The Pathologic Effects of an Instantaneous Dose of Radiation**

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(Received for publication April 2, 1946)

The distinctive feature of the atomic bomb is the large amount of radiant energy that it produces. While this energy covers a wide range of the electromagnetic spectrum, its chief physiologic and pathologic effects may be divided into two groups: first, the effects of heat, producing primary thermal injury of the flash burn type, and secondary thermal injuries due to induced fires; second, the effects of short-wave radiation and neutrons, paralleling closely the effects familiar to us from the experimental studies of the biologic effects of x-rays. This radiant energy was produced in an instant. Security prevents statement as to the exact duration of time.

Of course, combined with and modifying and obscuring these effects are the more usual effects of the conventional types of bomb. Chief among these is air blast injury, almost always secondary, due to flying debris or impact against fixed structures.

In our studies of the atomic bomb effects at Nagasaki and Hiroshima, which were carried on under the direction of the Naval Medical Research Institute and the Naval Technical Mission to Japan, we concentrated particularly on the injuries due to radiation. For security reasons the type and quantity of this radiation cannot be discussed. Suffice it to say that radiation effects ranging from lethal to minimal were observed. We were very fortunate in our study to have the collaboration of the investigating group from the Manhattan District under Colonel Stafford L. Warren and the Joint U. S. Army Imperial Japanese Government Atomic Bomb Commission under Colonel A. W. Oughterson.

* This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the U. S. Navy. The opinions and views set forth in this article are those of the writer and are not to be considered as reflecting the policies of the Navy Department.

† Presidential address delivered at the 37th meeting of the American Association for Cancer Research, Inc., at Atlantic City, New Jersey, March 11, 1946.

As we studied our patients it became apparent that...
there was no segregation of types of injury among them, but that an individual might well be suffering from blast effect, thermal injury and radiation injury simultaneously. Of the 80,000 people who died at Hiroshima and 45,000 that died at Nagasaki, it is very difficult to say what proportion were killed by one or another type of energy. Our primary interest is in those persons who died as a result of short-wave or neutron irradiation. Since the biologic responses to these different types of ionizing radiation are essentially similar, they will be considered en masse.

The characteristic clinical course of those persons primarily suffering from radiation injury as result of the atomic bomb explosions may be divided into two stages. The immediate effects were manifested as weakness, malaise, fever and often death, and appeared usually within 48 hours, while the delayed effects manifested themselves in a variety of ways.

Unfortunately, the disorganization of the Japanese was so great that no adequate material exists to determine the exact nature of immediate effects. We may assume, however, that they parallel experimentally induced changes in animals and represent the syndrome of radiation sickness carried to an extreme degree. We may assume that there is little morphologic evidence other than leukopenia and loss of adrenal lipoid.

Our material on the delayed effects is much better. When one considers that most of these cases received total body radiation it becomes obvious that the chance of survival with a dose equivalent to 500 r of conventional x-ray radiation would be extremely unlikely. Consequently we must look for effects in those tissues that are known to be particularly radiosensitive. These are, of course, the blood, hematopoietic and lymphoid tissues (Fig. 1), the gonads; sensitive to appreciably lesser degree are the hair follicles. Of course many of the patients showed evidences of injury to the total organism of the radiation sickness type. In this group in addition to weakness, anorexia and weight loss, diarrhea was a prominent feature. Owing to the fact that the hygiene of the region was totally disrupted and both bacillary and amoebic dysenteries were prevalent, it was extremely difficult to determine the cause of this diarrhea.

We received excellent cooperation from the Japanese authorities in studying survivors. Over 800 were hospitalized by our group at the Omura Naval Hospital, and about 13,000 were made available to us for a casualty survey.

It was easy, in the cities and villages around Nagasaki and Hiroshima, to pick out the irradiated refugees by the characteristic flash burns which they presented and by the not infrequent occurrence of epilation (Fig. 2). When we left in late December, over four months after the bombing, some degree of regeneration of new downy hair was beginning to appear in a fair number of the epilated cases. Scalp hair was lost while that of eyebrows, beard, axillae and pubis persisted.

The effect on the blood can be readily followed by clinical manifestation as well as from a laboratory standpoint. There were three chief groups of symptom complexes due to damage to hematopoietic tissue. While the groups overlapped to some degree they were quite distinctive. The first was the leukopenic group in which infection and particularly Ludwig's angina was the outstanding manifestation. The great bulk of leukopenic deaths occurred during the first three weeks following the bombing. Judging from the studies of Japanese investigators, the leukocytes in the circulating blood were destroyed at the same time that the hematopoietic tissue was damaged, so that white blood cell counts as low as 200 per cu. mm. were found in the first few days.

From 3 to 5 weeks after the bombing a considerable number of hemorrhagic deaths occurred, associated with the thrombocytopenia induced by radiation damage to the megakaryocytes of the bone marrow. Although we have no data, it is fair to assume that the absence of hemorrhagic deaths in the early days suggests that the blood platelets in the circulation were not destroyed by the radiation and only as a low point was reached as result of deficiency in blood did hemorrhagic manifestation occur. These ranged from extensive ecchymoses to purpuric patches and small petechiae. Some cases had massive hemorrhages from various body orifices. At autopsy it was not infrequent to find hemorrhage filling the pelvis of the kidney; multiple mucosal hemorrhages of the stomach or elsewhere in the gastrointestinal tract; multiple diffuse hemorrhages in the meninges or even in cerebral substance.

Those with serious bone marrow damage who weathered the first few weeks showed later anemic manifestations with red blood cell counts in some instances dropping to one million or below. The bone marrow as shown by sternal marrow biopsy frequently was extremely hyperplastic, while others were aplastic (Fig. 3). In relation to the aplastic group there was one point of interest. We commonly think of red marrow as being actively hematopoietic in contrast to the yellow fatty marrow. In many of these cases the aplastic marrow was red but its redness was due only to sinusoidal hyperemia and there was no appreciable formation of blood elements. At times the marrow was so depleted that little but reticulo-endothelial cells appeared.

The gonadal effect was much more prominent in case of the testis than of the ovary as would be suspected. Although a random sample of high school girls who previously had been menstruating regularly
Fig. 1.—Spleen showing atrophy of lymphoid tissue. Hematoxylin-eosin stain. Mag. X 35.
Fig. 2.—Eupilation following atomic bomb explosion at Nagasaki. Official U. S. Navy photograph.
Fig. 3.—Partial regeneration of hematopoietic bone marrow. Hematoxylin-eosin stain. Mag. X 50.
Fig. 4.—Testis showing atrophy of germinal epithelium. Hematoxylin-eosin stain. Mag. X 50.
showed suppression of menstruation in a considerable number, the probability of psychic shock and malnutrition must be weighed as well as direct ovarian effect. Ova were present in ovaries in many cases; only occasionally in women of the child-bearing age did atrophy occur. However, it was relatively infrequent to find a recent corpus hemorrhagicum or corpus luteum. In the testis, on the other hand, in those individuals who had been exposed to appreciable amounts of radiation, atrophy of the germinal epithelium was striking (Fig. 4). Spermatogenesis was suppressed and frequently the tubules were represented only by Sertoli cells and thickened membranes. The interstitial cells were not damaged.

The question of injury from residual radioactivity was of major importance. We were fortunate in locating a number of persons who had entered the bombed areas soon after the explosion and had remained there. None showed any deleterious effects.

In the forthcoming Crossroads Operation vital biologic data will be obtained, data that are essential to close in the gaps in our knowledge that exists as to the pathology in the periods shortly after the explosions. The total disorganization of the Japanese medical and reserve services following the bombings resulted in almost complete absence of information in the early phases.

We were also interested in therapy. The treatment given by the Japanese was utterly inadequate, as were their hospital facilities. Blood transfusions were not used. Little more than supportive treatment was given. Burns were treated with oily dressings or picric acid. Repeated blood transfusions, penicillin to control infection during the leukopenic period should have materially reduced the number of deaths.

The hematopoietic tissue attempts to regenerate, sometimes to such a degree that a pseudoleukemic pattern appears in the sternal marrow biopsy. Interestingly enough, one case of monocytic leukemia developed in a young man in November, only a few weeks after he had been discharged from a Japanese hospital where he was under treatment for leukopenia and anemia.

I am quite sure it will be necessary to follow the populations of Hiroshima and Nagasaki for many years to determine the long range results in production of blood dyscrasias, in alteration of resistance to disease and in genetic changes induced by this instantaneous dose of radiation.
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