IONIZING RADIATIONS AND LEUKAEMIA

by

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ABSTRACT

In this article an attempt has been made to correlate the incidence of leukaemia with the exposure to ionizing radiation. The available data have been analysed both qualitatively and quantitatively. The constant probability of leukaemia per individual per rem per year strongly indicates the existence of approximately linear relationship, at least at low levels of exposure. Important conclusions arrived at are—(*a*) some of the leukaemia cases can be attributed to background radiation, and (*b*) any exposure, however small it may be, must increase the risk of the disease developing.

Introduction

Recently physicists and radiation health specialists have sounded alarm regarding delayed effects on the human race of exposure to various ionizing radiations. There is confusion in public mind due to much publicised conflicting statements issued by different authorities. The purpose of this communication is to examine evidences for the induction of leukaemia in man by ionizing radiation. The study has been mainly inspired by the apparent steep rise in the incidence of the disease in different parts of the world. The available data have been analyzed to see if there exists any relationship between the dose and the incidence of the disease. Before touching the other aspects it will be appropriate to know what is 'leukaemia'.

Radiation exposure and leukaemia

Leukaemia is an unrestrained overgrowth of tissue normally forming white blood cells. Defined in this manner the disease is fundamentally a disturbance in the formation of leukocytes and thus may be termed as blood cancer of white cells. With this knowledge in mind we can now turn to the figures of incidence of leukaemia among the survivors of the atomic bomb bursts over Hiroshima and Nagasaki. It was observed that by the end of 1954 there had been nearly a five-fold increase in the number of cases occurring among the survivors in comparison with the number that might have been expected from the general mortality data for Japan.

In another survey the case records were examined of 13,352 patients presumed to have had ankylosing spondylitis and who had had X-ray treatment. A diagnosis of leukaemia was recorded on the death certificates of 28 of the patients who had died by December 1955, whereas the expected number is 2·9. In contrast no case of leukaemia was found among 399 pensioned men with spondylitis who had not had X-ray treatment.

1,400 individuals were traced who had been irradiated in their infancy for enlarged thymus glands. As a control 1795 unirradiated siblings were also traced. Among the irradiated persons there were 8 cases of leukaemia while there was none in the control group. The calculated number of cases that would have been expected in a sample of comparable size and age from the general pupulation was 0·6.

Lastly comes the number of reports suggesting that mortality from leukaemia among radiologists and other associated workers is unusually high. They suffer an approximately nine fold increase in their death rate from leukaemia in comparison with other physicians. Thus from the evidence of Japan's atomic bomb casualties, the survey of patients irradiated for ankylosing spondylitis and apparently high death rate among the radiologists, it must be accepted that ionizing radiations are leukaemogenic. Population surveys showed that incidence of leukaemia was higher in those who had been irradiated though the part played, if any, by diagnostic and background irradiation, were difficult to assess.

Thus, the above facts show the intimate relationship between radiation and genesis of leukaemia. The nature of the relationship between the incidence of leukaemia and the dose of radiation and an understanding of the scale of risk involved remain to be discovered. It is also to be determined if there is any evidence of threshold dose below which no increase in the incidence of the disease will be produced. Although the exact relationship between the incidence of leukaemia and the dose of radiation has not been established beyond doubt there is some convincing evidence in support that the probability of the incidence of the disease is directly proportional to the intensity of the exposure.

Dose response relationship

First indication that a dose response relationship may exist comes by the progressive manner in which the incidence of leukaemia among the survivors of Hiroshima decreases the farther they were situated from the ground zero at the time of explosion.

TABLE I

Incidence of Leukaemia among the combined exposed population of Hiroshima and Nagasaki by distance from hypocenter

(W. M. Court Brown)

Zone	Distance from hypocenter (meters)	Estimated population of exposed survivors	Number of confirmed cases of leukaemia	Percentage of leukaemia
A	0—999	1,870	18	0·96
B	000—1499	13,730	41	0·30
C	500—1999	23,060	10	0·043
D	2000 & over	156,400	26	0·017

The affected area has been divided into four zones (A, B, C and D). The Zone A extends from hypocenter to a distance of 999 metres, while the extension of Zone B is from 1000 to 1499 metres. C covers an area from 1500 to 1999 metres. The distance of zone D is 2000 metres and over. Against each zone the estimated exposed survivors and the number of confirmed cases of leukaemia occurred in that zone are noted. We find that as we proceed from the hypocenter the dose decreased and so do the percentage of the decrease as has been shown in the last column of the table. Here the calculation of dose is a bit difficult, because the parameters include the complete knowledge of energy spectrum and relative biological effectiveness of neutrons which are not easily computable.

That the relationship may be linear at least over lower levels of doses was shown by the study of patients irradiated for ankylosing spondylitis conceduted by Court Brown and Doll, and to some extent by the exposed survivors at Hiroshima and Nagasaki. Though the best fitting curve is concave upwards, the lower points may well lie on a straight line. This data provides no evidence for threshold dose in induction of leukaemia.

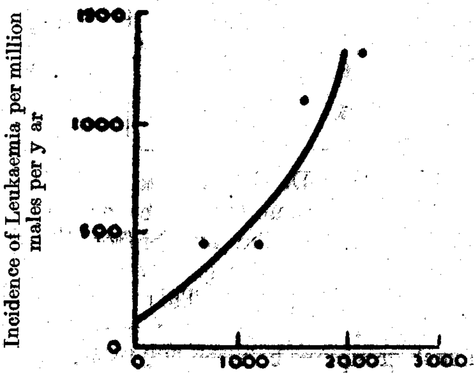

FIG. 1: Estimated average meximum dose in r [Court Brown & Doll][2].

TABLE II

Incidence of Leukaemia per year among the combined exposed population of Hiroshima and Nagasaki in relation to dose of Radiation (Lewis)[3]

Zone	Average maximum dose (rem)	Incidence of leukaemia per million per year	Incidence of radiation induced leukaemia per million/year	Probability of leukaemia per individual per rem, per year
A	1300	1200	1179	$0{\cdot}9\times10^{-6}$
B	500	390	369	$0{\cdot}7\times10^{-6}$
C	50	56	35	$0{\cdot}7\times10^{-6}$
D	5	21		

TABLE III

Incidence of Leukaemia among ankylosing spondylitis patients receiving different doses of radiation (X-rays)

(Court Brown and Doll)[2]

Maximum dose to spinal marrow (r)	Estimated average maximum dose (r)	Number of males developing leukaemia	Crude incidence per million males per year	Incidence of radiation induced leukaemia per million males per year	Probability of liaukaemp for individual per r (to spinal marrow) per year
0			50		
Under 500		2	220	170	
500—999	750	8	410	360	$0{\cdot}5\times10^{-6}$
1000—1499	1250	8	420	370	$0{\cdot}3\times10^{-6}$
1500—1999	1750	8	1130	1080	$0{\cdot}6\times10^{-6}$
2000—2749	2375	6	1300	1250	$0{\cdot}5\times10^{-6}$
2750 and more		5	1760		

In their study Court Brown & Doll[2] estimated the incidence of leukaemia in a comparable group of unirradiated normal males as 50 cases/million individuals/year. Substraction of this expected number from the observed incidence of leukaemia per year in irradiated patients gives an estimate of the incidence of the radiation induced leukaemia/per year. This calculation has been carried out for each of the groupings of leukaemia cases according to the amount of treatment. For each of such groupings between 500 to 2750 roentgens an average maximum dose to the spinal marrow is taken as the midpoint of the dose. By dividing the calculated incidence of radiation induced leukaemia by the respective average maximum dose a set of four minimum estimates of the probability of leukaemia per individual per roentgen to spinal marrow per year is calculated. The same type of calculations were done in Table III considering Zone D as control zone. The striking feature of these Tables is that the probability of leukaemia per individual per rad per year is nearly constant over a rather wide range of doses. This is a presumptive evidence that the relationship between the incidence of induced leukaemia and dose of radiation is either linear or approximately linear (Witts)[4].

Conclusion

Thus the above facts show the linear relationship at least at the lower levels and the non-threshold nature of the dose response relationship. This postulate has two important implications. Firstly it follows that some of the leukaemia cases can be attributed to natural background (Mazumdar and Nagaratnam)[5], and secondly any exposure to radiation over and above that from the natural background, however small, must increase the risk of the disease developing.

One consequence of the increasing use of X-rays and nuclear radiations in medicine, science and industry is that human beings are now exposed to a greater dose of ionizing radiation than any other time in the past. What has been said about, it can now be accepted without reserve that these ionizing radiations are leukaemogenic. Further, as it is generally believed that nuclear age is here to stay, the population is liable to increased radiation exposure. Therefore, it is natural to ask, "Should we abandon the use of radiation?" The answer cannot be but a negative one. We cannot ignore the atomic energy even for peace time and for civil purposes, if we mean to maintain at least our present position in industrial, economic and scientific spheres. What we can do is to understand the full and ultimate consequences of this exposure and limit it at a level where we and those that come after us can reap maximum benefits of this new age. Our approach must be positive to promote the benefits of atomic energy as well as negative to prevent damage to man and his environment. This can be achieved to some extent, by keeping the fractionated exposure well below the permissible dose, *i.e*, a dose of ionizing radiation which in the light of the present knowledge is not expected to cause appreciable body injury.

If we strictly adhere to the recommendations of ICRP the hazards due to ionizing radiation can be kept to its minimum. The exact statement runs like this. The maximum permissible accumulated dose in rems at any stage, is equal to 5 times the number of years beyond age 18 provided no annual increment exceeds 15 rems. Thus the accumulated Maximum Permissible Dose (MPD)= $5(N\text{-}18)$ rems where N is the age in years. This applies to all critical organs except the skin for which the value is double. Much has been done in this direction but there is ample scope for improvements.

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References

1. Court-Brown, W.M. *Brit. Med. Bull.* **14**, 168, 1958.
2. Court-Brown W.M. and R. Doll, *Medical Research Council Special Report Series No. 295* ( ).
3. Lewis, E. B. *Science*, **125**, 965, 1957.
4. Witts, L. J. *Brit. Med. Jour.* 1197, May 25, 1957.
5. Mazumdar S.K. and Nagaratnam A.—*Brit. Med. Jour.*, March 30, 1957.