlessness
- (3) The effect of 0 G on paramecium and HeLa cells
- (4) Biological effects of weightlessness as a factor in gas-liquid separation in metabolites of micro-organisms
- (5) The effect of 0 G on protozoa
- (6) Effects of radiation and a gravity-free environment in space on cell division and growth

Observations of the external morphology and dynamics of growth in plants and animals as affected by the absence of gravity are listed in our third subgroup. Studies in this category emphasize detection of changes in the normal patterns of geotropic response occasioned by the absence of Earth's gravity. The following experiments were considered:

C. MORPHOGENESIS AND GROWTH

- (1) Modification of phage production in bacteria
- (2) Effects of prolonged weightlessness on the growth rate of *Escherichia coli*
- (3) The effects of 0 G on the fertilization rate and development of various types of eggs
- (4) The independent and synergistic effects of radiation and 0 G on differentiation in the flour beetle (*Tribolium*)
- (5) Activated sludge in waste management (a bacterial study)
- (6) The effect of weightlessness on plant morphogenesis, seeds, culture, and leafy plants

Another subject under study is biorhythm. Two major schools of thought emerge in this area. One group maintains that periodicity in biological organisms is of endogenous origin. The other school believes that it is caused by exterior factors. Experiments will be conducted in the biosatellite, and supplements are considered for manned spacecraft. These may include investigations of the responses of biological systems to subtle astrogeophysical factors which may induce or affect terrestrial biological periodicity. Moreover, systematic observations of the Earth from manned satellites can lead to a better understanding of the relationship of biology to its environment. Periodic or random movement of fishes, birds and game, the changes of growth patterns of plankton in the oceans and that of crops, forests, and jungles may have far-reaching importance in world economy.

Although the study of simple biological systems is scientifically very important, higher animals must be used to determine the effects of space factors on specific physiological functions. Under the heading of "Physiology," we want to study, first, dynamic processes in animal systems to supply the basis for an understanding of 0-G phenomena, which might be detected in human biomedical experimentation. There is also a higher degree of transfer validity for extrapolations from animals to man.

In the subgroup of Systemic Physiology, the following experiments were judged to be of value:

- (1) Effects of weightlessness on
 - (a) Gross body composition; and
 - (b) Cerebral, neuronal, and glial chemistry of animals
- (2) Effects of weightlessness on cardiovascular, respiratory, and renal systems; metabolism; and behavioral correlates in the primate
- (3) Metabolic adaptation to 0 G appropriate dietaries
- (4) Mineral and water metabolism under weightlessness and ionizing radiation

Under the caption "Pathophysiology," the study of effects of the space environment on processes, such as the healing of wounds and intercurrent infections, were proposed. The specific experiments were:

- (1) Effect of weightlessness on immune defenses
- (2) Liver regeneration (mitosis) at 0 G
- (3) Study of tissue regeneration and wound healing during weightlessness
- (4) Limb regeneration during weightlessness

There is also a possibility that a set of experiments using the reduction or absence of gravity as a tool for the investigation of selected disease states, such as cardiovascular hypertension, may be developed in this area.

It must be recognized that theoretical analyses have significantly contributed to the prediction of human behavior under weightlessness before appropriate means of experimentation existed. After high-performance aircraft and spacecraft were available, experiments were conducted on various psychological functions. The results showed that certain functions, in particular eye-hand coordination, spatial orientation, touch-and-pressure sensation, and reaction time, are rather unaffected by weightlessness. However, episodes of "space sickness," that is, vertigo and nausea, were experienced in two of the Soviet manned space flights. The experiments envisioned in the area of psychobiology are designed to shed light on the effects of weightlessness on fundamental behavior of infrahuman organisms and the physiological substrate associated with this behavior. The following neurophysiological studies were selected:

- (1) Monitoring of electrophysiological performance of the nervous system by neuromyography
- (2) Effect of weightlessness on the behavior of statocyst-bearing organisms
- (3) The pathophysiological effects of weightlessness on primates, with special attention to the role of the vestibular organs
- (4) Monitoring of neurophysiological, physiological, and performance functions in the primate under prolonged weightlessness

It is still hypothesized, and there are still the unexplained episodes of the Soviet astronauts which point in this direction, that the absence of gravity may be a disorganizing factor in psychobiological phenomena. Experiments which may contribute to the solution of this problem are:

- (1) Discrimination and communication of animals under 0 G conditions
- (2) Experimental analysis of animal adjustment to various degrees of gravitational force (including 0 G)
- (3) The effect of drugs on behavior and performance in space flight

Finally, two sets of experiments are considered in the area of "Exobiology." The first one concerns a test of the so-called Panspermia theory. According to this theory, life may have migrated in the planetary system. It will be informative to determine whether or not living material can survive in the space environment with and without various degrees of protection. The second task consists of a continuation of the search for extraterrestrial and terrestrial life forms at orbital altitudes in a more sophisticated manner and over more extended periods than this was possible at previous attempts.

These were the experimental areas and the individual experiments which we suggested for study in the AES. Of these, the following were selected by the Manned Earth Orbital Review and Integration Team (of which I was not a member) as representative examples for the Extended Apollo Development plans:

- (1) Genetic effects in micro-organisms (DNA recombination, mutation rate, and phage production)
- (2) Effects of space flight on morphology, growth, and gas/liquid separation in micro-organisms, unicellular organisms, cells, and animal tissue
- (3) Limb regeneration and wound healing during weightlessness
- (4) The effects of drugs on animal behavior in flight
- (5) The effects of weightlessness on cardiovascular and respiratory functions, hormone, mineral and water metabolism, ANS, CNS and brain mechanisms, operant behavior, and biorhythms in the primate
- (6) Soft capture, enumeration and identification of space-borne micro-organisms

However, the preliminary draft of the "Advanced Earth Orbital Mission Definition Document" contains the following 11 experiments as representative examples:

- (1) Study of tropic and toxic phenomena in plants and animals
- (2) Study of lifetimes and ability to reproduce of bacteria in the space environment
- (3) Synergistic effects of 0 G and radiation upon growth rate and mutation rate in bacteria
- (4) Determination of effect of 0 G and/or radiation on cell-free protein synthesis
- (5) Fertilization experiments
- (6) Effects of weightlessness on immune defenses against pathogenic agents
- (7) Effects of weightlessness on dividing human cells in culture
- (8) Effects of weightlessness on the replication and recombination of DNA
- (9) Study of photosynthetic action spectra during exposure of algae cultures to true space illumination
- (10) Origin of biochemical components
- (11) Collecting and sampling of micro-organisms in near-Earth orbits

The discrepancy between these two representative samples of biological experiments for the same AES program has never been explained to my satisfaction. However, it is clear that they all fall in the same problem areas which we had previously established.

It was understood that—since this was an exercise and not a final selection of experiments—principal investigators should not be appointed. As you know, this can be done only after proper review and acceptance of a proposal by the scientific subcommittees—in our case by the Bioscience Subcommittee—and the Space Science Steering Committee of the Office of Space Science and Applications. So, even if you should recognize one or the other of these representative experiments as coming out of your own shop, you must know that none of these experiments has been submitted to or accepted, respectively, by the Space Science Steering Committee.

There are several reasons for this delay in action. The first one was the opinion of the biologists that the submission of experiments for a manned orbiting laboratory would result in hasty and unsound proposals; particularly, since the participation of man in such a facility was still very doubtful. Moreover, partly because of this, only a relatively small segment of the prospective experimenters would participate; and therefore the proposals would not express the opinion of the biologic community.

Second, two other approaches had been employed in the meantime to solicit the cooperation of the scientific community in the AES program. One was a contract with the American Institute of Biological Sciences. The other one was a "Feasibility Study of Promising Stability and Gravity (Including 0-G) Experiments for Manned Orbiting Missions." The major problem areas and study objectives of the AIBS contract are as follows:

Problems to be investigated:

- (1) Can the space environment be used as a unique experimental condition?
- (2) Can man be utilized as a scientific experimenter and/or as a competent observer?
- (3) Can adequate instrumentation and environmental conditions be provided in proposed vehicles and missions to accommodate life science experimentation and man as an efficient experimenter?
- (4) Can an orbiting laboratory designed specifically for biological and/or life science experiments be justified?

Proposed study objectives:

- (1) Review of pertinent information

- (2) Optimum utilization of man as an experimenter during Earth-orbiting missions
- (3) Critical research requirements and essential problem areas for investigation
- (4) Pertinent research tasks, adequate methodology, appropriate experiments, competent scientists, and organizations
- (5) Comprehensive bioscience research program

Mr. Beem will give a brief survey on the progress made by the AIBS.

BEEM: One of the purposes of the American Institute of Biological Sciences is to cooperate with national organizations concerned with biology and biologists. One way of doing that is by cooperating with this MORL program. The project that we have undertaken will encompass these study objectives, although some are more important than others. Basically, the program will define the problem areas requiring inflight investigation, including the hypothesis to be tested, general research design, essential experimental equipment, and operational procedures, and a listing of optimum experimental specimens and their husbandry requirements. Although the research program will be as specific as possible, it is not anticipated that detailed experimental plans can or need be developed. On the contrary, the objective will be a scientifically justified biological research program that can be used as a guide by future experimenters.

Any such program should benefit from the thoughts and knowledge of as many of the Nation's biologists as possible. Therefore, to achieve this objective, we ask for the help, and receive the help, of our adherent scientific societies, of which we have 42. They submit the names of people who they think will be capable and qualified to sit on regional study councils. There are now five such councils. The Chairmen are Dr. Gilbert Levin, Dr. James Henry, Dr. Theodore Sudia, Dr. George Davis, and Dr. Ralph Baker.

The regional councils have just been organized. They have all had at least one meeting, or will have had one meeting within the next few weeks. Of course, we have not yet done anything definitive on the problem. It is just an organizational procedure so far. We would hope by probably a year from this time we will be able to put something into print.

We also have an internal advisory committee on this program. Robert Lindberg is here. Robert Krause is on this advisory committee, Kenneth Timon, and John Olive.

GERATHEWOHL: Another reason for the delay in action was that none of the old proposals were written on the forms handed to us for the Garbarini Exercise, and most of them did not contain the information which the AES planners needed. It was hoped and planned that this meeting of potential experimenters would help in establishing the necessary professional contact between scientists and engineers, and also between biologists who may want to cooperate in one experiment; that is, pool their knowledge and experiences in order to come up with a good experiment which has a better-than-average chance to be accepted by the scientific committees. We have to be very selective because of the long leadtimes; the technical difficulties of preparing a complex experiment for flight; and the high costs involved, which amount to an average of about \$250,000 for a single experiment.

The "Advanced Earth Orbital Mission Definition Document" has been used in the meantime for defining the envisioned equipment for the representative examples, and for obtaining preliminary cost estimates. The next step involves a revision of the Flight Mission Assignment Plans, which were also established. To assure the planning of a realistic program, detailed descriptions of the experiments are now required. They are available in most of the other participating disciplines, such as geology, remote sensing, technology, and space medicine. These descriptions will be used by the Apollo spacecraft contractor, under the direction of the Manned Spacecraft Center, to conduct more detailed experiment integration studies. Hence, it is necessary and urgent that the biological flight program be finalized in a way which satisfies the scientific and the operational—I mean to say the OMSF—requirements.

I would like to conclude my presentation with a few comments about the need for an accelerated effort in our area of interest. The opinion has been voiced that such an effort is unnecessary, since any biological experiment, which can be done in an unmanned vehicle, can also be done in the AAP. This is a very superficial statement. First of all, we do not want to duplicate the biosatellite project for various reasons. At best, we want to implement it. The criteria which were used for selecting the AAP or AES experiments were different also. They are: The experiments would provide data of immediate interest and/or would aid in establishing the technological capability and the most effective methods for conducting future missions and projects—both manned and unmanned. Furthermore, the experiments should require the presence of man as an experimenter. We want to get the scientist-astronauts involved in space experiments as early and as much as possible. With respect to the latter criterion, it is recognized that, in a few cases, some of the suggested experiments do not require man's immediate presence and participation. However, in many cases, the technical difficulties inherent in studies, which require many specimens or statistically reliable samples, man's presence will be essential. In all these cases—even if the scientific objective of the experiment should be similar—the experimental conditions in the space laboratory will differ significantly from those in a small automated capsule, the design of the experiment will differ, and the equipment to be used will be different. That is why we have to make provisions now for the development of promising experiments in the AAP.

In short, we do not envision that the same equipment, the same techniques, and the same instruments, which are used in the unmanned biosatellite, will be adequate for the much more sophisticated work which scientists will perform in a manned orbiting laboratory. It is expected that the biological laboratory science, which still is mainly a hand-operated science, will undoubtedly profit from the degree of miniaturization and automation, which is mandatory for remote experimentation in space. On the other hand, we expect that the space biology program, which has been anchored so far mainly to the biosatellite project, will profit from the work of biologists in a manned orbiting laboratory. Hence, attention should be given to the preparations for this work, to the experiments which should be conducted, and to the equipment and facilities needed in manned spacecraft. They should be specifically designed to meet the characteristics of the space environment, but they should be general and flexible enough to permit work in the main areas of biology as outlined before. In this way, the true concept of a laboratory in space will be established, and the capability of the scientist-astronaut will be fully exploited.