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NATIONAL LONG-TERM PRIMATE RADIATION PROGRAM

405117

Proposal: The Committee on Radiation studies proposes the establishment of a research laboratory for the <sup>study</sup> <sup>investigation</sup> of long-term effects of irradiation exposure through the observation and study of primates, combined with a study of the aging process. *investigation of long-term effects of irradiation exposure, especially the primate, with the facilities being available.*

Justification: Tremendous efforts have been expended in studying the early effects of radiation damage in animals and man, but relatively little has been accomplished in studying the long-term effects. This problem has been investigated by a Subcommittee and presented on several occasions to this Committee for thorough consideration. The views of numerous scientists throughout the country interested in radiation effects and problems of aging have been considered. The Gerontological Society is very much in favor of the proposed program and numerous universities have expressed their desire to operate such an institute. The general opinion is quite unanimous that a research laboratory should be established for studying long-term effects of irradiation and problems of aging. Because of the many unsolved problems of radiation damage, the founding of this laboratory should not be delayed. Acquisition of knowledge of late effects of radiation may aid in the prevention of their occurrence or their diminution. Knowledge of the aging process may enable lessening of the accompanying ill effects. The use of various types of radiation for diagnosis and therapy has expanded tremendously in recent years. With the availability of substitutes for radium sources through the Atomic Energy Commission programs, the future use of radiation in medical programs will steadily increase. Hence the need for knowledge of long-term effects of irradiation becomes more urgent. Before and during World War II, groups of rodents were studied for long-term effects of gamma rays, fast neutrons and slow neutrons. However, these

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studies are incomplete, and were done on small numbers of animals at a time when neutron dosimetry was poor and neutron flux heavily contaminated with gamma rays. The studies now being made of the Japanese population subjected to atomic bombings will be fragmentary, and in spite of the great effort, the results are preliminary, at best, to serve as a guide to studies of radiation problems and means of counteracting their ill effects. The dosages were difficult to estimate and the population has been widely scattered. The recent long-term studies on the late effects of an atomic explosion on mice (not yet published) yielded results which indicate the need for further studies on larger animals to more closely approximate effects on man.

Although the late effects of irradiation are qualitatively the same for X rays, gamma rays, fast and slow neutrons, special problems with neutrons should be investigated in primates. Longevity is reduced in proportion with the dose, but the reasons or mechanism for this accelerated aging are unknown. Certain tumors have marked increases in incidence in mice exposed to ionizing radiation, but few data are available on animals higher than rodents. Many tumors seen in rodents are unlike those found in man. The types of tumors observed in different species vary, and there is no information in this respect on primates, the species closest to man. Extrapolation from mouse to man is not permissible; the information most applicable to man is best obtained from primates.

The problem of radiation damage appears to be closely linked with that of aging. The few studies of fundamental mechanisms of aging have been done with rodents on the effects of nutrition on life span with some additional studies in Baltimore under USPH. Gerontologists have pointed out the need of a study on the aging process in sub-human primates, but the magnitude

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of the undertaking prevented establishing a primate colony for that sole purpose.

More background information on other species of animals is certainly desirable, but it is believed that additional data from lower animals would not help substantially in solving many basic problems. Experiments with dogs would be just as costly, in time and money, as with monkeys, and would not take the place of experiments with monkeys.

The widespread use of radiation today both for diagnosis and treatment, the potential hazard of atomic explosion and radiological warfare, and exposure hazards from reactors which will utilize nuclear fission to yield energy make it imperative that no time should be lost in initiating studies in primates. An incidental material yielded by these studies will include cancers of diverse types which can be made available to interested investigators. Some observations on causes and factors of cancer development can be made on these animals without interference to other basic research.

Knowledge thus gained may aid in the establishment of preventive procedures.

The magnitude of the project: Estimates of the desirable number of primates to be used vary; a reasonable goal appears to be about 600, but it would not be necessary to start with that many. The Macacus species is favored, imported from India, prepubertal, with the age estimated from the teeth. Six hundred primates ( $\frac{1}{2}$  males,  $\frac{1}{2}$  females, including controls) should give enough for several dosage levels, and allow experiments of different types to be done on sub-groups with adequate controls. Facilities for a small number of anthropoid apes should be available.

Location of the project: The climate need not be considered as a factor in selecting the location of the project unless chimps are also considered.

The Macacus is not a tropical animal and if given adequate space will thrive

in almost any climate in the United States.

It is agreed that this laboratory is best established near to and in association with an existing good scientific center, a government laboratory such as one of the National Institutes of Health, or one of the Atomic Energy Commission laboratories. Universities are known to carry out long-term contracts efficiently, and there are some advantages of operating such a project through a university. The essential criteria are that: 1) a large active scientific community should be present including not only those working full time on the primate problem, but others representing varied basic disciplines and cooperating; 2) a good library; and 3) other basic common facilities. This project will require ample space, estimated at 30 acres; this would allow future expansion. Experiments will be started here at this proposed facility, but some primates on which grantees and/or other investigators have made a thorough study of early effects can be accepted by the permanent staff for studies on late effects. Currently the problem is faced by many grantees of what to do with the primates on which studies of the early effects have been concluded.

Observations to be made: All types of worthwhile observations, within reason, should be carried out. Psychological tests are as important as physiological tests. Biochemistry, endocrinology and pathology are equally important. Some animals will be sacrificed at definite intervals, others allowed to die, but all should be thoroughly studied postmortem.

Scientific staff: The scientific personnel requirements are as follows:

- A. A permanent staff consisting of a director who might serve also as one of the scientists, an experimental psychologist, pathologist, physicist, biochemist, endocrinologist and physiologist and perhaps others would carry out the basic scientific program.

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- B. Visiting scientists who would come for periods of a few weeks to carry out research can handle a large share of the work. In this way the program would be kept on a national level for the benefit of a great many interested scientists.
- C. A scientific advisory board appointed by the Surgeon General including representation of the interested U. S. Public Health Service National Institutes of Health, the Atomic Energy Commission and the various Defense Agencies would guide the research activities.

Duration of project: The life span of a primate is about 20 years, and without reasonable assurance of a 20-year duration the project should not be undertaken. However, important results may be expected from the first year on. Studies on early effects should be integrated with those on long-term effects.

Cost of the project: The initial cost of the project is in the laboratory building and animal quarters. No suitable facilities are known to be available at present, so this project would require largely new construction.

A preliminary estimate is as follows:

10 laboratories, 400 sq. ft. ea. at \$60 per sq. ft.	\$240,000
10 offices, 150 sq. ft. ea. at \$30 per sq. ft.	45,000
Corridors and services, 1000 sq. ft. at \$25 per sq. ft.	25,000
30 animal rooms with outdoor runs, 400 sq. ft. ea. inside at \$8,000 ea.	240,000
Initial equipment	<u>50,000</u>
	\$600,000

The annual cost would be as follows:

Scientific personnel:	senior, including the director and consisting a physiologist, biochemist, endocrinologist, pathologist, veterinarian, psychologist and social scientist, physicist	\$ 80,000
	Research assistants, 6-8 (Ph.D.'s & M.D.'s)	36,000
	Technicians, 6-8	24,000
	Librarian, 1	4,000
Office personnel:	administrative officer or business manager	5,000
	Secretary	3,700
	Typists, 3	8,700
Maintenance:		
	Engineer, 1	5,000
	6-8 others, e.g., carpenter, plumber, electrician, cleaners, etc.	30,000
Animal caretakers		12,500
Animals:	first acquisition and replacements (including several chimpanzees - present price: \$1,000 each)	20,000
Animal food:	\$100 per animal per year	60,000
Other supplies:	such as chemical reagents, laboratory glassware, cleaning supplies, etc.; scientific books and periodicals; office supplies; photographic supplies	25,000
Capital equipment:	laboratory equipment and apparatus; cages and accessories; photographic equipment, dish-washing equipment, kitchen equipment	44,000
Office and library furnishings and equipment		30,000
Contingencies:	building maintenance, etc.	50,000
Travel:	for research participants and consultants including the latter's fees	40,000
	Subtotal	\$463,000
	Overhead at 8%	37,040
	Total	\$500,040

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The cost estimates above are based on current experience in the operation of similar facilities of institutions working with primates. While detailed estimates by an architect-engineer would be required for actual construction, the estimates above are sufficiently accurate for budgetary purposes. The possibility that AEC and perhaps the Defense Agencies might underwrite the radiation program in whole or in part requires consideration.

Recommendations: The Committee on Radiation Studies strongly recommends that this program be initiated as soon as reasonably feasible. The Surgeon General, if approving this proposal, is requested to appoint a special committee to put this program into effect. The initial functions would include selecting the program director and the site, and acting in a general advisory capacity in getting the program started.

Selection of site: The site can be selected after acceptance of the plan. Responsible representatives of a few institutions known for their interest in related problems were contacted while information was gathered about this plan in general. Several institutions have expressed a desire to operate this laboratory, some offered land and some facilities. Unquestionably, there are many other institutions who would like to operate this laboratory and should be given a chance to bid for it. Those which have shown an interest are:

1. Univ. of Wisconsin
2. Univ. of Minnesota
3. Brookhaven Laboratories
4. Oak Ridge Laboratories
5. Washington Univ. (St. Louis)
6. Ohio Univ.
7. Univ. of Florida (Gainesville)
8. Univ. of Texas (Galveston)
9. Univ. of Miami (Florida)
10. Univ. of California (Berkeley)
11. Buffalo Univ.
12. Rocky Mt. Laboratories (Montana)