Risk Evaluation for Protection of the Public in Radiation Accidents

A REPORT PUBLISHED ON BEHALF OF IAEA and WHO

INTERNATIONAL ATOMIC ENERGY AGENCY

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RISK EVALUATION
FOR PROTECTION OF THE PUBLIC
IN RADIATION ACCIDENTS
SAFETY SERIES No. 21

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I. INTRODUCTION

The evaluation of the risk that would be involved in the exposure of the public in case of a radiation accident requires information on the biological consequences that might be expected from such an exposure. A seminar held at Geneva in 1963 and jointly sponsored by the World Health Organization, the Food and Agriculture Organization of the United Nations, and the International Atomic Energy Agency [1] dealt with many aspects of accidental situations. The present report deals more specifically with the risk evaluation problem.

The International Commission on Radiobiological Protection (ICRP) has also been considering some aspects of accidental situations involving the general public. The ICRP Publication No. 9 [2] states that:

"(103) Exposure of the population resulting from uncontrolled sources presents a much more complex problem. Here there is the possibility that exposures might be received under a much wider variety of conditions and circumstances (geographic, meteorological, social). This makes it impossible to lay down recommendations for action levels that would be universally applicable. However, in this regard, the Commission wishes to draw attention to the work of the United Kingdom Medical Research Council* and of the Federal Radiation Council in the United States †.

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"(104) Local circumstances will, in part at least, determine the action that will be taken in a particular case, and the action level will itself depend on the type of action that could be taken. Nevertheless, regardless of the circumstances, there are certain dose levels at which action is mandatory. For example, a likelihood of whole body exposures of 100 rads would always call for action. The report of the Task Group on the Evaluation of Risks from Radiation (20) gives some guidance concerning the relationship of dose to late effects such as the induction of malignancy.

"(105) Because the individual circumstances vary, it is not feasible to specify in detail all the possible types of remedial action. However, the basic actions can be summarized as:

(a) Actions to control the original source of exposure.
(b) Remedial actions to reduce the environmental levels, and measures taken to minimize the dose received in tissue.

Theoretically, there is also the possibility of action to reduce the damage done by the dose received, although as yet there is little practicable action of this kind known."

Similarly the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has considered for many years the biological effects of radiation.

The information and data used in this IAEA report were taken mainly from the 1964 and 1966 UNSCEAR reports [3, 4], from information collected from Member States, and in particular, from the Federal Radiation Council Reports Nos. 5 and 7 [5, 6] and the reports of the Medical Research Council [7]. In addition the report of the ICRP task group on the evaluation of risk for radiation was a useful source of information [8].

The present report defines a range of reference doses of radiation and their corresponding biological risks to the public in the event of a radiation accident. Such reference doses and the considerations upon which they are based will be useful for assessing

the hazards of nuclear installations and for policy decisions by the authorities responsible for the special measure to be taken to safeguard the public in the case of an accident at a nuclear installation. This report was produced by a panel of experts who were convened to study the subject, and is published on behalf of WHO and IAEA.

II. PREFACE

The basic objectives of radiation protection are to prevent or minimize somatic injuries and minimize the effects of radiation on the genetic constitution of the population. Therefore radiation exposure doses should be kept as low as reasonably practicable, the possible number of people exposed having been taken into consideration. The Agency's Basic Safety Standards for Radiation Protection [9] indicates that in practice the actual exposures should be as low as practicable to the extent permitted by reasonable economic and social conditions.

It is recognized that in designing and planning for nuclear establishments, the recommendations of the ICRP and the Agency's Basic Safety Standards for Radiation Protection require that the best practicable design, material and workmanship be used so that the exposure of the individual worker or the general public be kept during normal operations as low as practicable and always within the recommended levels.

It is anticipated from past experience that many minor accidents will not result in exposure doses any larger than those in the recommendations set forth in the Basic Safety Standards for Radiation Protection. It must be recognized however, that some situations may occur where a number of people may receive radiation doses from sources that are not under control. Therefore the concept of a fixed maximum permissible dose ceases to be meaningful. Instead other considerations arise, such as the need to balance the risk from radiation against the consequences of particular remedial measures.

III. SCOPE

In considering potential radiation exposures in accidents, two situations are envisaged, for which evaluations are required; firstly,
hypothetical situations contrived for safety evaluations and for planning for possible emergencies where a considerable release of radioactive material is assumed and secondly, the occurrence of an actual accidental release.

In the case of a hypothetical accident the radiobiological consequences that may result must be balanced against many other factors in selecting a particular site for a nuclear installation and in accepting the technical design of that establishment. These factors include social, economic and technical advantages of the site and the installation, the probability of the occurrence of accident, etc. Very often some factors in site selection may be almost overriding, and a choice of site is made from a limited number of sites owing to overriding engineering and economic requirements which may necessitate positioning the nuclear installation such as a power station in a certain general area. The ultimate responsibility for such decisions rests with the appropriate authority-in-charge. The information in this document is intended to help the authority in evaluating the nature and magnitude of the biological risks involved.

In the case of an accident resulting in the release of radioactivity to the public environment, the factors to be considered by the authority-in-charge are different. After an accident, an initial exposure of individuals may have occurred with little or no control, whereas subsequent exposures may be subject to protective supervision and planning. The appropriate authority-in-charge is therefore responsible for balancing the estimated consequences of further exposure against the feasibility of its reduction and the effects of any counter measures.

For both the safety evaluation and accident management mentioned above it is necessary to envisage the nature of possible accidents and to formulate plans for dealing with any such accident. Such plans are closely related to decisions on site selection and counter measures after an accident. In both cases the following factors are to be considered:

(a) The nature and magnitude of the release of radioactive material.
(b) The irradiation of the public resulting from that release in various circumstances.
(c) The radiobiological consequences of that irradiation.
(d) The feasibility of the counter measures and their consequences.

In this document the concept of the maximum credible accident is not used, nor is it intended to elaborate a maximum permissible dose for either of the two situations mentioned. The information
is solely intended to provide relevant information for evaluating the risk.

The figures given in the various tables are reference figures to assist in planning the steps to be taken in various circumstances as mentioned previously. Further calculations need to be made on the basis of risk estimates mentioned in this document, so that decisions can be made. For planning purposes the identity and quantity of the assumed release will be used to calculate possible consequences. In an actual accident these, as well as other parameters such as actual deposition measurements, must be taken into consideration.

In this document a nuclear installation generally applies to nuclear reactors and associated operations. The principles outlined in the document will, however, be applicable to the consideration of any accident in which significant radiation exposure of the public is involved.

IV. REFERENCE DOSES AND RELATED RISK ESTIMATES

1. General

The appropriate authority in a country, faced with a situation where significant accidental radiation exposure of individual members of the public has occurred or could occur as described in section III, needs risk estimates of the possible harmful consequences of such an exposure. These risk estimates would serve to indicate the consequences of exposure to the amounts of radiation that might be encountered.

The risk estimates would help the appropriate authority to balance the risk from a given exposure against the consequences which would result from counter measures to reduce the exposure of the people. The risk estimates would also give, at the planning stage of a nuclear installation, one of the guide lines to meet the requirements for the case of a hypothetical accident.

In making risk estimates of possible radiation exposure of the general public, it is recognized that the data used for these estimates suffer from many uncertainties and limitations. One of these limitations is the paucity of information about normal populations. There are uncertainties in regard to the estimate of the dose received by the irradiated tissue, dose distribution pattern, volume of tissue irradiated and dose-rate and dose-effect relationship.
For the present purposes, in which relatively small doses are considered, a linear dose-effect relationship has been assumed, so that estimates of risk for each rad may be expressed as so many cases per year for a million subjects exposed. Even when the frequency of observed somatic effects increases rapidly with increasing dose, it is most unlikely that the risk of such somatic effects derived from the high dose-range will underestimate the effect per rad at low doses. In fact the effect may well be much less than estimated. For any genetic effects that may be postulated a linear dose-effect relationship has generally been accepted as the norm.

In this report the convention is adopted of expressing the risk of radiation damage as the number of cases per year and per generation per million persons exposed per rad. One should consult the UNSCEAR reports [3, 10, 11] for information about the difficulties and uncertainties in applying these risk estimates to all populations and to all levels of radiation dose.

In spite of the uncertainties associated with the data, the need is such that one must provide risk estimates on which to base possible courses of action. In applying these risk estimates to any population, caution must be exercised because the data upon which these estimates are based are derived from various irradiated groups who may not necessarily be representative of the entire population with respect to radiation damage.

2. Whole-body irradiation and leukaemia risk

The information available at present on dose-effect relationships is more extensive for leukaemia than for other malignant conditions. It includes data on responses to moderate doses of radiation so that estimates are made with somewhat greater confidence than in the case of the other radiation-induced malignancies.

Leukaemia can be classified according to several distinct varieties. Even when these are aggregated into a single class, leukaemia is still a rare disease with a morbidity (and effectively the same mortality) of about 30 to 70 cases per million persons per year. The figure varies from nation to nation and where it is high a substantial fraction is caused by chronic lymphatic leukaemia. This class of leukaemia has not been causally attributed to radiation. It occurs especially in the elderly.

Risk estimates of the incidence of leukaemia were made by UNSCEAR for three groups of people.
(a) Japanese A-bomb survivors
(b) Patients with ankylosing spondylitis given therapeutic X-irradiation
(c) Children irradiated in utero.

Surveys of the incidence of leukaemia among the survivors of atomic bombing in Hiroshima and Nagasaki, who received doses ranging up to several hundred rads, have shown an increased incidence of between 1 and 2 cases per year per rad per million exposed individuals (para. 4, page 7 of Ref. [3]). A similar rate of incidence was observed among a group of people irradiated therapeutically for ankylosing spondylitis with doses of X-rays up to 1500 R.

A group of children, born to mothers who received one or more diagnostic X-irradiations during pregnancy, was surveyed for malignancies. The results indicate that low doses of radiation, of the order of a few rads, may induce malignancies in children irradiated in utero and that in such children the risk of leukaemia per unit dose may be several times (perhaps five) higher than in adults.

Despite the uncertainties of the linear dose-effect relationship, the deduced numbers for the incidence of leukaemia are of value for consideration of risks of radiation versus the estimated risks of countermeasures to minimize exposure. The total number of induced cases that a population of one million exposed to one rad might have in 20 yr is calculated to be $1.5 \times 20$, i.e. 30. The corresponding number of cases from natural incidence in the same population in 20 yr is 600-1400.

3. Thyroid irradiation and the possible cancer risk

The natural incidence of thyroid cancer is a function of age. The United States data show an incidence of four cases per year per million for persons under 25 yr of age. The incidence rises linearly with age afterwards. In this report the risk estimates for cancer of the thyroid are given for children; they constitute the critical population at risk, because of potentially higher doses and greater sensitivity.

The information available on cancer in the thyroid following irradiation comes from the following sources:
(a) Data from children irradiated therapeutically for enlarged thymus and other benign conditions
(b) Therapeutic and diagnostic irradiation of adult patients by $^{131}$I administration; or therapeutic irradiation by X-ray of adult patients
(c) Japanese A-bomb survivors
(d) Animal experiments.

The incidence of thyroid cancer after irradiation at high dose rates was the subject of detailed human surveys which are summarized in Table VI. From these surveys risk estimates were derived, which are also indicated in Table VI.

As in the case of leukaemia the incidence of thyroid cancer shows approximate proportionality (para. 10, page 8 of Ref. [3]) in a dose range of 100 to 300 rad and leads to a risk estimate of about one case per year per rad per million exposed individuals, averaged over a period of approximately 16 yr after irradiation.

It is possible to calculate the total intake of radioiodine which if incorporated will give a certain dose to the thyroid. By making further assumptions it is possible to extend such calculations to determine the radioiodine concentration in the diet (milk) or in air which would result in this thyroid dose. An example of such a computation is given in section VI, para. 2.

4. Irradiation of bone from internal sources and related malignancy risk

The natural incidence of primary tumours per year per million persons is about five cases. The development of primary bone tumours many years after exposure (10 to 35 yr) is considered a major hazard from the incorporation of radionuclides in bone. Experiments with animals have demonstrated the production of lesions of the haematopoietic system, such as leukaemia, from internal contamination with bone seekers. However, in humans the most extensive dose-response data come from studies of persons who have been contaminated with radium. It is important to note (para. 4, p. 7, Ref. [3]) that in the case of dial painters the evaluation of dose-effect relationship is complicated by the fact that some of the paints contained other short-lived radionuclides and were therefore difficult to measure at the late stages when the patients were seen.

Tumours have not been observed in persons with terminal body burdens of radium below about half a microcurie (para. 4, p. 7, Ref. [3]). Apart from radium, human data are very scarce. Some data are available from some cases where certain radionuclides have been incorporated in humans either therapeutically or accidentally. For many radionuclides human data are lacking and in such cases extrapolation from animal data to man is resorted to or estimates of risks
from malignancy can be based on comparison with radium. A variety of biological factors enters into such a comparison (para. 10, p. 8, Ref. [3]).

Because the uncertainties in the relationship between tumour incidence and radiation dose to bone are so great, even for radium, therefore the provision of risk estimates for other radionuclides incorporated in bone, as was done in section IV, paras. 2 and 3 for the risk of leukaemia and thyroid cancer, is difficult and should be approached with great caution.

However, the results of earlier surveys which indicated a marked dependence between the frequency of development of bone tumours and the skeletal content of radium are summarized in the UNSCEAR report (para. 135, page 95, Annex B [3]). In this study, persons who had been employed formerly in the radium watch dial industry or as radium chemists or who had received radium as a form of medical therapy were selected and measured for radium content. The results of tentative and very rough estimates of body-burden incidence relationship are summarized in Table I.

The risk estimates in Table I are mainly based on information from radium in a few hundred individuals. It is not appropriate to extrapolate risk estimates, since the dose-response relationship is probably not linear.

Accidental exposure to $^{90}$Sr may take place by inhalation or ingestion. In the former case 4%, and in the latter 3%, of the intake will be retained in bone at one year after exposure. For more detailed information and the derivation of these factors, consult VI.3.

Any estimates of the risk of bone cancer following deposition of $^{90}$Sr in bone can be arrived at only indirectly by using the information about radium presented in Table I. To compare the biological effect per microcurie of $^{90}$Sr in bone with that per microcurie of radium in bone one can adopt the present practice of the ICRP, which equates 1 $\mu$Ci of $^{226}$Ra to 20 $\mu$Ci of $^{90}$Sr for purposes of radiation protection [12].

Radium and strontium absorbed into blood are eliminated from the body at different rates. From a comparison of the time integral of internal contamination during a period of 1 to 30 yr after intake it can be estimated that 3 $\mu$Ci of $^{90}$Sr at the end of one year give the same integrated exposure to bone as a terminal content of 1 $\mu$Ci of radium at the end of 30 yr (see section VI, para. 3).

Thus a terminal body burden of 1 $\mu$Ci of radium is considered equivalent in biological effect to 60 $\mu$Ci of $^{90}$Sr in the skeleton 1 yr.
TABLE I. RELATIONSHIP BETWEEN $^{226}$Ra BODY BURDEN AND CANCER INCIDENCE

<table>
<thead>
<tr>
<th>Residual body-content range ($\mu$Ci)</th>
<th>Total number of persons</th>
<th>Man-years of exposure</th>
<th>No. of malignancies observed</th>
<th>Probability of malignancy per man-year of exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group (1) 1 - 10</td>
<td>41</td>
<td>1300</td>
<td>14</td>
<td>$1 \times 10^{-2}$</td>
</tr>
<tr>
<td>Group (2) 0.1 - 1</td>
<td>62</td>
<td>2200</td>
<td>3</td>
<td>$1 \times 10^{-3}$</td>
</tr>
<tr>
<td>less than 0.1</td>
<td>135</td>
<td>-</td>
<td>0</td>
<td>-</td>
</tr>
</tbody>
</table>

after intake. It can be calculated that this corresponds to an intake of 1500 $\mu$Ci of $^{90}$Sr by inhalation or 2000 $\mu$Ci by ingestion.

From Table I it can be seen that a terminal body burden of 1 $\mu$Ci of radium (and by implication a 2 mCi intake of $^{90}$Sr) corresponds to a probability of a bone tumour of $10^{-3}$ to $10^{-2}$ per year of exposure.

5. Whole-body irradiation and the related early effects

Whole-body irradiation can be the result of exposure to:
(a) External irradiation (including irradiation from a radioactive cloud)
(b) Uptake of radionuclides distributed uniformly in the body, such as $^{137}$Cs and tritium
(c) Combined whole-body irradiation from external and internal sources.

The whole-body irradiation effect caused by a high-intensity dose from a passing cloud will differ from that caused by a low-intensity dose from an internal source incorporated over a period of a few months. It is important therefore in arriving at a decision that the appropriate authority take into account that whole-body irradiation delivered over short periods of time will be more damaging than a comparable dose delivered slowly over a period of a few weeks. Severe early effects following whole-body irradiation of the general public are not likely to be encountered in radiation accidents from the peaceful uses of atomic energy since an accident of sufficient magnitude is most improbable.
Table II indicates levels above which medically discernible signs of damage are observed from absorbed doses of gamma rays of brief duration (1 min - 1 h) and involving the whole body. More information about the acute effects of irradiation are found in section VII.

Whole-body irradiation from caesium-137 can occur, as mentioned previously, either from external irradiation from $^{137}$Cs deposited on the ground after an accident or from caesium incorporated by the ingestion of contaminated foodstuffs or the inhalation of contaminated air. However, the most likely method of radiation exposure from nuclear accidents in peaceful uses would probably be mainly from contamination of foodstuffs, especially milk.

In section VI a method is described for calculating levels of intake or levels of concentration of noble gases in the air which would lead to a whole-body irradiation of a certain dose. The calculations for caesium-137 are indicated in section VI, para. 4 and for tritium and the noble gases in section VI, para. 5.

6. Reference doses and related risk estimates for risks other than leukaemia, thyroid carcinoma, primary bone tumours

It is important to know the incidence of other radiation-induced malignancies in addition to those of leukaemia, thyroid carcinoma.
and bone cancer. The data from Hiroshima (para. 12, page 8 [3]) and Nagasaki provide suitable bases for the determination of the overall risks of radiation-induced malignancy resulting from whole-body exposure with substantial doses. It is still too soon after the exposure of these populations for all malignancies to have developed, but present data suggest that leukaemia may well be the predominant type of malignancy produced. The expected number of all other malignancies is likely to be approximately the same as the number given for leukaemia.

The natural incidence of all malignancies in a population varies according to geographical location. An example is given in Table III for some areas where data are available.

7. Gonadal irradiation and related genetic risk

It is well established that gene mutations as well as breaks and other alterations in the chromosomes may be induced by irradiation of living cells. Hence gonadal exposure can be expected to lead to genetic effects. There is general agreement that any increase in mutations from radiation would be detrimental in man. General agreement does not exist however on the amount of genetic damage that would be associated with any given dose of radiation. This is because of the inadequacy of available data, the many scientific uncertainties involved, and an incomplete understanding of the genetic structure and dynamics of individuals and human populations. Quantitative risk estimates are therefore not attempted here. The matter has however received consideration recently by other bodies including the UNSCEAR and ICRP, and these reports may be consulted for estimates of the risks involved and of the assumptions made in arriving at such estimates [14]. For convenience, the relevant tables and associated texts from the ICRP report [14], as well as the relevant text from the UNSCEAR report [4], are reproduced in section VII.

The expression of genetic damage arising from the irradiation of germ cells of members of a population may occur in the first generation or be delayed and occur in later generations. The types of genetic damage may vary from what might be regarded as socially inconsequential, such as a failure of a fertilized egg to implant in the uterus, to the inheritance of a disabling disease.
TABLE III. INCIDENCE OF MALIGNANCY FOR CERTAIN GEOGRAPHICAL AREAS [13]

<table>
<thead>
<tr>
<th>Country</th>
<th>Morbidity rates per 10^6 persons from the natural incidence of malignant neoplasms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada - Ontario (1961)</td>
<td>1376</td>
</tr>
<tr>
<td>USA - Connecticut (1961)</td>
<td>3450</td>
</tr>
<tr>
<td>Federal Republic of Germany - Hamburg (1962)</td>
<td>3016</td>
</tr>
<tr>
<td>UK - England and Wales (1961)</td>
<td>2347</td>
</tr>
<tr>
<td>Australia - Victoria (1961)</td>
<td>1739</td>
</tr>
</tbody>
</table>

8. Risk estimates in perspective

The appropriate authorities should observe the need for evaluating radiation risks in relation to other hazards to life and property. In doing so the appropriate authority must always consider those risks pertinent to the country and the community in making its final evaluation.

It is not intended in this document to present a comprehensive review of radiation injury in perspective to other dangers to life in man's environment. This subject has been dealt with by the World Health Organization [15].

V. PRACTICAL APPLICATIONS FOR THE USE OF REFERENCE DOSES AND RELATED RISKS OF SECTION IV IN MAKING POLICY DECISIONS NECESSARY TO MEET AN ACCIDENTAL RADIATION EXPOSURE SITUATION (ACTUAL OR POTENTIAL)

1. General introduction

Accidental radiation exposure referred to in this report is actually or potentially a consequence of an event out of the ordinary that threatens to expose people in the general public to ionizing radiation in excess of the limits of exposure for the public under normal operating conditions, as set forth in the Agency's Basic Safety Standards for Radiation Protection [9]. While such circumstances need
not necessarily imply an emergency situation, some appropriate counter measures might be considered and if necessary instituted to keep the exposure of the public as low as practicable. Under such circumstances this document becomes applicable once an accidental exposure beyond the limits indicated in Ref. [9] occurs. In the case of accidental radiation exposure the appropriate authority may decide to use measures ranging from an extension of the monitoring procedure to counter measures of an emergency nature, depending on the estimated accidental radiation exposure and the corresponding radiological risk.

In assessing the radiobiological hazards of an accidental exposure, it is necessary to recognize the different modes of exposure, for example by inhalation, food or water contamination, external radiation, etc., the time during which an accidental exposure occurs, the dose ranges which are to be expected for various groups of individuals and the number of individuals possibly exposed in such a dose range.

It is recognized that this evaluation can hardly be done for all modes of accidental exposure, all groups of individuals (pregnant women, children, adults) and with regard to all possible damage (early and late effects in different critical organs). However, in each particular accident probably only one or a few sets of combined conditions will be the critical ones and only one or a few forms of radiation damage may represent the dominant risk. (For example, in an accident involving contamination of pastures by fresh fission products, the immediate critical nuclide will be $^{131}$I, the critical pathway may be through milk, the critical age group children and the risk for children thyroid cancer.) Other radionuclides may predominate later with respect to possible hazard.

For any critical set of conditions the best feasible estimate of the total risk should be made.

(a) With regard to early effects, every precaution should be taken to plan measures to meet accidental situations so that, as far as possible, in the event of an accident no individual doses would produce serious acute damage.

(b) The increased probability of late effects at doses below acute injury but above normal levels is not only of concern to the individual but also to the community as a whole.

The risk to the individual can be assessed on the basis of the individual doses and the associated risks. However, the community is also concerned with the overall impact of the radiation exposure.
which is evaluated by the expected number of later effects in the population. The total expected number of late effects can be calculated on the basis of the product of the mean dose per individual and the number of individuals exposed (man rad). The number of potential disabilities and deaths in the exposed population with and without counter measures can then be estimated and this serves as one basis for the decisions of the appropriate authority.

The evaluation of a hypothetical accidental exposure must necessarily take into account the probability of occurrence of the accident, in addition to the considerations outlined in the preceding paragraph. Probabilities of occurrence of accidents leading to exposure of population groups are difficult to assess accurately at present, but past experience shows that they are quite small, as expected from reliability considerations of designs, components and procedures. Safety evaluation of reactors shows that the probability of occurrence of an accidental exposure of the public decreases markedly with the magnitude of the exposure.

It can therefore be concluded that the risk incurred by a population from the presence of a nuclear installation is orders of magnitude lower than the risk from the exposure assumed for safety calculations, because of the low probability of the occurrence of a severe accident. In particular it should be noted that the risk of an accident with extreme consequences need not be unacceptable if the probability of occurrence is sufficiently small.

The setting up of a new nuclear installation should involve the following steps:

(a) Selection of a site for technical and economic reasons
(b) Preparation of a design proposal by engineers
(c) Preparation of a hazards analysis by appropriate experts. This should show that for normal operations and minor incidents the maximum permissible doses and intakes specified in the Basic Safety Standards [9] will not be exceeded. It should then go on to describe one or two representative accidents\(^1\) based on realistic assumptions which are specific for the installation and made with competent engineering advice. The resulting hypo-

\(^1\) In the present context of assessing the safety of a nuclear installation, the term "representative accident" is used to convey briefly the idea of a hypothetical accident with the following characteristics: it should be a type of accident which is specifically appropriate to the type of reactor under consideration; it should be in the middle range of probability and severity, in other words severe enough to test the safety provisions but not so severe as to be incredible.
Theoretical exposure to external radiation or internal contamination of the neighbouring population should then be calculated. The designers should also, if possible, provide estimates of the probability of occurrence of the accidents mentioned above. An estimate of the dose which would be received by the neighbouring population should be made, taking into account the application of reasonably practicable counter measures. This dose should then be compared with reference doses accepted by the appropriate authority, as discussed below, for safety evaluation purposes.

If this procedure for safety evaluation is used the appropriate authorities must provide assurance that the facilities and resources necessary to effect such counter measures promptly and effectively are available.

The Reference Doses for Safety Evaluations (RDSE) used by the appropriate authority are at present in the range of 1 to 100 times the annual dose limits for members of the population [9]. In selecting RDSE values for a particular set of circumstances the authority should be guided by the estimates of Chapter 4 of Ref. [9], by the estimated probability of the accident which could result in such a dose and by the number of people involved.

The national authorities of some countries have chosen as one RDSE for safety evaluation of a major nuclear installation a dose of about 25 rem to the whole body for individuals in the population. This is the level below which minimum early clinical damage is not readily observed in an individual. Reference to Chapter 4, section 4.2-4.9 of Ref. [9], will show that the probabilities of even the delayed effects from such a dose are relatively small.

These national authorities have used the RDSE in the following manner. If the estimated dose from a representative accident in connection with a specific proposal is below the reference dose, the specific proposal is accepted. If the dose is above the RDSE, the proposal is accepted only if by engineering means the probability and consequences of the accident are made acceptably small.

By way of further explanation different national authorities have selected different hypothetical accidents to which they apply the RDSE. It is relevant to emphasize that the development of atomic energy programmes might be placed in jeopardy if the authorities select RDSE values which, when account is taken of all the criteria referred to above, are too stringent. Clearly, the benefits which a community will derive from a nuclear reactor are an extremely important factor in deciding how much risk the population should be
asked to accept. Thus, the determination of the RDSE will be influenced by this consideration.

2. The process of making policy decisions for dealing with radiation accidents

It is recommended that advanced planning and the process of making policy decisions for dealing with radiation accidents take into account the following:

(a) Information from surveillance and monitoring
(b) Prediction of outcome of exposures
(c) Evaluation of the available counter measures and the identification of the responsible authority(ies).

2.1. Surveillance and monitoring

It is necessary to be prepared in advance for a potential accident by establishing a system of communications and procedures for assembling the radiological and other data necessary for an evaluation of the situation. Some of the data mentioned below can be prepared in advance (e.g. data on the distribution of population in the environment) and every effort should be made to prepare information of this nature in advance. When an accident involving release of radioactivity to the environment occurs, information relating to the following will be urgently required.

(a) Data relating to the meteorological situation will be of primary importance to enable the rapid delineation of the zone likely to be affected by the accident. Seasonal factors have to be considered as well in determining the possibility of contamination of foodstuffs.
(b) A continuous flow of information from the plant relating to the nature and probable magnitude of the actual or expected release of radioactivity will be important.
(c) Radiological monitoring data comprising dose rates and corresponding ground and agricultural products contamination over the area affected. Information will be required at later times on the contamination by long-lived isotopes of crops and water which may need to be determined by radiochemical methods. The IAEA has under preparation a manual on the monitoring of the environment under emergency conditions [16].
(d) Identify population at risk. Information pertaining to individuals and population groups and the population at risk, noting that this may not coincide with the contamination area.

2.2. Prediction of outcome of exposure

It is necessary to establish a system for predicting the outcome of any estimated exposure with respect to the radiobiological risk involved with and without counter measures. The predicted outcome is understood to be the result of total exposure from the event causing the accidental exposure. The reference doses of section IV and the information in section VII serve to estimate the outcome of such an exposure.

It is recognized that the risk from accidental radiation exposure from the peaceful uses of atomic energy would be mainly caused by the risk from the late effects of radiation. This is because exposure to doses which would produce severe early effects, as shown in Table II, section IV, para. 5, is extremely unlikely.

2.3. Evaluation of available counter measures and identification of appropriate authorities

It is necessary to investigate in advance the possible measures which might be taken in the event of an accident to reduce exposures to the population. Once these measures are identified it is necessary to:

(a) Determine the statutory power and resources necessary to carry out the measures
(b) Estimate the total advantages and disadvantages of the measures which would be associated with each.
(c) Develop plans and procedures for putting the measures into effect at the time of an accident.

Plans should be devised so that, after an accident, the appropriate authorities can act promptly and effectively with respect to the following considerations.

On the basis of the estimated dose from external and internal radiation and the associated biological risks for the population exposed, derived as described in section V, para.2.2, the appropriate authority must determine if an action is to be initiated to reduce the prospective dose to the public. Initiation of such an action may involve undesirable consequences. These include acceptance of any
risk associated with the available actions, the socio-economic im-
 pact resulting from disruption of the normal lives of the people af-
fected, and their reaction to the disruption. Naturally, the higher
the estimated dose (including prospective dose) to the public, the
more urgent it is to take counter measures to avoid the prospective
dose.

The prospective dose per individual, avoided by the application
of the counter measure, is important in deciding the action to be
taken. The magnitude and composition of the release, the mode of
exposure (inhalation, external radiation from material on the ground
and contamination of foods) and the time sequence of the event re-
quire many decisions. Therefore, decision-making is a continuous
process and requires continuous liaison between the appropriate
authority, the nuclear establishment, the control room and the per-
sonnel who can provide current information about the nature and mag-
nitude of the release. For example, the inhalation exposure fol-
lowing a single, abrupt release may not be avoidable, whereas it
may be possible to avoid an important fraction of the exposure if
the release occurs over a more extended period (one or more days).

Controls to be placed on the utilization of food, water, and crops
may also require a succession of decisions over a period of time.
When the event has contaminated an area involving dairy farms and
the production of milk, the area in which the milk may be consumed
can be many times greater than the production area because of the
distribution patterns. In particular, iodine-131 is transmitted
through milk very rapidly so that controls, to be effective, must be
initiated as early as 24 to 48 h after the accident. When it is decided
to initiate control measures, criteria for removing them must also
be established. These decisions must be made very carefully by the
appropriate authority if the health protection achieved is to be com-
mensurate with the total impact of the action itself. Although
general plans and advanced criteria can, and must, be prepared in
advance, as described in section V, para.2.1, the application of these
criteria in any actual case will require many practical decisions to
be made continuously throughout the entire course of the event.

Continuous decisions may also be required in regard to other
modes of exposure. For example, by evacuation it might be
practicable to avoid a significant fraction of the external exposure
following the deposition of material rich in short-lived nuclides on
the ground if only a few people are involved. However, it may not
be practicable if the aged, the ill, and young children must be eva-
cuated to neighbouring areas. If the external exposure is being caused largely by the deposition of longer-lived nuclides so that the daily dose rate is relatively small, but the cumulative dose over a year or more is considered sufficient to warrant its reduction, evacuation is a very drastic action and should be considered only as a last resort. One or all of these types of decisions may be required at different times after a sufficiently severe release.

It must be recognized in applying these criteria that practical decisions concerned with the protection of the public in the event of accidental exposure must be kept flexible and must not necessarily be connected with a particular value of exposure. The total impact and practicability of available procedures balanced against the radiation risk becomes the controlling criterion for such decisions. In this regard, it should also be recognized that the total radiation risk to the population can be modified substantially by applying the controls selectively to provide preferential protection for infants and foetuses.

VI. COMPUTATION OF DOSES INTO INTAKES OF RADIO-activity AND LEVELS OF CONCENTRATION IN DIET (SUCH AS MILK), AND TIME INTEGRALS OF CONCENTRATION IN AIR THAT IS INHALED

1. General

The appropriate authority must decide and select a certain dose(s) D, calculated in rads, to the critical organ or whole body, which is considered acceptable under the prevailing circumstances of a particular accidental situation, actual or potential. In arriving at the decision, the appropriate authority should take into account the risk estimates as indicated in section IV and the provisions of section V. It would then be necessary to calculate the corresponding possible intakes of radioactive material resulting from the dose D. These intake values in turn must be converted into levels of concentration in foodstuffs and into time integrals of concentration in inhaled air. Such computations would depend on many varying factors, among which are:

(a) The critical age group of the population to be affected and the critical organ. For $^{131}I$ the critical organ would be the thyroid
gland, for $^{90}\text{Sr}$ or $^{89}\text{Sr}$ bone and for $^{137}\text{Cs}$, $^3\text{H}$ or the noble gases the whole body;

(b) Metabolic data and parameters pertaining to the pathway and turn-over of the specified radionuclide in the critical age-group and data pertaining to the food habits of these individuals.

(c) Data pertaining to the food chain which begins from the time of deposition of radioactive material and its pathway through the various food chains in animals and plants until the material finally comes to man's food. Methods are given for the calculation of dose to tissues from radioactive nuclide concentrations in food or vice versa.

The steps involved in such a calculation can be summarized as follows.

(a) The appropriate authority arrives at a decision for selecting a dose $D$ which is appropriate for the situation concerned, to meet an accidental exposure (potential or actual) as indicated in section III of the main text. In arriving at that decision the authority must evaluate the risk estimates from such an exposure. The reference doses in section IV provide guidance in this respect. In addition, the authority, in deciding the dose $D$, must take into consideration the practical guidance in section V.

(b) The next step would be to calculate the total intake from either inhalation or ingestion which would deliver the dose $D$ to the critical organ of the critical age group likely to suffer most from the accidental exposure.

(c) In the case of ingestion, the intake is then converted to levels of concentration in food which, upon consumption by the critical group of individuals, would not deliver a dose to their critical organ greater than $D$.

(d) In the case of inhalation, the intake is converted to time integrals of concentration. In the case of noble gases a special calculation is made as indicated in section V.

1.1. Formulas to calculate intake of radioactivity, levels of concentration in diet (e.g. milk) and time integrals of concentration in air

1.1.1. Formulas for total intake of radioactivity by ingestion

Formulas for the calculation of the total intake by ingestion ($I$), delivering a dose $D$ to the critical organ of the individuals likely to
be exposed to accidental irradiation, involve the following parameters:

\[ f_w \] The fraction reaching the critical organ by ingestion (Table 12 of Ref. [17]).

\[ \text{Mass of critical organ in grams} \]

\[ T \] Effective half-life of the radionuclide in the critical organ

\[ t \] Time after exposure in days

\[ T_0 \] Life expectancy after intake

- 50 yr for adult = 18,250 d
- 70 yr for infant = 25,550 d

\[ \Sigma EF \] Effective energy of the radiation per disintegration (MeV)

1 μCi produces 3.7 × 10^4 dis/sec
1 MeV = 1.602 × 10^{-6} erg
1 rad = 100 erg/gram of tissue
8.64 × 10^4 = number of seconds in a day

The dose rate to the critical organ bearing 1 μCi of the radionuclide in question is

\[
\frac{3.7 \times 10^4 \times 1.6 \times 10^{-6} \times 10^{-2} \times 8.64 \times 10^4 \times \Sigma EF}{w} \text{ rad/d}
\]

\[ = 51.15 \frac{\Sigma EF}{w} \text{ rad/d} \]

By using the parameters listed above, one may express the dose to the critical organ after the ingestion of 1 μCi, \( D_{1w} \) as,

\[
D_{1w} = 51.15 \frac{f_w \Sigma EF}{w} \int_0^{T_0} e^{-0.693t/T} \ dt = 73.81 \frac{f_w T \Sigma EF}{w} (1 - e^{-0.693t/T}) \text{ rad} \quad (1)
\]

The value for \(^{131}\text{I}\) and \(^{137}\text{Cs}\) is 73.81 \( f_w T \Sigma EF/w \), since the value of the bracket is equal to one.

The intake \( I_w \) which would deliver a total integrated dose \( D \) to the critical organ during the life expectancy after intake would be

\[
I_w = \frac{D}{D_{1w}} = \frac{Dw}{73.81 f_w T \Sigma EF (1 - e^{-0.693T_0/T})} \mu \text{Ci} \quad (2)
\]
The value for $^{131}$I and $^{137}$Cs is $Dw/73.81 f_w T\Sigma EF \mu Ci$, since the value of the bracket is equal to one.

1.1.2. Formulas for daily intake of radioactivity by ingestion and the corresponding level of concentration in food

The radioactive material deposited may enter a reservoir of a food chain leading to contamination of foodstuffs. In the case of ingestion of such foodstuffs, if the rate of transfer of radioactivity, to the critical organ, after an initial deposition in the reservoir, is fast, then the concentration of the nuclide in the foodstuff will rise to a maximum level which is reached when the rate of uptake into the foodstuff is balanced by the rate of loss. Let $X_0$ be the maximum concentration of the nuclide in the foodstuff. The concentration $X$ at time $t''$ afterward is $X_0 e^{-\lambda' t''}$, where $\lambda'$ is the decay constant for the transfer through the food chain. The total activity ingested from the occurrence of maximum concentration to time $t''$ afterwards is represented as follows:

$$V \int_0^{t''} X dt = VX_0 \int_0^{t''} e^{-\lambda' t''} dt = \frac{VX_0}{\lambda'} (1 - e^{-\lambda' t''})$$  \hspace{1cm} (3)

where $V$ is the quantity of the foodstuff ingested per day, $\lambda' = 0.693/T'$ and $T'$ is the half-life in the food chain. For $^{131}$I and $^{137}$Cs this activity is merely $VX_0/\lambda'$, since the exponential term becomes very small at $t'' = T_0$.

From Eqs. (2) and (3) the maximum concentration in the foodstuff, which corresponds to a total intake $I_w$ as defined in Eq. (2), is equal to

$$X_0 = \frac{Dw}{10^2 TT' V f_w \Sigma EF (1 - e^{-0.693 t''/T'}) (1 - e^{0.693 T_0/T'})} \mu Ci/unit vol$$  \hspace{1cm} (4)

For $^{131}$I and $^{137}$Cs $X_0 = Dw/10^2 TT' V f_w \Sigma EF$, since the exponential terms become very small at $t'' = T_0$.

This calculation refers to a peak concentration which allows decay to bring about a reduction with time until the intake is insignificant. If this approach is used the peak concentration takes care of any individual incident regardless of the duration of the exposure. A similar formula is to be used for food contaminated directly by
exposure to a radioactive cloud, except in this case the food chain half-life $T'$ is replaced by the physical half-life of the nuclide, $T_r$,

$$X_0 = \frac{Dw}{111 f_w VT \sum EF T_r} \quad (5)$$

or $T''$ for the half-life of the foodstuff, if this is different.

$$X_0 = \frac{Dw}{111 f_w VT \sum EF T''} \quad (6)$$

1.1.3. Formulas for intake of radioactivity by inhalation and the time integrals of concentration

(a) For soluble compounds

The same argument applies as that for Eqs. (1) and (2). If $f_w$ is substituted by $f_a$ (Table 12 of Ref. [17]), where $f_a$ is the fraction of the inhaled radioactivity reaching the initial organ, then

$$I_a = \frac{D}{D_{1a}} = \frac{Dw}{73.81 f_a T \sum EF (1 - e^{-0.693 T/T})} = \frac{Dw}{73.81 f_a T \sum EF} \mu Ci \quad (7)$$

where $I_a$ is the intake through inhalation delivering a dose $D$ to a critical organ weighing $w$ grams.

Therefore the parameters necessary to compute the intake through inhalation are:

(i) The weight of the critical organ ($w$) of the critical age group,
(ii) $f_a$, the fraction of the radionuclide reaching the gland by inhalation,
(iii) $T$, the effective half-life of radioactive nuclide in the critical organ.

(b) For insoluble compounds

For insoluble compounds incorporated through inhalation the critical organ is the lungs. The dose to the lung from inhalation
of insoluble compounds can be calculated as follows. It is assumed (Table 10, Ref. [17]) that the retention of particulate matter in the lungs, when specific data are lacking for insoluble compounds, is: 25% is exhaled at once, 62.5% is eliminated in one day and 12.5% is retained in the lungs with a half-life of 120 d. In the case of plutonium and thorium the biological half-life is one year and four years, respectively. The dose to the lung is made up of two components. The first component of dose is a result of the assumed 62.5% that remains in the lung for one day with only physical decay taken into account. The second dose component is from the 12.5% of the inhaled activity which is assumed to be eliminated with an effective half-life of 120 d. If the mass of the lung in adults is assumed to be 10^3 g (in the case of children and infants a smaller value must be used), a dose rate of 1 µCi of an insoluble compound to the lung is 3.7 \times 10^4 \text{SEF} \times 1.602 \times 10^{-6} \times 10^{-3} \times 10^{-2} \times 8.64 \times 10^4 \text{rad/d}, or 5.1 \times 10^{-2} \text{SEF rad/d}. Hence the dose to the lung (D_L) per microcurie inhaled would be

\[
D_L = 0.625 \times 5.1 \times 10^{-2} \text{SEF} \int_0^1 e^{-0.693/T_r} \, dt \\
+ 0.125 \times 5.1 \times 10^{-2} \text{SEF} \int_0^{T_0} e^{-0.693 t/T} \, dt \\
= \text{SEF} \times 10^{-2} \left[4.6 T_r (1 - e^{-0.693/T_r}) + 0.92 T (1 - e^{-0.693 T_0/T}) \right] \text{rad/µCi}
\]

(8)

Once a decision is made with respect to the dose D, it would therefore be possible to determine the corresponding total intake and the maximum time integral of concentration.

(c) The maximum time integral of concentration

The concentration (C) of radioactivity in breathing air may vary with time. If the breathing rate V is expressed in proper units, then the intake during a small interval of time dt is equal to the concentration of radioactivity multiplied by V dt. Therefore the total intake I_a would be equal to V/C dt, i.e. the breathing rate multiplied by the maximum time integral of concentration; or the maximum
time integral of concentration is equivalent to the total intake divided by the breathing rate.

2. Iodine-131

2.1. Total intake of $^{131}$I by ingestion

The intake $I_w$ can be calculated by using Eq. (2) and substituting $0.23 \text{ MeV}^{[12]}$ for $\Sigma E F$. The intake $I_w$ which would deliver a total integrated dose $D$ to the thyroid gland during the life expectancy after intake would be

$$I_w = \frac{D}{D_{1w}} = \frac{Dw}{f_w 16.99 T} \mu \text{Ci} \quad (9)$$

Therefore the parameters necessary to compute the intake are the weight of the gland ($w$) of the critical age group, $f_w$ the fraction reaching the gland by ingestion and $T$ the effective half-life of radioactive iodine in the gland.

The intake for a given dose $D$ depends on the size of the thyroid and the uptake of iodine from foods, which varies for different ages. The average mass of the gland for a given age group may vary in different locations and therefore the responsible authority should have data on the mass of the thyroid gland and its uptake for different ages of the individuals for whom they are responsible. In the absence of such data reasonable values are quoted here as an illustration. The mass of the gland is assumed to be 2 g from birth to six months, 3.5 g at the age of three years, 10 g at the age of 10 years and 25 g in the adult. The uptake is assumed to be 30%. A conservative view would be to assume that the amounts of $^{131}$I in the thyroid decrease at a rate no faster than that caused by radioactive decay, i.e. with a half-life of eight days.

For children fed on milk only the maximum thyroid irradiation would be likely to occur at an age of about six months since the thyroid size increases very little from birth until this age whereas the milk intake may increase with body weight until this age. Therefore if we take the six-month-old infant as the critical age group and substitute the corresponding parameters in Eq. (2)

$$I_w = \frac{2D}{0.3 \times 16.99 \times 8} = \frac{D}{20.39} \mu \text{Ci}$$
where the dose D selected by the responsible authorities in charge of the situation was found appropriate to the situation. If, for example, the value chosen for D is 25 rad, then \( I_w = 1.23 \mu Ci \).

2.2. Emergency levels of daily intake of \(^{131}\text{I}\) by ingestion

For calculation of emergency levels of the daily intake of iodine-131, fresh milk in dairy producing areas is regarded as the most important source of the isotope. If pastures are contaminated with iodine and no loss of isotope occurs from the herbage except that by radioactive decay, the iodine content of the milk from the cows grazing on these pastures will reach a maximum concentration about 3 d after contamination. After the first week, this value falls with the half-life of iodine-131.

By using the example given in para. 2.1 for six-month-old infants, i.e. a dose of 25 rad to the thyroid and a total intake of 1.23 \( \mu Ci \) of iodine-131, the maximum concentration of \(^{131}\text{I}\) in milk can be found from Eq. (4). Thus

\[
X_0 = \frac{0.693 \times 25}{8 \times 20.39} = 0.106 \mu Ci/\text{litre}
\]

This calculation refers to a peak concentration which allows decay to bring about a reduction with time until the intake is insignificant. If this approach is followed, the peak concentration takes care of any individual incident regardless of the duration of exposure.

2.3. Intake of \(^{131}\text{I}\) by inhalation and time integrals of concentration

The conversion of the selected dose D into time integrals of concentration in air, if the hazard to the public is through the air breathed in that particular case, would, as in the case of intake by ingestion, depend on many varying factors, among which are:

(a) The critical age group

(b) Metabolic data and parameters pertaining to the pathway in the body and the pattern of radioactivity inhaled.

The total intake of \(^{131}\text{I}\), \( I_a \), can be computed for a dose D to the thyroid gland weighing w grams by Eq. (7).

\[
I_a = \frac{D}{D_{1a}} = \frac{Dw}{f_a 16.99 T} \mu Ci
\]
The parameters necessary to compute the intake are the same as those for Eq. (7), T being the effective half-life of radioactive $^{131}$I in the gland.

The intake through inhalation depends on the breathing rate which is a function of age. The critical age group is the one-year-old child whose breathing rate is 330 litres per hour$^2$. The $f_a = 0.23$ [17] and the weight of the gland is 2.2 g for a one-year-old child. Assuming again $T = 8$ d,

$$I_a = \frac{2.2 \times D}{0.23 \times 16.99 \times 8} = 0.07 \text{ D } \mu\text{Ci}$$

Therefore, the maximum time integral of concentration (nCi-h/litre) is $I_a/330 = 0.21 \text{ D nCi}$ and the maximum time integral of concentration $I_a/V$ is 5.3 nCi-h/litre.

For insoluble compounds of $^{131}$I incorporated through inhalation the critical organ is the lungs. The dose to the lung from inhalation of insoluble compounds can be calculated from Eq. (8). However, in the case of iodine some insoluble compounds such as AgI find their way readily to the thyroid gland.

In the case of $^{131}$I intake by inhalation, the contribution from other iodine isotopes and tellurium-132 should be accounted for; the value for $^{131}$I should be reduced by a factor of two or in the case of a release of short-lived fission products from a critical accident by a factor of ten. This factor is not applicable in the case of nuclear reactor accidents where there is no previous build-up of fission products. In calculating the dose to the thyroid gland, the contribution to dose from both inhalation and ingestion should be added together.

3. Radioactive strontium$^3$

3.1. Metabolism

The metabolic pathway of strontium in man is closely associated with the metabolism of calcium. It is therefore similarly subject

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$^2$ Breathing rate for an adult is 830 litres per hour.
Breathing rate for six-month infant is 250 litres per hour.
Breathing rate for infant at birth is 100 litres per hour.

$^3$ In preparing this section quotations and other information were used from Ref.[6] and the NAS-NRC Advisory Committee to the Federal Radiation Council: "Implications to man of irradiation by internally deposited $^{89}$Sr, $^{90}$Sr and $^{137}$Cs" (1964).
to variations in diet, age and various physiological states, e.g. lactation. After ingestion of radiostrontium part of it is absorbed through the gastro-intestinal tract and part is excreted in the faeces. The amount which enters the blood from the gastro-intestinal tract after ingestion is indicated as $f_1$ and is equal to 0.3 [16]. The part which is absorbed is deposited in the skeleton, distributed in the soft tissues and circulating fluids or removed from the body by urinary excretion and endogenous faecal excretion.

After short-term exposure⁴ the pattern of skeletal distribution can be pictured as follows; radiostrontium from the blood rapidly enters the bone by ion-exchange on the surface of bone crystal and by incorporation into new bone which is being formed in zones of growth and remodelling. This leads to focal areas of highly localized radioactivity known as "hot spots", and diffuse areas of generally lower concentration. In young growing individuals and in cancellous bone, formation rates are high resulting in comparatively high local deposition of radioactivity. The removal of radiostrontium from bone once it has been deposited is relatively slow, depending mainly upon the extent of bone resorption and mineral exchange. From observations on intravenous injection of $^{90}$Sr in man it can be deduced that in the adult only 1/6 to 1/10 of the material entering the exchange space will fail to be excreted within a year. Thus 0.1 of that which enters the circulation will remain tenaciously fixed in bone thereafter. Therefore the fraction reaching the bone after ingestion and remaining firmly fixed there after one year and thereafter is $0.3 \times 0.1$, or 0.03 as indicated in section IV, para. 4.5.

Similarly in the rare event of soluble $\text{Sr}^{i5}$ being inhaled during an accident, the fraction which reaches bone and remains tenaciously fixed at about one year and thereafter can be calculated. The fraction of the total amount of $\text{Sr}\text{aerosol}$ which would reach the absorptive area of the lung is conventionally assumed to be 0.25[17]. This fraction is absorbed into the circulation nearly instantaneously. A further fraction 0.5 is conventionally assumed to be carried up the respiratory passages to be swallowed later. So the total fraction of strontium reaching the circulation as a result of the event will be more than 0.25, perhaps 0.4 in all. Considering again as mentioned previously that only 1/6 to 1/10 of the total material entering

---
⁴ In this report short-term exposure refers to exposures equal to or similar to the exposures indicated in para. 3.2.1. of this section.

⁵ For the purpose of this report the symbol $\text{Sr}^{i5}$ refers to either $^{90}\text{Sr}$ or $^{93}\text{Sr}$.
the exchange space will fail to be excreted within a year, 1 µCi of radioactive strontium is inhaled, about 0.4 µCi will enter the circulation and about 0.04 µCi will remain in bone after one year (section IV, para. 4.5).

The behaviour of strontium in the body can be considered either in terms of the relation between strontium and calcium or in terms of strontium itself. Although the data on the retention of strontium in the body suffices for estimating body burdens for short-term ingestion, analysis of the Sr-Ca ratio facilitates estimating concentrations of radiostrontium in newly formed bone, and in the entire skeleton under conditions of protracted intake. The reasons for this are (a) homeostatic control of calcium leads to a remarkable constancy of calcium concentration in most tissues and fluids; (b) metabolism is regulated more by calcium levels than by normal amounts of stable strontium and, (c) strontium and calcium movements are usually affected similarly by extraneous factors. Extensive experimental evidence in man and animals shows that the Sr-Ca ratio in tissues and secretions is directly related to the ratio that exists in the diet within the normal dietary limits. Thus in para. 3.2 of this section the Sr-Ca ratio will be used.

The ratio of strontium to calcium in children's bones compared to the Sr-Ca ratio in the diet is based on the results obtained from measurements made on $^{90}$Sr from fallout. The proportion of radioactive strontium incorporated into the skeleton from the diet depends mainly on:

(a) The discrimination by the body in favour of Ca in the passage of these elements from the diet to a given tissue in the body, which is usually expressed as the observed ratio (OR). The OR relates the Sr-Ca ratio in a given compartment of the body at equilibrium to that ratio in the diet. In the case of bone,

$$\text{OR (bone/diet)} = \frac{\text{Sr/Ca in bone}}{\text{Sr/Ca in diet}}$$

The OR (foetal bone/mother's diet) = 0.1. The OR changes from about 1 at birth to about 0.5 at 6 months-1 yr and to about 0.25 shortly thereafter. The Federal Radiation Council in the United States of America selected an OR of 0.35 as the most representative value for the age group of interest, i.e. 6 months-2 yr.

(b) The sum of the calcium involved in skeletal growth (net accre-
tion), and the quantity of calcium in the existing skeleton that is turned over. Mitchel et al. [18] has estimated the net annual calcium accretion from birth to 20 yr, after which time skeletal growth ceases.

### TABLE IV. QUANTITY OF CALCIUM AND ESTIMATED NET ACCRETION FOR VARIOUS AGES

<table>
<thead>
<tr>
<th>Age</th>
<th>Quantity of calcium in the skeleton (g)</th>
<th>Net accretion of calcium (g)</th>
<th>Bone mineral turn-over per year (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foetus-birth</td>
<td>0 - 28</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>Birth-1 yr</td>
<td>28 - 100</td>
<td>72</td>
<td>50</td>
</tr>
<tr>
<td>1 yr-2 yr</td>
<td>100 - 150</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Adult life</td>
<td>1000</td>
<td>nil</td>
<td>1, in shafts of long bones and 10, in cancellous bone</td>
</tr>
</tbody>
</table>

The quantity of calcium and the estimated net accretion for various ages is given in Table IV. The fraction of skeletal calcium incorporated by accretion and turnover during the period of intake is denoted by F. F can be calculated from the data in Table IV as follows:

(i) For the infant 1 to 2 yr old

\[
\frac{50 + 50}{150} \times \frac{\text{number of days with average intake}}{365}
\]

(ii) For the ante-natal period, the maximum strontium burden of the developing skeleton would result when the period of intake coincides with and lasts for the length of the last trimester of pregnancy, i.e. when essentially all of the mineralization of the foetal skeleton occurs.

### 3.2. Dosimetry considerations

The estimation of the dose to the target tissue resulting from a certain radioactive strontium burden depends on the model used. At
a given time, the maximum local concentration of radioactivity in the skeleton "hot spots" depends on the Sr\textsuperscript{*}-Ca ratio in new bone. On the other hand, the average concentration of radioactivity in the skeleton, and thus the average dose to bone, is related to the ratio of Sr\textsuperscript{*} in the body to the total calcium in the body. One can use either of these models to estimate the corresponding doses in rads. The difference between the two doses is large.

The United States Federal Radiation Council, after evaluating results from a computer using a dynamic model for estimating dose after the ingestion of radioactive strontium, which simulates incremental changes in skeletal strontium on a day-to-day basis, found that a less-refined approach using strontium diet levels averaged over the period of intake and other simplified assumptions regarding net calcium accretion and bone turn-over would provide comparable estimates of dose. This is the method followed in this section.

3.2.1. Radiation dose to mineral bone, short-term exposure\textsuperscript{6}

If Sr\textsuperscript{*} is uniformly distributed throughout the mineral bone of the adult 1 nCi \textsuperscript{89}Sr/g Ca would result in a dose of 0.3 rad to mineral bone [19]. One nCi \textsuperscript{90}Sr/g Ca uniformly distributed in adult bone would result in a dose of 2.7 rad in a year [20]. This is approximately the same if one considers the ICRP model which indicates that 2 \mu Ci body burden (bone burden) of \textsuperscript{90}Sr is equivalent to a body burden (bone burden) of 0.1 \mu Ci of \textsuperscript{226}Ra which delivers a dose of 30 rem/yr (6 rad/yr)\textsuperscript{7} to the adult bone containing 1000 g Ca.

Therefore 1 \mu Ci \textsuperscript{90}Sr/g Ca diffusely distributed in adult bone will deliver 3 rad in a year. The dose to mineral bone of the foetus and infant may be about half the adult values because the young skeleton absorbs less of the available beta energy [21].

The dose (D) can be calculated by

\[ D = R_b \times \text{dose conversion factor} \]

where R\textsubscript{b} is the average Sr-to-Ca ratio in the skeleton, and the dose conversion factor can be taken as mentioned: namely, if Sr\textsuperscript{*} is uniformly distributed throughout the mineral bone of the adult, 1 nCi \textsuperscript{89}Sr/g Ca would result in a dose of 0.3 rad to mineral bone, 1 nCi

\textsuperscript{6} Short-term exposure refers to exposures equal or similar to the exposure indicated in para. 3.2.1 of this section.

\textsuperscript{7} 30/5 rem = 6 rad (distribution factor).
\(^{90}\text{Sr}/\text{g Ca}\) uniformly distributed in adult bone would result in a dose of 2.7 rad in a year. The dose to mineral bone of the foetus and infant may be about half the adult values. \(R_b\) can be estimated from:

\[
R_b = R_d \times \text{OR} \times F
\]

where \(R_d\) = Sr-to-Ca ratio in the diet averaged over the period of intake, \(\text{OR}\) = observed ratio and \(F\) = fraction of skeletal calcium incorporated by accretion and turn-over during the period of intake.

Estimates have been made for a contaminating event that would result in a total intake of 1 \(\mu\text{Ci}\) of \(^{89}\text{Sr}\) or \(^{90}\text{Sr}\) in 100 d, the period of interest for the transmission of these radionuclides through the pasture-cow-milk-man pathway. Assuming that the typical calcium intake is about 1 g/d, the radioactive intake would then be associated with 100 g of Ca. Thus the intake of 1 \(\mu\text{Ci}\) of \(^{89}\text{Sr}\) in 100 d would result in an average dietary level of 10 nCi \(^{89}\text{Sr}/\text{g Ca}\). The dose to mineral bone from such a contaminating event to the foetus and the infant who are the age groups of interest would therefore be as follows:

(i) In the case of the ante-natal period, the maximum \(^{89}\text{Sr}\) burden of the developing skeleton would be when the 100-d intake coincides with the third trimester, i.e. when essentially all of the mineralization of the foetal skeleton occurs. Thus \(F = 1\). If an \(R_d\) of 10 nCi \(^{89}\text{Sr}/\text{g Ca}\) in the mother's diet and an OR of 0.1 for mother's diet to foetal bone are assumed, the average \(^{89}\text{Sr}\)-to-Ca ratio in the foetal skeleton would be \(R_a = 10 \times 0.1 \times 1 = 1\) nCi \(^{89}\text{Sr}/\text{g Ca}\). If \(D = R_a \times \text{dose conversion factor}\) then \(D\) in the case of \(^{89}\text{Sr}\) would be \(= 1 \times 0.15 = 0.15\) rad and in the case of \(^{90}\text{Sr}\) would be \(= 1 \times 1.35 = 1.35\) rad/yr. Since one trimester is 1/4 of a year, the dose to the mineral bone of the foetus from \(^{90}\text{Sr}\) before birth would be approximately 0.34 rad.

(ii) In the case of infants 1 to 2 yr old, the fraction (\(F\)) is estimated from the annual net accretion and turn-over. The net accretion during the second year of life is estimated to be about 50 g of Ca. The turn-over is estimated to be an additional 50 g of Ca during this year. The fraction of calcium in the skeleton that is incorporated during the 100-d intake is

\[
F = \frac{50 + 50}{150} \times \frac{100}{365} = 0.18
\]
If one assumes an $R_d$ of $10 \text{nCi Sr}^{90}/1 \text{g Ca}$ in the diet and an OR of 0.35, then $R_b = 10 \times 0.35 \times 0.18 = 0.65 \text{nCi Sr}^{90}/\text{g Ca}$ and the dose $D$ therefore will be

(a) For $^{89}\text{Sr}$ $D = 0.65 \times 0.15 = 0.09 \text{rad}$

(b) For $^{90}\text{Sr}$ $D = 0.65 \times 1.35 = 0.87 \text{rad/yr}$

Total dose from the contaminating event to the mother during pregnancy or to the infant 6 months to 2 yr

The $^{90}\text{Sr}$ burden at birth would be $1 \text{nCi}^{90}\text{Sr}/\text{g Ca}$, i.e. a total burden of $1 \text{nCi}/\text{g Ca} \times 28 (\text{g Ca}) = 28 \text{nCi}$. With a bone turn-over rate of 50% per year, there would be $28 \times 0.5$ or

$14 \text{nCi}^{90}\text{Sr}/100 \text{g Ca}$ at the age of 1 yr, and

$7 \text{nCi}^{90}\text{Sr}/150 \text{g Ca}$ at the age of 2 yr

These concentrations would give dose rates to bone equal to

$14/100 \times 1.35 = 0.18 \text{rad/yr}$ at the end of one year of age, and

$7/150 \times 1.35 = 0.05 \text{rad/yr}$ at the end of two years of age.

Computer analysis showed that the 70-yr dose from a short-term intake of $^{90}\text{Sr}$ would be about five times the dose in the year when the infant is 1 yr old. Assuming that the dose in a year can be reasonably approximated by the average of the dose rates at the beginning and end of the year, the total dose to the bone of an individual whose mother has had an intake of $1 \mu\text{Ci}$ of $^{90}\text{Sr}$ during the last three months of pregnancy would be

$$D = 0.34 + \frac{1.35 + 0.18}{2} + \frac{5(0.18 + 0.05)}{2} = 1.68 \text{ rad}$$

The total dose to bone for a person exposed as an infant would be

$0.87 \times 5 = 4.35 \text{ rad}$

3.2.2. Dose to bone marrow

Though in section IV the dose considered was that of the mineral bone, it seems appropriate to give some information on the possible dose to bone marrow after a contaminating event resulting in an intake of $\text{Sr}^{*}$. 

34
As mentioned previously if uniformly distributed throughout the mineral bone of the adult, 1 nCi \(^{89}\)Sr/g Ca would result in a dose of 0.3 rad to mineral bone. One nCi \(^{90}\)Sr/g Ca uniformly distributed through mineral bone would result in a dose of 2.7 rad in a year. The dose to bone marrow from \(^{89}\)Sr and \(^{90}\)Sr uniformly distributed in the adult skeleton has been estimated to be about 1/5 of that calculated for mineral bone for \(^{89}\)Sr and about 1/4 for \(^{90}\)Sr [10]. The Federal Radiation Council used a value of 1/3 for both nuclides.

3.2.3. Summary on dosimetry (Computation of dose from a contaminating event affecting the diet of a pregnant woman or of a 6-month to 2-yr-old child)

3.2.3.1. For mineral bone

(a) Assume the contaminating event would result in a total intake of 1 \(\mu\)Ci \(^{89}\)Sr* in a 100-d period, the period of interest for the transmission of the \(^{89}\)Sr* through the pasture-cow-milk-man pathway.

(b) One nCi \(^{89}\)Sr/g Ca uniformly distributed would deliver about 0.15 rad and 1 nCi \(^{90}\)Sr/g Ca uniformly distributed would deliver about 1.35 rad in a year. 0.15 rad and 1.35 rad are the dose conversion factors.

(c) \(F = 1\) for the ante-natal life if the maximum \(^{89}\)Sr burden of the developing skeleton takes place in the third trimester of pregnancy \(F = (50+50)/150 \times 100/365 = 0.18\) for the 1 to 2-yr-old infant.

(d) \(R_d = \text{Sr-to-Ca ratio in the diet averaged over the period of intake. In this contaminating event therefore the intake of } 1 \mu\text{Ci } \text{Sr}^* \text{ in 100 d would result in an average dietary level of } 10 \text{nCi } \text{Sr}^* / 1 \text{g of Ca.} \)

(e) \(\text{OR (bone/diet)} = \text{Sr/Ca in bone/}(\text{Sr/Ca in diet}). \)
\(\text{OR (foetal bone/mother's diet)} = 0.1 \)
\(\text{OR (6-month to 2-yr infant)} = 0.35 \)

(f) \(R_b = \text{average Sr-to-Ca ratio in the skeleton} = R_d \times \text{OR} \times F \)

(g) Dose, \(D = R_b \times \text{dose conversion factor} \)

(i) Dose in case of foetus

If \(R_b = 10 \times 0.1 \times 1 = 1\) then \(D = 1 \times 0.15 = 0.15\) rad for \(^{89}\)Sr and \(D = 1 \times 1.35 = 1.35\) rad/yr for \(^{90}\)Sr.
Since one trimester is 1/4 of a year, the dose to the foetus from \(^{90}\)Sr before birth would be \(\approx 0.34 \text{ rad}\).

(ii) Dose in case of an infant 6 months to 2 yr

If \(R_b = 10 \times 0.35 \times 0.18 = 0.65 \text{ nCi Sr/g Ca}\) then \(D = 0.65 \times 0.15 = 0.09 \text{ rad}\) for \(^{89}\)Sr and \(D = 0.65 \times 1.35 = 0.87 \text{ rad/yr}\) for \(^{90}\)Sr.

(iii) Total dose from the contaminating event of \(^{90}\)Sr affecting the foetus or the infant 6 months to 2 yr

The \(^{90}\)Sr burden at birth would be 1 nCi/g Ca. Therefore, total burden \(1 \text{ nCi/g Ca} \times 28 = 28 \text{ nCi}\). With a bone turn-over rate of 50\% there would be \(28 \times 0.5 = 14 \text{ nCi}^{90}\text{Sr}/100 \text{ g Ca}\) at the age of 1 yr and \(7 \text{ nCi}^{90}\text{Sr}/150 \text{ g Ca}\) at the age of 2 yr.

These concentrations would give dose rates to bone equal to \(14/100 \times 1.35 = 0.18 \text{ rad}\) and \(7/150 \times 1.35 = 0.05 \text{ rad/yr}\). Therefore the total dose to an individual's bone whose mother had an intake of \(1 \mu\text{Ci}^{90}\text{Sr}\) during the last three months of pregnancy would be \(0.34 + (1.35 + 0.18)/2 + 5 (0.18 + 0.05)/2 = 1.35 \text{ rad}\) and the total dose to bone of a person exposed as infant would be \(0.87 \times 5 = 4.35 \text{ rad}\).

3.2.3.2. For bone marrow

The same steps as those shown above apply, except that in (ii) the conversion factor is 0.1 for \(^{89}\)Sr and 0.9 for \(^{90}\)Sr. Because of the lower density of mineralization in the infant and foetal skeleton, the dose to mineral bone from the same concentration of Sr\(^{\ast}\) in the adult skeleton results in lower dose to mineral bone and a higher dose to the bone marrow. Therefore 1/3 of the dose that would be calculated for mineral bone per unit of Sr\(^{\ast}\) in the adult skeleton is also a reasonable estimate of the dose from the same concentration to bone marrow of the foetus and infant.

The assumptions therefore for the calculation of the dose to bone marrow of foetus and infant are:

(a) The Sr\(^{\ast}\) is uniformly distributed in the mineral bone
(b) A concentration of 1 nCi \(^{89}\)Sr/g Ca in the skeleton will give a total dose of 0.1 rad to bone marrow and
(c) A concentration of 1 nCi \(^{90}\)Sr/g Ca in the skeleton will give a dose of 0.9 rad in one year to bone marrow.

By the same method as that used in the dose estimation to mineral bone and by substituting the appropriate conversion factors
in the formulae, the dose to bone marrow after a contaminating event that would result in a total intake of 1 µCi $^{89}$Sr or $^{90}$Sr in 100 d (the period of interest for the transmission of these radionuclides through the pasture-cow-milk-man pathway) can be estimated.

(i) In the case of the foetus, for $^{89}$Sr $D = 1 \times 0.1 = 0.1$ rad and for $^{90}$Sr $D = 1 \times 0.9 = 0.9$ rad in 1 yr.

The dose to the foetus in the trimester before birth would be about $1/4$ of that, or 0.2 rad.

(ii) In the case of the infant, for $^{89}$Sr $D = 0.65 \times 0.1 = 0.065$ rad and for $^{90}$Sr and for $D = 0.65 \times 0.9 = 0.6$ rad in 1 yr.

Also in the case of $^{90}$Sr the total dose to bone marrow of an individual whose mother has had an intake of 1 µCi $^{90}$Sr during the last three months of pregnancy would be $D = (0.2 + (0.9 + 0.1)^2 + 5 (0.1 + 0.04)/2 = 1.1$ rad. The total dose to bone marrow for an adult exposed as an infant would be $D = 0.6 \times 5 = 3$ rad total dose.

3.3. Comparison of radiation doses to bone from $^{226}$Ra and $^{90}$Sr

In section IV, para.4 it was mentioned that 3 µCi of $^{90}$Sr at one year after incorporation give the same integrated exposure to bone as a terminal content of 1 µCi of radium at the end of 30 yr. This conclusion is arrived at as follows:

Radium-226

\[ \Sigma EF(RBE)n = 110 \text{ [17].} \]

The retention of $^{226}$Ra can be expressed by the retention equation,

\[ 0.5 t^{-0.5} \]

Therefore, from 1 to 25 yr the bone content declines by a factor of 5 and a terminal burden of 1 µCi corresponds to a 1-yr burden of 5 µCi and the integrated number of microcurie-years from 1 to 25 yr is

\[ 5 \times \left[ \frac{5}{0.5} - \frac{1}{0.5} \right] = 40 \text{ µCi-yr} \hspace{1cm} (11) \]

The number of rems from 1 to 25 yr for 1 µCi is $110 \times 40 \times N = 4400 N$, where $N$ is the number of disintegrations/µCi - yr × ergs/MeV × 1/100 g
Strontium-90

\[ \text{LEF}(\text{RBE})n = 5.5 \text{[17]} \]. The retention equation is

\[ 0.5 e^{-0.693 \times t^{2.4}} + 0.5 t^{-0.2} \]

Therefore, from 1 to 25 yr, the bone content declines by a factor of 2 and a bone content of 1 \( \mu \text{Ci} \) at 1 yr gives a bone content of 1/2 \( \mu \text{Ci} \) at 25 yr. The integrated number of \( \mu \text{Ci} \)-years from 1 to 25 yr is

\[ 0.5 \times 2 \left[ \frac{25^{0.8}}{0.8} - \frac{1^{0.8}}{0.8} \right] = 14.775 \approx 15 \mu \text{Ci-yr} \] (12)

From Eqs. (11) and (12) it is evident that 3 \( \mu \text{Ci} \) of \(^{90}\text{Sr} \) at one year gives the same integrated \( \mu \text{Ci} \) of contamination to bone as a terminal content of 1 \( \mu \text{Ci} \) \(^{226}\text{Ra} \) at the end of 30 yr (\( \approx 25 \) yr)(IV, para. 4).

The number of rems from 1 to 25 yr from a bone content of 1\( \mu \text{Ci} \) \(^{90}\text{Sr} \) at 1 yr = 5.5 \( \times \) 15 N \( \approx \) 80 N. It is evident that 1 \( \mu \text{Ci} \) of \(^{226}\text{Ra} \) at 25 yr (terminal burden) delivers to bone the same rem dose as 55 (\( \approx \) 60) \( \mu \text{Ci} \) \(^{90}\text{Sr} \) at 1 yr, as mentioned in section IV, para 4.

4. Caesium-137

4.1. Method for computation

The following assumptions are made to compute the amounts of intake for caesium-137 as mentioned in section IV, para. 5.

(a) Young children are the critical age group because of their high intake relative to their body mass.

(b) The mass of the body is assumed to be 3.7 kg at birth, 8.8 kg at 6 months, 10 kg at one year and 70 kg in the adult.

(c) Uptake of caesium regardless of age is 100% by ingestion and 25% if intake is by inhalation.

(d) Recent evidence indicates that half-life of radiocaesium in the body is 100 d for adults and 30 d for children.

4.2. Intake of \(^{137}\text{Cs} \) by ingestion

The same argument as that in section VI, para. 1 is used, substituting in Eq. (1) the different parameters by the relevant values for caesium-
137, applicable to children, and taking $\Sigma EF = 0.59$ and $f_w = 1/1^7$. The total dose to the whole body for $1\mu Ci$ of caesium-137 ingested is

$$D_{1w} = f_w \times \frac{1306.4}{w} \text{ rad}$$

The total intake $I_w$ which would deliver a total integrated dose $D$ to the whole body during the life expectancy after intake would be

$$I_w = \frac{D}{D_{1w}} = \frac{Dw}{f_w 73.81 \times 30 \times 0.59} \mu Ci$$

If fresh milk is the main food for children, then young children, because of their high intake relative to their body mass, would be those exposed to the greatest risk. Therefore it we take the infant one-year-old as the critical age group and substitute the necessary parameters in the above formula,

$$I_w = D 7.64 \mu Ci$$

### 4.3. Emergency levels of daily intake of $^{137}$Cs by ingestion

Assume that the critical age-group is the one-year-old child. If fresh milk is the most important source of radiocaesium, young children, because of their high intake relative to their body mass would be those exposed to the greatest risk. From the way in which caesium enters milk it can be assumed that the contamination of milk would decrease rapidly and a value of 10 weeks has been assumed for its half-life ($T'$). However this figure may be too conservative and a smaller figure of 2-3 weeks may be used. Using Eq. (4)

$$X_0 = \frac{5.1D}{VT'}$$

and if $D = 10$ rad and $V = 1$ litre/d then

$$X_0 = 0.73 \mu Ci/L$$
4.4. Intake of $^{137}$Cs by inhalation and time integrals of concentration

Using Eq. (7)

$$I_a = \frac{D}{D_{1a}} = \frac{D_w}{f_a 1306.5} = \mu Ci$$

where $I_a$ is the intake through inhalation delivering a dose $D$ to the whole body weighing $w$ grams.

If the critical age-group is the one-year-old child and $f_a$ is 0.75 [17] then $I_a = 10.16 D \mu Ci$; assuming $D = 10$ rad, $I_a = 101.6 \mu Ci$.

Using Eq. (9) and taking the one-year-old child as the critical age-group we find that the maximum time integral of concentration is $10.16 D/330 = 30 \ D nCi-h/litre$.

5. Tritium and the noble gases

5.1. Intake of tritium and corresponding levels of concentration in food and air

(i) Food: By substituting the relevant values for tritium for the critical age-group at risk in Eq. (1) we obtain $I_w$ from which levels of concentration in food and water could be calculated, knowing the food habits of the critical age group $f_w = 1$, $\Sigma E\mu F(RBE) = 0.01$.

(ii) Air breathed: Reference [17] indicates that from animal and human experiments, it is known that when HTO vapour is present in air approximately equal amounts enter the body by inhalation and absorption through the skin. Thus the value of $I_a$ computed from Eq. (1), after substituting the relevant parameters ($f_a = 1$) and $\Sigma E\mu F(RBE) = 0.01$ and the weight of the body $w$ for the critical age-group, should be halved. From $I_a$ thus computed, it is possible to find the time integral of concentration in nCi-h/litre.

5.2. Levels of concentration of noble gases in air

The fission-product noble gases (Xe and Kr) are a mixture of isotopes of which about 12 have half-lives in excess of a few minutes. Most of these have short half-lives compared with the possible ex-
posure time during a reactor accident and hence the composition of the mixture is very dependent on the elapsed time since reactor shut-
down. In addition, some, such as $^{133}$Xe have a high neutron cross-
section which keeps them low during reactor operation and causes them to increase in abundance after the reactor is shut down. The hazard resulting from the release of these fission products is therefore dependent on the immediate past history of the reactor fuel. However, it can be shown that, at shutdown and up to a few hours afterwards, most of the dose delivered by the mixture results from $^{88}$Kr and its daughter $^{88}$Rb. By the same arguments and equation as that in Ref.[17] exposure to a dose of 1 Ci-sec/m$^3$ of the mixture is equivalent to a whole body dose of about 1.4 rad. Ref.[17] indicates that in dealing with inert gases such as $^{41}$Ar and $^{135}$Xe, the calculations are not based on the dose delivered by the concentration of the radioactive material inside the body, but rather on the dose the person would receive if he were surrounded by a semi-spherical infinite cloud of radioactive gas. In this case one would expect the radiation from the radioactive cloud to deliver a much higher dose than that held in the lungs or other body organs. It follows that the body is assumed to be irradiated from half the solid angle by this radioactive cloud of large volume.

Under these conditions the maximum permissible concentration in air which delivers a dose rate R per unit time to the whole body for continuous exposure can be calculated using Eq. (20) of Ref.[17].

$$\left(\frac{\text{MPC}}{4.38}\right)_a = \frac{0.024 R}{\Sigma E} P_a P_a / P_t \mu \text{Ci/cm}^3$$

in which $P_a$ = density of air (= 0.0012 g/cm$^3$); $P_a / P_t$ = stopping power of air relative to tissue; $P_a / P_t = 1/1.13$ for $\beta$ and secondary electrons produced by X-ray and $\gamma$-radiation; $\Sigma E(\Sigma E)$ = effective energy per disintegration (MeV); in this case RBE = 1 and $n = 1$. Once $R$ has been decided by the appropriate authority the calculation of $(\text{MPC})_a$ becomes evident.

The above equation is applied only in the case of large clouds of noble gases or other relatively inert gases that emit $\gamma$ or high-energy $\beta$ radiation ($E_m > 0.1$ MeV) where a person is surrounded by an infinite semi-spherical cloud of radioactive material that emits $\gamma$, X- or $\beta$-radiation of sufficient energy to constitute whole-body irradiation. In cases of $\alpha$-emitters or for relatively inert gases that emit low-energy $\beta$-radiation, e.g. $^3$H$_2$, because the radiation would not penetrate the skin, the above formula still applies but the
### TABLE V. TABLE OF PHYSICAL AND BIOLOGICAL PARAMETERS

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life (d)</th>
<th>Physical $T_r$</th>
<th>Effective $T$</th>
<th>For the transfer in the food chain ($T^*$)</th>
<th>$\Sigma$ EF (MeV)</th>
<th>Critical organ and its weight</th>
<th>Fraction reaching critical organ by</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{131}$I</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td></td>
<td>0.23</td>
<td>Thyroid gland, whose weight is assumed to be: 2 g from birth to 6 months, 3.5 g at 3 yr, 10 g at 10 yr, 25 g at adult age</td>
<td>Ingestion ($f_w$)</td>
</tr>
<tr>
<td>$^{137}$Cs</td>
<td>$1.1 \times 10^4$</td>
<td>100 for adult, 30 for children</td>
<td>70</td>
<td></td>
<td>0.59</td>
<td>Total body where weight is assumed to be: 3.7 kg at birth, 8.8 kg at 6 months, 10 kg at 1 yr, 70 kg in the adult</td>
<td>0.75</td>
</tr>
<tr>
<td>$^{90}$Sr</td>
<td>$10^4$</td>
<td>$6.4 \times 10^3$</td>
<td>1.1 $^a$</td>
<td>Bone where weight is assumed to be $7 \times 10^3$ g in the adult</td>
<td></td>
<td></td>
<td>0.67</td>
</tr>
<tr>
<td>$^{89}$Sr</td>
<td>50</td>
<td>50</td>
<td>0.56 $^a$</td>
<td>Bone where weight is assumed to be $7 \times 10^3$ g in the adult</td>
<td></td>
<td></td>
<td>0.75</td>
</tr>
</tbody>
</table>

$^a$ This value can be derived from Ref. [17]. Table 5 of the effective energies gives $\Sigma$ EF (RBE) as for bone $^{89}$Sr to be 2.8 and for $^{90}$Sr for bone to be 5.5. Dividing by the n factor which is 5, the indicated values for $^{89}$Sr and $^{90}$Sr can be derived.
dose rate can be higher than in the first case, since the critical organ would be the skin in the second case versus the whole body in the first case.

6. **Summary table of biological parameters**

A summary chart of the physical and biological parameters for $^{131}$I, $^{137}$Cs, $^{90}$Sr and $^{89}$Sr is given in Table V.

VII. ASSESSMENT OF THE HAZARDS TO MAN FROM EXPOSURE RESULTING FROM RADIATION ACCIDENT

Hazards to man after exposure to ionizing radiation under various conditions have been comprehensively reviewed by such organizations as the United Nations Scientific Committee on the effects of Atomic Radiation, the Medical Research Council of the United Kingdom, the National Academy of Sciences — National Research Council, and the Federal Radiation Council in the United States. Information on the effects of ionizing radiation on humans has been obtained from:

(a) Observations on man after the atomic bombing of Hiroshima and Nagasaki, as well as the data from the Marshall Islands
(b) Accidents involving exposure to ionizing radiation
(c) Occupational diseases related to radiation, such as those encountered in the mining and milling of radioactive ore
(d) Human exposure to radiation in diagnostic and therapeutic procedures using X-ray and radium and recently teletherapy units
(e) From animal experiments

Biological effects of radiation are normally divided into two distinct categories: (1) somatic effects referring to direct effects on the individuals exposed and (2) genetic effects referring to possible effects that may appear in the progeny of the individuals exposed as the result of the irradiation of the reproductive tissue. Both kinds of effects can result from exposure to either external irradiation, internal irradiation, or both.

Somatic effects are further subdivided in terms of the severity of response to radiation injury as follows:
(a) Early or acute effects referring to those effects that develop within a few weeks or months.

(b) Delayed effects referring to those which may not make their appearance for many months or years after exposure.

1. Somatic effects

1.1. Early or acute effects

The general conditions for the production of early effects or acute radiation injury are: (1) uniform irradiation of the whole body, (2) a radiation dose measured at the mid-line of the body in the range of 75 to 200 rad (see Table II) and a dose rate such that these doses would be delivered in time periods of hours to days. Experience with both animals and humans has shown that acute radiation syndrome results in nausea, and, if the dose is high enough, in death caused by direct injury to the gut and to the haematopoetic system. The production of nausea is related primarily to the direct irradiation of the trunk and head. The response of the haematopoetic system is very dependent on uniformity of the absorbed dose within the body since a relatively small fraction of uninjured bone marrow may repopulate the bone marrow depleted by the radiation injury.

The quantities of radionuclides that would have to be absorbed internally in a short period of time to produce symptoms of acute radiation injury are very large. Experiments with animals have shown that the quantities of most nuclides necessary to produce this syndrome in humans would be measured in curies. These quantities are in the range of one thousand to a hundred thousand times the quantities which members of the public might receive as the result of any credible radiation accident. In general the exposure dose conditions required to produce symptoms of acute radiation injury in individuals in the public as the result of a radiation accident are so severe that protection against such effects, though a possible problem to authorities concerned with the protection of the public, would not be a major problem. Protection against the possibility of delayed effects is far more crucial from the standpoint of public protection in radiation accidents.
1.2. Late or delayed effects

1.2.1. Incidence of leukaemia after exposure to irradiation and risk estimates

The incidence of leukaemia after exposure to radiation has been extensively discussed in the literature. The UNSCEAR reports [3, 10, 11] have surveyed the subject comprehensively. A summary of the most relevant data on the subject of this document is given here.

The mortality rate from leukaemia, though it has increased in some countries over the past decades, is still very low compared with lung cancer and coronary artery disease. The increase in mortality figures from leukaemia may result partly from improved methods of diagnosis and recognition of the disease, but there seems to be nevertheless a real increase in the incidence. It is important to note that no significant increase has been recorded in chronic lymphatic leukaemia.

There is no evidence at present that exposure to radiation can induce chronic lymphatic leukaemia. It is known that acute leukaemia and chronic myelogenous leukaemia can be induced by radiation. Until more is known about the effects of small doses of radiation, it is impossible to estimate directly whether a part of the increased incidence now being observed in the general public in some countries is caused by increased exposure to radiation. There are indications that other factors are implicated and that the effect of radiation is a minor one.

The information available concerning the incidence of leukaemia after exposure to irradiation comes from the following sources.

(a) Japanese atomic bomb survivors
(b) Exposure of radiologists
(c) Patients with ankylosing spondylitis who have been irradiated therapeutically
(d) Children irradiated therapeutically for enlarged thymus and other benign conditions
(e) Children irradiated in utero
(f) Leukaemia after internal irradiation of adults for diagnostic and therapeutic reasons
(g) Environmental irradiation exposure, where populations in different geographic locations receive different levels of environmental irradiation.
Onset: In Japan cases of leukaemia after brief exposure to the whole body presumably began to occur one or two years after exposure. The peak of highest incidence was reached in 1951 when an incidence was 11 times higher for those exposed than the non-exposed. From 1952 to 1959 the incidence in the exposed fluctuated below the peak. From 1960 to 1962 it fluctuated at a still lower range. In the case of chronic exposure (radiologists), it is difficult to determine the time relationship of incidence.

Age susceptibility: Data from survivors of A-bomb casualties indicate that the young age groups are more susceptible to radiation-induced leukaemia. Information from the spondylitic patients indicate that the old age groups are susceptible. With respect to children who have been irradiated in utero through medical exposure of the expectant mothers, the possibility of increased leukaemia in the children is to be borne in mind. There is some evidence however that most leukaemias in children are promoted when irradiation occurs during the first few weeks of conception, X-ray being the initiating event for a prezygotic or zygotic predisposition to leukaemia. It is believed that the child in the foetal stages of development is particularly sensitive to radiation, especially during the first few weeks of pregnancy where organogenesis is taking place.

Sex susceptibility: The data from atom bomb casualties show a preponderance of leukaemic males. In patients who have been treated by $^{131}$I hyperthyroidian, the incidence of leukaemia is not statistically significant in the cases observed so far as compared with a control group. However, it is estimated that only 20% of the hyperthyroid patients were males. Over 70% of the cases of leukaemia however occurred in males.

Dose-effect relationship for induction of leukaemia by irradiation: There is a lack of data concerning the shape of the curve of the dose-effect relationship in the low-dose range. In radiation protection practice it is customary to adopt the linearity of the dose-effect relationship curve.

Incidence of leukaemia among irradiated population and the derived risk estimates:

(i) From Japanese data in Hiroshima

The relation of dose to annual leukaemia incidence in the 9-yr period (1950-1958) can be described by a straight line over the dose range of about 100-900 rad. Between 10 and 100 rad the incidence
in each dose group, though consistent with the same straight line, does not differ significantly from another. The data indicate that at least in the range between 100 and 900 rad the average rate of increase of the incidence with dose was $1.1 \text{ cases/10}^6/\text{yr/rad}$ at Hiroshima and $1.6 \text{ cases/10}^6/\text{yr/rad}$ at Nagasaki or between 1 and 2 cases/$10^6/\text{yr/rad}$ in both cities. Since in Nagasaki the exposed population was smaller and the cases of leukaemia fewer, the estimates are less reliable. However in both the estimates for Hiroshima and Nagasaki the uncertainty lies in the limitation of the dosimetry.

(ii) Leukaemia incidence in American radiologists

UNSCEAR (para. 37, p. 85, Ref. [3]) reports that in a survey of the incidence in the American radiologists for a period of 14 yr where the number of man-years at risk was 47,348 for a group of radiologists between 35 and 74 years of age, the mortality ratio for leukaemia was 3, with 12 cases observed among the radiologists as compared with 4.02 cases expected. The average annual incidence of death from leukaemia in radiologists during these 14 yr was 235 cases/$10^6/\text{yr}$ as compared with an expected incidence of 85 cases/$10^6/\text{yr}$, giving an excess incidence of 168 cases/$10^6/\text{yr}$. Little is known about the magnitude and distribution of dose received by early radiologists but the evidence indicates that doses far in excess of 100 rad were received chronically over periods of up to 40 yr. The excess of leukaemia incidence observed in the radiologists, if based on the risk estimates for Hiroshima, would result from a single acute whole-body exposure of 100 rad. These observations suggest that the long-term radiation exposure is less effective than short-term exposure in inducing leukaemia.

(iii) Leukaemia incidence in ankylosing spondylitic patients

The UNSCEAR report (para. 37, p. 85, Ref. [3]) indicates that if a regression line, which is fitted through the incidences observed in exposures between 300 and 1500 R to the spine, has a slope of 0.5 cases/$10^6/\text{yr/R}$, extrapolation of the line below 300 R is not warranted. It may be recalled that the straight line describing the relationship between dose and incidence of leukaemia in the Hiroshima population of survivors to the A-bomb explosion has a slope between 1 and 2 cases/$10^6/\text{yr/ rad}$ in the range of 100 to 900 rad. The characteristics of the irradiated population and
the conditions of irradiation in Hiroshima were very different from those in the spondylitics. However the similarity of the two slopes of the curves for the incidence of leukaemia in the spondylitics and in the A-bomb survivors suggests that a common risk estimate may apply to both populations.

(iv) Leukaemia in children irradiated in utero

The same UNSCEAR report [3] surveys this question in detail. The relevant conclusions are mentioned here. While individual studies of the incidence of leukaemia in children irradiated in utero have yielded different risk estimates, these are of a different reliability on purely statistical grounds as indicated by their confidence limits. UNSCEAR, in its report, mentions that actually there is no inconsistency in the findings of the eleven surveys, five of which involved small samples with large sampling variability and gave estimates of relative risks less than one. The joint maximum likelihood estimate of the relative risk from all these surveys was in fact found to be 1.4 with 95% confidence limits of 1.2 and 1.6.

Although accurate estimates of doses are not available, it seems difficult to avoid the conclusion that irradiation of foetal tissue gives rise to a greater risk per unit dose than post-natal irradiation, possibly by a factor as high as five.

(v) Leukaemia from natural background

The increase in incidence of leukaemia from natural background is thought to be so small that it makes it very difficult to conduct an experiment to detect the increase in incidence of leukaemia.

The risk estimates mentioned in section IV, para. 2 were derived on the basis of this information and the assumption of a linear dose relationship.

1.2.2. Irradiation of the thyroid and related carcinoma risk

Again for more detailed information and for bibliography on the subject the reader is referred to UNSCEAR reports, in particular to Ref. [3]. Only information relevant to the purpose of this document is outlined here.

Socolow et al. [22] have reviewed the cases of carcinoma of the thyroid that were detected by routine medical examinations between
1 July 1958 and 1 July 1961, in matched groups of exposed and non-exposed subjects included in the long-term medical investigations (Adult Health Study) of the Atomic Bomb Casualty Commission. According to Socolow et al., although the overall incidence of thyroid cancer in the Adult Health Study may not depart greatly from that cited by others for Japan, the age distribution differed significantly in that the cases in the A-bomb survivors were younger. Of the 21 cases of thyroid cancer, 8 were diagnosed in the group under the age of 35 yr. At the time of exposure these patients ranged in age from 6 to 20 yr. The latent period after exposure can only be defined as less than 13 or 15 yr owing to the fact that all cases in this study were diagnosed between 1961 and 1965. Among cases occurring in the younger age groups over 80% were exposed within 1400 m from the hypocentre of the explosion where as in older age groups fewer than 50% were similarly exposed.

If the findings are representative of the incidence in the total exposed and non-exposed population in this study, the incidence of thyroid carcinoma in the exposed would be 19 out of 14 970 or 0.13% and the non-exposed 2 out of 4992 or 0.04%.

In 1964 Zeldis et al. [23] reviewed thyroid lesions in autopsy and surgical pathology specimens in Hiroshima A-bomb survivors. The increased incidence of thyroid carcinoma in the autopsy cases in the group exposed within 1400 m was found not to be statistically significant (P = 0.07), but the increased incidence in the thyroid cancers in the surgical specimen groups exposed within 1400 m was found to be statistically significant. Taken together both surveys suggest that the incidence of thyroid carcinoma has been increasing in the irradiated population of Hiroshima and Nagasaki, the incidence varying inversely with distance from the hypocentre. Difficulties of ascertainment, arising from the fact that the incidence of carcinoma of the thyroid is difficult to record and the fact that the latent periods are long, make it difficult to set up the surveys that would be necessary to obtain information on the dose-effect relationship and therefore on the risk induction.

Various surveys were carried out on the incidence of thyroid cancer in children irradiated by X-ray, for enlarged thymuses, cervical adenitis, bronchitis, hyperplastic tonsils, mastoid and other conditions. A summary of the results of the more important surveys are indicated in Table VI.

In all these surveys uncertainties and limitations of the risk estimates for malignancy arise. These are caused by many factors among which some of the more important are:
<table>
<thead>
<tr>
<th>Author</th>
<th>Age at irradiation</th>
<th>Man-yr at risk</th>
<th>Ave. exp. (R)</th>
<th>Cases</th>
<th>Cases 10⁵/yr</th>
<th>Risk estimate (x 10⁻⁶/yr/R)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conti</td>
<td>Children</td>
<td>21 896</td>
<td>168</td>
<td>0</td>
<td>0</td>
<td>0.0 (0.0 -1.1)⁵</td>
</tr>
<tr>
<td>De Lawtor</td>
<td>Adults</td>
<td>5 000</td>
<td>2100</td>
<td>0</td>
<td>0</td>
<td>0.0 (0.0 -0.03)</td>
</tr>
<tr>
<td>Hanford</td>
<td>Children, adults</td>
<td>5 711</td>
<td>900⁵</td>
<td>8</td>
<td>1400</td>
<td>1.6 (0.7 -3.1)</td>
</tr>
<tr>
<td>Latourette</td>
<td>Children</td>
<td>15 130</td>
<td>214</td>
<td>1</td>
<td>66</td>
<td>0.3 (0.01 -1.7)</td>
</tr>
<tr>
<td>Pifer, Series I</td>
<td>Children</td>
<td>26 843</td>
<td>329</td>
<td>8</td>
<td>298</td>
<td>0.9 (0.4 -1.8)</td>
</tr>
<tr>
<td>Pifer, Series II</td>
<td>Children</td>
<td>11 000</td>
<td>126</td>
<td>1</td>
<td>91</td>
<td>0.7 (0.01 -4.0)</td>
</tr>
<tr>
<td>Saenger</td>
<td>Children</td>
<td>24 871</td>
<td>330</td>
<td>11</td>
<td>442</td>
<td>1.3 (0.9 -2.3)</td>
</tr>
<tr>
<td>Simpson⁶</td>
<td>Children</td>
<td>18 829</td>
<td>520⁵</td>
<td>10</td>
<td>531</td>
<td>1.0 (0.5 -1.9)</td>
</tr>
</tbody>
</table>

⁵ In brackets, approximate 95% confidence limits of the estimate
⁶ Mean exposure to cases developing cancer

(a) The radiation dose delivered to patients for diagnostic or therapeutic reasons, to infants and to young patients can only be estimated crudely from the data given about the treatment and medical procedure used.
(b) The data is derived from groups receiving different doses to different parts and volume of the body (same total dose to body) and with different periods of follow up. The latent period in thyroid carcinoma may be relatively long and perhaps longer periods of observation are necessary. The dose rate is also different in the different groups.
(c) It is unknown whether the cause precipitating the medical examination bears a relation in inducing carcinoma of the thyroid or whether cancer develops as a combination of irradiation and the clinical condition.
From Table VI a single straight line can be fitted through the incidence observed in surveys of children when plotted against exposures. Its slope indicates that the rate of increase of the incidence with exposure is 0.9 cases/10^6/yr/R. If the statistical uncertainty of the data and the probably larger uncertainties of the dosimetry are considered, it appears that the joint risk estimate may be between 0.5 and 1.5 cases/10^6/yr/R. The estimate is based on an average follow-up time of about 16 yr and is valid for acute exposure of children only in the estimated exposure range of 100 to 300 R. However the incidence of thyroid cancer shows approximate proportionality in a range of doses between 100 and 300 rad and leads to a risk estimate of about one case per year per rad per million exposed individuals averaged over a period of approximately 16 yr after irradiation.

In adults the irradiation caused by ¹³¹I given to patients cannot as yet be indicated as causing carcinoma of the thyroid since 10-20 yr of observation are needed. So far no statistically significant increase in thyroid cancer has been reported in patients who had received either therapeutic or diagnostic doses of ¹³¹I. The incidence in some surveys is lower than that in the control group.

1.2.3. Primary malignant bone tumours

As mentioned in section IV, para. 4, the lowest terminal body burden of radium which was associated with primary malignancy of bone is 0.6 µCi of ²²⁶Ra. The lowest exposure from external radiation thought to have caused osteogenic sarcoma is at the present time about 3000 R. UNSCEAR (para. 138, p. 95, Ref. [3]) reports a study of 264 persons selected and measured for radium content, who had been employed formerly in the radium watch dial industry or as radium chemists, or who had received radium as a form of medical therapy. The result of this survey is summarized in Table I. Analysis of these data suffers from the fact that the determination of radium content of the body has been done at least 36 yr after acquisition of the radioactive material. The extrapolation of the present burdens to radium burden at early times carries large factors of uncertainty. However, UNSCEAR reports the attempts of Hasterlik et al. [12, 24] to derive the risk estimates per man-year of exposure in this group which is indicated in the last column of Table I.

UNSCEAR assumes that the cells lining bone surfaces are those that give rise to malignancies when irradiated. The committee gives
rough estimates of risk per unit dose which may be assumed to be about 4 cases\(^{\times10^{-6}}/\text{yr/rad}\) or a figure of the same order of magnitude as that for leukaemia and thyroid cancer after irradiation from external sources. Many uncertainties however arise; e.g. the doses are average doses to cells lining bone surfaces and do not take account of the highly inhomogeneous distribution of the absorbed dose. For a more detailed guidance on this subject UNSCEAR report should be consulted [3].

1.2.4. Foetal irradiation (para. 62-73 and 182-193 of Ref. [3])

In retrospective studies on mothers who had children dying from cancer, it was found that more of the mothers of these children had had abdominal X-ray examinations during the relevant pregnancy than mothers of control children. Recently Stewart [25] extended the survey to include more children. It appears from her studies that the frequency of cancer and leukaemia of children who were irradiated in utero has a peak of incidence between the ages of 5 and 10 yr. Earlier investigations were carried out to determine the frequency of abdominal irradiation during pregnancy of mothers of cancer children and mothers of control children. Such work was done by Stewart [25], Ford et al. [26], Kjeldsberg [27], Kaplan [28], MacMahon [29], Lewis [30] and others. These studies show that in children with cancer a higher proportion of mothers had received abdominal irradiation during pregnancy than in the control group.

Recent statistical estimations suggest that cancer mortality is about 40% higher in patients X-rayed in utero than in those not X-rayed in utero. These types of cancer were leukaemia, neoplasms of the central nervous system and other neoplasms. By an indirect method of standardization, McMahon [29] calculated that the cancer mortality rate in the X-rayed population adjusted for several variables was 10.31 per 10,000 live births.

It is now evident from the different studies made that there exists an association between exposure to X-ray while in utero and cancer mortality, with a peak risk after 5 yr of age. There is some evidence that in utero irradiation initiates leukaemogenesis in the first few weeks of conception. In these studies there are no exact measurements of doses received by the patients. It is therefore clear that no quantitative conclusions concerning dose and response can come from these studies. The conclusion, therefore, is that it seems wise to reduce exposure of pregnant women's abdomen and pelvis to the lowest practicable level. It is believed that the child
in the foetal stages of development is particularly susceptible to radiation, especially during the first few weeks of pregnancy where organogenesis is taking place.

1.2.5. Shortening of life span

In animal experiments total or partial body irradiation (whether the radiation is delivered singly or fractionated, by single exposure or protracted irradiation) produces a shortening of the average length of life. However, if irradiation is given at a low dose rate of 5 rad per week or less there appears to be no such effect even if the accumulated dose be some hundred rads before death.

Extrapolation to man from animal experiments, suggesting shortening of life span, had led to an estimate that each rad of total-body exposure shortens life from 1 to 10 d, but no observations are available to confirm this. In addition, the dose rate which would be received by the population in the case of an accident would probably be very low and therefore would not give rise to serious consequences as far as shortening of life is concerned.

2. Genetic effects

2.1. Excerpts from the Report on The Evaluation of Risks from Radiation

"(a) To provide a background for the assessment of genetic risks to man, the present state of knowledge on harmful genetic variation has been reviewed. Account has been taken both of studies of variation induced by radiation in animals and of that which arises from natural causes in man. Studies of the latter question have revealed that aneuploidy is a considerably more important cause of harmful variation in human populations than was hitherto supposed. Unfortunately, however, there is at present no adequate basis for estimating the extent to which such effects may be influenced by radiation, though there is good reason to believe that they will not account for a major part of the total genetic detriment which could result from low doses of radiation.

8 The following excerpts, including Tables 13 and 14, are a direct quotation from the report of the ICRP task group on The Evaluation of Risks from Radiation [14].
"(b) In the present state of knowledge any evaluation of genetic risks from radiation is beset with much uncertainty, largely because it is necessary to rely on much indirect evidence obtained from experiments with animals. In view of this, and because of the importance of avoiding the inadvertent underestimation of risks, many assumptions, which may in due course prove to be unduly pessimistic, have been made. Thus, for example, it has been assumed that the effects of radiation delivered at a low dose rate over an extended period are identical with those of the same total dose delivered at high dose rate in a short period. It has also been assumed that the dose-mutation relation is linear for all genetic effects to which it is now possible to assign estimates of risks. In addition, many simplifying assumptions have been necessary.

"(c) In Table 13 the expected detriment caused by all types of gene mutations in the first generation offspring of a parental generation exposed to a single irradiation is estimated. Table 14 contains estimates of the rates at which mutations, which are individually responsible for small effects, may determine genetic deaths in subsequent generations. By assuming that 2.5 per cent of the total effect is expressed in each generation it can be estimated that, if 1 rad were received by a parental population of one million persons, $1.9 \times 10^3$ genetic deaths would occur over the first 10 generations and $8.5 \times 10^3$ to infinity. The estimate for the first 10 generations may be compared with $2.4 \times 10^6$ cases which are expected to arise from spontaneously arising mutations of this type.

"(d) The principal assumptions made in the calculation are indicated briefly in notes appended to the tables; they are described more fully in earlier sections of this chapter. It is important that their extent and nature should be realised when the estimates are used to guide action in practical problems.

"No simple comparison of the values in Tables 13-14 can provide an adequate basis for comparing the harm which can be experienced by the first generation offspring of the exposed persons with ill effects to subsequent generations. General aspects of the imponderable factors which could vitiate any close comparison were outlined in Chapter I, Section 3; the special difficulties which arise in assessing the long term detriment from "genetic deaths" are apparent from Sections 2.10 and 11.3 of the present chapter. None the less, it is apparent:
(i) the detriment to the first generation offspring will exceed that to any other single generation;
(ii) the total number of deleterious conditions suffered by all subsequent generations will greatly exceed that experienced by the first generation."

2.2. Excerpts from the UNSCEAR Report A/63149

"24. The Committee has considered genetic effects of radiation, with particular regard to recent data, and has tried to derive from them information as to the importance of genetic effects of irradiation of man.

"25. A new estimate has been obtained for the spontaneous frequency of gene mutations over the whole of the hereditary material of man. An estimate has also been made of the rate of induction of gene mutations per unit of radiation dose. From these it would appear that a dose of one rad per generation would add something like one-seventieth to the total number of mutations arising spontaneously in a generation. Taking into account the various uncertainties, the range of that estimate would be very wide, but it is probably not in disagreement with the limits set in the 1962 report of between one-tenth and one one-hundredth. It is known that the great majority of all harmful mutations are expressed as small reductions of viability over intra-uterine and post-natal life, and their effects on health are detectable with difficulty in man. However, it is known that the cumulative effect of these small changes causes the major part of the damage from induced mutations. Furthermore, these changes will be expressed over many generations.

"26. The proportion of one-seventieth above might also apply to hereditary diseases of man which are known to be important and which can be transmitted directly from parent to offspring, but it should be emphasized once more that these diseases contribute only a small proportion of the damage from induced mutations. There is evidence that complexly inherited characteristics, such as stature and intelligence, may be affected by induced gene mutations and that the effects would probably be adverse.

"27. One-quarter of all abortions are caused by, and 1 per cent of all live-born infants suffer from, severe effects of chromosomal

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TABLE 13. ESTIMATED DETRIMENT TO FIRST GENERATION OFFSPRING IN A POPULATION WHERE THE WHOLE PARENTAL GENERATION HAS RECEIVED 1 rad OR 30 rad

<table>
<thead>
<tr>
<th>Type of detriment</th>
<th>Number expected without parental man-made irradiation</th>
<th>Number estimated to have arisen in preceding generations without parental irradiation</th>
<th>Estimated* additional numbers resulting from 1 rad</th>
<th>30 rads</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Autosomal dominant gene traits (births)</td>
<td>8000&lt;sup&gt;a&lt;/sup&gt;</td>
<td>320&lt;sup&gt;a&lt;/sup&gt;</td>
<td>16&lt;sup&gt;a&lt;/sup&gt;</td>
<td>480</td>
</tr>
<tr>
<td>B Sex linked traits (births)</td>
<td>250&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;83&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;4&lt;sup&gt;b&lt;/sup&gt;</td>
<td>&lt;120 (Mother exposed)</td>
</tr>
<tr>
<td>C Chromosomal aberrations (births)</td>
<td>7000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>7000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Unknown&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Unknown&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>D Abortions associated with chromosomal aberrations (recognized pregnancies)</td>
<td>35 000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>35 000&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Unknown&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Unknown&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>E &quot;Genetic deaths&quot; (zygotes)</td>
<td>235 000&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5875&lt;sup&gt;e&lt;/sup&gt;</td>
<td>211&lt;sup&gt;f&lt;/sup&gt;</td>
<td>6330</td>
</tr>
</tbody>
</table>

* The number of effects anticipated per million births are shown; the total number of pregnancies in the population which would last long enough to be recognized would be about 1 175 000, there being about 175 000 abortions of which about 20% are assumed to be associated with chromosomal aberrations. To facilitate alternative calculations figures have not been rounded and the number of significant digits is not indicative of precision.

<sup>a</sup> 0.8% have dominant gene traits, i.e. 8000 per million. The proportion of sporadic cases is 4%, i.e. 320. Both parents receive irradiation so the number expected from 1 rad would be 1/20 if the doubling dose is 20 rad, i.e. 16.

<sup>b</sup> From footnote b to Table 12 the birth frequencies of those traits is $5 \times 10^{-4}$ in male births, i.e. 250 in 1 000 000 births of both sexes. If one third of these were mutants, we should expect 83 mutant subjects. Increase in the next generation by 1/20th would give an expected 4 cases.

<sup>c</sup> No predictions are made (see Section 10.1.5) but current frequencies are shown to draw attention to their magnitude.
anomalies which arise spontaneously. It is, in our present state of knowledge, only possible to give estimates of rates of induction by high doses of radiation of chromosomal damage of types which include not more than a small proportion of the anomalies that occur naturally. The number of these that would arise after exposure to high doses can be estimated, but it is not known how many would occur following low doses, although the yield per unit dose would be much less than that expected if the yield were directly proportional to the dose. It should be noted that a large part of this type of genetic damage is not expected to persist in a population for more than one generation.

"28. Part of the total impairment in the first generation offspring of irradiated parents has been studied in mice, namely, certain skeletal defects. From experiments using high doses, it is known that malformations of the skeleton do occur fairly frequently in these offspring. Whether proportional numbers of such defects would result from low doses to parents is not known.

"29. The estimates arrived at in this report relate to the genetic effects of acute exposures, at high doses, of male reproductive cells in the stage (spermatogonia) that is most important in human hazards. Lower numbers of these mutations per unit dose will occur where the radiation dose is low or is spread out over a long time. It is also known that the reproductive cells of the two sexes differ in sensitivity; fewer mutations, on the average, will occur when the reproductive cells of females (oocytes) are exposed to radiation.

"30. The Committee is of the opinion that these estimates, because they are subject to many uncertainties, should not be applied in a simple and direct fashion to radiation protection. Any practical application of these numerical estimates must be made with full re-

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d If the average individual carries 8 small dominant mutations each conferring independent risks of 2.5 per cent, then the total risk is 0.025 \times 8 = 0.2. Therefore, in 1 175 000 zygotes we should expect 235 000 eliminations per generation. By postulating equilibrium gene frequencies, a figure is arrived at whereby the same number of mutations which arise in each generation are eliminated; otherwise the total gene frequency would either rise or fall.

e If of these 235 000 newly arisen mutations 2.5 per cent are eliminated in the first generation, then the number eliminated would be 0.025 \times 235 000 = 5875.

f If 1 175 000 zygotes received 2 350 000 gametes from their parents and if these parents received an average 1 rad of radiation, then the mutations received by their offspring would be 2 350 000 \times 0.0036 = 8460 mutations. Of these, 0.025 \times 8460 = 211 would be expected to be eliminated in the first generation as "genetic deaths".
TABLE 14. ESTIMATES OF THE NUMBERS OF "SMALL DOMINANT" MUTATIONS ELIMINATED IN SPECIFIED NUMBERS OF GENERATIONS (n) FROM A TOTAL OF 8460 (x) MUTATIONS ESTIMATED TO HAVE BEEN RECEIVED FROM A PARENTAL GENERATION WHO HAD ONE RAD OF GONADAL EXPOSURE. IF THE PARENTAL GENERATION RECEIVED ONE RAD PER YEAR, THEN "THE GENETICALLY EFFECTIVE DOSE" WOULD BE 30 rads AND THE NUMBERS ELIMINATED ACCORDING TO THE TABLE WOULD BE INCREASED 30 TIMES

<table>
<thead>
<tr>
<th>Generations</th>
<th>( x(1-s)^n )</th>
<th>( s = 0.01 )</th>
<th>( s = 0.025 )</th>
<th>( s = 0.05 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( x-x_0 )</td>
<td>85</td>
<td>1%</td>
<td>211</td>
</tr>
<tr>
<td>1-10</td>
<td>( x(1-s)^{10} )</td>
<td>808</td>
<td>10%</td>
<td>1892</td>
</tr>
<tr>
<td>1-50</td>
<td>( x(1-s)^{50} )</td>
<td>3342</td>
<td>39%</td>
<td>6074</td>
</tr>
<tr>
<td>1-100</td>
<td>( x(1-s)^{100} )</td>
<td>5360</td>
<td>63%</td>
<td>7787</td>
</tr>
<tr>
<td>1-( \infty )</td>
<td>0</td>
<td>8460</td>
<td>100%</td>
<td>8460</td>
</tr>
</tbody>
</table>

Generations by which 4230 (50%) will have been eliminated | 69th | 28th | 14th |

31. Although there are insufficient data for making satisfactory estimates of risk, it is clear that, with any increase of radiation levels on earth, the amount of genetic damage will increase with the accumulated dose. While any irradiation of the human population is genetically undesirable because of its implications for future generations, it should be pointed out that the proper use of radiation in medicine and in industry is important for the health of the individual and for the welfare of the community.

32. The limited number of estimates made, the many uncertainties as to their accuracy and the reservations which have to be

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attached to each of them may seem disappointing. The reasons will be clear to readers of annex C where the complications of establishing meaningful estimates are fully discussed. Although absolute measures of risk are still very uncertain and will probably remain so for some time, major advances have been made in our knowledge of the relative risks under various conditions of radiation exposure and for different biological variables such as the reproductive-cell stage. These findings are of considerable practical value. Thus, it is useful to know that the genetic hazard will be less per unit dose of radiation when the exposure is spread out in time, is delivered in small dosage, or when a long interval occurs between irradiation of the female germ cell and conception. These factors must be clearly borne in mind when making comparative risk estimates."

2.3. Excerpts from the UNSCEAR Report A/6314

IV. Risk estimates

"244. Risk estimates express a probable quantitative relationship between doses of radiation and frequencies of certain effects. In this report, risks of genetic effects will be expressed in terms of expected frequencies of genetic changes (point or chromosome mutations) induced per unit dose or function (e.g. power) of dose. In earlier reviews of genetic effects by the Committee, risks were expressed in terms of doubling doses, these being the doses required to produce a number of mutations equal to those occurring naturally in one generation. Doubling doses can easily be computed when both the natural incidence and the rate of induction of a certain category of mutations are known. When both figures are available, the doubling dose is a compact way of summarizing the information regarding a given effect in given circumstances. The use of the doubling dose, however, is not necessary in arriving at risk estimates, and for that reason the more direct approach is employed in this report.

"245. Risk estimates as defined in paragraph 244 have the advantage that they can be obtained in the non-linear case in which a single doubling dose would have little meaning. They are also

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10 Direct quotation of sections IV and V, Annex C of the UNSCEAR Report [4], p. 121.
absolute estimates which give at once the risk in terms of effects, whereas this type of information is less directly obtained from the doubling dose and involves unnecessary assumptions regarding the proportionality between spontaneous and induced rates. Finally, risk estimates as expressed in this report are consistent with the practice followed by the Committee with regard to the risk of induction of malignancies.

"246. It may be pointed out that, while estimates of risks of induction of malignancies in man can be derived from the results of irradiated human populations, this is not possible with regard to genetic risks. As will be discussed below, in vivo human data are inadequate to provide estimates of genetic risks. These must be based on results of experiments with animals — mainly mice — and with human somatic cells in vitro. While there appears to be no alternative at present to the use of such experimental material, its limitations must be clearly borne in mind and will be stressed throughout the following paragraphs. Because of unavoidable differences from one species to another or from one type of cell to another, the estimates thus obtained are less reliable than the data from which they are derived.

"247. An additional difficulty with genetic risks is encountered in expressing them in meaningful terms. The eventual result of the great majority of genetic changes is, sooner or later, the failure of cells carrying those changes to be transmitted to the following generations. Only in a minority of cases — such as certain dominant traits and certain chromosome anomalies that occur frequently in the population and that are easily detected — can we make assumptions as to the manner in which the damage will be expressed. For most genetic changes even conjectures are not permissible regarding the actual manifestation of the damage throughout generations in terms of individual or collective hardship.

"248. The estimates reviewed in the following paragraphs were obtained for acute irradiation of spermatogonia by low LET radiation at high single doses. The consequences of irradiation of oocytes, and those of exposure to radiation of different quality at different doses and dose rates, will be considered separately.
POINT MUTATIONS

Total risk of induction

"249. Much as the total rate of spontaneous mutation can be derived from an analysis of the excess of female over male newborn children, so the total risk of induction could, in principle, be obtained from the shift of the sex-ratio to be expected in the offspring of irradiated mothers as a consequence of the induction of sex-linked recessive lethal mutations. Such a shift has, in fact, been observed and was used by the Committee in its 1958 report to obtain risk estimates. Further observations were summarized and discussed in the 1962 report, in which the Committee discarded estimates of risk of point mutations based on the sex-ratio shift, because, while the shift undoubtedly was largely due to genetic damage and might have reflected a point mutational component, it was not possible to rule out or separate the possible confounding effect of induced chromosome anomalies, the high frequency of which was not known in 1958.

"250. Such a reservation is still valid now, despite new data[381,382] on the offspring of irradiated mothers which confirm earlier observations, and although no increase in the frequency of sex-chromosome anomalies was noted in a survey[383] of the female offspring of irradiated mothers. The size of the survey was too limited, however, to exclude the possibility that induced anomalies of the sex-chromosomes may account for at least part of the effect on the sex-ratio.

"251. A further reason why risk estimates based on the sex-ratio shift are not being made in this report lies in the limitation of the data themselves. The largest and dosimetrically best known material is still that collected among the irradiated populations of Hiroshima and Nagasaki.[384] Doses in the parental populations were between 0 and 200 rads, however, and the observed shift was not significant.

"252. Some effect on the sex-ratio may also be expected after paternal irradiation, primarily as a consequence of the induction of sex-linked dominant lethals. The expectation has not been conclusively borne out by observations in man, and experimental studies have shown that in mice the results of paternal irradiation cannot be explained on the sole basis of the induction of sex-linked dominant lethals.[384,385]
253. No other human data are yet available that would make it possible to obtain risk estimates for the induction of point mutations. As in the 1962 report, it will therefore be necessary to base risk estimates in man on rates of induction observed in the mouse. However, it is no more possible now than it was in 1962 to assess how close the rates of induction in man and in the mouse might be. For want of better data, it will be assumed that rates of induction of mutations are the same in man and in mice, but the arbitrary nature of such an assumption needs to be underlined. The possibility that rates of induction may be higher in man than in mice should not be overlooked.

254. The average rate of induction of mutations at twelve specific loci in mouse spermatogonia exposed in the range 300-600 R acute x rays is estimated to be about $1 \times 10^{-7}$ per locus per roentgen (paragraph 133). The confidence limits, when this figure is used as an estimate of the average rate for all loci in the mouse, are presumed to be about one order of magnitude apart.

255. The size of the human genome in terms of loci at which detectable mutations arise was estimated in paragraph 24 to be between 7000 and 70,000. As mentioned earlier, the estimate, although very crude, is in agreement with similar but more precise estimates valid for Drosophila. It also agrees with a number of other published estimates of the number of mutable loci in man.

256. If the rate of induction of specific locus mutations assumed to apply to man (paragraph 254), is multiplied by the estimated size of the human genome, the resulting estimate of total risk of point mutation in man is $2 \times 10^{-3}$ mutations per gamete per roentgen. Taking into account the variability of the data on which it is based, it can be assumed that the approximate confidence limits of the estimates are between one and two orders of magnitude apart. While this range reflects the sampling variability of the estimate, the dubiousness of some of the underlying assumptions must also be borne in mind.

257. It will be recalled that direct estimates of the total rates of induction of lethal recessives in mice have been obtained from two independent sets of experiments and are remarkably close (paragraphs 143, 144). Allowing for the fact that these estimates measure only a known part of the damage measured by experiments at specific loci makes it possible to compare direct estimates of the rate of induction over the whole genome with those obtained indirectly. The direct method gives a lower estimate ($\sim 0.5 \times 10^{-3}$) than the indirect method. The upper confidence limit of the direct estimate
(1.6 \times 10^{-3})$, however, is well within the range of the indirect one. Such an agreement gives strong support to the estimate discussed in paragraph 256, especially as the direct estimate is based on a smaller number of assumptions.

"258. The nature of the damage measured by the total rates of induction is as difficult to assess as is that measured by the total rate of spontaneous mutation which was discussed in paragraphs 25-27. The total rate of induction includes all mutations of every degree of dominance and harmfulness. They will all eventually be eliminated from the population:

"259. The mechanisms through which the spontaneous mutational damage could be eliminated were mentioned in paragraph 27. These mechanisms also apply to the induced damage, but the relative contribution of any mechanism to the process of elimination cannot in the current state of our knowledge be assessed. It is therefore not possible to express damage, as measured by the total rate of induction, in terms of individual or collective hardship.

"260. If observations made in Drosophila can be used as a model for the situation obtaining in man, the induced damage will initially be eliminated at the rate of 4-7 per cent per generation. The rate will, after a few generations, taper off into a rate between 1 and 2 per cent that will persist approximately at the same level until all the induced damage has been removed. Genes will persist in the population for periods of time inversely proportional to their rate of elimination and therefore dependent upon the severity of their expression in heterozygotes. If a population was steadily exposed to a constant amount of radiation per generation for a number of generations, the rate of elimination of the damage would tend to become equal to the rate of induction.

Risk of induction of dominant mutations

"261. The difficulty of evaluating the total mutational damage in socially meaningful terms justifies attempts to obtain independent estimates of that part of the damage that can be expected to find its expression in an indisputably injurious way. Experimental data that lead to high estimates of dominant skeletal damage in the mouse were discussed in paragraphs 151-155. While it is too early to evaluate from these data the effects at low doses, the Committee wishes to emphasize that this type of observation may in the future
offer a clue to the estimation of risks of induction of dominant mutations in man. In the meantime, dominant damage in man can only be estimated for that portion of the genome that is responsible for a selected group of dominant traits (paragraphs 8-11).

"262. When the Committee reviewed genetic effects in 1958 and 1962, it gave estimates of the expected frequency that these traits would reach in the population at equilibrium under conditions of steady irradiation. It is, however, more informative and more consistent with the approach adopted for estimating the over-all mutation rate if the rates of induction after a single exposure are obtained, and this approach will be followed here.

"263. For that purpose, the rate of induction per locus per roentgen (1 × 10⁻⁷) as observed at specific loci in the mouse will be used. The rate, however, applies to recessive mutations. It will be recalled (paragraphs 149, 150) that limited mouse data show that the over-all rate of induction of dominant visibles is considerably lower than that of recessive visibles. The interpretation of that phenomenon is difficult, but it cannot be excluded that it may in part reflect a lower average rate of induction of dominant mutations. The rate of induction used therefore can only be considered as an upper limit, for it probably over-estimates the rate of induction of dominants, though by not more than two orders of magnitude (paragraphs 149, 150).

"264. As discussed in paragraph 9, the part of the human genome under discussion, namely that responsible for some fifty dominant traits most commonly observed and easily detected, consists of at least fifty loci and is unlikely to consist of as many as 500. Multiplying the assumed number of loci by the rate of induction discussed in the previous paragraph gives a total rate of induction ranging from 5×10⁻⁵ to 5×10⁻⁸ mutations per gamete per roentgen depending upon the assumptions concerning the number of loci involved and the proportion of dominant mutations induced.

"265. Assuming full penetrance, the damage thus estimated will become apparent in the offspring of irradiated subjects and, because of the reduction of fitness that it entails (paragraph 11), will, on the average, persist in the population for some twenty-five generations. The genes responsible for those traits that more drastically impair fitness will be eliminated in the first generation, whereas the mildest ones will persist for a very long time. Under conditions of steady irradiation for several generations, the frequency of the induced traits in the population would build up to a value equal to the rate of induction.
"266. As mentioned in paragraph 248, all mouse data used for numerical estimates have been derived from experiments in which mouse spermatogonia were irradiated with high, unfractionated doses of acute, low LET radiation. However, it needs to be emphasized that the final yield of mutations has proved to be different when the germ cells of mice are irradiated with (a) low doses, (b) fractionated doses, (c) chronic radiation, and (d) high LET radiation.

"267. As has been discussed in part III of this annex, experimental results in a number of species show that matters may differ considerably when other germ cells are irradiated. On the basis of results obtained at seven specific loci in the mouse, acute x-ray irradiation of oocytes at high doses yields more mutations per unit dose than acute irradiation of spermatogonia. Although the rate of induction in oocytes is known with little precision, data suggest that it may be twice as high as in spermatogonia. When individuals of both sexes are irradiated, the total number of mutations induced will therefore be about 50 per cent higher than if oocytes had the same sensitivity to radiation as spermatogonia.

"268. Preliminary results indicate that in oocytes the yield of specific locus mutations per unit dose after 50 R acute x rays (paragraph 170) is significantly lower than would be expected from results of irradiation at higher doses. It seems therefore that low doses of radiation are relatively less mutagenic than high doses of radiation, at least in oocytes. Since human populations are more commonly exposed to low than to high radiation doses, it might well be that the estimates of genetic risks which are presently made will eventually prove to be too high.

"269. Experiments with spermatogonia and oocytes have shown that chronic radiation is mutagenically less effective than acute radiation. Under conditions of chronic irradiation of spermatogonia the yield of mutations per unit dose at rates of about 1 R per minute or less is about one-fourth of that at 90 R per minute (paragraph 156). With oocytes, the reduction of the mutation yield is even more pronounced (paragraph 157). When both sexes are exposed to low dose-rate x or gamma radiation, the over-all yield of mutations can therefore be expected to be between one-eighth and one-fourth of that expected when the same population is exposed to high dose-rate radiation. Preliminary data indicate that a small dose-rate effect obtains with low doses of neutrons in mice oocytes but not in sper-
matogonia (paragraphs 187, 196). More detailed information is needed before this dose-rate phenomenon with neutrons can be taken into account.

"270. Results of new fractionation experiments (paragraph 175), in which the total radiation exposure is partitioned into small acute exposures of 50 R, indicate that this type of fractionation procedure yields mutation frequencies which are below those obtained with single, unfractionated procedures. Although mutation frequencies in the fractionated and unfractionated series differ by less than one order of magnitude, it is thought that this effect may be of importance for the estimation of human genetic hazards, because the fractionation procedures used are similar to those used in some medical practices.

"271. Results of investigations at seven specific loci in spermatogonia show that low doses (up to about 100 rads) of acute or chronic fast fission neutrons are mutagenically more effective than x and gamma rays, suggesting an RBE of five for acute irradiation and of twenty for chronic irradiation (paragraph 188). Since human populations are usually exposed to low doses given at low dose rates, it seems that in spermatogonia the rate of induction of mutations per unit dose of neutrons may be some twenty times higher than the corresponding rate for x or gamma rays.

"272. The final yield of mutations is not only affected by factors associated with radiation procedures but also by biological factors. One of the latter factors has recently been discovered and may have an important bearing on the estimation of genetic risks from irradiation of germ cells of females. Experiments with female mice have shown that the interval between irradiation and conception has a very pronounced effect on the mutation frequency observed in the offspring (paragraph 182). The frequency obtained after irradiation of females with low doses of neutrons is high in the first few weeks after irradiation, but, after that period, drops to a very low value, in fact zero in the sample size studied so far. Similar results have been obtained with x rays. There is a possibility of a similar effect in man and, therefore, an indication that the genetic radiation hazard from the exposure of women may, on the average, be less than that calculated on the basis of female mouse mutation rates obtained in the early time interval after irradiation,
CHROMOSOME ANOMALIES

"273. The estimation of risks of induction of chromosome mutations can only be made on grounds as tenuous as those on which the estimates of risks of induced point mutations are based. While with regard to the induction of point mutations detailed and reliable quantitative information from Drosophila and from the mouse can be used, no comparable amount of data is available concerning the induction of chromosome anomalies. But the induction of point mutation is not borne out by direct observations in man, and the corresponding quantitative relationships between dose and effect are unknown. To estimate risks of induction of point mutations in man, a very major step is therefore necessarily involved in extrapolating from the experimental animals to our own species.

"274. With regard to the induction of chromosome anomalies, on the other hand, there is clear evidence that a number of them can be induced by radiation in human cells in vitro. Preliminary observations suggest that some can be radiation-induced in vivo in germ cells. However, information on rates of induction in vivo in man is absent, and that obtained from human peripheral blood cells irradiated in vitro must be supplemented with observations in experimental animals.

"275. Inferences regarding the induction of chromosome anomalies in our species based on animal material are especially open to criticism, inasmuch as the radiation sensitivity of chromosomes is known to change from one species to another. Thus, there is some evidence that human somatic cells might be more sensitive to the induction of chromosome anomalies by radiation than those of mice. Likewise, extrapolations from in vitro studies of human cells can also be quite misleading because of the known dependency of chromosome sensitivity on a number of factors associated with the stage and metabolism of the irradiated cells.

"276. It was shown in part II of the present review that constitutional chromosome anomalies are responsible for a large part of the defects of genetic origin carried by human populations. Most of the anomalies are eliminated either pre- or post-natally in the generation immediately following the one in which they have arisen, and are associated with very severe hardship. Some, however, notably translocations, can be transmitted for a number of generations and are also the cause of serious harm to those who carry them in the unbalanced state.
"277. Only for some types of chromosome anomalies can tentative risk estimates be obtained. These will be discussed in the following paragraphs. The estimates apply to a minor fraction of the total spontaneous chromosome damage detectable in the population. No estimate of the over-all risk of induction of chromosome anomalies can be obtained in the current stage of our knowledge.

Changes in chromosome numbers

"278. Experimental results indicate that in Drosophila the frequency of sex-chromosome loss rises linearly with dose below 1000 R (paragraph 82). The rate of induced loss per pre-meiotic cell is very close to that obtained from irradiation of mouse spermatocytes at 200 R — between one and four chromosomes per 100,000 cells per roentgen. A comparable figure for non-disjunction cannot be obtained, because in that case the dose-effect relationship as observed in Drosophila is more complicated.

"279. The possible importance of the induced sex-chromosome loss in man becomes apparent when it is recalled that XO karyotypes have been identified in 5 per cent of a sample of aborted foetuses and may therefore be responsible for a sizable proportion of spontaneous miscarriages. However, the possibility that at least part of the observed losses may have occurred after fertilization cannot be excluded.

"280. No estimate of risk can, in the present stage of our knowledge, be obtained for the induction of losses or additions of autosomes. Some still inconclusive evidence, indicating that they may be induced by radiation in man, was mentioned in paragraph 66.

Translocations

"281. Translocations in experimental animals are associated with, and frequently recognized through, the incidence of semi-sterility. In man, semi-sterility is a hardly applicable criterion, since the family-size usually falls very short of the natural fecundity of the species. The importance of translocations in human populations lies, therefore, much more in the suffering that they involve for those who receive them in the unbalanced state than in the effect they may have on the fertility of carriers of balanced translocations.
282. The estimation of risks of induction of translocations in man may be approached either from results obtained in mice or from results obtained in human cells in vitro. As discussed in part III (paragraph 116), from the incidence of semi-sterility in mice irradiated with 1200 R of x rays, the number of induced translocations has been estimated to be approximately $14.8 \times 10^{-2}$ per pre-meiotic cell. The estimate is based on the assumption that translocations are not further transmitted unless they are balanced, that no selection takes place between normal cells and cells carrying a balanced translocation, and that non-disjunction does not bias the observed frequencies of the translocations that are recovered.

283. In this connexion, it must be borne in mind that some of these assumptions may not strictly apply to man, since in our species the association of translocations with trisomies 21 does occur with a frequency of about $5 \times 10^{-5}$ of all live-born children (paragraph 42), and the viability of cells carrying balanced translocations may, in fact, be different in mice, since the spontaneous frequency of translocations seems to be lower than in man.

284. The use of cell cultures to estimate the frequency of radiation-induced translocations is also far from being free from objections. For example, it is not possible to determine directly the rate of induction of translocations by radiation, because, even if the karyotype of each scored cell were established, present techniques would not make it possible to detect those translocations that involved small quantities of chromosome material or fragments of equal size. Finally, in vitro observations are available only on somatic cells, and it does not necessarily follow that, if the anomalies that were observed in vitro occurred in pre-meiotic cells in vivo, they would be transmitted to a viable gamete, as is indicated by the fact that haplo-21 zygotes appear not to be viable, whereas haplo-21 somatic cells are.

285. Rather than determine the frequency of translocations in vitro, most authors have therefore assessed the frequency of breaks, dicentrics and ring chromosomes. Breaks are events whose frequency rises linearly with dose, whereas the frequency of dicentrics and ring chromosomes, like that of translocations, at least when induced by x rays, is proportional to the square of the dose at low doses and to its 1.5th power at high doses. At very low doses, the effect may be proportional to the first power of the dose.

286. The number of dicentrics and of ring chromosomes obtained through irradiation of blood cells at exposures between 50 and
200 R is $0.52 \times 10^{-5}$ per cell per roentgen squared of which $0.45 \times 10^{-5}$ are dicentrics. The rate of $0.27 \times 10^{-5}$ dicentrics per cell per roentgen squared was also obtained, but it is perhaps less relevant because it is based on observations at exposures ranging between limits too far apart (25 to 1200 R).

"287. If it is assumed that translocations on one side and rings and dicentrics on the other are induced at the same rate, and that rates at high doses increase with the 1.5th power rather than with the square of the dose, the expected translocation rate after 1200 R based on in vitro data is approximately $21 \times 10^{-2}$ translocations per cell (or $18 \times 10^{-2}$ if only the results on dicentrics are taken into account). This rate is fairly close to that deduced from semi-sterility data in mouse spermatogonia. Under the same reservations as were formulated for that case, the rate of transmission of translocations through the gametes would be four to six times less.

"288. The rate of induction of translocations is known to be highly dependent on the rate of delivery of radiation. The estimates of rates of induction discussed in the previous paragraphs refer to acute irradiation. The actual rates under chronic irradiation may be considerably lower, as indicated by the mouse data discussed in paragraphs 118 and 124.

Deletions

"289. Estimates of rates of induction of deletions in human germ cells are not available, but an idea of the possible magnitude of the risk of induction of certain clinically significant deletions can be obtained on the basis of the rates of induction of deletions by radiation in human cells in vitro. Induced rates in vitro are probably reliable, since they are consistent with scantier observations on peripheral cells of subjects irradiated accidentally in vivo.

"290. It is not known whether one single break is sufficient to bring about a stable "terminal" deletion or whether, in fact, an additional break is required to make it possible for the telomere to attach itself to the centric fragment. The linear rise of the frequency of terminal deletions in vitro (paragraph 69) speaks in favour of the one-hit theory.

"291. To obtain estimates of the risk of induction of given syndromes due to terminal deletions, it is necessary to know the size of the fragments whose loss is responsible for each syndrome.
mentioned in paragraphs 39 and 40, the following terminal deletions are known to be associated with clinical syndromes severely detrimental but compatible with survival: deletion of part of the short arm of chromosome 5 (cri du chat syndrome), of the short arm and of the long arm of 18, and of the short and of the long arm of the X chromosome. It is not known whether any other deletion, be it terminal or interstitial, is compatible with survival nor to what sort of detriment it may be associated.

"292. In the cri du chat syndrome, the size of the target, i.e. the length of the segment of chromosome 5 where a break must occur to produce the required deletion, amounts to over 50 per cent of the short arm of this chromosome or to about 1 per cent of the length of the diploid chromosome complement. This has been estimated by studying the variations in length of the residual fragment of the short arm of chromosome 5 in the known cases of cri du chat syndrome.

"293. Observations on blood cells irradiated in vitro have shown that x rays induce $1.1 \times 10^{-3}$ deletions per cell per roentgen. If a single break were enough to bring about the cri du chat syndrome, the deletion would be expected to occur with a frequency of $1.1 \times 10^{-3} \times 10^{-2} = 1.1 \times 10^{-5}$ per cell per roentgen. If two breaks were required, the expected frequency would be lower than the square of this (i.e., $1.2 \times 10^{-10}$ per cell per roentgen squared).

"294. Similar estimates can be obtained for the other deletions mentioned previously. Deletions of part of the short and of the long arm of chromosome 18 compatible with survival involve 0.25 and 1 per cent of the length of the diploid chromosome complement, respectively, leading to estimates of $0.3 \times 10^{-5}$ and $1.1 \times 10^{-5}$ deletions per cell per roentgen in the case of single events, and of $0.8 \times 10^{-10}$ and $1.2 \times 10^{-10}$ deletions if two breaks are required. Likewise, deletions of the short and of the long arm of the X chromosome, involving 3 and 4 per cent of the complement length, respectively, would occur with probabilities of $3.3 \times 10^{-5}$ and $4.4 \times 10^{-5}$ deletions per cell per roentgen if one break was required, and $11.0 \times 10^{-10}$ and $19.0 \times 10^{-10}$ deletions per cell per roentgen squared otherwise.

"295. Nothing is known about the selection that deletions arising in germ cells might undergo. It is conceivable that a fraction of those that radiation may induce would be eliminated sometime before birth or perhaps before fertilization. Neither human nor experimental data are available which would make it possible to assess the extent of the elimination.
V. Conclusions

"296. The estimates given in the preceding paragraphs must be examined in the light of the practical value they have in assessing the detriment that will result from exposure of human populations to any source of radiation. For that purpose, risk estimates must, ideally, be comprehensive, therefore taking into account all major genetic effects of social, rather than merely biological, import. If this did not prove possible, it would still be valuable to know the range in which the over-all risk estimate lay or even an upper limit to the estimate.

"297. Even taken together, the estimates given earlier do not meet these requirements. The risk of induction of dominant mutations (paragraphs 261-265) applies to those major and easily recognizable traits that are clearly undesirable from the individual and social points of view. These traits are frequently observed in all known populations. That damage would always be a minor fraction of the over-all damage due to point mutations, though a particularly conspicuous one, both because of its immediate manifestation and its persistence for a number of generations, and because of the nature of the detriment to which the risk estimate applied.

"298. An approach to the estimation of damage from induced dominant mutations could in the future result from the application to man of the observed frequencies of skeletal defects in first generation irradiated mice (paragraphs 151-155). However, it is not certain that comparable rates of induction apply at low doses.

"299. The over-all risk of induction of all point mutations, which are all assumed to have some degree of dominance and to be eliminated predominantly in heterozygotes (paragraphs 253-260), includes the risk of induction of dominant mutations discussed in paragraph 297. One major practical limitation of the over-all risk estimate is due to the fact that the damage that is thus assessed is expressed in terms of loss of mutants through generations. This loss has a clear biological meaning, and has an undesirable character for the individual and for society. However, we do not know how many of the harmful mutations induced by radiation will at some point be eliminated through, say, loss of a zygote before implantation — an event which is not usually detectable in man — rather than through drastic reduction of fertility, miscarriages or serious genetic defects. But the estimate does, at any rate, provide the required upper limit to the damage due to point mutations.
"300. This is, however, only part of the induced damage, since it does not include that due to chromosome anomalies. At present, we have no way of estimating the over-all risk of induction of chromosome anomalies. Their high frequency in human populations makes it likely that such a risk may not be negligible. We only have estimates of the induction of sex-chromosome loss (paragraphs 278-280), of translocations (paragraphs 281-288) and of those deletions that are known to be associated with severe clinical syndromes (paragraphs 289-295). The total damage from induced chromosome anomalies is likely to be higher, but our present knowledge is inadequate even to guess its possible magnitude, while such partial estimates as we have discussed are based on assumptions that make conclusions conjectural or, at best, very tentative indeed.

"301. In considering the significance of radiation damage to the genetic material, it may be of interest to compare it with the rate of naturally-occurring genetic changes. It was estimated in the report that, on the average, a total of 140 point mutations arose spontaneously in 1000 gametes in each generation and that under conditions of acute irradiation at high doses one rad induced a total of two mutations per 1000 gametes. Thus a dose of one rad per generation would add about one-seventieth to the total number of mutations arising spontaneously per generation. To this point mutational damage must be added that due to chromosome anomalies which occur spontaneously in 1 per cent of live-born children. It is not possible at present to estimate the over-all rate of induction of these anomalies by radiation, but the rate is expected to be very low at low doses.

"302. Since neither a comprehensive estimate of the genetic risk, nor an upper limit to that estimate is available, the assessment of genetic damage from main sources of radiation must still be made by means of comparative risks. This is possible only at low doses and dose rates, in so far as linearity of the dose-effect relationship can be accepted as a computational approximation even for those effects that take place as a consequence of more than one event. No such approximation is allowed at high doses and dose rates, and even comparative risks cannot be determined for them."
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