Cosmic Radiation and Cancer

Frank H. J. Figge
University of Maryland Medical School, Baltimore

THE FACT THAT THE TOTAL ENERGY received by the earth as cosmic radiation is no greater than that of starlight has led many to assume that this could have little, if any, biological effect. Other considerations would indicate, however, that even radiation of such low intensity may have an influence on so-called spontaneous mutations and genetic effects in general. One must admit that these effects may occur with any amount of radiation, and even though the probability decreases with lower intensities, it must be remembered that all living things receive a continuous exposure throughout life. The term "lifetime exposure" is somewhat indefinite in this instance, since protoplasm is passed from one generation to another, and the biological effects of such low-intensity radiation may be additive over a period of several generations.

The theoretical speculations which have emphasized the low intensity and ignored or minimized the possibility of biological effects have probably served only to inhibit the search for such effects. There appears to be a need for less speculation and more experimental testing. This is especially true in the field of cancer research for, in spite of the attractive nature of such investigations, the writer was unable to find a single reference involving the experimental evaluation of the possible influence of cosmic radiation on carcinogenesis. The technical difficulties involved in evaluating such an omnipresent factor may also have had a deterrent influence, for in order to obtain conclusive data on the influence which cosmic radiation may have in regulating cancer incidence, it would be necessary to study the induction of cancer with various agents in an environment free from cosmic radiation. This would require a chamber with lead roof at least 49 feet thick or laboratory space 700 feet underground. Since the former was regarded as impractical and the latter was impossible with the funds available, a simple substitute procedure was devised.

It was hoped that the results of this preliminary experiment would indicate whether it would be worth while to investigate this problem more extensively. The experiment[1] involved the attempt to intensify cosmic radiation effects by means of various combinations of lead plates and the comparison of the rate of carcinogenesis in mice receiving the intensified cosmic radiation with the rate of carcinogenesis in mice receiving non-intensified (normal) cosmic radiation. The rate of induction of cancer in the mice kept under the lead plates was found to be consistently and definitely higher than that in the controls.

One hundred and eighty-four male mice[2] of the C_3H strain were injected with 0.25 mg. of methylcholanthrene in sesame oil and distributed equally in 8 aluminum cages, 11 x 11 x 4 inches. They were given food and water ad libitum.

Lead plates ¼ inch thick were placed over 5 of the 8 cages. Lead of this thickness was chosen because it had been shown by other investigators (*3*) that the optimum thickness for the production of small cosmic radiation showers was 0.6 cm. while the optimum thickness for the production of large showers was approximately 2 cm. Four of the cages were, therefore, covered with only one sheet of lead while two lead sheets were placed over the fifth. Cage 1, without a lead plate, and Cage 2, with one lead plate, were placed on the top shelf of a metal rack on the fifth floor of a six-story concrete steel building. Cages 3 and 4, a similar pair, were placed on the top shelf of a metal rack on the first floor of the same building. Cages 5 and 6, with one lead plate on each, were arranged on the second and third shelves from the top of the rack vertically below Cage 4. Cage 7, with two lead-plate covers, was placed vertically below Cages 4, 5, and 6. Cage 8, without a lead cover, was placed 4 inches south of Cage 7 and vertically below Cage 3. Cage 8, although not vertically below Cages 4 and 5, was near enough to have received some scattered cosmic ray showers from the lead plates over the latter cages. It was also beneath three iron shelves of the rack. No data could be found on cosmic ray showers in iron, but these probably would occur. Both of these unanticipated circumstances would, theoretically, have had a tendency to increase the intensity of cosmic radiation in control Cage 8 as compared to that in the other two control cages (1 and 3), which were on the top shelves. The metal shelves were painted on each side of the cages so that the position of the cages was maintained relatively constant throughout the 5-month period of observation.

The results were tabulated (see Table 1) using the method of Shimkin and Andervont (*2*). It will be noted that 5 cages contained one or two mice less than 23. In these instances, the mice died or disappeared before the eighth week and were not included in the tabulation. The mice in the three control cages without lead plates

[1] This work was supported by grants from the Anna Fuller Fund and the Donner Foundation.

[2] These mice were progeny of mice obtained from L. C. Strong, of New Haven, Connecticut, several years ago.

are placed together in the table. The numbers in vertical columns below the time in weeks represent the number of new tumors found at each weekly examination. It is apparent that the tumors in the controls developed at a slower rate than in the mice covered with lead plates. It may also be noted that in the lead-plate-covered cages a relatively large number of tumors was recorded on the earliest week tabulated. With a dose of 0.25 mg. of methylcholanthrene, one would expect the first tumor to appear at the seventh or eighth week. It is, therefore, unfortunate that the weekly examinations were not started at an earlier date, because it seems probable that some of the tumors listed under the sixth week may have been palpable earlier. Even with this handicap, the average latent period for the lead-plate-covered mice was only 8.5 weeks as compared with 11.3 weeks for the controls. The 50 per cent latent period—the average latent period for the first 50 per cent of the animals to develop tumors—was 9.6 for the controls and 6.7 weeks for the lead-plate-covered mice.

In experiments of this kind, where practically all the animals eventually develop tumors, one is not concerned with the percentage of animals developing tumors but primarily with the rate of tumor development as expressed in average latent periods.

Only 2 of the 67 controls and 1 of the 111 lead-covered mice did not develop tumors within the period of 22 weeks. These mice had to be excluded from data on the average latent period calculations. However, the carcinogenic index, derived from a formula suggested by Iball (*1*), takes these animals into account. Iball's formula is $\frac{p}{t} \times 100$, where p is the per cent of mice developing tumors and t is the average latent period of the whole group in days. Higher numbers thus indicate more potent carcinogenic stimuli. The index for the control group was 123, while for the lead-plate-covered animals it was 168.

None of these calculations or sets of numbers appears to do justice to the acceleration of the rate of tumor formation which was observed in the early part of the experiment. The remarkable difference between controls and experimental animals which was apparent early in the experiment is indicated by the total number of mice with tumors in each cage at the end of 10 weeks. Control Cage 8 contained 10 mice with tumors at this time. The lowest number of tumors in any of the lead-plate-covered cages was 14. Cage 8, however, was the control cage beneath three metal shelves and may have received scattered cosmic radiation showers from the lead over Cages 4 and 5. Even with the inclusion of this cage in the calculations at the end of 10 weeks, only 22 or 33 per cent of the 66 control mice had developed tumors while 75 per cent of the 110 lead-covered mice had developed tumors which grew progressively larger.

TABLE 1

INFLUENCE OF LEAD-PLATE CAGE COVERS (INCREASED COSMIC RADIATION INTENSITY) ON RATE OF INDUCTION OF PALPABLE SUBCUTANEOUS TUMORS IN C_3H MALE MICE INJECTED WITH 0.25 MG. 20-METHYLCHOLANTHRENE

Cage	Lead plate	No. of mice	No. of tumors per week and time (wks.)																Non-tumor	No. tumors	Avg. latent period (wks.)	50% latent period	Carcino-genic index	Tumors (10 wks.)
			6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21						
1	0	22			1	1	2	6	6	2	3	1							0	22	11.7	10.5	123	4
3	0	22		1	3	1	2	1	5	2	4							1	2	20	11.7	9.5	111	8
8	0	23		1	4	1	4	5	5	2	1								0	23	10.6	9.	135	10
Total.....		67		2	8	3	8	12	16	6	8	1						1	2	65	11.3	9.6	123	22
2	1	22	7	4	3	2	2	3		1									0	22	8.1	6.4	177	18
4	1	22	4	4	2	2	2	2	3	2						1			0	22	9.5	7.	151	14
5	1	21	1	6	6	0	1	4	2	1									0	21	8.9	7.3	161	14
6	1	23	6	4	4	1	2	4	1	1									0	23	8.4	6.5	166	17
7	2	23	6	5	8	1	1	1											1	22	7.5	6.5	181	21
Total.....		111	24	23	23	6	8	14	6	5						1			1	110	8.5	6.7	168	84

It was of interest that the highest percentage of tumors occurred in Cage 7, which was covered with two lead plates instead of one and placed beneath three iron shelves and three other cages with lead-plate covers. Twenty-one of the 23, or 91 per cent, of the mice in this cage had developed tumors within 10 weeks. The thickness of lead directly over this cage was near the optimum for the production of larger cosmic ray showers. However, the total thickness of lead above the cage (5 cm.) was greater than the optimum. The cages had been arranged in this way in the hope of detecting a possible protective effect due to absorption, but, obviously, such an effect was not observed.

This remarkable increase in the rate of tumor induction brought about by placing lead plates 3 inches above methylcholanthrene-injected mice was thought to be related to the intensification of the cosmic radiation which results from the production of showers or bursts of ionizing radiations which occur when cosmic rays pass through thin sheets of metal. According to this hypothesis, carcinogenic substances such as methylcholanthrene induce cancer by converting some of the energy of cosmic radiation into carcinogenic stimuli; in other words, they sensitize the tissues to this kind of energy. It should be emphasized, however, that these experiments are only preliminary and that conclusive data can be derived only from experiments carried out in the absence of cosmic and other types of radiation.

If this general hypothesis continues to receive verification in future experiments, we may then begin to speculate on how to reduce the incidence of cancer by minimizing the effect of such radiation. The first reaction to such an hypothesis is that, if true, it would be futile to attempt to prevent cancer, because cosmic radiation cannot be avoided. In the first place, it may not be impossible to minimize the life exposure of such radiations by regulating building materials and other environmental factors which may modify the effective intensity of such radiation. Secondly, it has not been the intention of the writer to give the impression that cosmic radiation is the only factor involved in carcinogenesis. Other factors, such as the heavy metals and chemicals within tissues that absorb and modify such radiation, may thus offer possibilities for nullifying the effect of such radiations. Further, the radiation sensitivities of cells of the same and different individuals must vary within wide limits. It is possible that the variation in this respect controls the age at which cancer develops. As the life expectancy of a population increases, more and more people survive long enough to have their least resistant cells undergo malignant transformation as a result of the cumulative and additive effect of cosmic and other similar radiations. In addition to the increased length of the exposure time, we may be increasing the intensity factor by spending a high proportion of our life in buildings beneath roofs and other materials which serve to produce cosmic radiation showers and thus intensify the radiation effects. According to the results of this experiment, an individual whose least resistant cells could stand 50 years of unaltered radiation would conceivably develop cancer at 40 years or earlier if most of the lifetime had been spent in a building which served to intensify cosmic radiation. There are doubtless many other factors that would offer avenues of attack and investigation.

It is most important at present, however, to test this hypothesis further in a conclusive way by repeating these experiments in an environment free from cosmic radiation. Plans to do this are in progress. The prospect of a general exposure of large numbers of people to radiations of this type as a result of developments in the atomic energy field and the consequent popularization of the use of radioactive material provides an added incentive for hastening the investigation. It would seem in order to re-examine qualitatively and quantitatively the question of what is a safe dose of radiation. This should be determined not only for what we call normal cells but also for the occasional extremely radiation-sensitive cell and on the basis of a lifetime exposure.

References

1. Iball, J. *Amer. J. Cancer*, 1939, **35**, 188.
2. Shimkin, M. B., and Andervont, H. B. *J. nat. Cancer Inst.*, 1940, **1**, 57.
3. Starr, M. A. *Phys. Rev.*, 1938, **53**, 6.

Section Secretaries, AAAS, 1947

Mathematics (A): Raymond W. Brink, University of Minnesota, Minneapolis, Minnesota

Physics (B): Joseph C. Boyce, New York University, New York City

Chemistry (C): Ed. F. Degering, Purdue University, LaFayette, Indiana

Astronomy (D): Charles C. Wylie, University of Iowa, Iowa City, Iowa

Geology and Geography (E): George W. White, Ohio State University, Columbus, Ohio

Zoological Sciences (F): J. William Buchanan, Northwestern University, Evanston, Illinois

Botanical Sciences (G): George W. Martin, University of Iowa, Iowa City, Iowa

Anthropology (H): Marian W. Smith, Columbia University, New York City

Psychology (I): Harold E. Burtt, Ohio State University, Columbus, Ohio

Social and Economic Sciences (K): Successor to Albert E. Waugh (resigned) not yet announced.

History and Philosophy of Science (L): Raymond J. Seeger, Bureau of Ordnance, Navy Department, Washington, D. C.

Engineering (M): Frank D. Carvin, Newark College of Engineering, Newark, New Jersey

Medical Sciences (N): Malcolm H. Soule, University of Michigan, Ann Arbor, Michigan

Agriculture (O): Ernest E. DeTurk, University of Illinois, Urbana, Illinois

Education (Q): Dean A. Worcester, University of Nebraska, Lincoln, Nebraska