RESPONSE OF HUMAN BEINGS ACCIDENTALLY EXPOSED TO SIGNIFICANT FALL-OUT RADIATION (U)

To support discussion of Item JM 1(a) at the Tenth Tripartite Conference.

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RESPONSE OF HUMAN BEINGS ACCIDENTALLY EXPOSED TO SIGNIFICANT FALL-OUT RADIATION (U)

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ABSTRACT

Following the detonation of a nuclear device in the Marshall Islands in March 1954, a group of 239 Marshallese and 28 Americans on nearby islands were exposed to a significant amount of radioactive fallout material. Sixty-four Marshallese on one island received the largest exposure, (a calculated whole-body dose of 175 r) in addition to sufficient skin contamination to result in lesions and some degree of internal contamination. The other island groups received considerably less exposure and in view of time limitations, the response of the highest exposure group only was discussed in detail. A significant number of individuals suffered from mild nausea and one or two individuals vomited on the day of exposure. In addition, a considerable number of people experienced itching of the skin and a few reported burning of the eyes with lacrimation during the first two days after exposure. Later signs of radiation injury included definite epilation and the development of spotty, hyperpigmented skin lesions that desquamated from the center of the lesions outward. In some cases the skin damage was sufficient to result in raw, weeping lesions. All lesions healed rapidly with no further breakdown of the skin noted up to the period of latest observation which was six months after the event. (There was one persistent ear lesion that required several months to heal). Microscopic examination of the biopsies of the lesions showed changes usually associated with radiation injury. Clothing and shelter in building during the fallout offered considerable protection against the development of lesions. Hematological

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(Abstract cont'd)

changes were pronounced.

Lymphopenia appeared promptly and was persistent for a prolonged period of time. Neutropenia occurred in all of the individuals with initial minimum values occurring around the 11th day followed by an increase in the counts and a secondary minimum around the 40th to 45th day. The most consistent hematologic changes was the depression in the platelet counts. There was still depression of these blood elements on resurvey of these people at six months post-exposure. The incidence of various diseases that developed was identical in all exposure groups and bore no relationship to the hematologic changes. The degree of internal contamination was not believed to have contributed to the acute radiation syndrome observed and was not believed sufficient to produce a long-term hazard.

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Following a nuclear device detonation in the Marshall Islands in the Spring of 1954, a serious fallout of radioactive materials occurred on several neighboring inhabited islands. Many of the inhabitants of these islands received a significant amount of radiation. Radiation exposure of these inhabitants was not from the bomb detonation itself but was due to the aftermath in which a mixture of radioactive materials and pulverized coral was forced high into the air by the violence of the detonation and carried by wind strata to be deposited on these islands many miles from the sight of detonation. The deposit of this radioactive material on the islands was large enough to produce a field of radiation sufficient to result in significant whole-body irradiation of the inhabitants. In addition, the skin was contaminated with the material and some of it was inhaled and ingested. The calculated whole-body dose of radiation in r in air and the amount of fallout observed for each of these island groups was as follows:

Island Group	Population	Whole-body dose in r	Fallout Observed
I	64 Marshallese	175 r	Heavy
II	18 Marshallese	69 r	Moderate
III	28 American service men	78 r	Slight
IV	157 Marshallese	14 r	None

These doses were calculated largely by field instrument readings taken at the time of evacuation with backward extrapolation of calculations to conform to the appropriate decay schemes occurring during the estimated times of exposure.

In view of the time limitation, only the more severely exposed Group I will be presented in detail and the other groups only referred to for comparative purposes.

The detonation of the device was observed in the early morning and hours later the islanders noticed a snow-like material falling from the sky which continued for several hours. The material was visible on the ground and sifted into their poorly constructed thatched-roof houses.

The material whitened their hair and clung to their skins. During that night and the next day or two, about three-fourths of the population developed nausea and a few vomited and had diarrhea. During this period also, many developed itching and burning of their skin and some reported burning of the eyes with lacrimation. They became concerned about the powder being "poisonous" but made no serious efforts to avoid the powder or to cleanse themselves adequately. Supervised personnel decontamination and medical care was not possible until evacuation to the nearby naval base at Kwajalein Island about two days after exposure. By this time initial symptomatology had completely subsided and no further symptomatology developed. During the next few weeks there were repeated extensive efforts at personnel decontamination. The hair was particularly difficult to decontaminate, due to the heavy coconut oil which they used to groom it. The body radiation readings, however, gradually were reduced to background levels during this period.

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An emergency medical team was quickly organized and was composed largely of naval medical personnel from the Naval Medical Research Institute and the Naval Radiological Defense Laboratory.

On arrival at Kwajalein, laboratory facilities were quickly set up in an empty building and the team was functioning the day after arrival, i.e., the 10th day after the accident. On arrival, complete initial histories and physical examinations were carried out on all personnel with frequent follow-up examinations. Numerous skin surveys and hematological and radiological urinary studies were undertaken, the results of which will be described subsequently. All personnel were found to be in relatively good health and the only indication of radiation injury was change in the blood picture. In fact, there was no other development of signs and symptoms that could be attributed with certainty to radiation effects throughout the period of study except for the development of skin lesions and hematological changes.

Skin lesions and Epilation.

Considerable irradiation of the skin was produced largely by soft beta and gamma radiation from the deposited fallout material on the skin. The harder gamma components added little to the total dose on the skin. Due to the complexity of the makeup of the radioactive materials and other uncertainties, it was impossible to calculate with any degree of accuracy the dose to the skin. The dose was sufficient, however, to produce epilation and widespread lesions of the skin which appeared starting about the 12th to the 14th day after the accident.

In the less heavily exposed island groups (Groups II and III), the lesions did not start developing until some 20 days after the accident. The people of Group IV never developed any skin lesions. The lesions occurred primarily on the exposed parts of the body which were not protected by clothing. Those who remained under shelter in their homes developed less severe lesions or no lesions. There was some protection also to those who bathed during the fallout period.

Almost simultaneously, with development of skin lesions, epilation of the scalp of a spotty nature was noted. Epilation was almost always accompanied or preceded by lesions of the scalp, and was more extensive and severe among the children (0-15 years), over 90 percent showing some degree of epilation. Only 28 percent of the older age group showed epilation. The preponderous of scalp lesions in the areas of epilation indicated that beta radiation from the deposit of radioactive materials in the scalp was primarily responsible for epilation rather than being due to the penetrating gamma radiation. The epilation, however, was not permanent since regrowth of the hair was noted beginning about nine weeks after irradiation and complete regrowth of normal hair was evident six months after the accident.

The development of the skin lesions did not conform in all respects to beta skin lesions described in literature. No primary or secondary erythema was observed. The dark skins of these people may have obscured this phenomenon or perhaps the dose to the dermis was insufficient to evoke the response. The lesions showed differences in latent periods

before appearance on different parts of the body in roughly the following sequential order: scalp, neck, axillary region, antecubital fossae, feet, arms, legs, and trunk.

Table 1 shows the incidence of these various lesions and the median time of appearance of these lesions. It can be seen that the neck and scalp lesions were far more common than other lesions. There were also, however, a substantial number of antecubital fosaee lesions and foot lesions.

Lesions on flexor surfaces tended to appear before lesions on extensor surfaces. These differences in latent periods did not appear to be related entirely to the dose to the skin since severe foot lesions presumably receiving a larger dose of radiation did not appear until after other less severe lesions. It was believed that differences in sensitivity of skin areas to irradiation might partly account for this variation in latent period.

The first indication of a developing lesion was an increase in pigmentation in the form of macules, papules, and raised plaques. Usually these dark pigmented lesions had a dry, thickened, leathery feel. However, some areas developed merely simple hyperpigmentation of the skin over extended areas.

The majority of lesions was superficial with no vesicle formation and after several days showed dry, scaly, desquamation from the center of the lesion outward. Desquamation left depigmented pink to white epithelium not remarkably different in texture from the surrounding

skin. Over the next few weeks, the lesions gradually became repigmented so that the skin became relatively normal in appearance.

Approximately 20 percent of the group developed lesions of a deeper nature. These lesions occurred primarily on the feet and to some extent on the neck and scalp and in one case on the ear. These lesions also began with hyperpigmentation but in a few days showed wet desquamation with weeping and crusting and in some foot lesions, bullae formation occurred. Some of these lesions became secondarily infected. However, all lesions healed rapidly and re-epithelized in a week or ten days. Repigmentation gradually took place in most lesions and some of these healing lesions, particularly on the neck, showed development of hyperpigmentation of a greyish, dusky color and a thickening of the skin with "orange-peel" appearance.

Six months after the accident, the hyperpigmentation had in most cases subsided considerably. The deeper foot lesions tended to heal without repigmentation leaving pink to white depigmented areas, though the skin did not appear abnormal in texture. The deeper lesions were more painful, particularly the foot and neck lesions.

Biopsies taken from lesions during the third to the fourth week post-exposure revealed histopathological changes characteristic of radiation damage.

Spotty trans-epidermal damage with atrophy and flattening of the retepegs was a common finding with areas of relatively normal skin between emphasizing the particulate nature of the radioactive material.

Cells of the Malphigian layer showed pleomorphic nuclei, pyknosis, and cytoplasmic halos. Focal disorganization of the Malphigian and basal layers was present in extensively damaged areas. In the dermis, telangiectatic vessels were noted in areas where the overlying epidermis showed greatest damage and there was considerably lymphocytic infiltration surrounding these telangiectatic spaces.

Treatment of the skin lesions was largely non-specific except in the deeper lesions which became infected in which case aureomycin ointment after thorough cleansing was used. In one deep foot lesion, parenteral prophylactic penicillin was used for two days. Otherwise, treatment consisted simply of relieving itching and pain by cleansing, application of calamine lotion with phenol, pontocaine ointment, or keeping the skin plaint with water soluble vanishing type ointment.

In regard to prognostication, there are factors for and against the future development of skin cancer in these people. In favor of such development are (a) the number of young people exposed with long life expectancy probably exceeds the induction period of cancer development; (b) the long exposure to tropical sunlight; and (c) the influence of the sublethal whole-body exposure is not known but may adversely affect the prognosis. A favorable prognosis is suggested by the superficial nature of the lesions with little scarring, lack of gross telangiectasia or extensive vascular changes which would portend chronic radiodermatitis.

An interesting unexpected finding in nearly all of the Group I people was a development of a bluish, brown semi-circle band of pigmentation of the fingernails and toenails which was first noted about the 23rd day. The pigmentation band started in the semilunar area and

progressed distally with growth of the nail. It was apparently beneath the nail plate. Since all of the American negroes but none of the white Americans in Group III developed this pigmentation, it appeared that this phenomenon was characteristic of dark-skinned races. It also was probably due to whole-body irradiation and not local skin irradiation since people without skin lesions developed the pigmentation and vice versa. One case of similar pigmentation bands of the fingernails has been reported in the literature in a negress given therapeutic irradiation to the hands.

As a result of this accident the following conclusions can be drawn with respect to beta damage to the skin:

a. Serious skin contamination of personnel from fallout may occur many miles from the detonation of a nuclear device. Resultant radiation damage to the skin may be the major radiation effect under conditions where early evacuation from the field of radiation reduces the whole body exposure.

b. Decontamination of the skin must be prompt to be effective because of the initial high beta dose rate.

c. A latent period of a few days to 3 to 4 weeks may elapse before signs and symptoms of skin damage are evident.

d. Clothing and/or any type of shelter gives almost complete protection to the skin.

Hematological Observations.

Since there had been no previous human exposure to significant

amounts of fallout radiation, no hematological data known to be strictly applicable were available for use as a guide in the evaluation of the exposed personnel. Accordingly, emphasis was placed on serial studies utilizing a few highly standardized hematological determinations to insure that individual and group trends would have maximum validity. These determinations consisted of total leukocyte, neutrophil, lymphocyte. and platelet counts, and hematocrit determinations. Standard techniques were utilized and every effort was made to maintain uniform procedures in every phase of the laboratory work.

Control groups, as comparable as possible, in respect to age, race, sex, and background were selected from Marshallese on a nearby island. (Controls for the service men were obtained from the American group on Kwajalein). Findings are expressed in terms of percent of the control group. In view of the significantly higher lymphocyte counts in children below 5 years of age and some age and sex difference in platelet counts in the control group. the data is presented according to age groups and in the case of platelets, sex groups.

The absolute neutrophil count of both younger and older age groups fell to a value of approximately 70 to 80 percent of that of the controls during the 2nd week, followed by unstable counts until the 5th week. At this time the beginning of a second depression (P 0.01) was noted for both age groups, and a low value of approximately 50 percent of the controls was reached. The count was maintained at approximately 75 percent of the control values from the 7th week to the end of the

first study (10 weeks). At 6 months the counts were within normal range but still depressed below the control limit as a group. The lower age group was below the older age group throughout most of the observation.

The absolute lymphocyte count of the older age group had fallen by the 3rd day to a value of approximately 55 percent of the control group. This value was maintained throughout the study with no definite evidence of an upward trend. The values for the younger age group also fell before the third day to a value of approximately 25 percent of the control group following which there was a significant upward trend, recovery being more rapid in the younger age group. Examination at 6 months showed the lymphocyte counts were still depressed.

Since the lymphocyte count remained essentially constant throughout the study, the fluctuation in white blood count was a reflection of the neutrophil count changes.

Platelets were first counted 10 days after exposure, at which time counts in the age group above 15 years were approximately 70 percent of the control group. Following this the platelet count fell reaching a low of approximately 35 percent of the control value during the 4th week. At this time counts in 20 percent of the group were below 90,000 platelets/mm^3. The platelet count rose during the 5th week and reached the value noted for the initial counts on the 10th day. A second decrease in platelet count ($P>0.01$) developed during the 7th and 8th weeks and values remained at approximately 70 percent of the control group during the remainder of the observation period. The pattern

of platelet counts in the age group below 15 years was remarkably similar to that noted in the older age group.

Six months after the accident, platelet as well as the other blood counts showed about the same degree of depression as was noted during the last week (10th) of the first study.

Hamatocrits first done on the 22nd day were slightly below those of the control population. A significant trend in values after this time could not be detected statistically.

Expressed as percent of controls in the younger age groups, all elements were affected more markedly. These results would indicate that the children are more sensitive to radiation or that other biological or physical factors resulted in a relatively greater dose.

The less exposed island groups showed similar, but in most cases, less pronounced hematological change which was consistent with the lower doses calculated for these groups.

The time course of hematological changes corresponded most closely with those low exposure Japanese victims of the Hiroshima and Nagasaki bombs in which definite signs of severe radiation exposure were present in some individuals, but in which no mortality occurred. Comparison with hematological data in Japanese groups in which fatalities occurred make it evident that exposure in the largest exposure group of Marshallese was moderately severe, probably within 50 or at most 100 r of the level where some fatalities would have resulted.

The skin and internal radioactive contamination were not considered to have contributed significantly to the depression of the hematological elements.

As an index of severity of radiation exposure, particularly in sublethal range, this study indicates that the total white or neutrophil counts are of limited usefulness because of wide fluctuations and because several weeks may be required for maximum depression to become evident. The lymphocyte count is of more value in this regard, particularly in the low dose range, since depression occurs within hours of exposure. However, since a marked depression of lymphocyte counts occurs with low doses, and since further increase in dose produces little more depression, this index is of little value at higher doses. Platelet counts showed a regular pattern of change in the present studies, with the same time of maximum depression in all exposure groups and with the degree of depression roughly proportional to the calculated doses. It appears, therefore, that the platelet count has considerable promise in the sublethal range as a convenient and relatively easy direct method of determining the degree of exposure.

Clinical Observations and Therapy.

Clinical care of the exposed individuals, in addition to treatment of skin lesions, centered around the possible sequelae of depression of hemopoiesis. In view of the widespread conflicting opinions in regard to the value of various prophylactic and therapeutic measures in treatment of radiation effects, it was decided in advance that therapy

would not be given arbitrarily, but would be instituted as indicated clinically for specific conditions on an individual basis. However, if severe granulocytopenia developed the prophylactic use of antibiotics would be considered. Whole blood transfusions would likewise be resorted to only in those cases developing frank anemia.

With the exception of the development of skin lesions and epilation, physical examinations at no time revealed findings in any group that could be attributed with certainty to radiation. The various clinical conditions encountered in the most severely exposed groups were not remarkably different from those seen in the least exposed group that received only 14 r.

In view of the low leukocyte counts developed in the Group I people, prophylactic antibiotic therapy was given careful consideration but never resorted to. Twenty-seven individuals had total leukocyte counts of 4000 or below or absolute neutrophil counts of 2500 or less at some time during the period of observation. (10 percent of the individuals reached an absolute granulocyte level of 1000 cells/c.c. or below). Of these 27 individuals, 13 had symptoms of disease that required evaluation for possible antibiotic therapy. Eleven of the individuals had severe upper-respiratory infections. However, antibiotic therapy (two injections of penicillin) was given to only two children in the group who had symptoms which were out of proportion with the physical findings. Prophylactic antibiotics were not instituted based on leukopenia because the granulocyte fall was gradual and all individuals were under continuous medical observation so that infection would be

discovered in its earlier stages. In addition, it was felt that the premature administration of such drugs might not only obscure medical indication of treatment but might potentially lead to the development of drug-resistant organisms in an individual with an already lowered resistance to infection. Table 2 shows the conditions in which antibiotic therapy was used in Groups I and II. Antibiotic therapy would have been used in these individuals even had they not received irradiation.

There was no evidence of hemorrhage into tissues even though 11 individuals reached platelet count levels between 35,000 and 65,000. Two women menstruated when their platelet counts were 150,000 and 130,000, respectively. Both menstruated several extra days and thought that the bleeding was more than usual but not sufficient to cause them concern.

None of the diseases that developed appeared to be related to the effects of irradiation, either directly or as a result of the hamatological disturbances. The diseases were comparable to those diseases seen in the least exposed group.

An epidemic of upper respiratory infection developed in all of these exposed groups between the 27th and 47th post-exposure days. Fifty-eight percent of the people of Group I were involved. The disease did not appear to be more severe in this more heavily exposed group than in the other less exposed groups. When compared to those individuals not infected, there did not seem to be any correlation between the presence of the infection and the hematological picture.

The body weight of individuals in Groups I and II was followed routinely. Both adults as well as children lost some weight during the period of observation in spite of the fact that they lived inactive lives and ate heartily. Whether the failure to gain weight was connected with radiation or changes in environment is open to question. Unfortunately, the weight of Group IV was not systematically followed, and there was no satisfactory control to aid in interpreting the loss in weight.

Four women in Group I were pregnant when brought to Kwajalein. None of these women had abnormal symptoms referable to pregnancy. Three of the pregnancies have since terminated in normal deliveries, and apparently normal babies.

It can be concluded from this experience that the dosage of radiation and associated pancytopenia observed is not sufficient to interfere materially with an individual's defenses against common everyday infections. Therefore, neither prophylactic antibiotic or transfusion therapy in a situation of this nature are indicated when an individual can be under close medical supervision. Indications for specific therapy should be based on good clinical judgment for the individual case.

Internal Radiation Hazard.

Radiochemical analysis of numerous urine samples of exposed personnel showed that the degree of internal absorption of radioactive materials was roughly proportional to the calculated external dose and therefore to the concentrations of airborne fission products. The degree

of internal radiation hazard was too low to have contributed significantly to the acute radiation syndrome observed. The concentration and type of internal radioactive contaminants minimize the probability of any significant long-term effects from the internal radiation.

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(To support discussion of Item [illegible] 1(e) at the Tenth Tripartite Conference)

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