Minutes of the 28th AFRRI Board of Governors Meeting

1. VADM Robert R. Monroe, U.S. Navy, Director, Defense Nuclear Agency (DNA), opened the 28th Meeting of the AFRRI Board of Governors (BOG) at 0800 on 5 September 1979.

2. VADM Monroe introduced the DNA personnel who were present, distinguished guests, and other advisors. CAPT Paul E. Tyler, MC, U.S. Navy, Director, Armed Forces Radiobiology Research Institute (AFRRI), introduced the AFRRI personnel (see enclosure 1 for list of attendees).

3. The agenda, which had been distributed to the Board prior to the meeting, is at enclosure 2. Listed below are the major topics discussed and the conclusions and/or decisions reached by the Board.

a. VADM Monroe opened the meeting with a discussion of possible mechanisms by which the Board of Governors could be more effective in guiding--in the broadest sense--the work of AFRRI. He suggested that the group of three ad hoc assistants, which had met several times since the last Board meeting, might well be made permanent, but should have their role re-focused. He then briefly discussed the agenda and invited Members of the Board to make opening comments.

b. LTG Pixley then picked up on one of the agenda topics--that of "offensive" vs. "defensive" nuclear weapons effects research. He read a statement expressing the opinion that the central issue of the meeting was "...should AFRRI be a medical research organization, or should it be something else." He felt that DNA sees AFRRI as its major biomedical research institute for both offensive and defensive aspects of nuclear weapons effects. A lengthy and lively discussion followed concerning the ethics of medical personnel being involved in research on issues which had overtones of offensive nuclear warfare. While no firm conclusion was reached, it was agreed that in most cases it is a two-sided coin; with the same research data being used by those addressing offensive and defensive issues (with medical matters confined to the latter). Most of those present felt that AFRRI was properly a <u>radiobiology research</u> organization, not more narrowly a <u>medical</u> research organization, and that the medical doctors at AFRRI (5 of 210) would have to limit their involvement to issues in the latter area. It was recognized that the present charter and its mission statement are in need of revision. It was agreed that a revised charter would be prepared and submitted informally to the BOG, OSD, and the Services for review and comments.

c. On the matter of research planning, VADM Monroe presented a sample letter in which DNA had attempted to develop a set of research requirements for transmission to AFRRI. There was some discussion as to whether this should be stated in terms of military issues or medical issues (the latter avoiding the ethical issue discussed in b. above). It was agreed that DNA would continue to refine this set of requirements and forward it to the BOG, OSD, the Services, and the Joint and Unified Commanders for comments and suggestions. When finalized, it would be transmitted to AFRRI. Based upon the requirements, AFRRI would develop a five-year research program for DNA approval. This overall guidance would be provided annually, with yearly revisions in AFRRI's program to accommodate the annual guidance changes. It was also decided that DNA would review whether AFRRI's current funding profile of being entirely in 6.2 is the most appropriate way to keep it or whether some other provision should be made.

d. Dean Sanford recommended that the BOG select certain topics of research to be presented by AFRRI at future meetings. It was generally agreed that this was an excellent approach.

e. Following a general discussion concerning the make-up of the BOG, it was decided that the current Board make-up was appropriate, but the new charter should make provisions for advisors and observers.

f. VADM Monroe then discussed the Brain Trauma Program, and stated that he was determined to make a final, firm decision either to continue it or close it down. He sought the Board's advice. Dr. David Carpenter, Chairman, Neurobiology Department, AFRRI, gave a presentation on the rationale for the program, the goals of the investigator, and the justification for its continuation. Dr. Tyler presented the AFRRI Directorate position for discontinuing the program. There followed a wide-ranging discussion, which included the fact that an adequate supply of primates in the near future (3-5 years) was unlikely. The opinion of all Board Members was that the project should be terminated. MajGen Dettinger abstained, and informed the Board he would discuss this issue with LtGen Myers. VADM Monroe stated that he would defer his decision until he had discussed the issue with LtGen Myers, and at that time he would notify AFRRI of his decision. (Note: Following the meeting LtGen Myers concurred in the termination of the project. VADM Monroe made the decision to terminate, and all concerned were notified.)

g. VADM Monroe then raised the matter of the growing shortage of medical personnel trained in radiobiology. It was noted that it has been many years since the Services sponsored anyone for graduate training in this area. The majority of

those who were trained in the past are gone now or nearing retirement, and soon the Services would be without this type of expertise. VADM Arentzen stated "...as for the Navy, we are going to start training some medical personnel in this area..." It was agreed that DNA would investigate the need and possible training programs and prepare a position paper for review by the BOG and OSD.

h. It was agreed that one meeting of the Board per year was not enough. It is planned that the next BOG meeting will be in approximately six months.

4. Major actions taken.

a. DNA will prepare a new charter for AFRRI and route to appropriate persons for review and comment.

b. DNA will prepare, circulate, and then finalize a set of research requirements to be forwarded to AFRRI annually.

c. AFRRI, based upon the requirements, will develop a five-year research plan annually.

d. At future meetings the BOG will select topics for presentation by AFRRI, based upon their current research program.

e. The structure of the BOG will be modified in the new charter to reflect official observers and advisors to the Board.

f. It was recommended that the Brain Trauma Program be terminated.

g. DNA and AFRRI will prepare a position paper on the need for trained personnel in radiobiology.

h. Future meetings of the BOG will be held semiannually.

2 Encls
as stated

R. R. MONROE
Vice Admiral, U.S. Navy
Director, DNA

August 1980

List of Attendees

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AGENDA

28th Meeting of the AFRRI Board of Governors

5 September 1979

0800-0815	Introduction - VADM Monroe
0815-0830	Discussion - Board
0830-1115	Action Items - Board

(1) AFRRI's Charter: Are changes desirable?

(2) AFRRI's Research Objectives: What should they be? Should they be expressed in military or scientific terms?

(3) AFRRI's Research Objectives: How should they be established?

(4) Role of Board of Governors: What should be the functions? What should be the procedures?

(5) Makeup of Board of Governors: Members? Assistants? Observers? Staff?

(6) Specific (short) topics:

- (a) Brain trauma program
- (b) Officer education/training in radiobiology
- (c) Primate availability.

1115-1130 Closing Remarks - VADM Monroe and Board

Enclosure 1

Background
material
on
28th BOG

BEHAVIORAL SCIENCES DEPARTMENT

I. Research Objectives.

The Behavioral Sciences Department (BHS) evaluates possible alterations in the performance of military personnel as a function of exposure to elements within the operational environment. These evaluations may be in relation to operational considerations for military exposure to ionizing radiation environments or the investigation of potential problems arising from present day-to-day activities of military personnel.

II. Present Status and Goals of Future Research.

Currently, we are conducting studies which are in direct support of the Army Nuclear and Chemical Agency's (USANCA) requirement for nuclear combat casualty criteria planning information concerning crew degradation and synergistic effects, as well as, supporting the Naval Medical Research and Development Command (USNMRDC) with behavioral toxicology information concerning the potential neurobehavioral impact of the day-to-day operational use of synthetic fuel derived from shale-oil.

The areas presently under investigation within BHS are: (1) the effects of task stress and fatigue on radiation-produced performance decrement, (2) the biological mechanisms by which ionizing radiation produces performance decrement, and (3) the behavioral toxicology military chemicals.

Ionizing radiation and combined stress studies involving task stress and fatigue are supported by two work units. These studies indicate that as the mental and physical requirement of a task are increased, the level of radiation required to degrade performance is decreased. This has resulted in a decrease in the average radiation level required to produce performance decrement from 1800 to approximately 900 rads.

The biological mechanisms by which these decrements are produced are investigated in three work units. These studies, which involve the use of radiomimetic drugs and electrophysiological mapping, have been successful in establishing regional areas of radiation effects within the brain. The use of molecular probes to examine the effects of radiation on neural membranes has begun and will provide a molecular basis for discussing radiation effects.

As a part of an ongoing collaboration with the Navy to develop a comprehensive neurobehavioral toxicology program, BHS is curently assessing the potential neurological and behavioral impact of diesel fuel marine and JP-5 jet propulsion fuel derived from shale crude oil in support of the Navy's Project Independence. This collaboration has resulted in the evaluation of eight potential operational chemicals in the past seven years and the development of a comprehensive neurobehavioral evaluation procedure which is equally applicable to the assessment of low dose chemical and radiation toxicity.

In the future BHS will be involved in the definition of low dose radiation effects on behavior and in collaborative studies to investigate the basic mechanisms underlying radiation-produced performance decrements.

Over the last 20 months, BHS has lost 3 Ph.Ds. The single most significant factor in determining the future research accomplishment of BHS will be the level of professional staffing.

BIOCHEMISTRY DEPARTMENT

I. Research Objectives.

A. Elucidate mechanisms of damage to the mammalian organism due to radiation and/or chemical agents.

B. Develop effective methods for detecting and evaluating this damage and relate them to similar injury in man.

II. Present Status and Goals for Future Research.

A. Development of Biochemical Indicators of Radiation Injury.

Gallium (Ga-67) binds competitively with iron on serum transferrin. Preliminary results of this biologic radiation dosimeters are promising.

B. Late Effects of Radiation (Carcinogenesis).

The appearance of cancer is associated with changes in the levels of certain serum glycoproteins. The possibility of utilizing these glycoproteins for a biochemical radiation dosimeter is under study.

C. Myocardial Depressant Factor (MDF).

A serum factor (MDF) in irradiated animals has been found which, when added to a cardiac muscle preparations, drastically decreases contractility. Goals are to (a) isolate, purify, and identify MDF; (b) identify the sites of production or release; and (c) find ways to prevent its production or counteract its effects.

D. Effect of Low Level Radiation on the Prenatal and Juvenile Mammal.

Newborn rats exposed to low levels of ionizing radiation (50 to 100 rads) develop atrophic brains. Research has been initiated to elucidate the biochemical mechanisms underlying the observed effect and determine radiation dose response.

E. Hematopoietic Stem Cell Isolation.

Isolation of the stem (precursor) cells of the Hematopoietic system by using the Fluorescent Activated Cell Sorter will enable direct study of ionizing radiation effects upon these vital cells.

F. Effects of Microwaves and Toxic Chemicals on the Mammalian Brain.

Preliminary results in which commercially available organophosphorous compounds, used as "probes", indicate that exposure to pulsed microwave radiation results in a probable reversible opening of the Blood Brain Barrier (BBB). Present and future research is to (a) verify this temporary opening of the BBB can be used for effective treatment of anticholinesterase poisoning.

G. Effects of Radiation on Lysosomes.

Ionizing radiation apparently causes leakage of certain lysosomal enzymes. The radiation induced changes in lysosomal membranes are being studied.

H. Radiation Induced Immunosuppression.

Immunostimulants (levamisol) are being tried to counteract the radiation induced immunosuppression. Preliminary results indicate that administration of levamisol to irradiated mice results in some increase of survival rate.

Program: Postirradiation [illegible]

I. Research Objectives.

Exposures to ionizing radiation doses between 100 and 1000 rads damages or destroys bone marrow cells resulting in a reduction or cessation in the production of granulocytes, macrophages and platelets which are the first and major defense against infectious bacteria and their toxins. With increasing radiation doses these infections result in fatalities. Procedures which would protect bone marrow cells from these effects, enhance their endogenous production postirradiation or which would temporarily supply functional granulocytes until the radiation-damaged bone marrow recovers, would decrease infections and fatalities. In addition, means that would prevent the invasion of intestinal gram-negative bacteria into other tissues and organs of irradiated personnel or at least reduce their concentration, would contribute towards successful treatment. This would permit exposures of personnel to higher radiation doses if extreme military situations demand it and the utilization of enhanced nuclear weapons, since it would raise the radiation dose for collateral damage by raising the $LD_{5/30}$.

II. Present Status and Goals of Future Research.

A. Enhancement of white cell production postirradiation.

The humoral control mechanisms responsible for regulating production of granulocytes and macrophages are currently being elucidated. These humoral regulators will be identified and characterized. The therapeutic applicability of these humoral agents to re-stimulate the production of these white cell types postirradiation will be evaluated.

B. Studies of origin and prevention of infection postirradiation.

Changes in permeability to gram-negative bacteria and their endotoxins are being studied, along with the mechanisms available for clearing these agents from the host. Protocols to reduce intestinal injury (decrease permeability) and to supplement systemic clearance of agents postirradiation will be explored.

C. Combined injury.

The involvement of the hematopoietic system in wound and burn healing and in secondary release of degradative enzymes is being examined. Mechanisms to reduce or eliminate the combined stresses of radiation and multiple injury to hematopoietic system function will be explored.

D. Physiological assessment of fresh and cryopreserved granulocytes and macrophages utilized for postirradiation transfusion.

Protocols have been developed for the isolation of pure and functional granulocytes. Further testing of these cell isolates will assess the clinical effectiveness of such transfusion postirradiation. Isolation of other hematopoietic cells for potential postirradiation therapy, including macrophages and progenitor cell populations, will be pursued. Radiation effects on membrane physiology of these cells are being studied.

E. Transplantation of bone marrow into lethally irradiated animals.

Lymphocyte "supressor cell" populations have been identified which can inactivate the lymphocyte "killer cells" responsible for post-transplantation graft-versus-host disease. The applicability of these "suppressor cells" to the removal of "killer cells" from marrow before postirradiation transplantation will be studied. Additionally, the effect of fission neutrons versus gamma radiation on the processes of bone marrow sterilization and of transplantation will also be investigated.

NEUROBIOLOGY DEPARTMENT

1. Research Objectives:

A. The mission of the Neurobiology Department is to study the effects of ionizing radiation on nervous tissue and the interactions of radiation injury with other forms of injury, such as those resulting from blast and thermal effects. The direct effects of radiation include study of mechanisms underlying early transient incapacitation (ETI), radiation-induced fatigue, the central nervous system (CNS) syndrome, and the study of the relative radiosensitivities of various types of cells in the nervous system.

2. Present Status and Goals of Future Research:

A. Mechanisms of ETI: ETI is known to result from radiation-induced release of active substances from mast cells. These substances, particularly histamine, serotonin, dopamine and several peptides, are released into the circulation and act at receptor sites throughout the body. We have made major progress in understanding the variety of receptors for these substances on both nerve and smooth muscle cells. Our future work will expand to study receptors on other areas in brain and blood vessels.

B. Mechanisms Underlying Radiation-Induced Fatigue: Research in this area was begun one year ago with the initial aim of determining whether the origin of this fatigue was peripheral (at the neuromuscular junction) or within the central nervous system. We are studying the mechanisms in both the rat and the monkey. Our preliminary results suggest fatigue is a central process and we are now focusing particularly on the motor neurons in the spinal cord as a possible site.

C. Mechanisms Underlying the CNS Syndrome: Our studies suggest that the CNS syndrome results because of a disruption of the ability of cells to regulate intracellular calcium concentration. Disturbance of calcium concentration alters the ionic concentrations to other ions and alters the permeability of the membrane. We have studied the effects of alteration of intracellular calcium and are now establishing a program to measure the concentration of free intracellular calcium directly.

D. Radiosensitivities of Cellular Components of the Nervous System: Using tissue cultured nerve, glial and smooth muscle cells we study the relative radiosensitivities of the various cell types from different species in an effort to test the validity of extrapolation models to man from animals. We now study several human cell lines. This program will be expanded to include the growth of monkey cells in tissue culture. This is particularly important since so much of the experimental data on responses of the whole animal to radiation comes from primates.

E. Responses of Specific Organ Systems to Ionizing Radiation: We have programs investigating effects of radiation on the cardiovascular system and on the auditory system. The cardiovascular system is particularly important in that there are probably cardiovascular components to both ETI and the CNS syndrome. The auditory system is uniquely sensitive to the effects of radiation for reasons not presently understood.

F. Combined Radiation, Thermal and Mechanical Injury: Nervous tissue has a limited variety of ways of responding to injury, and many of these are common to mechanical, thermal and radiation effects. These programs are concerned with an elucidation of the mechanisms of injury to these variety of insults, alone and in combination.

NUCLEAR SCIENCES DEPARTMENT OVERVIEW

I. Research Objectives.

A. The Nuclear Biology Division utilizes radionuclide counting and imaging techniques for the study of physiological functions in experimental animal models.

B. The Radiological Physics Division conducts extensive in-house dosimetry research in order to provide dosimetry support for all radiation sources at AFRRI.

II. Present Status and Goals of Future Research.

A. Neutron Flux Spectra Measurement

New project to accurately determine the neutron flux spectra in the AFRRI TRIGA Reactor exposure rooms free-in-air and at depth in a phantom.

B. Development of a Lithium Fluoride Thermoluminescent Dosimetry System

New project to obtain procedures for precise and accurate doses from a few rads to approximately 300,000 rads with a spacial resolution of approximately 1 cm^3.

C. Pulmonary Irradiations Effects

Compare the long-term effects on regional pulmonary functions neutron and gamma irradiations.

D. Bone Marrow Localization with Indium-111

Investigate the usefulness of Indium-111 as a red bone marrow imaging agent and its potential use in assessment of bone marrow damage due to irradiation.

E. Evaluation of Cardiac Localizing Radiopharmaceuticals

Develop new cardiac imaging radiopharmaceuticals which are specific for certain receptor sites in the heart.

F. Radiation Dosimetry

Continuing project to maintain calibration factors for all radiation sources at AFRRI, investigate radiation detection devices and maintain the AFRRI Dosimetry Protocol manual.

G. Effect of Irradiation on Tissue Uptake of Radiopharmaceuticals

Define the time-course of radiation effects on skeletal and muscle uptake of bone imaging radiopharmaceuticals, and evaluate the role of local bone and muscle blood flow in tracer uptake.

H. Evaluation of Healing of Traumatic Bone Fracture and Bone Grafts

Evaluate bone graft healing with radionuclide techniques and study the effect of anemia and irradiation of graft healing.

Summary and Recommendations of the November 1978 Peer Review

of AFRRI's Scientific Research Program

A. Introduction.

The report has three main sections. The introduction discusses the Institute, while the second section is devoted to the five scientific departments. The last section is a list of twenty major recommendations, which the committee, as a whole, felt should be implemented as soon as possible.

In viewing the report it is apparent that there were some divergent views among the committee members. While these divergent views are evident, the Chairman did an outstanding job of synthesizing many differing opinions into a consensus document. Since each department was only reviewed by two or three members of the committee, one can identify opposite opinions if one selects isolated statements in the sections concerning the specific scientific departments.

B. The following observations have been abstracted from the first section.

1. Civilian interest and research in radiobiology is declining. (Note - in light of Three Mile Island, NTPR and congressional interest, this may not be true today.)

2. AFRRI has not been interested in low-level, long term effects.

3. Non-ionizing radiation is only minimally represented in AFRRI's program but appears to be well within its overall mission.

4. The scientific departments are disparate in size, level of effort, quality of research, and relevance to AFRRI's mission. There is a lack of coordinated or cooperative effort between the departments.

5. Related defects are due to transient management.

6. There is a need for overall policies establishing firm priorities and research goals in radiobiology.

7. There was concern about the three year tours of military personnel, it was felt that this was too short.

8. The ratio of technical support personnel to professional staff is grossly inadequate.

9. There is a lack of qualified staff and lack of equipment in advanced biophysical methods which may be indicative of a lack of adequate breadth in some areas.

10. The observation concerning the Board of Governors, because of its pertinence, is quoted.

> "One observation should be reported which was particularly underlined by those members of the committee who have been involved in military R&D. The Board of Governors, consisting of the service Surgeons General, does not appear to be adequate for the type of long-range decision making needed. They are overwhelmed with the problems of delivery of medical care around the world to service personnel, dependents, and retired personnel along with special operational specialties such as aviation, submarine, and military field medicine.
>
> The demands of present peacetime operations may leave them with not enough time, money, or personnel to be concerned with problems that may arise, in a future war. In general, they personally have little professional experience with the requirements for research in radiation biology related to military operations, and indeed the expertise developed in nuclear weapon testing is rapidly leaving the senior ranks of the services. The Surgeons General have heavy responsibilities and can give little detailed attention to the guidance of AFRRI—yet their prestigious presence on the Board is an indication of the importance of AFRRI to DoD. There is a need for the Board of Governors to enunciate a strong commitment to an ongoing multi-year program, and to demand performance in relation to the mission."

C. In general, the observations stated in the various sections directed toward the specific departments should properly be handled as internal management problems and proposed solutions are not of general concern as an Institute-wide comment. They are, therefore, not abstracted for discussion by the Board of Governors. The theme was the criticism that the research was not adequately oriented to the problem of the interaction of radiation with mammalian systems and to the practical concerns of the DoD.....for too many sidelines, primarily of scientific interest, are followed without establishing adequate priorities. The committee also noted that the relative emphasis on long-range versus immediately relevant research requires major management decisions.

D. Specific Recommendations.

The committee concurred virtually unanimously in a number of major recommendations which should be implemented as soon as possible. These include:

1. Selection of a civilian scientist at the super-grade level as permanent technical director.

2. Establishment of a scientific advisory group consisting of peer scientists drawn from industry, university, and the Government. This group should number from ten to fifteen reviewers and should provide for both periodic rotation and reasonable overlapping for continuity.

3. Development, together with DoD and the Board of Governors, of an explicit statement of current and long-term defense requirements for research in radiation biology and the concurrent mission responsibilities of AFRRI.

4. Development of an investment strategy for the Institute's research program covering the next five years in detail and extending to perhaps ten to fifteen years with lesser detail. Particular attention should be paid to insure that the resources available are optimized to the needs of the DoD and NATO. Planned research not directly mission related should be identified.

5. Designation in each department of a permanent career civilian chairman with appropriate scientific credentials in his field, and that an appropriate number of permanent senior appointments be made in each department of principal investigators to manage long-term projects.

6. Introduction of additional civilian billets at the technician level to permit proper utilization of both permanent and transient principal investigators.

7. The structure of the Board of Governors should be changed to include, in addition to the Surgeons General, at least two (rotational) representatives of the service in DoD medical research areas and at least two scientists of stature in the field of radiation biology.

8. There should be a much stronger awareness of many new developments in the fields of neurochemistry, hematology, and immunochemistry over the past five years that are relevant to the epidemiology of chronic low-level ionizing radiation and in the acute medical management of high-level exposures. The development of these needed, new programs requires aggressive new research teams, including current AFRRI scientists, and supplemented by infusion of new personnel. These developments may require substantial amounts of new research equipment and facilities.

9. Initiation of a study to determine the appropriate role for the Institute in assessing long-term effects of military-type exposures, particularly in carcinogenesis. This study should consider what actual experimental involvement is required of the DoD and how data from the civilian programs can be adapted.

10. A group consisting of institute senior scientists and external advisors should review the availability and application of sophisticated physical instrumentation to biological problems within the Institute.

11. The general areas of "combined effects" needs to be looked at carefully before large numbers of animals are subjected to experiments. The studies would need to relate to problems of function, diagnosis, or treatment, rather than just assessment of effects of various combinations and permutations of injury.

12. There is a need for more use of the radiobiological literature, much of which has come out only as progress reports from various laboratories. The need is for better indexing, as well as stress from a scientific direction, perhaps through appropriate seminars.

13. A lecture program on problems in radiation biology should be instituted using staff and outside experts to "raise the consciousness" of the investigators in radiation biology. This would insure that as problems of radiobiological significance become approachable, experimental programs will be implemented with little delay.

14. Greater departmental interaction at AFRRI is required. Many investigators seem unaware of other work going on throughout the Institute.

15. More work should relate to human data when possible—Japanese casualties (already being extensively evaluated at AFRRI), patients treated by wide field or total body irradiation, data on radiation accidents. Studies on white cell and platelet transfusions may be an area for clinical interaction with cancer programs, etc.

16. There is good interaction with other organizations involved primarily with research. More and stronger interaction with clinical groups would be desirable.

17. Provision for periodic scientific review of permanent personnel should be implemented to insure a base of productive and quality performance.

18. In line with the improvement of mission orientation, consideration should be given in performance reviews to the accountability, at the level of the working scientist, to the AFRRI mission.

19. There should be an increase in systemic dialogue between AFRRI staff, particularly at the program planning level, and the Pentagon, government laboratories involved in weapons such as the DoE labs, and other government laboratories.

20. Consideration should be given to amplifying the role in, and expanding the resources of the Institute for, the study of the biological effects of non-ionizing radiation.

DISCUSSION ON PERSONNEL NEEDS IN RADIOBIOLOGY

There is a chronic lack of medical personnel in the military service, particularly physicians, trained in radiobiology and nuclear weapons effects.

In the 1960s DASA supported military personnel for graduate training in radiobiology; isolated personnel have since been sponsored by their own service. At the present time, those who have been trained in radiobiology have either left the services or are now in the senior ranks and will be gone in the next few years. Today, there is almost zero input from junior personnel into this program and unless this trend is reversed there will soon be a total lack of military personnel on active duty qualified in this area.

In light of the general shortage of medical personnel and the demands for patient care, a simple solution is not apparent. It is recommended that a small task force, under the leadership of AFRRI, be established to explore ways whereby the military cadre trained in radiobiology can be increased. This task force should identify the present and projected service and DoD requirements, levels of training required, sources of personnel, methods of providing necessary training, and career utilization of personnel trained in this area.

At the request of the Board of Governors, AFRRI has prepared a one-week course to familiarize medical personnel with the Medical Effects of Nuclear Weapons. The first course was presented this past May and was well received. The next course is scheduled for November 1979. A 14-hour course has been developed and given to the freshman medical students at the Uniformed Services University of the Health Sciences (USUHS). Personnel from AFRRI have also been involved in presenting a mini course in the Biological and Medical Aspects of Ionizing Radiation at the Radiation Disaster Preparedness Symposiums. Recent symposiums include one presented at the 19th Naval Reserve Readiness Command in Long Beach, California, and one sponsored by the Emergency Medical Service of Orange County, California. Future presentations are scheduled for the Association of Military Surgeons, and the Aerospace Medical Association.

This education activity is welcomed and gives a positive image and recognition. The major impact has been to place a heavy burden on the few members of AFRRI presently qualified to teach radiobiology subjects. This underlines the major problem: a severe shortage of service personnel with adequate background and training in the general field of radiobiology.

July 1979

Director, AFRRI, Suggestions for Research Guidance

1. Biological effects of neutrons and identification of neutron RBEs, since there is early evidence that several factors may influence the assignment of an RBE and in fact it may not be a single number.

2. The effects of lower doses and long-term effects of radiation must be considered and a sound research program addressing this area developed.

3. The specific area of cytogenetics should be developed wtihin AFRRI to adequately evaluate low-dose, long-term effects.

4. Efforts should be started to study cellular damage and repair mechanisms.

5. Programs in biophysical modeling of radiation damage and repair should be given serious consideration

6. A systemic program should be developed to start with cellular models and expand to the evaluation of system responses to radiation.

7. Programs directed toward prevention of injury or increased resistance to radiation should be considered.

8. Studies should continue to identify performance decrements and possible methods to prevent such decrements.

9. Studies should be directed toward the development and evaluation of practical therapeutic approaches that can be utilized in combat zones under emergency conditions.

Department of Defense Directive

SUBJECT Armed Forces Radiobiology Research Institute (AFRRI)

Refs: (a) DoD Directive 5105.33, "Armed Forces Radiobiology Research Institute", May 11, 1972, hereby cancelled.

(b) DoD Directive 5105.18, "Department of Defense Committee Management Program", April 25, 1975.

(c) DoD Handbook 7220.9H, "Accounting Guidance Handbook", August 1972, Autnorized by DoD Instruction 7220.9, July 12, 1971.

I. REISSUANCE AND PURPOSE

A. This Directive reissues reference (b).

B. It assigns responsibilities and functions, sets forth the organizational relationships, and establishes the administrative and management arrangements for the Armed Forces Radiobiology Research Institute (AFRRI).

C. It provides for the establishment of a Board of Governors and a Scientific Advisory Board to aid the Director, AFRRI.

D. Reference (a) is hereby superseded and cancelled.

II. GENERAL

A. Established pursuant to the authority vested in the Secretary of Defense, the Armed Forces Radiobiology Research Institute is designated as a Department of Defense Research Laboratory and a subordinate activity of the Defense Nuclear Agency (DNA).

B. AFRRI shall serve as a radiobiology research laboratory for the Department of Defense. Other Federal and civilian agencies and institutions may utilize AFRRI services as agreed upon by the Secretary of Defense or his designee.

III. MISSION

The mission of AFRRI shall be to conduct scientific research in the field of radiobiology and related matters that are essential to the operational and medical support of the Department of Defense and the military services.

IV. ORGANIZATION

A. AFRRI shall consist of a Director, Deputy Director, and a staff of professional, technical, administrative and clerical personnel.

1. The Director, AFRRI, will be a military medical officer in Grade O-6 nominated by the appropriate service on the basis of high professional qualifications in the field of radiobiology and demonstrated medical research management ability. He shall be appointed by the Director, Defense Nuclear Agency (DNA), after consultation with the Board of Governors, normally for a period of (three) (four) years. Selection of the Director shall be rotated in order among the Army, the Navy, and the Air Force, provided that the military department next in line has a qualified individual who is acceptable to the approving authority.

2. The Deputy Director will be an officer in grade O-6 from one of the military services not represented by the Director and will be selected on the same basis as the Director.

3. The staff shall consist of professional, technical and clerical personnel, consisting of medical officers and other military personnel of the Army, the Navy, and the Air Force, and civilian personnel.

4. The Director, shall recommend staffing requirements to the Director, DNA for final determination and approval.

5. Staffing of military positions shall be coordinated with the military departments and prorated among them, in accordance with joint manpower authorizations.

B. See Options 1, 2, and 3 (attached)

C. The Director, AFRRI, shall have additional duty to the Defense Nuclear Agency as DNA Surgeon.

V. FUNCTIONS

Under established Department of Defense policies, the Armed Forces Radiobiology Research Institute shall:

A. Operate facilities for conducting research on the biological effects of radiation and disseminate the results.

B. Conduct training in the field of biological effects of radiation and nuclear weapons to meet internal requirements of the Institute, the individual services, other DoD components, and the Uniformed Services University of the Health Sciences.

C. Provide biomedical expertese in the field of radiobiology to support and assist DoD, its components and the military services. Represent DoD in interagency arrangements concerning biological effects of radiation.

D. Perform such other functions as may be assigned.

VI. AUTHORITY

The Armed Forces Radiobiology Research Institute shall be a joint agency of the Military Departments, subject to the authority, direction, and control of the Director, DNA, as delegated by the Secretary of Defense.

VII. ADMINISTRATION

A. The Armed Forces Radiobiology Research Institute shall serve as the principal facility for radiobiology research in the Department of Defense. AFRRI shall be self-contained and independent of other established activities.

B. The Director, DNA, shall be responsible for the determination and

C. The Director, AFRRI, shall have direct access to Director, DNA on matters pertaining to the Armed Forces Radiobiology Research Institute.

D. Under the Director, Defense Nuclear Agency, the Director, AFRRI, shall be responsible for the organization and effective operation of AFRRI, including the direction and supervision of its staff and activities.

E. Military personnel shall be responsible to the Director for their performance of duty while assigned to AFRRI.

F. The Armed Forces Radiobiology Research Institute will be identified as a separate accounting entity and follow the guidance in DoD Handbook 7220.9-H (reference c.), to assure full financial accounting of funds, property, and other resources made available or expended in the accomplishment of its mission.

VIII. EFFECTIVE DATE AND IMPLEMENTATION

This Directive is effective immediately, two (2) copies of implementing regulations shall be forwarded to the Under Secretary of Defense (Research and Engineering).

OPTION 1

B. In exercising command of AFRRI, the Director will be advised in matters of overall policy by a Board of Governors.

1. The Board of Governors shall consist of:

a. Voting members; the Director, DNA, as Chairman, and the Surgeons General of the Army, Navy and Air Force

b. The Dean, Uniformed Services University of the Health Sciences will be a non-voting associate member.

c. A designated representative of USDR&E and service experts in radiobiology will serve as observers and/or advisors to their respective Surgeon General.

OPTION 2

B. In exercising command of AFRRI, the Director will be advised in matters of overall policy by a Board of Governors.

1. The Board of Governors shall consist of the Director, DNA, as Chairman, and the Surgeons General of the Army, Navy and Air Force as voting members, the Dean, Uniformed Services Univeristy of the Health Sciences as a non-voting associate member. A designated representative of USDR&E and service experts in radiobiology will serve as observers and/or advisors to their respective Surgeon General.

OPTION 3

B. In exercising command of AFRRI, the Director will be aided in matters of overall policy by a Board of Governors and in matters of professional advice by a Scientific Advisory Board.

1. The Board of Governors shall consist of the Director, DNA, as Chairman, and the Surgeons General of the Army, Navy and Air Force as voting members. The Dean, Uniformed Services University of the Health Sciences as a non-voting associate member. A designated representative of USDR&E and service experts in radiobiology will serve as observers and/or advisors to their respective Surgeon General.

2. The Scientific Advisory Board shall consist of civilian and/or military experts in scientific areas relevant to radiation. The members will be appointed by the Director, DNA, for a term not to exceed four (4) years. The Scientific Advisory Board will operate in accordance with DoD Directive 5105.18.

May 11, 1972
NUMBER 5105.33

ASD(C)

Department of Defense Directive

SUBJECT Armed Forces Radiobiology Research Institute (AFRRI)

Refs.: (a) DoD Directive 5105.31, "Defense Nuclear Agency (DNA)," November 3, 1971
(b) DoD Directive 5105.33, "Armed Forces Radiobiolog Research Institute (AFRRI)," November 20, 196 (hereby cancelled)

I. GENERAL

A. Established pursuant to the authority vested in the Secretary of Defense, the Armed Forces Radiobiolog Research Institute (AFRRI) is designated a subordina unit of the Defense Nuclear Agency (DNA).

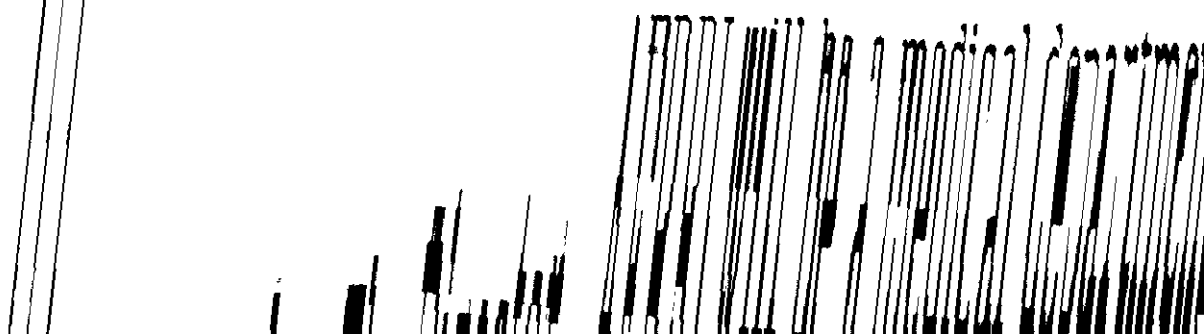
B. AFRRI shall serve as a radiobiology research laboratory for the Department of Defense. Other federal and civilian agencies and institutions may utilize AFRRI services as agreed upon by the Secretary of Defense or his designee.

II. MISSION

The mission of AFRRI shall be to conduct scientific resear in the field of radiobiology and related matters that are essential to the medical support of the Department of Defen

III. ORGANIZATION

A. AFRRI shall consist of a Director, a Deputy Director and a supporting staff.



consultation with the Board of Governors. Normally, the position of Director will rotate among the Services. His tour of duty shall be consistent with professional and military requirements and applicable DoD Directives and Instructions.

2. The Deputy Director will be an officer in Grade 0-6 or 0-5 from one of the Military Services not represented by the Director.

3. The staff shall be constituted of military and civilian personnel authorized by a Joint Table of Distribution (JTD), developed by the Director, DNA, and approved by the Joint Chiefs of Staff. Insofar as possible, the military members of the supporting staff shall be provided on an equal basis by the Military Departments.

B. In exercising command of AFRRI, the Director, DNA, will be advised in matters of professional policy direction and related matters by a Board of Governors.

1. The AFRRI Board of Governors shall consist of the Director, DNA, as Chairman, and the Chief Surgeons General of the Army, Navy, and Air Force.

2. The Director, National Institutes of Health, and the Director, Division of Biology and Medicine, Atomic Energy Commission, or their designees, may be invited to participate in meetings of the Board of Governors when matters of mutual interest are being considered.

IV. FUNCTIONS

Under the direction, control and authority of the Director, DNA, and in accordance with appropriate DoD Directives and Instructions, AFRRI shall:

A. Operate facilities for conducting research on the biological effects of ionizing radiation and disseminate the results.

B. Conduct advanced training in the field of biological effects of ionizing radiation to meet the internal requirement of the Institute, and those which may be developed and requested by other DoD Components.

C. Operate facilities for the production of short-lived radioisotopes for use in direct or collaborative research performed by the Institute.

D. Perform such other functions as may be assigned.

V. AUTHORITY

The appropriate provisions of reference (a) apply to the Director, DNA, in exercising command of AFRRI and fulfilling the functional responsibilities implicit in this Directive.

VI. ADMINISTRATION

A. The Military Departments will assign military personnel to AFRRI in accordance with approved authorizations. Procedures for such assignments will be as agreed upon between the Director, DNA, and the individual Military Departments.

B. Maintenance and operation of AFRRI normally will be programmed, budgeted and financed by DNA. This provision does not preclude AFRRI from participating in reimbursable activities subject to concurrence by Director, DNA.

C. The pay, allowances (including subsistence) and permanent change of station travel costs of military personnel assigned to AFRRI will be borne by the Military Department from which assigned.

VII. EFFECTIVE DATE AND CANCELLATION

This Directive is effective immediately. Reference (b) is hereby superseded and cancelled.

Kenneth Rush

Deputy Secretary of Defense

DEFENSE NUCLEAR AGENCY
WASHINGTON, D C. 20305

Draft

28 August 1979

MEMORANDUM FOR DIRECTOR, ARMED FORCES RADIOBIOLOGY RESEARCH INSTITUTE

SUBJECT: Radiobiological Research Objectives, FY80-85

1. In accomplishing AFRRI's mission of radiobiological research in support of the Department of Defense, you should address the following military requirements in your research program:

a. Determine the radiation levels which result in performance decrement sufficient to cause an inability for military units to perform military functions in a wartime environment, including fighting, support or service missions, and command, control and communications functions. The decrement in performance--both temporary and permanent--should be predicted as a function of time for periods:

(1) Immediately following exposure.

(2) Delayed in onset.

b. Determine the levels of radiation exposure which result in radiation sickness requiring hospitalization of 10%, 25%, and 50% of a unit within a few weeks of exposure.

c. Determine the Relative Biological Effectiveness (RBE) of nuclear radiation exposures consisting of either:

(1) Entirely neutron radiation with:

(a) An approximate fission spectrum.

(b) An energy of 14 MeV.

(2) Combination of mixed neutrons and gamma radiation typical of weapon detonation environments.

The RBE should be measured in terms of causing a performance decrement sufficient to result in ineffectiveness for accomplishing military tasks such as listed in 1.a. above.

d. Determine effective means of preventing, reducing, or reversing the performance decrement caused by ionizing radiation (physical, biochemical, behavioral, psychological, etc.).

e. Determine the recovery from ionizing radiation injury as a function of time, dose, dose-rate, and pattern in which radiation was received.

f. Determine biological indicators, amenable for field implementation, that correlate the magnitude of radiation exposure over sublethal to lethal ranges.

g. Evaluate the reliability of extrapolating controlled laboratory studies in animal model systems to expected effects in man, and determine the best laboratory models.

h. Determine the probability of sickness requiring hospitalization and prolonged care of noncombatants for ionizing radiation doses of 10-250 rads, such as might occur through collateral damage in theater nuclear warfare. Furthermore, contribute to present knowledge concerning the additional lethal burdens over remaining lifetimes resulting from the above radiation exposures. Consideration of age, health status, and complications added by other nuclear weapon effects such as thermal radiation or blast should be included.

2. About 80% of AFRRI's resources should be devoted to the above tasks, all of which fall under AFRRI's primary

mission of research in the effects of ionizing radiation resulting from nuclear detonations. At this time, AFRRI's secondary mission of research in the biological aspects of other nuclear weapon effects (blast, thermal, etc.) are of lower priority. About 20% of AFRRI's resources may be devoted to research under your direction on broad radiobiological subjects of importance to military medicine.

3. Please prepare a plan for modifying your FY80 research program--to the degree feasible--to focus more directly upon the research objectives set forth above. This plan should be presented for review and approval to the Deputy Director, Science and Technology, (DDST) by 1 October 1979. Additionally, by 1 November 1979 please prepare for DDST's review and approval a detailed five-year research program for FY81-85 in accordance with these objectives.

R. R. MONROE
Vice Admiral, U. S. Navy
Director

PROPOSED PLAN FOR IDENTIFYING MILITARY REQUIREMENTS AND PREPARING A REQUIREMENTS DOCUMENT

1. The Requirement Document should not be an in-house document.

2. Time is of the essence. The requirements should be identified and a five-year plan completed prior to 1 January 1980 in order to be able to affect the 1981 program.

3. To develop an adequate plan, inputs or comments should be received from many sources. These include: the services medical departments, operational portions of each service, Defense Nuclear Agency, Joint Chiefs of Staff, Joint Commands, civilian agencies, researchers in the field, etc. To assemble representatives from these varied sources at one time in one place for long enough to thoroughly develop a Requirements Document is almost impossible and would require at least several months in advance to meet everyone's schedule.

4. Another alternate method would be to request inputs and ideas by mail from the various sources. This may or may not result in significant inputs. Once the inputs have been received, they must be synthesized, evaluated, and incorporated as a single document. Presently, there is no available personnel within AFRRI to spend the time and effort on contacting all the sources and coordinating their inputs.

5. Various options have been explored and discussed with DDST. It appears that the most reasonable and effective method to meet the required time frame would be:

a. Contract out the development of a Requirements Document and Five-year Plan.

(1) The contractor can visit necessary agencies, researchers, etc., obtain their ideas, comments and synthesize into a written document.

(2) Meet with various in-house scientists and university scientists to develop broad research goals to meet identified requirements. Draft a Five-year Plan.

b. Appoint a permanent Scientific Advisory Committee. Have SAC review draft the Five-year Plan, and revise as necessary.

c. Following review and revision by SAC forward to DNA, DoD, and BoG for approval.

PROPOSED FUTURE DIRECTION OF AFRRI

(as seen by the Directorate)

Without debating the merits or the lack of expertise of the Defense Audit Service (DAS) and Peer Review reports, it is evident that it is time for complete review, assessment and a redefinition of the mission of AFRRI.

A five-year plan must be developed which will provide for an integrated approach to the solution of military relevant problems within the purview of the redefined mission of AFRRI.

In developing a five-year plan the following steps must be taken as soon as possible.

1. Management decisions on the Peer Review Committee recommendations.

2. Immediate effort to determine service and DoD requirements in radiobiology.

3. Establishment of review procedure for requirements for direction of the research programs.

4. Development of specific research plans to meet identified requirements.

5. Identify present research that will not meet the objectives of the approved five-year program and plan for orderly phase out.

While it is not definitely known what specific areas of radiobiology must be addressed for the future, the research efforts at AFRRI should include:

a. Biological effects of neutrons and identification of neutron RBEs, since there is early evidence that several factors may influence the assignment of an RBE and in fact it may not be a single number.

b. The effects of lower doses and long-term effects of radiation must be considered and a sound research program addressing this area developed.

c. The specific area of cytogenetics should be developed within AFRRI to adequately evaluate low-dose, long-term effects.

d. Efforts should be started to study cellular damage and repair mechanisms.

e. Programs in biophysical modeling of radiation damage and repair should be given serious consideration.

f. A systemic program should be developed to start with cellular models and expand to the evaluation of system responses to radiation.

g. Programs directed toward prevention of injury or increased resistance to radiation should be considered.

h. Studies should continue to identify performance decrements and possible methods to prevent such decrements.

i. Studies should be directed toward the development and evaluation of practical therapeutic approaches that can be utilized in combat zones under emergency conditions.

In revising the mission, AFRRI should remain as a radiobiological research institute. The term radiobiology should be defined in its broad context to cover the entire electromagnetic spectrum since many of the problems and techniques are similar. Since AFRRI has expertise that can be of assistance and value in solving militarily relevant problems, allowance should be made to conduct research outside the specific area of radiobiology. This research should be done at the request of a service of DoD, providing AFRRI has the available capabilities without impairing their primary mission.

The Defense Nuclear Agency is solely concerned with nuclear weapons effects, which, from a biological point of view, consist of radiation, thermal, and blast injuries. AFRRI should be limited to studying the radiation effects since it does not have the facilities or expertise in the other areas. Expertise in thermal and

blast injuries is available from other military or contractural sources.

In 1972 DNA/DDST, in a letter to the Executive Office of the President, stated that "research in the field of biological effects of electromagnetic radiation is an important part of the Defense Nuclear Agency's mission." The entire EMR area is of critical importance to the DoD with an impact across the entire spectrum of DoD activities. Presently, AFRRI has expertise that can provide significant assistance to the DoD effort in this area.

In some cases, AFRRI has specific capabilities that can be of immediate assistance to an individual service in solving a particular military problem. As a DoD activity, AFRRI should provide this assistance providing it does not function as a decrement to its main mission.

BRAIN TRAUMA PROGRAM

This project has been very controversial ever since it was started at AFRRI, several years ago. While it was discussed at the last meeting, the issue was not completely resolved.

To present both sides of the issue - Enclosure 1 presents the position prepared by the investigator for the last BOG meeting, Enclosure 2 presents the present analysis by the Directorate.

Summary

Despite the various points of view, the major dominant fact is the lack of primates available for this program now or within the next three to five years. Unless otherwise directed, it is planned to terminate this project effective 1 October 1979; and, direct that the analysis of the data collected to date be completed and a final report written. The alternative is to continue this project by terminating a primate radiation program and utilizing these primates for that study.

2 Enclosures
as stated

HISTORY:

THE HEAD INJURY RESEARCH PROGRAM AT AFRRI WAS UNDERTAKEN BEGINNING IN 1972. AT THAT TIME A SLED SUITABLE FOR ANIMAL EXPERIMENTS AND BUILT AT WALTER REED ARMY MEDICAL RESEARCH CENTER WAS TRANSFERRED TO AFRRI TO PERFORM HIGH-SPEED ANGIOGRAPHY DURING IMPACT EXPERIMENTS. THIS ALLOWED THE UNION OF AFRRI'S RADIOLOGICAL AND NEUROPHYSIOLOGIC EXPERTISE WITH THE USE OF A HEAD INJURY IMPACT MODEL.

AT THE SAME TIME THE NATIONAL INSTITUTE OF NEUROLOGICAL DISEASE AND STROKE (NOW THE NATIONAL INSTITUTE OF NEUROLOGICAL, COMMUNICATIVE DISEASE AND STROKE, NINCDS) HAD A NEED FOR HIGHLY SPECIALIZED LABORATORY SPACE FOR THEIR HEAD INJURY RESEARCH PROGRAM WHICH WAS ORGANIZED IN COOPERATION WITH THE DEPARTMENT OF TRANSPORTATION. REALIZING THE IMPORTANCE OF THIS RESEARCH TO THE DEPARTMENT OF DEFENSE, CAPTAIN VARON INVITED DR. OMMAYA OF THE NATIONAL INSTITUTES OF HEALTH TO USE AFRRI'S FACILITIES AND TO ACT AS A CONSULTING NEUROSURGEON.

LATER IN 1974 THE TWO PREVIOUSLY INDEPENDENT PROGRAMS WERE COMBINED AND CURRENTLY COMPRISE A MAJOR RESEARCH EFFORT OF THE NEUROLOGICAL SCIENCES DIVISION OF THE NEUROBIOLOGY DEPARTMENT AT AFRRI. SINCE THAT TIME WE

HAVE CONTINUED TO ENJOY AN EXCELLENT COOPERATIVE RELATIONSHIP WITH NINCDS AND DOT. THESE TWO AGENCIES IN COOPERATION WITH THE DEFENSE NUCLEAR AGENCY ARE CONTINUING TO SPONSOR AND SUPPORT OUR ONGOING RESEARCH.

CURRENT RESEARCH EFFORTS:

AT PRESENT THERE ARE FOUR SEPARATE BUT ASSOCIATED NEURAL TRAUMATOLOGY RESEARCH PROGRAMS BEING CONDUCTED AT AFRRI. THE FIRST OF THESE PROGR IS DIRECTED TOWARD DETERMINING THE BIOMECHANICS ASSOCIATED WITH TRAU- MATIC UNCONSCIOUSNESS. THE SECOND APPLIES METABOLIC INVESTIGATIONS T THE HEAD INJURY MODEL DEVELOPED IN THE FIRST. THE THIRD USES THE SAM MODEL WITH THE AIM OF DETERMINING THE TIME BASE AND MECHANISM OF BLOO BRAIN BARRIER DISRUPTION WHICH RESULTS IN SECONDARY INJURY. FINALLY THE FOURTH STUDY IS AN INVESTIGATION OF ALTERATION OF PHYSIOLOGIC RESPONSIVENESS OF NEURAL TISSUES IN ISOLATION SUBJECTED TO MECHANICAL TRAUMA.

BEFORE ENTERING THESE PROGRAMS IN GREATER DETAIL, I WOULD LIKE TO BRIEFLY DISCUSS THE IMPORTANCE OF THE HEAD INJURY MODEL WHICH WE ARE ATTEMPTING TO DEVELOP. OUR CURRENT UNDERSTANDING OF HEAD INJURY MECHANISMS HAS BEEN CONSIDERABLY AIDED BY THE AVAILABILITY OF HEAD INJURY MODELS OF INCREASINGLY RELIABLE NATURE. WE HAVE BEEN IMPRESSE HOWEVER, WITH THE UNPREDICTABLE BIOMECHANICAL INPUT TO A HEAD INJURY MODEL WHICH IS BASED ON IMPACT AGAINST THE UNRESTRAINED HEAD. THIS HAS RESULTED IN WIDE VARIABILITY IN BIOLOGIC RESPONSE FOR A GIVEN

MECHANICAL INPUT (A RESULT CLEARLY SEEN IN OUR PREVIOUS SLED-IMPACT EXPERIMENTS). FOR THIS REASON FOR THE PAST THREE YEARS WE HAVE BEEN DEVELOPING A MODEL FOR HEAD INJURY IN SUB-HUMAN PRIMATES WHERE INJURY IS PRODUCED BY INERTIAL LOADING WITHOUT DIRECT IMPACT. THIS MODEL OF VIOLENT HEAD SHAKING ALLOWS A MUCH HIGHER LEVEL OF MECHANICAL STRESS TO BE APPLIED IN A GRADED AND REPRODUCIBLE MANNER TO THE BRAIN WITHOUT THE COMPLICATING EFFECTS OF SKULL DEFORMATION OR FRACTURE. WE NOW HAVE THE POTENTIAL TO PRODUCE MOST OF THE CLINIC PHENOMENA OF HEAD INJURY IN A SUB-HUMAN PRIMATE IN A PREDICTABLE FASHION. IN ADDITION WE HAVE DEVELOPED A SYSTEM FOR SERIAL MEASUREMENT OF THE PHYSIOLOGIC STATUS OF THE ANIMAL ALLOWING US TO QUANTITAT TO SOME DEGREE, THE LEVEL OF BIOLOGIC RESPONSE TO A GIVEN MECHANICAL INPUT. USING THESE TECHNIQUES WE ARE IN THE PROCESS OF TESTING A HYPOTHESIS TO EXPLAIN CEREBRAL CONCUSSION AND THE VARIOUS GRADES OF TRAUMATIC DISTURBANCE OF CONSCIOUSNESS (1).

OUR APPROACH IN ALL OF THE CURRENT PROJECTS HAS BEEN TO CONSIDER THE BIOMECHANICAL PARAMETERS TO BE OF PRIMARY IMPORTANCE. WE CLASSIFY MECHANICAL TRAUMA AS STATIC OR PSEUDO-STATIC IF THE TIME BASE IS IN T ORDER OF SECONDS OR LONGER. THIS TYPE OF TRAUMA, USUALLY A CRUSHING INJURY, RARELY PRODUCES CONCUSSION BUT RATHER RESULTS IN SKULL FRACTU AND LOCAL INJURY SUCH AS BRAIN LACERATION. ON THE OTHER HAND WE CONS A MECHANICAL INPUT TO BE DYNAMIC IF THE TIME BASE IS IN THE ORDER OF MILLISECONDS. DYNAMIC TRAUMA MAY BE THEN DIVIDED INTO THAT PRODUCED BY IMPACT AND THAT PRODUCED BY IMPULSE OR INERTIAL LOADING. OUR RESEA

IS CONFINED TO THE LATTER FORM OF DYNAMIC TRAUMA. IN ADDITION, THE MODEL WE HAVE DEVELOPED GREATLY SIMPLIFIES THE ANALYSIS OF DYNAMIC TRAUMA TO AID OUR UNDERSTANDING OF THE MECHANISMS INVOLVED BY LIMITING ACCELERATION TO ONE PLANE.

NEVERTHELESS, FOR ANY FORM OF MECHANICAL TRAUMA OF SUFFICIENT STRENGTH, THERE IS A BIOLOGIC RESPONSE. THE BASIC RESPONSE IS THAT OF TRAUMATIC DYSFUNCTION. THIS MAY BE CONFUSION OR AMNESIA IN MILD CASES OR IN MORE SEVERE INJURY MAY RESULT IN UNCONSCIOUSNESS OR PARALYSIS IN TERMS OF SPINAL CORD INJURY. THERE ARE OTHER RESPONSES WHICH WE CLASSIFY AS EPIPHENOMENA INCLUDING CONTUSION, FRACTURE, INTRACRANIAL HEMORRHAGE, AND BRAIN (OR CORD) SWELLING.

CURRENTLY WE ARE INVESTIGATING ALL OF THESE BIOLOGICAL RESPONSES TO TRAUMA (WITH THE EXCEPTION OF SKULL FRACTURE) AS THEY RELATE TO INERTIAL LOADING OF THE BRAIN. THE QUESTIONS WE ARE ASKING INCLUDE THE FOLLOWING: 1. WHAT MECHANISM IS INVOLVED IN MEDIATING THE BIOLOGIC RESPONSE? THAT IS IN WHAT MANNER IS THE BRAIN STRUCTURALLY OR FUNCTIONALLY AFFECTED BY TRAUMA? 2. WHAT IS THE THRESHOLD FOR MECHANICAL INPUT TO PRODUCE A GIVEN BIOLOGICAL RESPONSE? 3. HOW MAY DATA DERIVED FROM ANIMAL EXPERIMENTS WITH THE SMALLER MASS OF THE HEAD AND BRAIN BE APPLIED TO THE EVALUATION OF POTENTIAL INJURIES IN MAN? 4. IN TERMS OF ANTHROPOMORPHIC SUBSTITUTES FOR MAN IN SIMULATED INJURY EXPERIMENTS, WHAT TYPE OF MATERIALS MAY BE USED TO MIMIC THE RESPONSE OF HUMAN TISSUE?

THE NEXT DIAGRAM SHOWS THE BASIC STEPS IN THE PRODUCTION OF A BRAIN INJURY. THERE IS FIRST A MECHANICAL INPUT RESULTING IN EITHER SKULL DEFORMATION OR INERTIAL LOADING OR BOTH. THIS THEN PRODUCES A VOLUMETRIC DISTORTION OF THE VISCOELASTIC SUBSTANCE OF THE BRAIN. THE DISTORTION STRESSES THE NEURAL ELEMENTS PRODUCING STRAINS THAT RESULT IN BRAIN INJURY.

TO EXPLAIN THE RELATIONSHIP OF THIS PHYSICAL MECHANISM TO WHAT IS USUALLY OBSERVED CLINICALLY, THE FOLLOWING HYPOTHESIS HAS BEEN PROPOSED. CEREBRAL CONCUSSION IS A GRADED SET OF CLINICAL SYNDROMES FOLLOWING HEAD INJURY WHEREIN INCREASING SEVERITY OF DISTRUBANCE IN LEVEL AND CONTENT OF CONSCIOUSNESS IS CAUSED BY MECHANICALLY INDUCED STRAINS AFFECTING THE BRAIN IN A CENTRIPETAL SEQUENCE OF DISRUPTIVE EFFECTS ON FUNCTION AND STRUCTURE. THE EFFECTS OF THIS SEQUENCE ALWAYS BEGIN AT THE SURFACES OF THE BRAIN IN THE MILD CASES (WITH CORTICAL AND SUBCORTICAL INJURY) AND EXTEND INWARD TO AFFECT THE DIENCEPHALIC-MESENCEPHALIC CORE AT THE MOST SEVERE LEVELS OF CNS TRAUMA.

WITH THIS HYPOTHESIS IN MIND WE MAY NOW MAKE SEVERAL PREDICTIONS. FIRST WE SHOULD FIND THAT WHEN HEAD INJURY PRODUCES TRAUMATIC UNCONSCIOUSNESS, THE EXTENT OF SIMULTANEOUS PRIMARY INJURY TO THE BRAIN IS MORE SEVERE IN THE CORTICAL AND SUB-CORTICAL STRUCTURES (ESPECIALLY THE VULNERABLE AREAS SUCH AS FRONTAL AND TEMPORAL POLES) THAN IN THE ROSTRAL BRAIN STEM. SECONDLY, BECAUSE THE MESENCEPHALON IS THE LAST PART OF THE BRAIN TO BE AFFECTED BY TRAUMA, PRIMARY DAMAGE TO THE ROSTRAL BRAIN STEM WILL NOT OCCUR IN ISOLATION IN THE VAST MAJORITY OF HEAD INJURIES WHICH ARE

ASSOCIATED WITH ACCELERATION-DECELERATION TRAUMA. FINALLY CONFUSION AND AMNESIA CAN OCCUR WITHOUT LOSS OF CONSCIOUSNESS BUT THE REVERSE CANNOT OCCUR.

THE BASIS FOR THIS HYPOTHESIS AND ITS PREDICTIONS WAS FIRST NOTED BY HOLBOURN IN 1943 WHEN HE SUGGESTED THE IMPORTANCE OF SHEARING STRAINS IN ROTATIONAL ACCELERATION OF THE BRAIN (2). MORE RECENT WORK BY OMMAYA AND GENARELLI INDICATES THAT, FOR A GIVEN FORCE INPUT, THE TRANSLATIONAL MODE PRODUCES ONLY FOCAL LESIONS WITHOUT CONCUSSION, WHILE ANGULAR ACCELERATION PRODUCES DIFFUSE LESIONS AND UNCONSCIOUSNESS (1).

AT PRESENT WE ARE TESTING THIS HYPOTHESIS USING MACACA FASICULARIS AND A DEVICE WHICH WE HAVE NAMED THE HAD-III. THIS IS ESSENTIALLY A SIX INCH BENDIX HYGE SHOCK TESTER WHICH WE HAVE MOUNTED HORIZONTALLY ON AN 80 TON BLOCK OF CONCRETE AND STEEL WHICH IS MOVABLE ON TRACKS SET INTO THE FLOOR. THE BENDIX UNIT HAS BEEN MODIFIED TO PRODUCE A TRUE HALF SINE ACCELERATION AND DECELERATION PULSE OVER A 5 MILLISECOND PERIOD PRODUCING UP TO 2,000 G'S IN OUR EXPERIMENTS. THE FORCES INVOLVED ARE REPRODUCIBLE AND ARE DETERMINED BY THE PRESSURES APPLIED TO THE TWO CHAMBERS OF THE DEVICE. ATTACHED TO THE END OF THE UNIT IS A STEEL LINKAGE ASSEMBLY WHICH SUPPORTS A HELMET. THE ANIMAL'S HEAD IS POSITIONED WITHIN THE HELMET REPRODUCIBLY USING EAR PINS AND A VACUUM-FORMED POLYCARBONATE FACE MASK. ONCE POSITIONED A MIXTURE OF DENTAL STONE AND PLASTER OF PARIS IS USED TO FILL THE HELMET. IN THIS MANNER THE ANIMAL'S HEAD AND THE HELMET ACT AS A RIGID BODY AND IMPACT IS AVOIDED. THE HELMET IS THEN SECURED TO THE LINKAGE IN SUCH A MANNER

THAT ANGULAR ACCELERATION IS ASSURED. ADJUSTMENTS ARE USED TO ALTER THE CENTER OF ROTATION AND THE PLANE OF ROTATION.

PRIOR TO ACCELERATION A NUMBER OF PHYSIOLOGIC PARAMETERS ARE MEASURED INCLUDING THE ECG, SYSTEMIC ARTERIAL PRESSURE INTRACRANIAL PRESSURE, RESPIRATIONS, PULSE, AND VISUAL AND SOMATOSENSORY CORTICAL EVOKED RESPONSES ARE OBTAINED SERIALLY. IN ADDITION THE TEST SERIES IS RECORDED ON VIDEOTAPE SO THAT CLINICAL CONDITIONS MAY BE CONTINUOUSLY MONITORED. AT ACCELERATION TWO HIGH-SPEED MOTION PICTURE CAMERAS RECORD THE EVENT AS DO ACCELEROMETERS ON THE HELMET. FOLLOWING THE INJURY THE SERIAL RECORDING OF PHYSIOLOGIC DATA IS REPEATED FOR AN APPROPRIATE TIME. PATHOLOGICALLY THE ANIMAL IS EVALUATED USING VASCULA MARKERS. AT 12 TO 24 HOURS A VITAL PERFUSION TECHNIQUE IS USED AND SUBSEQUENTLY THE BRAIN IS SECTIONED AT TWO MILLIMETER INTERVALS FOR GROSS INSPECTION AS WELL AS LIGHT AND ELECTRON MICROSCOPIC EXAMINATION. LESIONS ARE PHOTOGRAPHED AGAINST GRID AND ARE REPRODUCED ON AN X,Y, AND Z AXIS USING A COMPUTER SYSTEM WITH VIDEO DISPLAY AND LIGHT PEN. THUS A THREE DIMENSIONAL IMAGE OF THE INJURY IS STORED BY THE COMPUTER.

THE DATA THUS OBTAINED IS THEN REDUCED AND NON-LINEAR MULTIVARIANT ANALYSIS IS USED FOR CORRELATION. ALSO THE DATA IS PROVIDED TO THE NAVAL CIVIL ENGINEERING LABORATORY, PORT HUENEME, CALIFORNIA, WHERE IT IS USED IN THE VALIDATION AND MODIFICATION OF A FINITE ELEMENT MATHEMATICAL MODEL OF THE BRAIN AND SKULL.

A SECOND PART OF THIS PROJECT INVOLVES THE USE OF A LARGE HYDRAULIC VIBRATOR AND A SIMILAR HELMET AND LINKAGE ASSEMBLY. IN THIS CASE, IODENSE, RADIO-OPAQUE PELLETS ARE PLACED WITHIN THE SUBSTANCE OF THE BRAIN AND A SUB-MINIATURE, ISODENSE ACCELERATOR IS IMPLANTED OVER THE CORPUS CALLOSUM. PAPER-THIN INTRACRANIAL PRESSURE TRANSDUCERS ARE ALSO PLACED WITHIN THE SKULL. THE HEAD IS THEN PLACED IN THE HELMET AND SECURED AS PREVIOUSLY DESCRIBED. THE HYDRAULIC UNIT IS ACTIVATED WITH A CONTROLLED FREQUENCY SINE WAVE AND, WHEN A STEADY STATE OF OSCILLATION IS REACHED, A HIGH-SPEED X-RAY UNIT IS USED TO RECORD THE PELLET MOTION WHILE THE PHASE OUTPUT OF A SKULL-MOUNTED ACCELEROMETER IS COMPARED WITH THAT OF THE INTRACRANIAL ACCELEROMETER.

THIS DATA IS USED IN THE DETERMINATION OF BRAIN RESONANCE IN THE LOW FREQUENCY RANGE AND CONTRIBUTES TO THE VALIDATION OF THE MATHEMATICAL MODEL.

TO COMPLEMENT THIS PROJECT, THE AFRRI LINEAR ACCELERATOR WILL BE USED TO PRODUCE RADIOACTIVE $^{15}O_2$, AN ISOTOPE WITH AN APPROXIMATE TWO MINUTE HALF-LIFE. THE ISOTOPE WILL THEN BE USED TO LABEL BLOOD WHICH IN TURN ACTS AS A TRACER IN THE DETERMINATION OF REGIONAL CEREBRAL BLOOD FLOW, REGIONAL CEREBRAL METABOLISM OF OXYGEN, AND REGIONAL CEREBRAL BLOOD VOLUME (3). THIS INFORMATION WILL THEN BE CORRELATED WITH DATA OBTAINED AS IN THE PREVIOUSLY DESCRIBED HAD-III PROJECT. IN THIS WAY WE HOPE TO OBTAIN INSIGHT INTO THE METABOLIC CHANGES WHICH MAY ACCOMPANY HEAD INJURY.

THE THIRD PROJECT INVOLVING BRAIN EDEMA ADDS THE FACET OF LONGER TERM STUDY AFTER INJURY (FROM 24 TO 72 HOURS) AS WELL AS A BIOCHEMICAL STUDY OF CHANGES IN THE BLOOD-BRAIN BARRIER. THIS WILL ALLOW US TO CORRELATE CHANGES IN THE BARRIER WITH OTHER MORPHOLOGIC INDICES OF STRUCTURAL DAMAGE AND REPRESENTS AN APPROACH TO THE UNDERSTANDING AND PREVENTION OF SOME OF THE SECONDARY LESIONS OF HEAD INJURY.

THE FOURTH PROJECT INVOLVING MECHANICAL STRESSING OF ISOLATED NEURAL TISSUES, WE HAVE CHOSEN TO CALL MICROTRAUMA. IN THIS EXPERIMENTAL SERIES, A VARIETY OF MYELINATED AND UNMYELINATED PERIPHERAL NERVES AS WELL AS SINGLE NEURONES WILL BE STUDIED PHYSIOLOGICALLY BEGORE AND AFTER SHEARING STRAINS ARE APPLIED. A DETERMINATION OF THE THRESHOLDS FOR BOTH REVERSIBLE AND IRREVERSIBLE LOSS OF FUNCTION WILL BE DETERMINED.

THESE LEVELS OF SHEARING STRAIN DETERMINED ON AN ALMOST MICROSCOPIC BASIS WILL THEN BE COMPARED WITH THOSE THAT WE CAN ESTIMATE TO HAVE OCCURRED ALONG THE AXIS OF STRAIN IN WHOLE BRAIN INERTIAL LOADING IN THE FIRST PROJECT. PRELIMINARY DATA AT THIS TIME SUGGESTS THAT THERE WILL BE A GOOD CORRELATION BETWEEN FORCES THAT PRODUCE SIMILAR LEVELS OF DYSFUNCTION IN THE TWO MODELS (4). THIS INFORMATION SHOULD HELP TO INCREASE OUR UNDERSTANDING OF THE MECHANISMS OF HEAD INJURY.

IN SUMMARY:

IN TERMS OF THE FIRST PROJECT, THE BIODYNAMICS OF TRAUMATIC UNCONSCIOUSNESS, WE HAVE THREE OVERALL GOALS. FIRST IS THE DEVELOPMENT OF A REPRODUCIBLE MODEL, WHICH HAS NOW BEEN ACCOMPLISHED, BUT HAS NOT YET BEEN COMPLETELY

PROVEN. NEXT, IN COMBINATION WITH THE INFORMATION OBTAINED FROM THE REMAINING THREE PROJECTS, WE HOPE TO BE BETTER ABLE TO RATIONALLY DEVELOP PROTECTIVE PRINCIPLES OR MEASURES TO PREVENT SERIOUS HEAD INJURY. FINALLY, USING THE MODEL AND INFORMATION FROM THESE STUDIES, WE HOPE TO DEVISE A RATIONAL THERAPEUTIC BASIS FOR THE TREATMENT OF HEAD INJURED PATIENTS, THEREBY REDUCING THE MORBIDITY AND MORTALITY AFTER INJURY.

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Slide 3.

RELEVANCE OF THE STUDY

1. 100,000 deaths per year from accidents

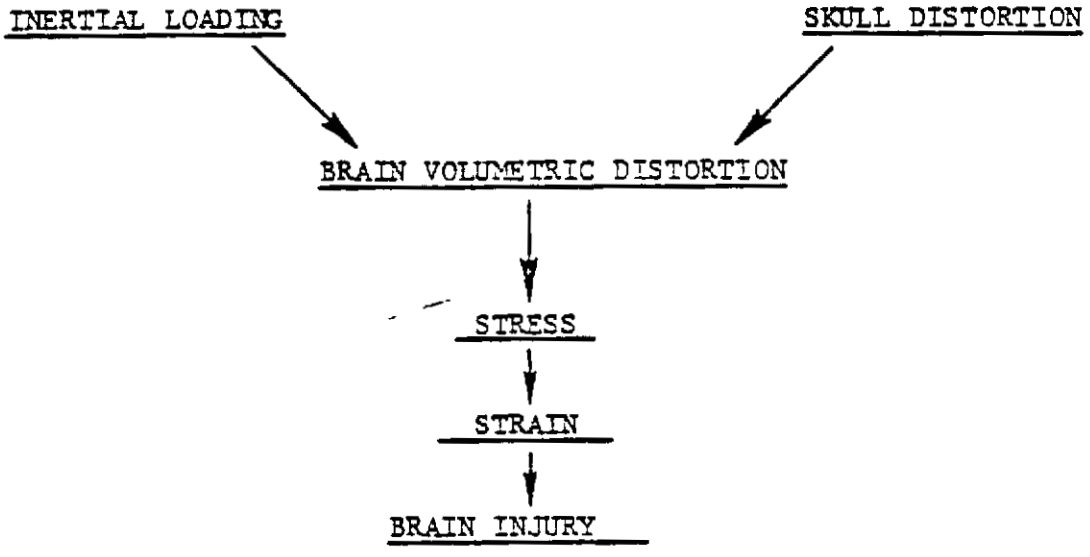
2. 50,000,000 accidents per year with unknown morbidity

3. 50,000 deaths per year from highway accidents with 70 percent of these due to head injury

4. For DoD: 6 deaths from accident for each combat death

Slide 7

PHYSICAL MECHANISM



AFRRI DIRECTORATE POSITION

This research project is primarily aimed at exploring pathologic mechanisms and responses related to inertial trauma. When evaluating the import of inertial trauma in nuclear warfare as a synergistic effect on sub-lethal whole body radiation (combined effect), it is exceedingly difficult to postulate any area where this combination would occur. The significant biodynamic blast radius in both fission and ER weapons is associated with such high radiation levels that the "combined effect" is apparently only incidental information.

Both the Air Force and Navy have major laboratories dedicated to biodynamics research. The Army's Aviation Medical Research Laboratory at Ft. Rucker also conducts biodynamic research.

In reviewing the objectives of the AFRRI research concerning pathologic mechanisms and responses to inertial trauma, a great deal of information is already available as a result of the Air Force and Navy research programs. A large portion of this program is a duplication of previous and present programs being conducted by the individual services.

Presently, the expertise and manpower resources to conduct this program do not reside within AFRRI. With current billet limitations it is not anticipated that personnel and the required billets will be available in the foreseeable future.

It is considered poor management practice to support a significant and expensive program where management has absolutely no control over the scientific personnel involved.

It is axiomatic that a biologic system can respond to trauma in only a specific, limited number of pathways. In studying these "final common pathways" it would appear relevant to study these with the incident trauma directly related to the overall research effort of this Institution; i.e., radiation and not develop a model to simulate another model.

Recent discussions with Dr. Ommaya of the National Institutes of Health, concerning this project, provided the following information.

a. Dr. Ommaya was acting as a consultant at the invitation of Dr. Varon, previous Director of AFRRI.

b. Dr. Ommaya was not happy with the progress or direction of the program and felt his advise was being ignored, for this reason he withdrew his support of the program and is no longer involved in the project.

Limitations imposed by Department of State and Department of Defense on utilization of first generation monkeys for radiation research leaves this program without an animal model. Second generation monkeys will not be in adequate supply for at least three to five years.

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