REPORT OF THE UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION

GENERAL ASSEMBLY

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NOTE

Symbols of United Nations documents are composed of capital letters combined with figures. Mention of such a symbol indicates a reference to a United Nations document.

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Chapter I

INTRODUCTION

Constitution and terms of reference of the Committee

1. The United Nations Scientific Committee on the Effects of Atomic Radiation was established by the General Assembly at its tenth session on 3 December 1955, under resolution 913 (X), as a result of debates held in the First Committee from 31 October to 10 November 1955. The terms of reference of the Committee were set out in paragraph 2 of the above-mentioned resolution by which the General Assembly requested the Committee:

"(*a*) To receive and assemble in an appropriate and useful form the following radiological information furnished by States Members of the United Nations or members of the specialized agencies:

"(i) Reports on observed levels of ionizing radiation and radio-activity in the environment;

"(ii) Reports on scientific observations and experiments relevant to the effects of ionizing radiation upon man and his environment already under way or later undertaken by national scientific bodies or by authorities of national Governments;

"(*b*) To recommend uniform standards with respect to procedures for sample collection and instrumentation, and radiation counting procedures to be used in analyses of samples;

"(*c*) To compile and assemble in an integrated manner the various reports, referred to in sub-paragraph (*a*) (i) above, on observed radiological levels;

"(*d*) To review and collate national reports, referred to in sub-paragraph (*a*) (ii) above, evaluating each report to determine its usefulness for the purposes of the Committee;

"(*e*) To make yearly progress reports and to develop by 1 July 1958, or earlier if the assembled facts warrant, a summary of the reports received on radiation levels and radiation effects on man and his environment together with the evaluations provided for in sub-paragraph (*d*) above and indications of research projects which might require further study;

"(*f*) To transmit from time to time, as it deems appropriate, the documents and evaluations referred to above to the Secretary-General for publication and dissemination to States Members of the United Nations or members of the specialized agencies."

2. The Committee consists of Argentina, Australia, Belgium, Brazil, Canada, Czechoslovakia, France, India, Japan, Mexico, Sweden, the Union of Soviet Socialist Republics, the United Arab Republic, the United Kingdom of Great Britain and Northern Ireland and the United States of America.

Activities of the Committee

3. Since its establishment, the Committee has held nineteen sessions. Its activities during the first sixteen sessions were surveyed in the introductions to the reports that the Committee submitted to the General Assembly in 1958, 1962, 1964 and 1966.[1]

4. The Committee held its seventeenth and eighteenth sessions, respectively, at the United Nations Office at Geneva from 26 August to 6 September 1967, and at Headquarters from 8 to 17 April 1968. Besides considering preliminary material later to be included in the present report, at those sessions the Committee reviewed the information that it required to continue its assessment of world-wide levels of radiation from nuclear tests. Since some of its earlier requests for data had become less relevant than before to the problem of estimating risks to human populations, the Committee outlined its continued requirements in a letter to States Members of the United Nations or members of the specialized agencies or of the International Atomic Energy Agency. The text of the letter, dated 30 April 1968, which was sent to the above-mentioned States by the Secretary of the Committee is attached to this report as annex E.

5. At both sessions the Committee adopted annual progress reports to the General Assembly. These were noted with appreciation by the General Assembly at its twenty-second and twenty-third sessions by resolution 2258 (XXII) of 25 October 1967 and resolution 2382 (XXIII) of 1 November 1968. By the latter resolution, the General Assembly also commended the Scientific Committee for the valuable contributions it had made since its inception to wider knowledge and understanding of the effects and levels of atomic radiation; drew the attention of Member States to the review of information required to continue the Scientific Committee's assessment of world-wide levels of radiation from nuclear tests, as contained in the letter annexed to the report of the Committee; requested the Scientific Committee to complete its current programme of work and to review and formulate plans for its future activities; noted the intention of the Scientific Committee to hold its nineteenth session in May 1969 and to report further to the General Assembly.

6. The nineteenth session of the Committee was held at Headquarters from 5 to 16 May 1969. At that session, the Committee adopted the present report to the General Assembly. The Committee also discussed and formulated plans for its future activities. It decided that it would continue to keep under review and to

[1] *Official Records of the General Assembly, Thirteenth Session, Supplement No. 17* (A/3838); *ibid., Seventeenth Session, Supplement No. 16* (A/5216); *ibid., Nineteenth Session, Supplement No. 14* (A/5814); *ibid., Twenty-first Session, Supplement No. 14* (A/6314). Hereafter these documents will be referred to as the 1958, 1962, 1964 and 1966 reports, respectively.

assess the levels of radiation to which the world population is or may become exposed, including those from radio-active contamination of the environment due to both military and peaceful applications of nuclear energy, those from the increasing industrial and medical uses of radiation and radio-nuclides and those from natural sources present in the environment. The Committee would also continue to provide the General Assembly with assessments of the risks entailed by exposure to radiation and of the mechanisms involved and would evaluate the significance of any new radiation effect that came to its attention. The Committee felt that it might prepare a report on some special aspects of the above-mentioned subjects to the General Assembly at its twenty-seventh session, noted that it would report yearly on its progress and requested that arrangements be made for a session in September 1970 at the United Nations Office at Geneva.

Organization of the work of the Committee

7. As in the past, the Committee met in *ad hoc* groups of specialists who held most of their technical discussions in informal meetings before presenting their conclusions to the full Committee for review.

8. Dr. A. R. Gopal-Ayengar of India and Dr. G. C. Butler of Canada served as Chairman and Vice-Chairman, respectively, during the seventeenth session of the Committee. Dr. G. C. Butler of Canada, Professor B. Lindell of Sweden and Dr. V. Zelený of Czechoslovakia served as Chairman, Vice-Chairman and Rapporteur, respectively, at the eighteenth and nineteenth sessions. At the nineteenth session, Professor B. Lindell of Sweden, Dr. V. Zelený of Czechoslovakia and Professor L. R. Caldas of Brazil were elected Chairman, Vice-Chairman and Rapporteur, respectively, to serve during the twentieth and twenty-first sessions. The names of those scientists who attended the seventeenth, eighteenth and nineteenth sessions of the Committee as members of national delegations are listed in appendix II.

Sources of information

9. The reports received by the Committee from States Members of the United Nations, and members of the specialized agencies and of the International Atomic Energy Agency, as well as from these agencies themselves, between 8 June 1966 and 16 May 1969, are listed in annex D of this report. Reports received before 8 June 1966 were listed in earlier reports of the Committee to the General Assembly. The information received officially by the Committee was supplemented by, and interpreted in the light of, information available in the current scientific literature or obtained from unpublished private communications from individual scientists.

Scientific assistance

10. The Committee was assisted by a small scientific staff and by consultants appointed by the Secretary-General. The scientific staff and consultants were responsible for preliminary review and evaluation of the technical information received by the Committee or published in the scientific literature.

11. Although the Committee itself assumes full responsibility for the report, it wishes to acknowledge the help and advice given by those scientists whose names are listed in appendix II. The Committee owes much to their co-operation and goodwill.

Relations with United Nations agencies and other organizations

12. Representatives of the International Labour Organisation (ILO), the Food and Agriculture Organization of the United Nations (FAO), the World Health Organization (WHO), and of the International Atomic Energy Agency (IAEA), as well as of the International Commission on Radiological Protection (ICRP) and the International Commission on Radiation Units and Measurements (ICRU), attended sessions of the Committee held during the period under review. The Committee wishes to acknowledge with appreciation their contribution to the discussions.

Scope and purpose of the report

13. The present report is not intended to cover comprehensively the whole field of interest of the Committee. It is limited to a discussion of radio-active contamination of the environment by nuclear tests, radiation-induced chromosome aberrations in human cells and the effects of ionizing radiation on the nervous system. The present report, therefore, being neither comprehensive nor self-contained, must be read in the context of the earlier reviews made by the Committee.

14. The main text of the report is followed by technical annexes in which the Committee has discussed in detail the scientific information on which it rests its conclusions. The Committee wishes to emphasize, as it did in the past, that its conclusions, being based on the scientific evidence now available, cannot be considered as final and will require revision as scientific knowledge progresses.

Chapter II

RADIO-ACTIVE CONTAMINATION OF THE ENVIRONMENT BY NUCLEAR TESTS

1. Debris from atmospheric nuclear tests continues to be the most important man-made radio-active contaminant of the environment. A number of tests have been carried out since the Committee's 1966 report: these have, however, added about 2 per cent to the amounts of long-lived radio-active nuclides still in the environment as a result of tests carried out in the early 1960s, although they have about doubled the current low content of the stratosphere and have thus contributed substantially to the deposition observed since the middle of 1967.

2. Small amounts of radio-active material have leaked from a few underground tests, and the crash of an aeroplane carrying nuclear weapons resulted in a localized contamination by plutonium-239 off the coast of northern Greenland in January 1968. These events have contributed only minutely to the global inventory.

3. Since the 1966 report, levels of long-lived nuclides in food-stuffs and human tissues have continued to decline except in the second half of 1968, when a slight increase in levels of caesium-137 due to recent tests was observed in food-stuffs in some countries of the northern hemisphere.

4. Most of the amount of long-lived nuclides injected into the stratosphere by earlier tests had been deposited by the middle of 1967. However, substantial fractions of the total doses to which the population is committed remain to be received from present body burdens and from the deposit in soil which will continue to be transferred to food-stuffs. This is particularly true in the case of strontium-90 which remains available for absorption by plant roots and is retained for long periods in the human skeleton. Present estimates indicate that roughly one-eighth of the total expected population dose due to strontium-90 had been delivered by the end of 1967, compared with between two-thirds and three-quarters of that due to the total amount of caesium-137 available for deposition in the body. On the other hand, only a small fraction of the expected population dose due to carbon-14, the radio-active half-life of which is much longer, has so far been delivered, and somewhat less than one-tenth of it will have been delivered by the year 2000. By contrast, more than half of the contribution to the dose commitment from external sources has already been delivered.

5. As in its earlier reports, the Committee has evaluated comparative risks of biological damage to the whole world population by means of "dose commitments" derived from the sum of radiation doses received and expected to be received by the world's population as a result of the nuclear explosions which have already taken place. As previously, dose commitments have been estimated for the gonads, for cells lining bone surfaces and for the bone marrow, as these are the tissues whose irradiation may give rise to hereditary effects, to bone tumours and to leukæmias, respectively. The Committee has not made special dose commitment estimates applicable to limited populations, such as those in individual countries, except in a few cases of populations with much higher than average exposures.

6. In the present report, for the purpose of estimating dose commitments, the Committee has used more extensively than heretofore actually measured levels of long-lived radio-nuclides in human tissues. This is particularly so in the case of strontium-90, which poses special problems because of its long retention in soil and bone and because of its complex metabolism in human tissues. By making use of measured levels in tissues, the Committee has been able to avoid some of the assumptions previously needed. Though a large number of other assumptions are still necessary and are common to all methods of calculation, the method now used will enable the Committee to use more efficiently the results of future measurements to verify and, if necessary, modify those assumptions in the future.

7. As far as the world-wide dose commitment is concerned, the major source of uncertainty continues to be the lack of information concerning the levels of any of the radio-active nuclides in the food and tissues of nearly two-thirds of the world population. In its previous reports, the Committee assumed that the numerical constants that describe the transfer of long-lived radio-nuclides were the same as those determined for areas from which measured data had been consistently available.

8. In the present report, the Committee has confined itself to estimating the dose commitment specifically for those populations from which sufficient measurements have been reported. For the rest of the world population, an upper limit to the dose commitment has been estimated.

9. The Committee feels that the uncertainty regarding the estimate applying to a large part of the world population, though unlikely to have caused a serious under-estimate of the global dose commitment, is undesirable, and it recognizes that, because of the very slow turnover of strontium-90 in adult bone, it will be possible, by sampling human bone from those areas of the world from which no data have yet been available, to estimate dose commitments to the population of these areas. The Committee notes with appreciation that the World Health Organization, in response to a recommendation made by the Committee at its eighteenth session, is now undertaking a limited programme of bone sampling, the results of which will be available in the near future.

10. Short-lived radio-nuclides are a source of radiation exposure of the population for a comparatively short time following their release into the environment, and external doses from short-lived nuclides due to tests carried out in 1966, 1967 and 1968 have not

significantly increased the global dose commitment. Measurable iodine-131 levels in milk have been reported mainly from the southern hemisphere following the tests carried out in that area.

11. Since the last report, there has been a continuing interest in the doses received by populations in the subarctic regions where, because of special ecological conditions, there is an enhanced transfer of caesium-137 from deposit to the body, mainly through consumption of reindeer or caribou meat. In these regions, individual doses from internal caesium-137 are of the order of one hundred times greater than the average for the northern hemisphere. There are also indications that, in these regions, levels of strontium-90 in food and tissues may be significantly greater, though not by as much as caesium-137 levels, than the average for the northern hemisphere.

12. There are several other limited regions of the world where levels of caesium-137 in food-stuffs and in humans have been found to exceed by many times the average for the corresponding latitudinal band. This has been attributed to high precipitation and to special soil conditions resulting in increased availability of caesium-137 to plants.

13. The estimated dose commitments are summarized in table I. The table includes estimates for the temperate zones of the northern and southern hemispheres. A third column shows values applicable to the whole world population. Although the Committee has used new and less indirect methods of estimating dose commitments, the present estimates differ little from those given in the previous report.

14. Comparative risks are, as in the 1964 and 1966 reports, expressed as the periods of time during which the natural background would have to be doubled in order to deliver an additional dose equal to the fraction of the dose commitments that will be received by the year 2000. These periods derived from the dose commitment estimates applicable to the whole world population are approximately 11, 26 and 18 months for gonads, cells lining bone surfaces and bone marrow, respectively.

15. The Committee now has increased confidence that its estimates are representative of the doses to which humans have been committed, particularly for those populations in the countries and areas from which measurements are available.

TABLE I. DOSE COMMITMENTS FROM NUCLEAR TESTS CARRIED OUT BEFORE 1968

				Dose commitments (mrad)		
Tissue	*Source of radiation*			*North temperate zone*	*South temperate zone*	*Whole world*
Gonads	External	Short-lived		36	8	23
		^{137}Cs		36	8	23
	Internal	^{137}Cs		21	4	21[a]
		^{14}C[b]		13	13	13
			Total[c]	110	33	80
Cells lining bone surfaces	External	Short-lived		36	8	23
		^{137}Cs		36	8	23
	Internal	^{90}Sr		130	28	130[a]
		^{137}Cs		21	4	21[a]
		^{14}C[b]		16	16	16
		^{89}Sr		<1	<1	<1
			Total[c]	240	66	220
Bone marrow	External	Short-lived		36	8	23
		^{137}Cs		36	8	23
	Internal	^{90}Sr		64	14	64[a]
		^{137}Cs		21	4	21[a]
		^{14}C[b]		13	13	13
		^{89}Sr		<1	<1	<1
			Total[c]	170	51	140

[a] The dose commitments due to internally deposited ^{90}SR and ^{137}Cs given for the north temperate zone are considered to represent upper limits of the corresponding dose commitments to the world population.

[b] As in the 1964 and 1966 reports, only the doses accumulated up to year 2000 are given for ^{14}C; at that time, the doses from the other nuclides will have essentially been delivered in full. The total dose commitment to the gonads and bone marrow due to the ^{14}C from tests up to the end of 1967 is about 180 millirads and that to cell lining bone surface is about 230 millirads.

[c] Totals have been rounded off to two significant figures.

Chapter III

EFFECTS OF IONIZING RADIATION ON THE NERVOUS SYSTEM

1. The nervous system performs various functions in the organism. In the first place, it provides the means for relating the organism to the external environment by means of perception through the sense organs and of control of the skeletal muscles. The nervous system is also the instrument by which immediate or delayed behaviour is expressed, and in man it is responsible for the most complex intellectual functions.

2. With regard to such functions as digestion, respiration, blood circulation and excretion, the nervous system, often in conjunction with the endocrine glands, plays an essential regulatory role by adapting these functions to the changing needs of the organism and thus contributes to maintaining the constancy of the internal environment. This task is largely performed by the autonomic nervous system whose control centres are located in the spinal cord and in certain brain structures.

3. Reflex activity usually involves an orderly progression of events, namely, an initiation of activity at sensory receptors, a relay of impulses to a neural centre and final transmission to a muscle or other effector. While reflex activities are readily analysed, the nervous activity concerned with the highest integrative functions of the organism, such as complex behaviour, are much more difficult to assess.

4. The importance and diversity of these functions emphasize the need for the study of the effects of ionizing radiation on the nervous system. Although ultimately it is the functional effects that may be more important, both structural and functional effects need to be studied. Investigations of functions and structures have been mostly carried out by different researchers, and relatively few attempts at integrating the two approaches have been made. Because the response of the nervous system is so different depending on whether irradiation takes place during its development or afterwards, it is customary and convenient to consider the effects during these two periods in sequence.

Irradiation of the nervous system during its development

5. Observations on experimental animals indicate that pre-natal irradiation can produce severe developmental anomalies. Those of the nervous system are prominent among them. When they are serious enough, further development of the foetus is prevented and death ensues. Anomalies of the nervous system are produced only if irradiation occurs in the period when the nervous system and its various parts are differentiating. Specific anomalies such as microcephaly, encephalocele and hydrocephalus occur in this period only after irradiation at certain so-called critical times.

6. The frequency and severity of anomalies of any given type depend on the radiation dose, but information is insufficient to establish dose-effect relationships for any of the malformations affecting the nervous system. It is likely that the induction of gross malformations of the nervous system requires doses higher than a threshold which, for mice and rats, is probably around 100 rads.

7. Disorganization of the cellular layers of the brain cortex has been observed, however, after an x-ray dose of 20 rads administered to rats on the sixteenth day of pre-natal life and are still apparent when the animals reach maturity. Less pronounced changes also occur in rats after 10 rads given on the first day after birth, but evidence of damage disappears progressively as the animal grows. Such changes have been observed by means of painstaking studies which need to be systematically pursued at various doses and various times of irradiation and observation, and attempts should be made to correlate them with the functional effects that have also been reported after pre-natal irradiation.

8. The functional impairment of animals irradiated pre-natally has been studied by various methods, particularly in rodents. Electro-encephalographic changes seem to reflect disturbances in the inhibitory function of the cortex on lower centres. Visual, olfactory and distance discrimination and other learning processes are also affected. These changes have been observed in adult rats which have received doses of the order of 100 rads or more during the second and third week of their intra-uterine life.

9. Some studies of conditioned reflexes, however, have been reported to reflect changes of learning processes at much lower doses. Slight changes in conditioned reflex performance have been observed in the adult after as little as 1 rad on the eighteenth day of pre-natal life. The assessment of the relevance of these and other behavioural changes for the problem of risk estimation in man requires better knowledge on the comparability of results of studies on animals and on man.

10. That severe damage to the nervous system can be induced in man also is shown by a number of observations of children born of mothers irradiated for medical reasons during pregnancy. Doses are unknown but are believed to have been high. A number of cases of reduction of head size, often accompanied by severe mental retardation, have been reported among these children as a result of irradiation from the second through the sixth month of intra-uterine life. However, contrary to what animal experiments would lead one to expect, major structural changes of the nervous system have seldom been observed, perhaps because these would be incompatible with sufficiently long survival of the human embryo for the damage to be detected at birth.

11. Similar observations have been made among the offspring of women exposed during pregnancy to the

Hiroshima and Nagasaki explosions. Reduced average head size and increased incidence of mental retardation are clearly observed among those exposed within 1.5 kilometres of the hypocentre between the second and the sixth month of intra-uterine life, and the frequency of mental retardation may also be above normal at greater distances, where doses were of the order of a few rads.

12. The value of this latter observation is limited by the fact that the number of cases among the off-spring of women irradiated at low doses is extremely small and that the role of other factors cannot be entirely excluded. Where the opportunity exists, any additional investigations on pre-natally irradiated subjects are very desirable in order to establish further the degree of radio-sensitivity of the foetus.

13. Surveys of children whose mothers were irradiated for medical reasons during pregnancy have shown an associated increase (40 per cent) of malignancies, including malignancies of the nervous tissue. The excess was noticeable after doses assumed to be of the order of a few rads, but it cannot be entirely excluded that it may have been associated with the condition in the mother that prompted the irradiation rather than with the irradiation itself. Such an increase has not been reported among survivors of *in utero* exposure to the Hiroshima and Nagasaki bombings, but the expected number of induced cases in that population was very low.

14. An increased incidence of tumours of the nervous tissue has also been observed in a number of surveys of children irradiated for medical reasons in infancy or early childhood. One of these surveys suggests that, at the doses absorbed by the relevant tissues, the incidence of these malignancies is increased by the same order of magnitude as the incidence of leukæmias. The same survey has also shown an increased incidence of serious mental disturbances associated with previous irradiation of the brain around the age of seven years. Most of the brain was estimated to have received doses of approximately 140 rads. However, as the role of a number of variables that may themselves have contributed to that excess cannot at present be assessed, the results of further analysis of these results are required before the relationship between radiation and mental disorders can be considered as proved. Other surveys of brain-irradiated children that are currently in progress should be vigorously pursued.

15. The evidence available induces the Committee to draw attention to the particular hazards that may result from irradiation of the fœtus and of children.

Irradiation of the nervous system in the adult

16. In the adult, the radiation dose required to induce severe structural changes in the nervous system under conditions of whole-body irradiation is higher than the dose needed to cause gross alterations of other systems such as the gastro-intestinal tract and of the hæmopoietic system. Under conditions of short-term irradiation, the median lethal dose for man lies around 400 rads, and death when it occurs is mainly due to the involvement of both of these. Sudden death primarily due to the involvement of the nervous system, on the other hand, occurs after doses of the order of several thousands of rads.

17. Only isolated cases of malignant intracranial tumours of the nervous tissue have been reported after irradiation of adult subjects. It seems, therefore, that the induction of malignancies is unlikely to be a substantial hazard of irradiation of the adult nervous system in man.

18. Functional and behavioural effects are observed in experimental animals after high doses (above 50 rad). These effects include some electro-encephalographic changes and some disturbances of certain conditioned reflexes. The accomplishment of many tasks involving learning and performance is little if at all affected. Such changes as have been induced by radiation disappear with time, but repeated irradiations with the same dose tend to produce greater disturbances. There are both positive and negative reports on the induction of similar, but milder, functional changes by low-dose radiation.

19. It is not clear to what extent such functional effects as have been observed after whole-body doses of 50 rads and above are the primary consequence of damage to the nervous system or whether they result from different stimuli originating in, or from toxic products released by, other damaged tissues and systems such as the cardio-vascular, gastro-intestinal and endocrine systems. Nevertheless, whether primary or secondary, these effects on the nervous system may play a role at the doses at which the acute radiation syndrome may occur.

20. Observations are available on radiation workers exposed in the past for a number of years to average levels of radiation estimated as being higher than current maximum dose levels for radiation protection. Subjective complaints, such as headaches and sleep disturbances accompanied by mild and reversible neurological and cardio-vascular changes, have been reported. No changes of consequence were observed among workers exposed, even for a number of years, within the currently accepted dose limits.

21. Even at very low doses, ionizing radiation may act as a non-specific stimulus. Evidence of this is found in the possibility of using radiation as a conditioning stimulus, the ability of radiation to awaken an animal, the avoidance of a radiation source by an animal, and in the fact that radiation can serve as a visual or olfactory stimulus. Under certain circumstances, ionizing radiation can be perceived by the human retina at doses as low as a few millirads. There is no evidence that these doses induce any injury to the sense organs involved.

22. It seems, in summary, that the most significant fact emerging from a review of the effects of ionizing radiation on the nervous system is the striking dependence of the type and intensity of effects on the age at irradiation. In the adult, except at extremely high doses, the effects that have been observed, whether structural or functional, appear to be of secondary importance compared to those that may arise in other tissues and systems. Functional reactions of the nervous system may also appear at very low doses (10 rad or less). However, they are of a physiological nature, and no damage of the nervous system has been observed. In children, on the other hand, the evidence suggests that, at least with regard to the induction of malignancies, the nervous tissue might be about as susceptible as other tissues such as the thyroid and

blood-forming tissues. It is, however, in the pre-natal period that the vulnerability of the nervous system is highest. There is clear evidence that, from the second to the sixth month of pre-natal life, doses from 50 rads onwards are associated with increases in mental retardation and microcephaly. Evidence on the effects of lower doses during this same period of pre-natal life is still extremely tenuous and does not permit exclusion of the possibility that increased incidence of the same effects may be a result of exposure in this lower range. Available data suggest that even low doses given to the fœtus later in pregnancy may increase the incidence of tumours of the nervous system as well as of other malignancies.

Chapter IV

RADIATION-INDUCED CHROMOSOME ABERRATIONS IN HUMAN CELLS

1. The cells of any given species have a characteristic number of chromosomes, and each chromosome has a characteristic structure and size. Chromosomal changes visible by some form of light microscopy are called chromosome aberrations. These can be separated into aberrations involving changes in structure—the chromosome structural aberrations—and those involving changes in the number of chromosomes. Since chromosomes contain genetic material, the various types of chromosome aberrations may result in genetic effects.

2. In man, as in all other animal and plant species, chromosome aberrations are to be found with low frequencies in both somatic and germ cells of individuals in populations that have not been exposed to radiation over and above natural background levels. Such spontaneous aberrations are changes that may, in some cases, be transmitted to descendant cells. In other cases, the changes are so gross that they result in the death of the cells containing them. Clearly there are differences between the relative importance of such changes in somatic as opposed to germ cells.

3. Chromosome aberrations in human germ cells are associated with and may be responsible for a considerable proportion of spontaneous abortions and, where they are compatible with viability, for a variety of congenital abnormalities. Indeed, as discussed in the 1966 report, it has been estimated that one child out of every 200 live-born has a constitutional chromosome anomaly responsible for a gross physical or mental abnormality. The importance of chromosome aberrations in somatic cells is less clear, although there is evidence that one particular kind of chromosome anomaly may be causally related to the development of human chronic granulocytic leukæmia. On the other hand, in normal healthy individuals peripheral blood lymphocytes may occasionally contain a chromosome aberration (less than one in 2,000 for one specific type of aberration). In itself the presence of such aberrations appears to be of no consequence to the well-being of the individual.

4. Exposure to radiation may result in an increase in the number, but not in the variety, of chromosomal aberrations. These aberrations are clearly of genetic importance and they may, in fact, comprise the major component of the genetic damage resulting from radiation exposure. Thus, a considerable amount of work has been carried out on the mechanisms whereby such aberrations are induced by radiation, on the behaviour of the aberrant chromosomes at cell division and on the genetic consequences of the aberrations.

5. Until relatively recently, most of this work had been carried out on organisms that were particularly well suited for cytological study, because they possessed small numbers of rather large chromosomes. However, in the last decade, and particularly over the last four or five years, a considerable amount of study has been devoted to the induction of aberrations in man. These studies have been made possible through the development of simple and reliable techniques for culturing human cells *in vitro* and through the application and refinement of cytological techniques previously utilized by plant cytogeneticists.

6. As a result of the developments in human cytogenetics, it has become possible to make observations on chromosome aberrations induced in human cells both *in vivo* and *in vitro*. Studies have been carried out on individuals exposed to radiation in the course of their work or for diagnostic or therapeutic purposes, as well as on individuals who had been exposed accidentally or as a consequence of nuclear explosions. In addition, a considerable amount of work has been undertaken on the responses of human chromosomes in cells exposed to radiation *in vitro*. These studies have shown that the human chromosome complement is sensitive to radiation and that it is possible to detect effects following x-ray doses as low as 10 rads delivered to substantial proportions of the body in a short period of time.

In vitro studies

7. The blood leucocyte culture system offers a means of experimenting on freshly obtained human cells which can be easily and painlessly collected in large numbers without any adverse effect on the donor and are amenable to short-term culture, using relatively simple techniques. The obvious advantages offered by this system for studies on the *in vitro* response of human cells to radiation exposure have been exploited by a number of groups of workers, and a considerable amount of data on radiation-induced chromosome aberrations in such cells has been obtained.

8. A variety of studies have been carried out on the influence of various factors, including radiation quality, dose, dose rate and time of sampling, on the yield of radiation-induced chromosome aberrations in human peripheral blood cells. In general, it has been found that, for any given set of factors, there exists a quantitative relationship between the yield of aberrations and dose, as has been observed in all other mammalian and non-mammalian cell systems that have been studied.

9. Although studies in various laboratories on the relationship between aberration yield and dose have shown that separate experiments yield consistent results, significant differences have been observed between laboratories. However, it is now clear that the main factors contributing to the quantitative differences between these results are (*a*) differences in the quality of the radiations employed; (*b*) the use of irradiated cultures as opposed to the irradiation of blood cells *in vitro* prior to culture and (*c*) the use of different durations of culture. When these factors are taken into account, close agreement between different laboratories

is evident. However, further standardization of methods is highly desirable to ensure better comparability.

10. This work has great importance because of the possible use of dose-yield relationships established *in vitro* in attempts to estimate radiation doses absorbed *in vivo* and as an indication of their likely biological importance. In theory, dose estimates can be obtained with this technique through the study of chromosome-aberration yields in the exposed individuals and extrapolation to equivalent yields obtained *in vitro* under defined conditions of exposure. A number of laboratories have had a good measure of success in estimating radiation doses in accidentally exposed individuals by the use of this "chromosome-aberration dosimetry" approach. However, there are a number of important problems, particularly in relation to problems of non-homogeneous exposures of the body. At the present time, it seems clear that the use of chromosome aberrations in biological dosimetry may have considerable potential, but much work remains to be done.

In vivo studies

11. Studies on peripheral blood lymphocytes from patients exposed to diagnostic x rays and from radiation workers receiving long-term irradiation have, in some cases, clearly revealed significant increases in aberration yields after doses of the order of a few rads. The ability to detect such effects at low doses is a consequence of the relatively high sensitivity of the human chromosome complement, of the high quality of cytological preparations from lymphocytes and of the very low frequency of spontaneous chromosome aberrations in such cells.

12. To relate aberration yield to radiation dose *in vivo*, data obtained over a range of exposures, preferably under standardized conditions, are desirable but rarely obtainable. A number of studies, however, have been carried out on individuals irradiated at various dose levels and under various conditions either as a result of accident or for therapeutic purposes. The integral absorbed dose has been estimated from aberration yields in some of the studies on individuals accidentally exposed, sometimes with good agreement with measurements obtained by physical means.

13. Evaluation of the dose under these conditions is fraught with uncertainty since, although the cells (small lymphocytes) that are sampled for studying aberration yields are widely distributed throughout the body, they tend to migrate so that only a small proportion is to be found in the peripheral blood at any one time. Thus, in the case of short-term partial-body exposure by radiation of a given quality, the aberration yield observed in the cells sampled will depend upon a variety of factors, including the volume irradiated, the proportion of small lymphocytes in the exposed volume and, since there is considerable mixing between lymphocytes in different tissues, the time at which blood is sampled after exposure. Similar difficulties arise in cases where limited areas of the body have been exposed to radiation for medical purposes, and blood samples are taken at short defined intervals after exposure.

14. Because at least some of the cells sampled for aberration yields are long-lived, it has recently been possible to obtain dose estimates from blood cells of survivors of Hiroshima who had been exposed to radiation from the nuclear explosion twenty-two years previously. These estimates are in reasonable agreement with indirect estimates of exposures obtained by physical methods.

15. It may be concluded that studies to date indicate that scoring of chromosome aberrations in the lymphocytes of circulating blood is a potentially important biological adjunct to physical dosimetry. Special difficulties, however, arise in the irradiations restricted to parts of the body because of the mixing of lymphocytes from irradiated and unirradiated parts of the body. Thus, this method only reflects an average effect upon lymphocytes irradiated in different parts of the body. Further data are urgently required to improve the validity and broaden the field of application of this method.

Possible biological significance of the aberrations

16. The possible biological significance of chromosome aberrations present in germ cells has been the subject of continued review by the Committee, and the views expressed in the 1966 report are still largely valid. There are no direct observations yet on the genetic consequences of radiation-induced chromosome aberrations in the germ cells of man, although information on the genetic consequences of radiation-induced chromosome anomalies in laboratory mammals is available and was reviewed in detail in the 1966 report. Further study on human meiotic cells is clearly necessary, particularly in order to provide better estimates of the spontaneous frequency of translocations in man and a better understanding of their genetic consequences.

17. At the somatic level, the interest of chromosome anomalies results mainly from their possible role in the causation of malignant changes, with which they are frequently associated. Such a role is, however, still unclear. Only in the case of chronic myeloid leukæmia does the evidence strongly implicate a specific chromosome aberration (the Ph^1 chromosome) as playing a significant role in the initiation of the disease if cells with this aberration are present in the bone marrow. Although it is possible that other specific chromosome abnormalities could be associated with other types of neoplastic change, the evidence is tenuous, whereas the presence of a wide variety of chromosome aberrations in most tumours and their complete absence in some others argues against a simple causal relationship. Chromosome aberrations may well be phenomena that are secondary to, and could be independent of, the neoplastic change, although it is clear that most agents and conditions that produce chromosome aberrations also cause tumours.

18. The incidence of chromosome aberrations and that of tumours both increase with increasing dose, but the relationship between the two effects is complex. Although there is some correlation between radiation-induced chromosome aberrations and malignancies, it is a matter of observation that, of the individuals exposed to low levels of radiation and who have aberrations in many of their cells, very few manifest malignant disease.

19. The considerable interest in the possibility that radiation-induced chromosome aberrations may contribute to life shortening and to immunological deficiency has not so far resulted in any clear conclusions

regarding the relationship between chromosome aberrations and these effects. Although life shortening and acute immunological deficiency may be induced by radiation, the part played by chromosome aberrations, other than by contributing to cell killing in the case of immunological deficiency, is by no means clear.

20. Information on the yields and types of chromosome aberrations in somatic cells does not as yet provide us with a new approach to, or better estimates of, risks except in the one specific case of the Ph^1 chromosome change which correlates with chronic granulocytic leukæmia. Knowledge of an increased frequency of chromosome aberrations in the peripheral blood lymphocytes of an irradiated individual does not enable us to make any quantitative statement regarding the risk of developing neoplastic diseases, immunological defects or other clinical conditions. For the time being, estimates of risk of somatic diseases must, therefore, remain largely based on empirical relationships between doses and observed incidences in groups of irradiated people, as were the estimates earlier obtained by the Committee.