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MAXIMUM PERMISSIBLE EXPOSURE STANDARDS

By

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HISTORY OF IDEA OF TOLERANCE

Professor Roentgen discovered x-rays and investigated their characteristics in the latter part of 1895. In December of that year when he announced his discovery he told of his use of heavy metals to confine the newly discovered rays. By the end of January, 1896, Grubbé (1), who was building and experimenting with the new "x-ray" tubes, had developed a new and peculiar dermatitis of his hands which was determined to be due to the action of the roentgen rays. In a relatively short time it was found that x-rays produced many changes in people who worked with them and in animals used for experimental purposes. The injuries recorded include the following: erythematous dermatitis; smarting of the eyes; epilation of hair; constitutional symptoms such as tiredness, weakness, nausea, and vomiting; cancer in chronic x-ray ulcer; inhibition of bone growth; sterilization of male rabbits and guinea pigs; reduction of white blood cells; alteration of bone marrow, etc. By 1906 it had been found that most of the organs of the body could be altered by the x-rays.

While the need for protection against the ionizing radiation was obvious from the very beginning because of the injuries, the idea of trying to define an amount of exposure that could be tolerated by the human body was slow in developing. When the British X-Ray and Radium Protection Committee was formed in 1921, it discussed "establishing a maximum tolerance dose in terms of a specifiable and reproducible biological standard, and if possible expressing this biological standard in physical units." (2) In 1925, the problem was stated more explicitly by Mutscheller (3): "In order to be able to calculate the thickness of the protective shield there must be known the dose which an operator can for a prolonged period of time, tolerate without ultimately suffering injury". In an attempt to find such a "dose", he and others selected some people who had been occupationally exposed for some years without showing evidence of any deleterious effect. The amount of radiation to which these people had been exposed was then determined in retrospect. When the units used are translated into roentgens, the doses of different workers advocated as tolerable nearly all fall in the range of 0.1 to 0.2 r per day.

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Table I. Historical Landmarks: Radiation Injuries

1895	Discovery of x-rays	Roentgen
1896	Dermatitis of hands (January)	Grubbé
	Smarting of eyes (March)	Edison
	Epilation (April)	Daniel
1897	Constitutional symptoms	Walsh
1898	Paraplegia and spasmodic muscular contraction	Rodet and Bertin
1899	Degeneration of vascular endothelium	Gassman
1902	Cancer in x-ray ulcer	Frieben
1903	Bone growth inhibited	Perthes
	Sterilization produced	Albers-Schönberg
1904	Blood changes produced	Milchner and Mosse
	Leukopenia produced	Heineke
1906	Bone marrow changes demonstrated	Warthin
1912	Anemia found in two x-ray workers	Béclère

Table II. Historical Landmarks: Tolerance

1902	Rollins photographic indication of "safe" intensity
1921	British X-ray and Radium Protection Committee considered "establishing a maximum tolerance dose"
1925	First attempt at defining a "tolerance dose" by Mutscheller
1931	U.S. Advisory Committee on X-ray and Radium Protection recommends tolerance dose of 0.2 r per day
1934	International X-ray and Radium Committee endorses tolerance dose of 0.2 r per day
1936	U.S. Advisory Committee reduces tolerance dose to 0.1 r per day
1942	Metallurgical (Plutonium) Project adopts tolerance dose of 0.1 r per day
1950	International Commission on Radiological Protection recommends 0.3 r (air) per week = 0.05 r per day

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In 1931 the Advisory Committee on X-Ray and Radium Protection in the United States, and in 1934 the International Committee on X-Ray and Radium Protection both endorsed a tolerance dose of 0.2 r per day. In 1936 the United States Committee reduced the tolerance dose to 0.1 r per day, apparently for two reasons. First, the practice in Europe was to measure the dose on the skin with backscatter, whereas the practice in the United States was to measure the dose in air without backscatter. For the quality of radiations then available and the size of the fields involved in whole-body exposure, the agreement between 0.1 r in air and 0.2 r on the skin was very good. Second, by 1936 there were many more 200 kv x-ray machines in operation producing more penetrating radiations than before, and therefore a greater percentage of the surface dose was reaching the deeper organs. The main basis on which these tolerance doses were established was still the observation of those occupationally exposed.

Table III. Estimation of Tolerance Doses

Date	Author	Days for dose[a]	Calculated r per day[b]
1902	Rollins	(Photographic)	10
1925	Mutscheller	3	0.2
1925	Sievert	3	0.2
1926	Solomon	0.3	2.0
1927	Dutch Board	15.0	0.04
1928	Barclay and Cox	3.5	0.17
1928	Kaye	5	0.12
1931	Advisory Committee, USA	. .	0.2
1932	Failla (γ rays)	30.0	0.1
1932	Stenstrom	3.7	0.16
1936	Advisory Committee, USA	. .	0.1
1950	International Commission	. .	0.05[c]

[a] Number of days over which 1/1000 of an erythema dose may be received.

[b] Calculated on basis of erythema dose = 600 r, except Failla γ-ray erythema = 1800 γr.

[c] I.C.R.P. recommended 0.3 r (air) per week.

These "tolerance doses" were largely of interest to medical radiologists until 1942 when the first nuclear chain reacting pile started to operate. Since then, the matter of radiation protection and safe amounts of

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exposure have become of interest to the citizen in the street as well as to the many thousands of workers occupationally exposed. The need for more accurate information on which to base the tolerance dose became known to many scientists and money for experiments was made available. New tests of various kinds were tried in attempts to find the earliest possible changes as a result of exposure to ionizing radiations with the hope of avoiding more serious effects. Several changes were found, such as bilobed lymphocytes, changes in intracellular structure, more immature leucocytes, etc. The new problem that is not yet solved is: Are these minor changes of real significance to the individual.

PERMISSIBLE DOSE

The problem of how to define a permissible dose became more difficult than that of specifying what dose had been tolerated by a few people. After much deliberation the International Commission on Radiation Protection (4) defined permissible dose as "a dose of ionizing radiation that in the light of present knowledge is not expected to cause appreciable bodily injury to a person at any time during his lifetime". "Appreciable bodily injury" is defined as "any bodily injury or effect that a person would regard as being objectionable and/or competent medical authorities would regard as being deleterious to the health and well-being of the individual". In attempting to give a numerical value to the permissible dose the fact that man is and always has been bombarded by the ionizing cosmic rays and the radiations from the natural radioactive elements must be taken into consideration. These radiations provide a lower limit that is inescapable (about 10 mr per week).

The upper limit of permissible exposure must be based on the experience of radiation workers (mostly medical) over the past 60 years, and on such animal experiments as seem to be pertinent. There are several factors that make the interpretation of the human experience difficult. First, we have no real measure of the level of exposures prior to about 1942. Second, the long latent period between cause and effect - sometimes 25 years - makes it difficult to connect the two. Third, the biological variability of man is so great that some people known to have been overexposed have had no complications while others not known to have been overexposed have died of such conditions as leukemia that probably were due to such exposures as they suffered.

CRITICAL ORGANS

Reviewing the experiences of man and the results of animal experimentation revealed clearly that some organs of the body are critical to the problem of permissible exposure. The skin is the most exposed organ of the body. It was the first known to be injured and is the one most frequently involved. In the damaged skin cancer sometimes developes and causes the death of the person. By 1911 Hesse (5) was able to collect 94 cases of x-ray induced human tumors. The great length of time between cause and effect makes it difficult to set a permissible dose for the skin. Some doctors have developed detectable skin changes as long as 25 years after stopping the

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practice of exposing their hands while doing fluoroscopic work. By estimating the probable doses received by the skin of the hands of radiologists who showed no skin changes, the International Commission set 1500 mr per week as the maximum permissible dose when only the hands and forearms are exposed, as in handling radioisotopes. When the whole body is exposed, the limit for the skin is 300 mr.

It was recognized early in the study of radiation effects that any peripheral blood change was one of the first objective signs of the effect of x-rays. The hemopoietic tissue was thus established as a critical organ, the changes in which can be followed by studies of the peripheral blood. Before there were physical instruments capable of making reproducible measurements, blood counts were used as a biological monitor of exposure. In the period before personal and area monitoring was easily possible, many if not most radiologists, radium workers, and technicians were overexposed, as was demonstrated by the first few weeks of accurate monitoring in the radiology departments of many hospitals. Hence the reports of Carman and Miller in 1924 (6) and Goodfellow in 1935 (7) dealt with marked changes in the blood counts due to real overexposures. With the establishing of tolerance doses and the development of means to measure exposures, hematologists have had to search for new criteria of damage. Now, Ingram (8) and others have found bilobed lymphocytes in the blood of cyclotron workers presumably exposed to very little radiation. Helde and Wahlberg (9) have associated "changes" with very low exposures in very short times. Mayneord (10) has found "trends" in serial counts which he considers significant. The counts were done on workers exposed to below maximum permissible levels. On the other hand, Jacobson and co-workers (11) have found no correlation of counts with exposure at low levels, and Chamberlain, Turner, and Williams (12), while finding some evidence of detectable radiation effects on the average count of large groups of workers even at low levels of exposure, conclude that while cell counting does not give much of a measure of protection to the individual. What really is of concern is whether or not these changes are significant and can be considered as "appreciable bodily injury". The real danger that threatens is the development of leukemia, a universally fatal disease. March (13) found that 14 of 299 radiologists, 4.68 per cent, dying between 1928 and 1948 died of leukemia while only 334 of 65,922 non-radiologist physicians, 0.51 per cent, died of the disease. No one has detected the premonitory signs of leukemia. It is well established that many people who have had severe blood changes from radiation exposure have not developed leukemia. Experimental studies using animals have not helped us to date except to prove that in susceptible animals leukemia occurs earlier and more frequently following whole-body irradiation.

This author believes that while variations from the normal must be studied and all avenues of studying blood changes investigated, slight deviation from an admittedly unstable "normal" should not be classed as "appreciable bodily injury".

The International Commission on Radiological Protection has recommended that the permissible weekly dose in the blood forming organs be 300 mr. The lowering of this dose from essentially 600 mr per week was an attempt to be on the safe side and was not based on proof that 600 mr was too high a dose.

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The 300 mr is to be measured in the cubic centimeter that receives the highest dose. Many experiments suggest that the whole body must be exposed before leukemia becomes a problem.

Another tissue that has entered the list of critical tissues is the lens of the eye. It was known that treatments with large doses of x-rays could cause cataracts. Cataracts had not been seen as a result of long-continued small doses in radiologists. The fact that neutrons seem to have a highly selective action on the lens as evidenced by the changes in the eyes of some physicists working with them and of some of the Japanese exposed at Hiroshima and Nagasaki has placed the lens tissue in the critical list. However, it should be noted that exposure of adult animals to levels of x-ray dosage much above permissible levels did not produce cataracts. The International Commission decided to set 300 mr per week as the permissible dose, mainly to have a basis for dose from neutrons.

The effects of ionizing radiation on the gonads have been under investigation since at least 1903. However, except for human experience, little was known about the effects of long-term low level exposure until Lorenz and Heston started genetic experiments in 1941 (14). Exposure of the gonads to ionizing radiations can produce sterility, abnormal children in the first generation, and long-term genetic effects.

Recent surveys (15, 16) of radiologists and pathologists (as controls) show that the exposed group reported more offspring than the unexposed group. While many factors are involved, at least a loss of fertility of those occupationally exposed was not demonstrated. However, one of the surveys (15) revealed that while the normal offspring of the unexposed group constituted 83.23 per cent, the normal offspring of the exposed group constituted only 80.42 per cent. This difference is not large and should not be viewed with alarm. The other survey (16) showed that the amount of radiation received by radiologists under usual conditions does not have any very large effect on fetal and infant death rates in their children. The animal experiments of Lorenz showed that mice could live, breed, and die while exposed constantly to 1.1 r per day (14). Experiments reported from the University of Rochester (17) indicate that the sperm count of dogs was reduced by daily exposures of 0.5 r. Insofar as long-term genetic effects are concerned, those who are competent to discuss this subject are doing so at this Conference. In determining the permissible <u>occupational</u> exposure of a limited number of people, the genetic factor is not considered to be the determining one.

All things considered, insofar as the gonads are concerned, the recommendation of the International Committee "that exposure to radiation be kept at the lowest practicable level in all cases" should be followed. Based solely on considerations involving avoidance of damage to the exposed individual himself, the basic permissible weekly dose in the gonads was set at 300 mr.

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LIFESPAN

While the idea of critical organs is clearly a direct method of attack on the problem of permissible dose, it must be remembered that a shortening of the lifespan is possible without the development of any of the specific conditions mentioned above. This effect became apparent when large numbers of animals of selected strains were studied under conditions of prolonged daily low-level exposure to radiations. The average life of the group of animals was shorter when numbers of them developed anemia, leukemia, or cancer, but there appeared to be another factor of an indefinite character which many have chosen to call premature aging. In the case of man, the biological variation is so great that it is difficult if not impossible to establish any small difference in length of life that might exist between those who have been occupationally exposed to radiation and the rest of the population. In the case of animals it has been shown with certainty insofar as mice are concerned that exposure to daily doses of x-rays of slightly greater than 1 r cause a reduction in lifespan (14). Boche (17) has shown that the lifespan of the rat is definitely shortened by daily exposures of 0.5 r and probably 0.1 r, the exposures starting at the time of maturity. On the basis of such figures it was felt that for whole-body exposure the permissible dose should not exceed 0.05 r per day. Even this provides a factor of safety of only 2.

RECOVERY FROM INJURY AND PROTRACTION OF EXPOSURE

One of the biological facts that makes it difficult to establish permissible doses for long-term exposures is that recovery from radiation injury takes place in certain instances even while the radiation is continuing. Other changes produced by radiation are irreversible and no recovery takes place. There probably are injuries that show all gradations of response between the extremes of complete recovery and of no recovery. Enough facts with regard to these different rates of recovery are not yet known to allow the projection of the various reactions over the lifetime of man. It is known that some of the acute reactions to radiation take just as long in a mouse whose total life is from two to three years as in a man whose total life is about 70 years. Thus, it is not possible to simply multiply the time for certain reactions to occur in laboratory animals by factors relating their total life to man's total life.

Damaging events in the genes producing genetic change have been shown to be totally additive; that is, there is no recovery. The changes causing epilation in man have been shown to have little relation to the protraction of a given total dose over the period of a week, but there is some recovery in a period as long as a month. The reaction known as the erythema reaction of the skin requires about 50 per cent more radiation when given on two successive days than when given all at one time. The amount of radiation to produce a given weight loss in the mouse testis is the same whether given in one day or in five days (18). The amount of radiation required to kill 50 per cent of a group of mice increases with the intensity of the radiation and with the fractionation of the dose over days, weeks, or months. Henshaw (19), using mice, found that 51.6 r given at one session once each week was

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effective as judged by the LD_{50} at 18 weeks than when given in six daily sessions of 8.6 r each week.

These studies have been cited to emphasize the problem of deciding whether the permissible dose should be stated as a certain dose per second, per minute, per hour, per week, per month, per year, or per lifetime. The maximum permissible dose of radiation to the whole body is stated as being 0.3 r per week. If an individual were exposed to the maximum amount for 50 weeks of each year for the period from 25 to 65 years of age, he would receive a total of 600 r in the forty years. If subjected to 600 r in one day, he would probably die very quickly. If exposed to 15 r in one day each year for 40 years, what would happen is not known because of lack of experience with animals or people exposed in that way. There is experience with daily or almost daily exposures of radiologists, physicists, and technicians. A decision had to be made on somewhat arbitrary grounds as to the length of time over which a permissible dose could be averaged no matter how it was received. The International Commission decided on the week as the unit of time. From the point of view of occupational exposure it is more convenient to monitor exposures each week than each day, and experience to date indicates little difference of biological effect at such low levels between daily and weekly distribution of dose. The Commission defined the permissible weekly dose as "a dose of ionizing radiation accumulated in one week of such magnitude that, in the light of present knowledge, exposure at this weekly rate for an indefinite period of time is not expected to cause appreciable bodily injury to a person at any time in his lifetime. One week as used here is any seven consecutive days". Inferred in this definition is the belief that such a dose could be received in a matter of a few minutes during the week or spread over the whole seven days. No one has sufficient information as yet to know whether such a dose would still be "permissible" if it were received in a small fraction of a second.

RELATIVE BIOLOGICAL EFFECTIVENESS

The Relative Biological Effectiveness (RBE) of radiations of various types and energies is a necessary factor in determining the permissible dose of radiation for other than x-rays up to 250 kv. The biological effectiveness of a radiation is the relationship between a given biological reaction and the dose of radiation required to produce it. Since for both man and animals the effects of x-rays up to 250 kv are known with greater precision than for other types, the biological effectiveness of such rays is arbitrarily established as the base line. The relative biological effectiveness of a given radiation is the factor that relates its biological effectiveness to that of 250 kv x-rays.

Since the biological effectiveness is known to be related to the density of ionization along the paths of the ionizing particles, this characteristic can be used to determine the RBE. The linear ion density per unit of path is called the specific ionization. Various combinations of photon or particle radiations with differing energies may have similar specific ionizations. Thus, a very high energy proton may have the same specific ionization as a low energy electron. It is thus better to relate the RBE to the specific

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Table IV. Effects of Small Weekly Doses of Ionizing Radiation

Dose (mr/week)		Effect Produced	Reported by
100	Man	Questionable slight decrease of mean total white cell count of group.	Mayneord
100	Man	Total number of blood abnormalities (group av.) increased.	Sievert
500	Dog	Sperm count slightly reduced.	Boche
500	Rat	Leukemia induced.	Barnett
600	Man	Blood, no significant changes.	Pearlman and Sacher
770	Mice, LAF_1	Mean survival time, no significant decrease.	Lorenz
770	Guinea-pig	Lymphocyte and platelet counts reduced.	Lorenz
770	Mouse	Ovarian, mammary, and lung tumors induced.	Lorenz
2500	Dog	Lymphocyte count reduced.	Ingram
2500	Rat	Mean survival time decreased.	Boche
4000	Man	Skin of hand, minimal changes.	Parker
5000	Dog	50 % of group aspermic after 9 months.	Boche
7700	Mouse	Mammary cancer induced.	Lorenz
7700	Mouse, bda	Breeding, no effect.	Lorenz and Heston
7700	Mouse	Ovarian follicles, decreased after 18 months.	Lorenz
7700	Mouse	Decrease of spermatogonia in mitosis.	Eschenbrenner
7700	Mouse Guinea-pig	Testicular weight decreased.	Lorenz
7700	Guinea-pig	Lung tumors increased in number.	Lorenz
15400	Guinea-pig	Platelet, heterophil, and red cell counts reduced.	Lorenz
15400	Mouse	Lymphocyte count reduced.	Lorenz
15400	Mouse	Mean survival time reduced.	Lorenz
30800	Mouse	Leukemia induced.	Lorenz
30800	Mouse	Sterility induced.	Lorenz and Heston

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