

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

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and

Lieut. Col. L. Eugene Browning (MC) U. S. Army

After detonation of a nuclear device in the Marshall Islands during the spring of 1954, radioactive material fell upon several neighboring inhabited atolls.¹ The fall-out material consisted of pulverized and incinerated coral (calcium oxide) coated with radioactive fission products, forced high into the atmosphere by the violence of the explosion. The particulate matter was then distributed over a wide area by the wind structure. The field of radiation resulting from the deposition of this radioactive material on the islands was sufficiently intense 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 roentgens as measured in air and the amount of fall-out observed for each of the island groups is shown below. The exposed American

Calculated Whole Body Dose of Radiation

Island Group	Population	Whole-Body Dose in r	Fall-Out Observed
Rongelap	64 Marshallese	175	Heavy (snow-like)
Ailinginae	18 Marshallese	69	Moderate (mist-like)
Rongerik	28 American servicemen	78	Moderate (mist-like)
Utirik	157 Marshallese	14	None

servicemen were returned to duty after extensive medical examinations at Kwajalein and at the Tripler General Hospital, Honolulu, T. H. The Utirik people were returned to their native atoll after the initial period of observation. The Rongelap and Ailinginae residents were moved to Majuro Atoll for temporary occupation of dwellings built for them. These gamma ray doses were calculated from field instrument readings taken at the time of evacuation and decay schemes appropriate for the estimated times of exposure. For the sake of brevity, details will be presented only on the more severely exposed Rongelap group and the other groups will be referred to only for comparative purposes.

The detonation of the device was observed in the early morning, and hours later the exposed individuals noticed a snow-like material falling from the sky; this continued for several hours. The material was visible on the ground

and sifted into the lightly constructed thatched-roof houses. The material whitened the hair and clung to the skin. During the night following the explosion and for the next two days, about two-thirds of the population developed nausea and 10% vomited and had diarrhea. During this period also, many developed itching and burning of the skin and some reported burning of the eyes with lacrimation. Supervised decontamination and medical care was not possible until the exposed individuals were evacuated to the nearby naval base at Kwajalein. By this time, initial symptoms had completely subsided.

An emergency medical team, composed largely of naval personnel from the Naval Medical Research Institute and the U. S. Naval Radiological Defense Laboratory, was organized and sent to the area, arriving on the ninth day after exposure. Complete initial histories and physical examinations and frequent follow-up examinations and treatment for medical conditions were carried out on all personnel. In addition, hematological studies to assay the degree of radiation damage and urinary excretion studies for radioactive materials were performed. It was apparent from initial blood studies that significant radiation had been received, and by 12 to 14 days further evidence of radiation injury was apparent in the form of skin lesions and epilation. 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.

CLINICAL OBSERVATIONS, THERAPY, AND HEMATOLOGICAL FINDINGS

Since the degree of depression of peripheral blood elements is believed to be the best index of severity of radiation injury, systematic serial determinations were carried out. These determinations consisted of total leukocyte, neutrophil, lymphocyte, and platelet counts and hematocrit determinations. Control groups, as comparable as possible to the exposure groups in respect to age, race, sex, and background, were selected. Findings are expressed in terms of percentage of control values. Significant age and sex difference in blood cell counts were noted in the control groups, and the data are presented in accordance with the differences noted.

The absolute neutrophil count (fig. 1) of both younger and older age groups fell to a value of approximately 70 to 80% of that of the controls during the second week, followed by a period of fluctuation until the fifth week. At this time the beginning of a second depression was noted for both age groups, and a low value of approximately 50% of that of the controls was reached. The

From the Naval Medical Research Institute, Bethesda, Md., and U. S. Naval Radiological Defense Laboratory, San Francisco. Commander Cronkite is now at Brookhaven National Laboratory, Upton, N. Y. Lieut. Farr is now at the University of Chicago, School of Biological and Medical Sciences.

Read before the Section on Military Medicine at the 104th Annual Meeting of the American Medical Association, Atlantic City, June 8, 1955.

Drs. David A. Wood, University of California Hospital, San Francisco, and Edward L. Alpen, U. S. Naval Radiological Defense Laboratory, San Francisco, made the histopathological evaluation of the skin lesions.

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level was maintained at approximately 75% of the control values from the 7th week to the end of the critical period of observation (10th week). The values for the lower age group were below those of the older age group throughout most of the period of observation. The absolute lymphocyte count (fig. 1) of the older age group had fallen by the third day to a value of approximately 55% of the control value. This value was maintained through-

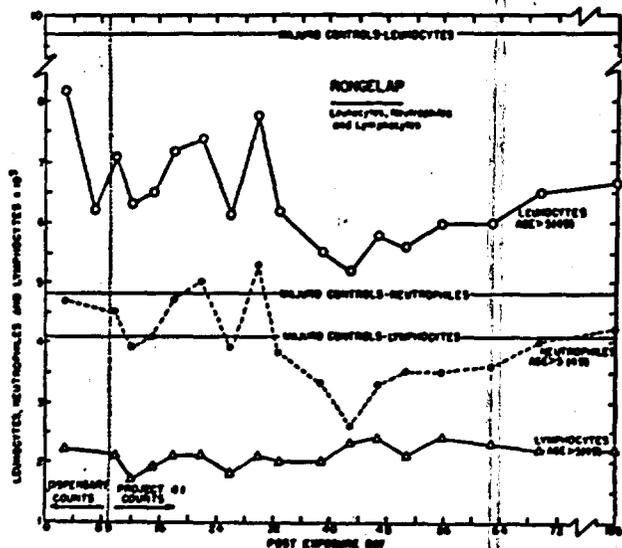


Fig. 1.—Mean leukocyte changes in highest exposure group (64 people).

out 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% of the control value, after which there was a significant upward trend, recovery being more rapid in the younger age group. Since the mean lymphocyte counts remained essentially constant throughout the study, the fluctuation in total white blood cell count was a reflection of changes in the neutrophil component (fig. 1).

The sequelae of depression of hemopoiesis are generally considered as the major source of morbidity and mortality from whole-body radiation injury.² Therefore, in view of the low leukocyte counts that developed in the Rongelap people, the use of prophylactic administration of antibiotics was given careful consideration. Twenty-seven individuals had absolute neutrophil counts of 2,500 per cubic millimeter or less at some time during the period of observation. Temporary depressions as low as 700-1,000 were observed. Prophylactic administration of antibiotics was not instituted because all individuals were under continuous medical observation and it was felt that such drugs might obscure medical indication of treatment and lead to the development of drug-resistant organisms. An epidemic of upper respiratory infection developed between the 27th and 47th days after exposure in all of the exposed groups. Fifty-eight per cent of the Rongelap people were involved. The disease did not appear to be more severe in this than in the other less exposed groups. There was no correlation between leukopenia and incidence of infection.

Platelets were first counted 10 days after exposure (fig. 2), at which time the level in the females were approximately 60% of the appropriate control group.

After this, the platelet count fell, reaching a low of approximately 30% of the control value during the fourth week. (At this time counts in 20% of the Rongelap people were below 90,000 platelets per cubic millimeter.) The platelet level rose during the fifth and sixth week and had reached the value noted for the initial counts on the 10th day. A second decrease in platelets developed during the seventh and eighth week, and values remained at approximately 70% of the control values during the remainder of the observation period. The pattern of the platelet counts in the male groups was similar to that noted for the females. Counts of the lower age group, males, were consistently higher than those of the adult group in absolute counts but consistently lower as percentage of control.

There was no evidence of hemorrhage into tissues, even though in 11 individuals platelet count levels reached between 35,000 and 65,000 per cubic millimeter. Two women menstruated when their platelet counts were 150,000 and 130,000 per cubic millimeter respectively. Both experienced excessive menstrual bleeding, insufficient to cause them concern, which subsided without therapy.

Six months after the accident, blood cell counts showed only slight increase over previous ones during the last week (10th) of the initial observation period and were still below control levels. Follow-up studies at one

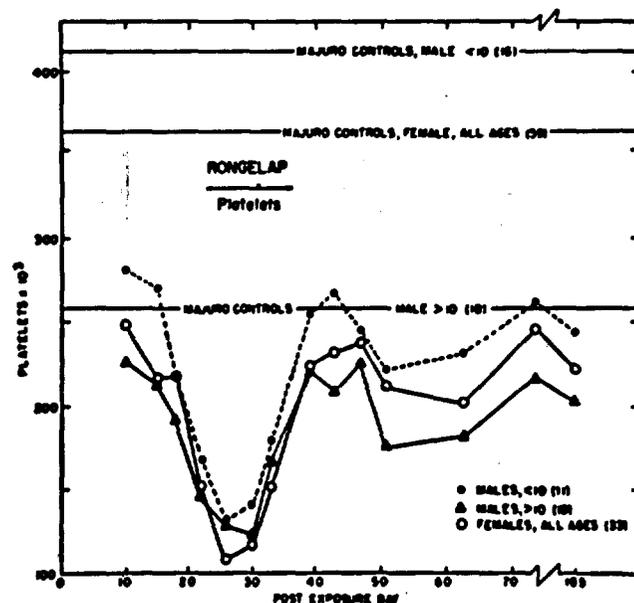


Fig. 2.—Mean platelet changes in highest exposure group (64 people).

year after the accident showed that the neutrophil counts of the exposed individuals were back to the control level; however, the lymphocytes, monocytes, eosinophils, and platelets were still below control levels, though they were higher than after six months. Hematocrit determinations

2. Dunham, C. L.; Cronkite, E. P.; LeRoy, O. V., and Warren, S.: Atomic Bomb Injury: Radiation, Council on National Emergency Medical Service, J. A. M. A. 147:50 (Sept. 1) 1951. Cronkite, E. P., and Brecher, G.: Defects in Hemostasis Produced by Whole Body Radiation, in Clotting and Allied Problems: Transactions of the Fifth Conference, January 21 and 22, 1952, edited by Joseph E. Flynn, New York, Josiah Macy, Jr., Foundation, 1952. Bond, V. P.; Silverman, M. S., and Cronkite, E. P.: Pathogenesis and Pathology of Radiation Infection, Radiation Res. 1:389, 1954. Cronkite, E. P., and Brecher, G.: The Protective Effect of Granulocytes in Radiation Injury, Ann. New York Acad. Sc. 59:815, 1955.

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

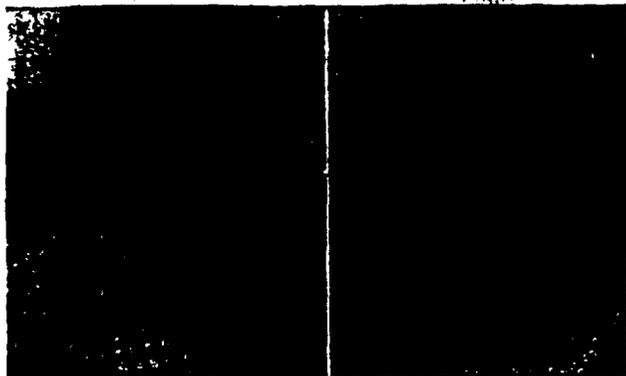


Fig. 3.—*A*, epilation in 7-year-old girl at 28 days. *B*, six months later, showing complete regrowth of hair.

The time course of hematological changes corresponded most closely with the low-dose Japanese groups exposed to radiation from the Hiroshima and Nagasaki bombs³ in which definite signs of severe radiation exposure were present in some individuals but in which no mortality occurred. Comparison with hema-

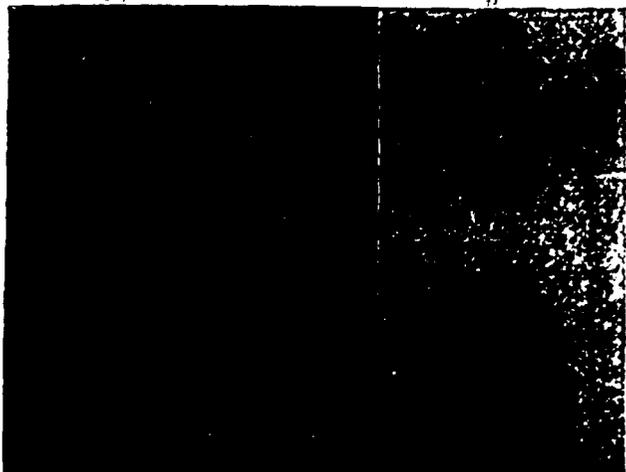


Fig. 4.—*A*, pigmented lesions of neck and antecubital fossae in 13-year-old boy (29 days after exposure). Desquamation with depigmentation of neck lesions has begun. *B*, extensive lesions in 13-year-old boy at 45 days after exposure.

tological data in Japanese groups in which fatalities occurred make it probable that exposure in the highest exposure group of Marshallese was moderately severe, probably within 50 to 100 r of the level where some fa-

3. LeRoy, G. V.: Hematology of Atomic Bomb Casualties. *Arch. Int. Med.* 86:691 (Nov.) 1950. Oughterson, A. W., and others: Medical Effects of the Atomic Bombs, report of the Joint Commission for Investigation of the Effects of the Atomic Bomb in Japan, vol. 3 and 5, Office of Air Surgeons, Army Institute of Pathology, Atomic Energy Commission, 1951.

4. Knowlton, N. P., Jr., and others: Beta Ray Burns of Human Skin. *J. A. M. A.* 141:239 (Sept. 24) 1949.

5. Robbins, L. L., and others: Superficial "Burns" of the Skin and Eyes from Scattered Cathode Rays. *Radiology* 48:1, 1946. Low-Beer, B. V. A.: External Therapeutic Use of Radioactive Phosphorus: 1. Erythema studies. *Ibid.* 47:213, 1946. Wirth, J. E., and Raper, J. R.: Chapter 12, in *Biological Effects of External Beta Radiation*, edited by R. E. Zirkle, ed. 1, New York, McGraw-Hill Book Company, Inc., 1951.

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

The body weight of individuals in the Rongelap and Ailinginae groups was followed routinely. 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 change in environment is open to question. Four women in the Rongelap group were pregnant when brought to Kwajalein. None of these women had abnormal symptoms referable to radiation. All of the pregnancies have since terminated in delivery of apparently normal babies.

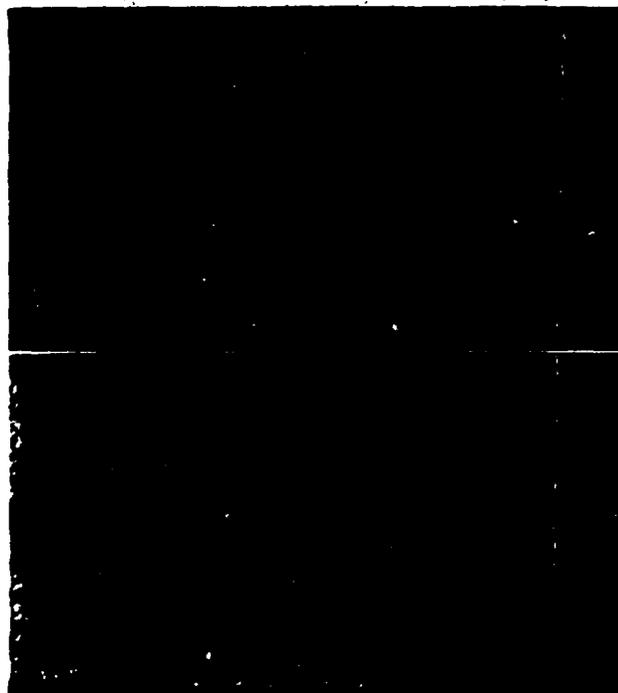


Fig. 5.—*A*, hyperpigmented raised plaques and bullae on dorsum of feet and toes at 28 days. One lesion on left foot shows deeper involvement. Feet were painful at this time. *B*, six months later. Foot lesions have healed with repigmentation, except for depigmented spots persisting in areas where deepest lesions were.

SKIN LESIONS AND EPILATION

Irradiation of the skin resulted largely from beta radiation from the fall-out material deposited on the skin. Due to the complex composition of the radioactive materials, and because of other uncertainties, it was impossible to calculate the skin dose accurately. The dose was sufficiently large, however, to produce epilation and widespread lesions of the skin in 90% of the Rongelap group, beginning about 12 to 14 days after the exposure. In the less heavily exposed groups (Ailinginae and Rongerik), the lesions did not appear until approximately 20 days after the accident. In the Utrik group, radiation lesions of the skin did not appear. The lesions occurred primarily on the exposed parts of the body not protected by clothing. Those who remained under shelter during the fall-out developed less severe or no lesions. Some protection was afforded those who bathed during this period. Almost simultaneously with develop-

ment of skin lesions, spotty epilation of the scalp was noted (fig. 3A). Epilation was usually accompanied or preceded by lesions of the scalp. This was more extensive and severe among the children (birth to 15 years). Over 90% of the children showed some degree of epilation, as compared to 28% in the older age group. Ra-

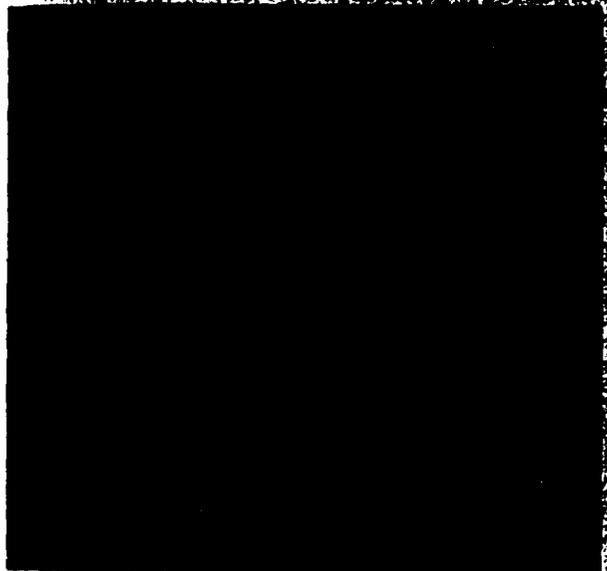


Fig. 6.—Desquamation of back of scalp at 28 weeks. Epilation occurred earlier in desquamated area. Note persistent irritation of left ear.

growth of hair of normal color and distribution was noted beginning about nine weeks after irradiation and was complete six months after the accident (fig. 3B).

The developing lesions did not follow the identical course as observed by Knowlton and co-workers⁴ in individuals after handling concentrated fission products or after other beta burns.⁸ Primary and secondary erythema was not observed. The lesions showed differences in latent periods before appearance on different parts of the body and appeared in roughly the following sequential order: scalp, neck, axillary region, antecubital fossae, feet, arms, legs, and trunk. The neck and scalp lesions were most common; however, a substantial number of antecubital fossae lesions and foot lesions were seen. Lesions on the 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 caused by the foot receiving a larger dose of radiation, did not appear until after other less severe lesions.

The first indication of a lesion was an increase in pigmentation in the form of macules, papules, and raised plaques (fig. 4A). Usually these dark pigmented lesions had a dry, thickened, leathery feel. Most lesions were superficial. After several days, dry, scaly desquamation developed from the center of the lesion outward. Desquamation left depigmented areas similar in texture to the surrounding skin (fig. 4B). During the next few weeks, the lesions gradually became repigmented and the skin became relatively normal in appearance. Approximately 20% of the group developed deeper lesions. These were seen on the neck, scalp, and ear, and most frequently on the feet (fig. 5 and 6). These lesions were painful and were characterized by wet desquamation with weeping and crusting, and, in some foot le-

sions, desquamation was preceded by bullous formation (fig. 5A). Some lesions became secondarily infected; however, all lesions except one ear lesion healed rapidly and reepithelized in a week or 10 days. The ear lesion took about four months to heal. Repigmentation gradually took place in most lesions, and some of the healing lesions, particularly on the neck, showed development of hyperpigmentation of a grayish, dusky color and a thickening of the skin with "orange-peel" appearance.

Biopsy specimens taken from lesions during the third to fourth week revealed histopathological changes consistent with radiation damage (fig. 7). Spotty transepidermal damage with atrophy and flattening of the rete pegs was a common finding, with areas of relatively normal skin between, emphasizing the particulate nature of the radioactive material. Cells of the malpighian layer showed pleomorphic nuclei, pyknosis, and cytoplasmic halos. Focal disorganization of the malpighian and basal layers was present in extensively damaged areas. In the dermis, telangiectatic vessels were noted where the overlying epidermis showed greatest damage. There was mild edema of the pars papillaris with lymphocytic infiltration, particularly around the telangiectatic vessels. Atrophy of hair follicles was observed.



Fig. 7.—Photomicrograph of pigmented skin lesion three weeks after exposure ($\times 100$). Extensive transepidermal damage with less involved areas on either side. Loose lamination of stratum corneum, absence of stratum granulosum, and disorganization of malpighian layer. Dermis shows mild edema of pars reticularis, indistinct capillary loops, moderately pronounced perivascular cellular infiltrate, and mild telangiectasia.

Follow-up studies at six months and one year showed that the hyperpigmentation had in most cases disappeared. At the site of deeper foot lesions and the ear lesions, there were pink-to-white areas that had not repigmented (fig. 5B). In these areas the skin appeared slightly atrophic. Treatment of the skin lesions consisted of daily cleansing and symptomatic therapy with

the exception of locally applied antibiotic ointments for infected lesions and in one case parenterally given penicillin.

The possibility that cancer might develop at the site of some of these lesions must be considered. Favoring such development are the long life expectancy of the numerous children in the exposed group, constant exposure to tropical sunlight, and the possible influence of additional sublethal whole-body exposure. Against such development are the superficial nature of the lesions, rapid healing with little in the way of residual gross defects, and only minimal evidence of histological damage by six months.

Pigmentation of the semilunar area of the fingernails and toenails was observed about the 23rd day in most of the Marshallese in the higher exposure groups and in the five American Negroes but in none of the white Americans. The pigmentation was beneath the nail and progressed distally with growth of the nail. A similar phenomenon has been observed in a Negro woman after local therapeutic irradiation.⁶

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 air-borne 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.

SUMMARY AND CONCLUSIONS

After detonation of a thermonuclear device in the Marshall Islands in the spring of 1954, radioactive fallout occurred over an area of thousands of square miles beyond the range of thermal and blast injury. Marshal-

lese and Americans were accidentally exposed on islands in this area, receiving whole-body gamma radiation, beta radiation injury to skin, and minimal internal contamination. The highest dose (an estimated 175 r) was received by a group of 64 Marshallese. The dose of radiation received proved to be sublethal. Though there was significant depression of hemopoiesis, no clinical signs or symptoms developed that could be attributed with certainty to this effect. Prophylactic administration of antibiotics or other specific therapy was not found to be indicated.

Skin lesions and epilation developed in 90% of the group beginning about two weeks after the exposure. The lesions occurred largely on exposed parts of the body not protected by clothing, and varying degrees of protection were also afforded those who remained indoors or bathed during the fall-out period. Most of the skin lesions were superficial and exhibited pigmentation; dry, scaly desquamation; and rapid healing with little pain. Some lesions were deeper, exhibiting wet desquamation, and a few became secondarily infected. Treatment was largely palliative except for use of antibiotics for secondarily infected lesions. Histopathological examination of lesions showed changes consistent with radiation damage. Bluish-brown pigmentation was noted in the fingernails and toenails of the dark-skinned people but not in the white Americans. Minimal amounts of radioactive material were detected in the urine. The internal deposition was insufficient to contribute significantly to the acute reaction, and it is believed there is no long-term hazard. Examinations conducted one year after the exposure revealed these people to be in generally good health. Slight depression of lymphocytes and platelets persisted. A few pigment aberrations and minimal atrophy remained at the site of the deeper skin lesions.

6. Sutton, R. L., Jr.: Transverse Band Pigmentation of Fingernails After X-Ray Therapy, *J. A. M. A.* 150:210 (Sept. 20) 1952.

RADIOIODINE TREATMENT OF EUTHYROID CARDIAC DISEASE

FOUR YEARS OF EXPERIENCE WITH TWO HUNDRED THIRTY-ONE PATIENTS

Henry L. Jaffe, M.D., Maurice H. Rosenfeld, M.D., Frederick W. Pobirs, M.D.

and

Laurence J. Stuppy, M.D., Los Angeles

Two hundred thirty-one euthyroid, seriously ill cardiac patients have been treated with radioactive iodine (I^{131}) since February, 1950, in the department of radiation therapy and the cardiac outpatient department of the Cedars of Lebanon Hospital in Los Angeles. Of

angina pectoris. Stuppy,⁸ Jaffe,⁴ Pobirs,⁸ and Rosenfeld⁸ reported upon 95 treated patients in November, 1951, and upon end-results in 100 patients in June, 1952.⁷ In 1952, Chapman⁸ described 23 treated cases. Serber and his group⁸ reported 24 cases in February, 1952. *Pharmacology and Therapeutics*, 1:1-10 (1952).