Genetic Effects of the Atomic Bombs in Hiroshima and Nagasaki

Genetics Conference, Committee on Atomic Casualties, National Research Council

The Atomic Energy Commission recently formally signified its intention of supporting long-range medical studies of the survivors of the atomic bombings in Japan, to be conducted by the Committee on Atomic Casualties of the National Research Council. One aspect of these studies will concern the much-discussed potential genetic effects of the bombs. The background of this program begins shortly after Japan's surrender, when a Joint Army-Navy Commission made extensive observations in Hiroshima and Nagasaki on the survivors of the bombings. At the conclusion of the Commission's work its chairman, Col. A. W. Oughterson, M.C., AUS, recommended to the Surgeon General of the Army that the Council be requested to undertake a long-range study of the medical and biological effects of the atomic bomb, and this recommendation was transmitted by Surgeon Gen. Norman T. Kirk to Lewis H. Weed, chairman of the Division of Medical Sciences. As a result, in June 1946 a conference group was convened by the Council, and in November, following its recommendation, a five-man commission composed of representatives of the Council, the Army, and the Navy left for Japan for the purpose of determining the current status of Japanese work on atomic bomb casualties, evaluating the feasibility of American participation in continued research on these casualties, and indicating the lines along which such studies should proceed. This commission, known as the Atomic Bomb Casualty Commission and composed of Austin Brues, Paul S. Henshaw, Lt. Melvin Block, M.C., AUS, Lt. James V. Neel, M.C., AUS, and Lt. (j.g.) Frederick Ullrich, (MC) USNR, submitted a report of its findings to the Council in January 1947.

The June 1946 conference group had recommended that appropriate action be taken to obtain a Presidential Directive authorizing the National Research Council to initiate a long range study of the atomic bomb effects. This Directive was issued at the request of the Secretary of the Navy, James T. Forrestal, in November 1946, and on its authority the Council, in January 1947, established a Committee on Atomic Casualties, composed of Thomas M. Rivers (chairman), George W. Beadle, Detlev W. Bronk, Austin Brues, George M. Lyon, C. P. Rhoads, Shields Warren, Stafford L. Warren, George H. Whipple, and Raymond E. Zirkle.

The potential genetic effects of the atomic bomb were apparent to all interested students from the day the first bomb was dropped—in fact, to some, well before that time. A consideration of genetic studies was one facet of the work of the Atomic Bomb Casualty Commission, and a section of its January 1947 report was devoted to this subject. This phase of the work was to a large extent the responsibility of Lt. James V. Neel.

On June 24, 1947, the Committee on Atomic Casualties arranged a conference on the potential genetic effects of the atomic bombs. At this meeting, which was attended by George W. Beadle (chairman), Donald R. Charles, Charles H. Danforth, Herman J. Muller, Laurence H. Snyder, and Lt. Neel, the latter submitted a report of preliminary genetic studies, based on his observations in Japan during the preceding six months. Following a thorough appraisal of the problem, the conference voted to recommend to the Committee on Atomic Casualties that a program be undertaken in Japan along the lines sketched out in the Neel report. This recommendation was accepted at a meeting of the Committee on June 26, 1947. The conference also recommended that a statement be prepared, briefly summarizing the current status of the problem. This statement follows.

WHETHER THE ATOMIC BOMBS dropped on Hiroshima and Nagasaki will have detectable genetic effects on the Japanese is a question of widespread interest. The purpose of the present note is to show briefly that (1) many difficulties beset any attempt to obtain a valid answer to this question and (2) even after a long-term study, such as that outlined below, it still may not be possible to determine just how much genetic damage was done at Hiroshima and Nagasaki.

This memorandum is essentially a partial summary of the material presented by Lt. James V. Neel at the meeting of the Conference on Genetics convened by the Committee on Atomic Casualties of the National Research Council on June 24, 1947, but with certain additional considerations which grew out of the deliberations of the Conference.

It must first be recognized that, inasmuch as the majority of mutations occurring in animals are recessive, only the relatively small proportion of mutations which are dominants may be expected to show effects in the first postbomb generation. The potential range in their effects is very wide. Dominant mutations with large, clear-cut manifestations can be expected to be much rarer than those with smaller, but possibly quite significant, effects on bodily dimensions, life span, etc. But the detection of these latter is a matter of great difficulty with present techniques. For practical considerations investigation will have to be concentrated chiefly on the class with such large effects as may lead to stillbirths, to live births with gross external abnormality, or to internal defects causing death or serious illness in infancy.

Since there is no general agreement as to what proportion of cases of abnormal fetal development is genetically determined, and what proportion is due to nongenetic factors, an increased incidence of morphologically abnormal fetuses following irradiation may not be used as an index of the frequency of genetic change until the non-

genetic effects of this irradiation on the reproductive history of the mother have been determined. This point will be very difficult to evaluate.

It is obvious that in this case the approach to the problem of genetic effects is the statistical one. It is unlikely that any individual and specific pathology in a post-irradiation generation can ever be attributed with certainty to the effects of the bomb, but if there is a definite increase in the occurrence of abortions, miscarriages, stillbirths, and abnormal products of conception, one may surmise that this is related to the bombing—although some of the effects need not necessarily be genetic. Appropriate control studies in other Japanese cities are therefore of the utmost importance.

The survivors of the bombing received amounts of irradiation ranging from negligible to just short of lethal. It is impossible to say on a priori grounds whether an adequate number of people absorbed sufficient radiation to produce enough dominant mutations to result in detectable effects. However, comparison of this situation with the experimental data on infrahuman material suggests that these effects, if detectable, will be small. The median lethal dose for whole body irradiation in man is probably in the neighborhood of 500 Roentgen units (Shields Warren. *Physiol. Rev.*, 1944, **24,** 225–238). It is likely that many individuals in Hiroshima and Nagasaki who received high but sublethal doses of irradiation sustained other injuries which, in combination with the radiation damage, resulted in death. Thus, the mean radiation dose received by the surviving population will be lower than expected from a consideration of the median lethal dose alone. In terms of radiation genetics this is a small exposure, expected from data on animals to produce a frequency of dominant mutations which would increase the normal frequency of abnormal offspring by so small a proportion as to be difficult to demonstrate. Large-scale studies, utilizing all available material, plus accurate vital statistics, are thus necessary if data of value are to be obtained. In this connection it is important to bear in mind that the available children born to parents who received significant amounts of irradiation will probably not exceed 12,000 or 13,000 within the next 10 years.

The Japanese had recognized the importance of genetic studies and, under great difficulties, were organizing a program in Hiroshima when the Atomic Bomb Casualty Commission arrived. They had planned to compare the present and future frequency of abnormal births in Hiroshima with the frequencies reported in their medical literature and vital statistics during the prewar years. But it is by no means sure either that the prewar figures were sufficiently accurate or that the present reporting of vital statistics would be wholly effective in detecting rare effects of the atomic bomb radiations. It cannot be too strongly emphasized that there is at present absolutely no reliable evidence on which to base any opinion concerning the absolute or relative frequency of congenital abnormalities among children being born in Hiroshima and Nagasaki. Unfortunately, a good deal of misinformation is currently in circulation.

Two independent programs, one Japanese and one American, would involve needless duplication of effort. A joint undertaking is therefore indicated. In view of the fact that the Japanese are actively attempting to initiate genetic studies, it seems that any American efforts which may materialize should contemplate cooperation with the Japanese in an attempt to ensure an efficient and satisfactory program. The Neel report contains the following seven specific recommendations as to the organization of a program:

(1) Organize, in Hiroshima, Nagasaki, and a control area or areas, a modified system of pregnancy registration, this to include the irradiation history of the parents.

(2) Obtain as complete information as possible on the outcome of each registered pregnancy.

(3) Follow up each report of an abnormal termination of pregnancy or a congenital malformation with detailed family studies.

(4) Develop a system of checking on the completeness and accuracy of registration of births and deaths, such as requiring at intervals dual registration by both the family and the obstetrician or midwife.

(5) Conduct these studies on a sufficiently large scale that the results will have statistical significance.

(6) Integrate this program with a system of periodic examination of the offspring of irradiated persons and with careful death certification, so that genetic effects not apparent at birth but detected subsequently may be recorded. In particular, causes of infant mortality should be accurately recorded.

(7) Place this program in competent Japanese hands, through the Japanese Government, with only enough American supervision and cooperation, including supplies, to facilitate a successful program.

This program must extend over a period of 10–20 years before a significant amount of data can be accumulated, and quite possibly an even longer period of study, extending to the second and subsequent generations, will be indicated.

Certain practical limitations of the program may be considered at this point. The most difficult problem will be to obtain the necessary completeness of reporting. This will require constant effort, a wide educational program, and frequent cross-checks. Congenital malformations occurring within Japanese families may sometimes not be reported. This is perhaps more likely to occur in Japan than in this country, because probably less than 10 per cent of Japanese births occur in hospitals as these are defined in the United States. To what extent stillbirths and malformations occurring outside a hospital will be recorded depends on the vigor with which the problem is pursued. It will be difficult to get evenly matched teams of investigators for bombed and control areas. Furthermore, once people living in Hiroshima and

Nagasaki learn that stillbirths and malformations may possibly be attributed to the effects of the bomb, they will probably lose some of their reluctance to report such matters, whereas this will not be the case in a control area.

Japan is now a defeated and occupied country, under severe postwar stress, whose people have a very different psychology from our own. A program such as that under consideration will proceed much more slowly there than it would in this country.

In order to reduce the possibility that a negative result of the investigation on Japanese material be interpreted by the medical and lay public as meaning that important genetic effects were not produced, it is essential that a comparable effort be expended in experimentation on other mammalian material, in which genetic effects of different kinds can much more readily be brought to light. In this way it should be possible to throw light upon the proportion of the total genetic effects produced by the radiation that would have been detectable by the methods used in the investigation on the human material, and the serious danger of misinterpretation of the latter results would be minimized.

Recognizing the difficulties briefly touched upon in the foregoing paragraphs, the Conference on Genetics voted unanimously to record the following expression of its attitude toward the genetic program: "Although there is every reason to infer that genetic effects can be produced and have been produced in man by atomic radiation, nevertheless the conference wishes to make it clear that it cannot guarantee significant results from this or any other study on the Japanese material. In contrast to laboratory data, this material is too much influenced by extraneous variables and too little adapted to disclosing genetic effects. In spite of these facts, the conference feels that this unique possibility for demonstrating genetic effects caused by atomic radiation should not be lost."

An Auditory Afterimage?

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FOR THOSE WHO LIKE TO EMPHASIZE THE similarities between our different sense modalities, the absence of auditory afterimages has been a persistent puzzle, a blank in the table of analogies which can be drawn between vision and audition. There is, of course, tinnitus—that annoying ringing in the ears that often follows exposure to deafening sounds. But tinnitus may last for hours, is often pathological in origin, and resembles "spots before the eyes" more than a true afterimage. Tinnitus excluded, therefore, the story of unrewarded searching (*1*) seems to justify the conclusion that auditory afterimages do not exist.

The error of such a conclusion can be demonstrated with the help of a pulse generator and a pair of earphones. The generator is used to produce a train of rectangular voltage pulses at a rate of about 100 pulses per second. [The rectangular pulses used in this experiment contain all harmonics of the fundamental pulse repetition frequency at approximately equal amplitude over the frequency range transmitted by the earphones (cutoff around 6,500 cps).] The earphones transduce the voltage pulses to acoustical pulses, and the listener is allowed to hear this buzzing sound at a high intensity for one or two minutes. When the earphones are removed, there is a striking change in the timbre of such familiar sounds as a handclap, a typewriter, the voice, etc. A peculiar metallic quality seems to be added to the sounds. Listeners have described the sounds as "jangly," "twangy," "like a rasping file," or "like two pieces of iron being rubbed together." The aftereffect of the pulses is transient, and in a few seconds the sounds regain their normal quality.

We have had no trouble in demonstrating this aftereffect to subjects with normal hearing. It has been experienced in reverberant and anechoic rooms, with test noises produced in the room, over a loud-speaker, or in headphones. Phonographically recorded handclaps, sibilant consonants, the sound of scraping sandpaper, and typewriter noises seem to work about as well as the original sounds themselves.

Several questions immediately suggest themselves. What characteristics of the exposure stimulus are necessary to produce the effect? What kind of test stimuli can be used? What is the quality and duration of the effect?

Exposure to intense random noise—a hissing sound—is ineffective in producing the aftereffect. Random noise interrupted at regular intervals to give a train of 150 bursts of noise per second was also a failure. Nor did a combination of 11 oscillators producing frequencies not in harmonic relation elicit the aftereffect. Very loud pure tones of low frequency may evoke the phenomenon for some listeners. A square wave elicits the aftereffect but is much less impressive than the pulses. Pulses produce

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