

BROOKHAVEN NATIONAL LABORATORY
ASSOCIATED UNIVERSITIES, INC.
UPTON, L. I., N. Y.

September 25, 1957

Dear Dr. *Chuck*,

I am anxious to formulate plans for studies to be carried out on the annual medical survey to be conducted on the Marshallese in March, 1958. It is anticipated that three weeks will be spent on Rongelap Island and several days on Majuro Island, in carrying out the examination. Complete history, physical and laboratory examinations of a basic nature will be carried out as in the past. However, there are special studies that should be considered and I would like to outline my thinking on the subject at this time and would appreciate your comments.

Keeping in mind the limited facilities and personnel with which the examination will be conducted as well as the language barrier difficulty, it would seem to me the priority for special studies should be based on the following considerations:

1. Those studies which have revealed positive findings in the past in regard to possible radiation effects should be pursued with greatest vigor. I refer to (a) the hematological effects, (b) growth and development studies in children, (c) beta lesions of the skin and (d) body burden of radioisotopes.
2. Studies based on known long term effects of radiation in human beings, particularly in the Japanese and animals. Such studies include effects on aging and longevity, incidence of degenerative diseases, malignancy (leukemia, etc.) fertility, cataracts, and genetic effects.
3. Studies of positive findings common to both exposed and unexposed Marshall-ese people which may have a direct influence on the future prognosis of the long term effects of radiation. Such findings include the tendency to anemia (low hematocrits), high incidence of parasitism, high total proteins and gamma globulin of the sera, high incidence of congenital defects. Of less priority would be studies of the homogeneity of the population, psychological studies, etc.

Further elaboration on the various studies in these different categories follows.

1. (a) Hematological. It is anticipated that three complete blood studies on each person including WBC, differential counts, platelet counts and hematocrits, will be conducted over the three week period as was done last year. In view of the fact that the lymphocyte and platelet mean counts have remained slightly below the mean counts of the unexposed groups it would be desirable to investigate the possibility of lowered reserve capacity of the hemopoetic tissues for these blood elements. For instance, it might be possible to test for lymphopoetic capacity by challenging with some lymphocytic stimulating substance (pertussis vaccine?), or platelet response by stimulating platelet production by some means. Possibly radioiron uptake studies might be of value in evaluation erythropoetic integrity. Do you have any suggestions along this line?

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(b) Growth and development studies in the children should be continued particularly in view of suggestive findings of some impairment in the exposed children. Such studies would include anthropometric measurements and x-ray of wrists and tibia for bone development.

(c) Studies of residual beta lesions of the skin will be continued. These will include gross observations with color photography and biopsy with histological study of selected cases.

The added burden of the small doses of radiation in the people necessary in doing bone x-ray and possible tracer rbe uptake studies is not considered to be much of an incremental hazard since the technique used would insure minimum dosages.

(d) Evaluation of body burdens of radioisotopes. It is planned that a whole body counter (steel room with 4 inch thick walls, floor and ceiling, equipped with crystal and 100 channel analyzer) will be installed on the LST to be used for the survey. Gamma spectroscopy will be carried out on exposed and non-exposed Rongelap people. In addition concerted effort will be made to obtain sufficient urine collections on individuals to be brought back for radiochemical analyses. It is hoped also that some correlation may be drawn between body burden (evaluated from gamma spectroscopy) and urinary excretion rates of isotopes (from radiochemical analysis of the urine). This study is of increased importance in view of the fact that the people have been moved back to their home island which is slightly contaminated.

2. In the second category, i.e. long term effects of radiation, the following fields of study should be considered.

(a) Premature aging and shortening of life span. Studies of longevity will in the long run give the most definite answer on the effects of radiation on aging, but such information will take years. In the meantime it would be desirable to evaluate premature aging by attempting to estimate the biological age of the individuals compared with their actual age. We are faced here with the difficulty that some of the ages, particularly of the older people are not precisely known (maybe off by several years). Even so, such studies should be attempted if possible. Studies to determine biological age are extremely difficult to plan since quantification of biological effects associated with aging are far from precise. I am not aware of any single biological end point that can be used to bracket an individual's age at all closely. Therefore, in arriving at an estimate of biological age I wonder if it would be possible to establish an overall "score" for various endpoints in an individual weighted according to relative importance. Weighted scores might be established for such characteristics of aging as: retinal and general arteriosclerosis, cataracts, arcus senilis, accommodation, skin elasticity, senile keratoses, greying of the hair, blood pressure, cardiac function, kidney function, degree of agility (or fragility), osteoarthritis, mental agility, reflexes etc. I plan to investigate the feasibility of this approach. Do you know of any specific tests for aging that might be considered? Consideration might be given to studies of hexosamine to collagen ratio of skin, ratio of ketosteroids to corticoids in the urine, vitamin B-12 levels as indices of age.

(b) Studies for leukemoid tendencies will be repeated. These include alkaline phosphatase determination on neutrophils (by Dr. Moloney) and basophile counts on 4000 white cells.

(c) Thyroid function. In view of the fact that the Rongelap people received a dose of about 300 rep to the thyroid gland (an estimated 175 r whole body gamma dose plus an estimated 100-150 rep to the thyroid from internally absorbed ¹³¹I) thyroid studies should be carried out. Several investigators have reported thyroid malignancy and leukemias in people who in infancy or childhood had received similar doses of radiation to the thyroid. We carried out total cholesterol determinations on the sera of the Marshallese this past year. No abnormally high cholesterols were found. However, on the next survey it might be desirable to do plasma bound iodine studies at least on those individuals, particularly children, with cholesterol levels in the higher ranges.

(d) Degenerative disease. Nephrosclerosis is said to be one of the diseases associated with radiation aging. Therefore tests for kidney function should be considered. On the past survey routine urinalysis was carried out (with microscopic examination done on those samples showing positive albumen only). Perhaps these should be repeated again next year. Serum creatinine levels were determined but no significantly high values were found. However, we might consider doing blood urea urine urea levels on those people showing creatinine levels in the upper ranges.

Should liver function tests or any other test along this line be considered?

(e) Slit lamp observation for radiation induced opacities of the lens will be repeated as in the past.

(f) Genetic studies. With such small numbers of people involved and in view of the negative nature of the genetic studies carried out in large numbers of Japanese people we have not been encouraged to undertake such studies. However, in my opinion, there are several factors which place these studies in the Marshallese in a more favorable light; 1. the relative isolation of the people insures repeat examinations over a period of years with a minimum of mixing with other island population; 2. consanguinous marriages are common; 3. there is considerable intermarriage among the irradiated group. The incidence of congenital defects among the Marshallese appears high (possibly due to consanguinous matings over a long period of years). Thus far we have only examined the offspring for abnormalities which might be found on routine physical examinations and nothing of significance has been found. Dr. J. Neel suggests that data on congenital defects in offspring of consanguinous marriages would be valuable in connection with their study along this line in the Japanese. (This study is aside from radiation effects.) 3. In the third category, ie, abnormalities common to both exposed and unexposed Marshallese, the relatively low hematocrit levels should be investigated. Dietary deficiencies should be ruled out. The prevalence of intestinal parasites (with high eosinophile counts) might be more completely evaluated by stool studies for ova and parasites. Attempts at large scale treatment for parasitism might be contemplated. Since many types of parasites are present the procedure would be more feasible if there were a "universal" vermifuge of some type.

The high serum protein levels prevalent in these people could be further investigated. Preliminary electrophoretic data indicate a high gamma globulin fraction. Perhaps parasitism, chronic infections, or diet may be partly responsible.

Anthropological studies to show the degree of homogeneity of the Marshallese might be interesting. The hemoglobin types seem to indicate a considerable degree of homogeneity. Blood group studies indicate a large Asiatic component in their background.

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psychological studies and psychiatric testing would be interesting in view of the apparent lack of emotional difficulties observed in these people.

I realize that in this letter I have only touched the high spots. We are limited in the number of studies we can undertake and would therefore appreciate very much your comments and suggestions.

Sincerely,

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