



MEDICAL RESEARCH COUNCIL

THE HAZARDS TO MAN OF
NUCLEAR AND ALLIED
RADIATIONS

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TO THE MOST HONOURABLE
THE MARQUESS OF SALISBURY, K.G., LORD PRESIDENT
OF THE COUNCIL

My LORD,

On the 29th March, 1955, the Prime Minister, through you, requested the Medical Research Council to appoint an independent committee to report on the medical aspects of nuclear radiation, including the genetic aspects. The Council accordingly appointed a committee, under the chairmanship of Sir Harold Himsworth, and this body has now reported.

The report has been accepted by the Medical Research Council, and I have been authorised to transmit it to you with a view to its presentation to Parliament. It is the wish of the Council that, in so doing, I should express their high appreciation of the care, thought and ability which all members of the Committee have devoted so freely to their most difficult and important task.

I have the honour to be, my Lord,
Your Lordship's obedient Servant,

LIMERICK,
Chairman,
Medical Research Council.

June, 1956.



THE HAZARDS TO MAN OF NUCLEAR AND ALLIED RADIATIONS

A REPORT TO THE MEDICAL RESEARCH COUNCIL

CHAPTER I

INTRODUCTION

1. In accordance with the undertaking of the Prime Minister given in the House of Commons on the 29th March, 1955, the Medical Research Council, in April of that year, appointed us members of a committee, under the chairmanship of Sir Harold Himsworth, to review the existing scientific evidence on the medical aspects of nuclear and allied radiations, and we have unanimously signed this report.

2. We held our first meeting on the 3rd May, 1955, and decided to carry out our enquiry for the most part through two panels, one of which undertook to consider the effects of radiation on the health of the individual, and the other the possible genetic consequences of radiation to the population as a whole as well as to the individual and his descendants. Sir Ernest Rock Carling, Professor A. Haddow, Professor A. Bradford Hill, Dr. J. F. Loutit, Professor W. V. Mayneord, Dr. F. G. Spear, Professor Sir Lionel Whitby and Professor B. W. Windeyer have served on the former panel, which has met nine times. Professor A. Bradford Hill, Professor K. Mather, Professor P. B. Medawar, Professor J. S. Mitchell, Professor L. S. Penrose, Sir Edward Salisbury and Professor C. H. Waddington have served on the latter, which has met eleven times. In addition, Sir John Cockcroft and Professor J. R. Squire have served on the main committee. Both panels have worked under the chairmanship of Sir Harold Himsworth and all papers have been circulated to every member of the committee. More than seventy specially prepared papers have been considered, some of them written by scientists not serving on the committee, and we have drawn widely on the relevant published material. Groups to consider special problems have been appointed as the need arose. We have also taken into account relevant work carried out under the auspices of the Medical Research Council's Committee on Protection against Ionizing Radiations, and the recommendations and discussions of the International Commission on Radiological Protection. On the completion of the work of the panels, we have met together in full committee to consider our conclusions and to draw up this report. We have held four meetings of the whole committee during the period of our enquiry.

3. Throughout the course of our work, and in the preparation of this report, we have been greatly helped by our two scientific secretaries, Dr. W. M. Court Brown and Dr. T. C. Carter, of the scientific staff of the Medical Research Council. We are also very much indebted to Dr. R. H. L. Cohen and to Dr. Joan Faulkner, of the Council's headquarters staff, who have been responsible for co-ordinating the work of the panels and the various special enquiries that we have initiated.

4. The immediate occasion for the Government's request to the Medical Research Council to set up this Committee was the widespread public concern

about the long-term effects of nuclear weapon testing. This is only one aspect, however, of the much larger problem arising from the increasing use of ionizing radiations. It is already apparent that the future development of our civilisation is closely bound up with the exploitation of nuclear energy. At present, the potential hazards from its possible military uses overshadow in many people's minds the vast potentialities for good of this new source of power. The hazards to health are qualitatively the same, however, whether they arise from nuclear weapons or from the use of ionizing radiation for peaceful purposes. The difference is one of degree and intensity only. As with other sources of energy that man has harnessed to his service, the use of ionizing radiation necessarily entails risk; but the risk is controllable within limits that he can accept. It is the purpose of this report to indicate the nature of the risks and the extent to which they can be controlled.

5. Our purpose has been to give as firm a guide as the evidence allows to informed opinion in the country as a whole, and more especially to those with whom lies the responsibility for practical decisions of policy. This has laid on us the duty of drawing more precise conclusions than we might wish to do on purely scientific grounds, and we feel bound to point out that in the course of our enquiry we have become increasingly aware of the impossibility, in the present state of knowledge, of coming to final conclusions on many questions of importance in the subject under study. Nevertheless, because of the many and urgent problems on which action cannot be delayed, we have felt it incumbent upon us to attempt to give guidance to the best of our ability. It is inevitable that, with the advance of knowledge, many of the views which we have expressed will come to require amendment, but we feel reasonably confident that the general picture which we have drawn is unlikely to be found grossly inaccurate in perspective or scope.

6. We wish to remind those who read this report that human populations have always been exposed to ionizing radiation, and that it is the scale and not the nature of the hazard which is new. Moreover, our remarks in many respects can be applied only to large populations living under conditions similar to those prevailing in this country. A technically advanced community, such as our own, is likely to be exposed to a greater risk from the industrial and medical uses of atomic energy. These risks have to be weighed against the established benefits derived from the use of ionizing radiation in industry and medicine, and against the benefits likely to be conferred in the future.

7. We have thought it helpful to the general reader to follow this introduction with a brief account of radiation and its mode of action on living cells (*Chapter II*). The types of radiation and the units in which they are measured are described, and the chapter concludes with an outline of the way in which radiation acts on living tissues.

8. In *Chapter III* consideration is given to the effects of radiation on the health of the exposed individual. A brief review of the available sources of information is followed by an account, first, of the clinical manifestations which may occur within a short time of exposure, and, secondly, of the effects which may appear a considerable time, perhaps many years, afterwards. The chapter includes a discussion of the evidence from a detailed study of the relationship between radiation dose and the incidence of leukaemia in patients suffering from a particular disease. This study was undertaken at our request by members of the Medical Research Council's staff, and we should like to thank Dr. W. M. Court Brown and Dr. R. Doll, who carried out the work, for the great help that they have given us. The full results of the enquiry are to be published separately and are summarised in Appendix B.

9. *Chapter IV* of the report opens with a short account of the biological processes controlling the hereditary constitution in human beings, and proceeds to a description of the way in which radiation might affect the genetic structure of human populations. An attempt is then made, in terms of the incidence of certain specific grossly harmful conditions, to assess the consequences for the individual and society of increasing the rate of mutation, and to define the levels of dose which might be expected to bring about such an increase.

10. In *Chapter V* the contributions made to the present level of radiation by naturally occurring radioactivity and by the medical, industrial and other uses of ionizing radiation are reviewed. Many new data have been obtained, and an investigation has been initiated at our request, and is still in progress, to establish more precisely the contribution from various diagnostic and therapeutic procedures (Appendix K). An assessment is then made of the results of contamination from the fall-out from atomic and thermonuclear test-explosions, and the chapter concludes with a brief description of the nature of nuclear warfare.

11. *Chapter VI* sets out our assessment of the hazards of ionizing radiation on the basis of the evidence put forward in the earlier chapters and proceeds to a discussion of the dangers from radiation in peace and war.

12. *Chapter VII* contains a summary of our report which is followed by a statement of our conclusions.

13. The highly technical nature of this report has made it necessary to devote some space in each chapter to a description of generally accepted scientific theory in terms comprehensible to the general reader. No attempt has been made to prepare a bibliography for these parts of the report. Where new material has been drawn upon or controversial topics are discussed, the evidence has been set out in greater detail in appendices, to which lists of selected references to published work have been attached.

14. It will be evident to any reader of this report that, at the present time, there are many large and serious gaps in our knowledge of the medical and biological effects of ionizing radiation. If the potentialities for good are to be exploited with confidence and safety, it is necessary that these gaps should be filled. Much research on many broad fronts will be required. Given the necessary facilities, there is no reason to doubt that the information can be obtained; and we attach the greatest importance to the recommendations for future work that we have been invited to submit for the consideration of the Medical Research Council.

CHAPTER II

THE NATURE OF RADIATION AND ITS ACTION ON LIVING CELLS

Introduction

Discovery of X-rays

15. The transference of energy from sun to earth by radiant heat and light was already well recognised when in 1895 the discovery of X-rays revealed something quite novel—namely rays which had the power of penetrating normally opaque objects. The power of penetration varied in relation to different tissues of the body, and this variation enabled shadow pictures of internal structures to be seen, and so laid the foundation of the first great use of the new discovery. Almost by accident it came to be recognised in the next few years that part of the radiation was absorbed in the tissues, with the production of physico-chemical changes which could lead to biological damage.

Discovery of natural radioactivity

16. The production of X-rays was soon followed by the discovery of natural radioactivity. It was found that compounds of certain heavy elements in the earth's crust, such as uranium and radium, spontaneously emitted rays which had similar properties to X-radiation, although they were of different penetrating power. Later, rays were identified which reached the earth from outer space and these were named "cosmic rays".*

Disintegration of radioactive elements

17. The radiation emitted from radioactive elements is due to spontaneous disintegration of their atoms, with the production of one or more types of radiation and of a new element lighter in weight than the original one. A radioactive element, such as radium, may be regarded as a population of atoms, each of which has a length of life ending in spontaneous break-up of the atomic nucleus with emission of radiation, partly in the form of a stream of particles and partly as wave-propagated radiant energy. In this way the amount of radium gradually diminishes. While the moment of disintegration of any particular atom is unpredictable, the rate of decay of the population of atoms as a whole follows a strictly constant rule. Thus, any group of radium atoms decays to half its original number in a period of about 1,600 years. This period, called the half-life, varies widely for different radioactive substances but for each it is constant and characteristic. Sometimes the new element formed by atomic disintegration is itself unstable and a cascade of successive disintegrations occurs, each with the emission of one or more types of radiation, until finally a stable non-radioactive substance is formed.

Radioactive isotopes

18. After much pioneer work, dating from Rutherford's experiments as early as 1919, it was found possible in the nineteen-thirties to turn many normally stable elements into unstable versions of their original form, by treating their nuclei with suitably energetic radiations, and so to produce artificial radioactive substances. At first it was only possible to make these

* For a description of cosmic rays see paragraphs 192-193.

artificial radioactive substances under very special conditions and on a very small scale. The expansion of nuclear research during the last war, however, led to the development of the nuclear reactor, by means of which it became possible to create radioactive substances in very large quantities either directly or as by-products of the fission* processes in the reactor itself. Both natural and artificial radioactive substances are now commonly called radio-isotopes.

Types of Radiation and Units of Measurement

19. Several different kinds of penetrating radiation are known, of which the common types are the following :

alpha particles : These are the nuclei of helium atoms and are swiftly moving particles of high energy, carrying a positive electric charge. They have little power of penetration, passing into soft tissues for only small fractions of a millimetre, and irradiation of the body from outside with alpha particles is consequently of little significance. They may, however, affect living tissues when they arise from radioactive materials actually within the body, and, in sufficient quantity, they are then biologically very destructive.

beta particles : These are fast-moving energy-carrying particles (electrons) of very small mass with a negative charge. The amount of energy that they carry may vary considerably and their power of penetration will vary accordingly. In general, beta particles are more penetrating than alpha particles and can traverse distances of up to about a centimetre in soft tissues. For this reason they are valuable therapeutically, and radioactive substances emitting beta radiations are used for the destruction of superficial tumours. For the same reason heavy doses from outside the body can damage the superficial tissues and, if beta-emitting substances are ingested, destructive effects within the body may be produced.

gamma rays : These are electro-magnetic radiations of high energy emitted by atomic nuclei. Like alpha and beta particles they are produced in the process of natural or artificially induced atomic disintegration. Gamma rays have great penetrating powers in comparison with alpha and beta particles and the more energetic gamma rays can traverse the whole body with relatively little absorption. As a result, almost the whole thickness of the body may be irradiated by gamma radiations and this is a deciding factor in producing the general illnesses which may follow this type of irradiation. The properties of gamma rays are essentially similar to those of X-radiations but in general gamma-rays have an energy and penetrating power corresponding to the more penetrating X-rays produced at such extremely high voltages as several million volts.

X-rays : These are similar wave-propagated radiations, which are usually produced artificially by electrical machines and which are widely used both diagnostically and therapeutically in medical radiology. They vary considerably in their penetrating power, according to the electrical energy used in their production. The biological effects of X-rays are brought about by high-energy electrons, which are liberated in the tissues during the passage of the rays, so that the biological action of X-rays and beta particles is essentially the same.

neutrons : These are normal constituents of atomic nuclei but may be liberated with considerable energy. They carry no electric charge and

**Fission*: The splitting of the nucleus of a heavy atom into two roughly equal parts with the release of a large amount of energy.

are therefore not repelled by the charged nuclei of atoms, but enter into them to build up unstable structures which often disintegrate with the production of artificial radioactivity. Fast neutrons act chiefly by collision with the hydrogen of the water and of the other compounds which the tissues contain, the resulting 'recoil hydrogen nuclei' somewhat resembling alpha particles in their action. The initially fast neutrons are gradually slowed down in the tissues and may then bring about biological effects by interaction particularly with nitrogen. They may also be captured by hydrogen, thereby releasing energetic gamma rays.

Ionization

20. These several types of radiation vary not only in their powers of penetration but also in relation to the number of electrically charged atoms and molecules, called ions, that they leave in their tracks as they pass through tissues. For this reason they are collectively known as ionizing radiations. It is the production of electrically charged particles, or ions, which is mainly responsible for initiating the physico-chemical changes in living tissue that lead ultimately to the production of overt radiation damage. The efficiency of a given dose of radiations in producing biological effects can be related to the numbers of ions produced per unit length of track.

Intensity of dose and length of exposure

21. The biological effects of radiation are closely related to the dose, or quantity, of radiation received. An analogy can be drawn with the effects of ultra-violet light on the skin in producing sunburn. It is well known that these effects depend on two main factors, the brightness of the sunshine and the length of the exposure to it. Similarly, the effects of radiations such as gamma rays, X-rays or beta rays are determined by the same two factors, the intensity of the radiation and the period of exposure. Radiation may be regarded as consisting of small units of energy called 'quanta', and the intensity of the beam of a given kind of X- or gamma rays is simply a measure of how many such quanta are striking a particular area in a given time. The dose of radiation might therefore be described as the energy which is absorbed in the small mass of tissue upon which the radiation impinges. Living tissues, however, are not inert. After some types of damage by radiation, repair processes take place and the rate at which the dose of radiation is given becomes an important factor in determining the observed biological effect. Thus, if a dose of radiation is spread out over a very long time, for example many years, the response may be very much smaller than or even quite different from that which would occur if the same amount of radiation were given in a very short time. On the other hand, with some well known forms of biological damage produced by ionizing radiations, recovery does not occur. The production of gene mutation is perhaps the most important example of this latter type of change.

Measurement of dose: the roentgen

22. The difficulty of making satisfactory measurements of the dose of radiation has been overcome by making use of the changes of electrical conductivity which are brought about in air when ionizing radiations pass through it. This particular method of measurement is used, not only because it is technically convenient but also because the atomic composition of air or water is in this respect essentially similar to that of the body, the

absorption of X-rays taking account only of the kind of atoms present and not of their particular chemical combinations. The unit of dose which has hitherto been adopted internationally is called the roentgen,* which is abbreviated to the letter "r"; for very small quantities of radiation the milliroentgen (0.001 r) is often used as the unit. The intensity of radiation to which we are ordinarily exposed from our natural surroundings is about 0.1 r per year.

Measurement of radioactivity : the curie

23. It has been seen that the biological effects of radiation depend upon the amount of energy which is absorbed in the tissues. At each radioactive disintegration, an atom emits a certain amount of energy in the form of high-speed particles and gamma rays. The total rate at which the tissues are irradiated therefore depends on how many atoms disintegrate per second. In considering the effects of radioactive materials actually within the tissues, use is accordingly made of units of radioactivity which depend on the number of atomic disintegrations per second. Based originally upon the rate of disintegration of radium, the unit of radioactivity is called the curie and represents the amount of an element in which 3.7×10^{10} disintegrations occur per second. This is too large an amount of radioactivity for most biological work and it is customary to measure the amounts of radioactivity in the body in microcuries (millionths of a curie). For some radioactive materials the maximum amounts which can be allowed in the body are of the order of only one microcurie or less; but even this very small amount of material corresponds to many thousands of atomic disintegrations per second.

Relative biological efficiency

24. The destructiveness of the different types of radiation can also be expressed in relation to that of an equivalent amount, in terms of energy, of gamma rays. This measure is known as the relative biological efficiency (R.B.E.) and varies between different tissues.

Action on Living Tissues

25. The basis of the biological action of ionizing radiation is not fully understood. The consensus of opinion is that radiation acts primarily upon the cell and its constituents, and upon the complex chemical processes occurring in these, rather than upon the fluids in which the cell is bathed. It is thought that the processes associated with the formation of ions during the passage of radiation lead to changes in some of the highly organised molecular systems within the cell. These changes are probably brought about by highly reactive chemical intermediates liberated within the cell subsequent to the physical process of ionization.

Effect of radiation on organisms, tissues and cells

26. All living tissue is killed if exposed to large enough doses of radiation. Different types of organisms, tissues and cells, however, vary greatly in the amount of radiation which they can withstand. Among mammals the dose of X-rays to the whole body which will kill 50 per cent of an animal population varies from 200 to 1000 r—depending on the species; for man it is thought to be between 400 and 500 r. There is also a wide variation in sensitivity between different animal tissues. For instance, in man the most sensitive tissues include the lymphatic glands, the epithelium of the small

* The roentgen shall be the quantity of X- or gamma radiation such that the associated corpuscular emission per 0.001293 gramme of air produces, in air, ions carrying 1 electrostatic unit of quantity of electricity of either sign.

bowel, and the precursors of the blood cells which are situated in the bone marrow, whereas adult nerve and muscle tissue are comparatively insensitive. Variations in sensitivity also occur at different stages in the life cycle of a cell; for example, cells about to divide are often more sensitive than those in the resting state.

Repair processes

27. At dose levels below those which damage tissue irretrievably, the situation is modified by processes of repair; but a distinction must be drawn between true recovery, in which the damaged cells return to normal form and function, and the replacement of injured cells by those coming from outside the field of radiation. The latter is the more conspicuous form of repair after heavy radiation damage in the higher animals and leads to the original tissue being replaced by simpler unspecialised material or scar tissue. Repair processes within the individual cell are little understood and still largely a matter of speculation, but they must play an important part after low doses.

CHAPTER III

THE EFFECTS OF RADIATION ON THE HEALTH OF THE INDIVIDUAL

Introduction

28. Experience of the effects of ionizing radiations has been accumulating with increasing rapidity since the benefits which they may produce in the treatment of malignant disease first began to be appreciated. This experience has been limited, in the main, to the effects produced by the relatively large doses which it is often necessary to give to the area of the body under treatment. More recently, knowledge of the effects of very large doses to the whole body has been obtained as a result of the atomic bomb explosions in Japan. In this chapter it will be necessary to draw heavily on the information from these two sources in considering both the acute and the long-term effects of exposure to radiation, but the reader must bear in mind that such information is only indirectly relevant to the circumstances of ordinary civilian life, since doses of this magnitude would only be conceivable in the immediate vicinity of an accident in a nuclear reactor.

29. There is much less information about the possible effects of chronic exposure to very low doses of radiation, such as those to which special groups of workers may be exposed in the course of their occupations. At a time like the present, when nuclear energy is being intensively developed for civil use, the importance of obtaining such information cannot be exaggerated. The investigation which we have sponsored on leukaemia was undertaken in an attempt to obtain information on the relationship between the size of the dose of radiation and the incidence of the disease among patients with ankylosing spondylitis, so that conclusions might be drawn about the effects of lower doses. The investigation must be regarded, however, as only the first step towards this goal.

Sources of Information

30. Information about the effects of radiation on man has been derived from four main sources: radiotherapeutic experience; occupational experience, including that from accidents; experience from atomic bomb explosions; and animal studies.

31. *Radiotherapeutic experience.* Both X-rays and the gamma rays of radium have been used for many years in the treatment of disease, mainly in the treatment of cancer. Observation of patients receiving radiotherapy has yielded information on the general effects of radiation and on the effects produced in different tissues; and the therapeutic use of radioactive isotopes has provided data on the effects of radioactivity within the body.

32. *Occupational experience.* Information on the occupational hazards of radiation has been obtained from studies of three groups of workers: medical radiological workers, painters of luminous dials for watches and clocks, and miners working radioactive ores in the Schneeberg mines in Saxony and in Joachimsthal. The experience of these three groups serves to illustrate three different forms of radiation hazard. The radiological workers were exposed mainly to external irradiation by X- and gamma rays, and some developed

skin damage leading to skin cancer, or bone-marrow damage leading to severe diseases of the blood. The luminous-dial painters ingested paint containing the naturally-occurring radioactive elements radium, mesothorium and radiothorium, which are retained within the skeleton, and some developed bone tumours. The miners of Joachimsthal and Schneeberg worked in an atmosphere containing high concentrations of the radioactive gas, radon, and many developed lung cancer. The study of these three different hazards has contributed greatly to our knowledge of the harmful effects of radiation, and has provided data for the formulation of safety standards.

33. *Atomic bomb experience.* The atomic bomb explosions over Hiroshima and Nagasaki brought widespread destruction to these cities. Blast and fire caused most of the casualties, but about 15 to 20 per cent were caused by the gamma and neutron radiations emitted during the explosions. In 1946 the United States established in Japan the Atomic Bomb Casualty Commission, which has studied the immediate and the long-term effects of radiation from the bombs on the populations of both cities; the findings have been of great value in expanding knowledge on this subject.

34. *Analogous effects produced in animals.* The discovery that X-rays could produce changes in human tissues led investigators to study the effects of radiation on animals. As a result, it was established that radiation produces effects in animals similar to those observed in man and it thus became possible to make an experimental approach to the problem of radiation hazards. The knowledge thus gained has been drawn on freely in this report.

Factors Affecting the Severity of Radiation Injury

35. The harmful effects of radiation can be divided into those developing within a few weeks of exposure and those developing some considerable time, perhaps many years, afterwards. Illnesses which develop within a few weeks are sudden in onset and run an acute course, whereas those occurring some years after exposure develop insidiously.

36. The severity of radiation injury in any particular instance is determined by the interplay of several factors: the type and dose of radiation received, the duration of the period of exposure, the extent and part of the body which has been irradiated, and also the age of the person exposed.

The dose of radiation received

37. If the dose of radiation is a large one and is received by the whole body in the space of a few minutes, a severe and possibly fatal illness is likely to develop within a few hours, and certainly within a few weeks, of exposure. Some of those who survive this early illness may die several years later from one of the delayed effects of radiation, such as anaemia or leukaemia. Exposure of the whole body to smaller doses of radiation, over a period of months or years, will not cause the early illness, but there may still be a slightly increased risk of death from the delayed effects in later years.

The extent of the body irradiated

38. On the other hand, if only a fraction of the whole body is irradiated, as in radiotherapy, immediate general effects are rare, although some patients may develop a mild form of the early illness, known as radiation sickness. It is often necessary to give a large dose locally and there may be local reaction in the irradiated area with temporary reddening of the skin or blistering similar to that which occurs in sunburn. Delayed local effects

that may occur in these patients are scarring, less commonly necrosis and rarely the later development of cancer in the irradiated tissues. It is now apparent that there may be delayed general effects, a small proportion of patients in later years developing anaemia or leukaemia.

The part of the body irradiated

39. Experience has shown that there is a difference in the general effects of radiation according to the part of the body which is irradiated. Even quite a large dose of radiation given to a portion of a limb will usually produce no general ill effects whereas a similar dose directed to an equally large volume of tissue in the upper abdomen, for example, may produce severe immediate illness.

The type of radiation

40. The severity of effect produced by radiation may also depend to some extent upon the type of radiation concerned, since radiations differ in their powers of penetration and in their destructive effects. For example, fast neutrons are about ten times more potent than X- or gamma rays in causing cataract in the lens of the eye, although these three forms of radiation differ very little in their capacity to cause the early acute form of illness.

The age of the individual exposed

41. It has long been known to radiotherapists that young children are more likely than adults to develop reactions after irradiation. Further evidence on this point comes from a recent report on the inhabitants of the Marshall Islands, who were exposed to radioactive fall-out after the thermo-nuclear test explosion in that area of the Pacific Ocean in the spring of 1954. A consistently greater fall in the number of white corpuscles in the blood occurred among children than among adults, and a similar age-difference in response was noted also in regard to loss of hair.

The frequency of radiation effects

42. Reasonably good estimates have been made of the numbers likely to develop the acute illness under varying conditions of whole-body irradiation. Thus, every member of a population receiving a single whole-body dose of 500 r of gamma-rays would become ill shortly afterwards; if the dose were 150 r, only about half would do so; and, if it were of the order of 50 r, sickness would be extremely rare. It is much more difficult to assess the proportion likely to suffer from the delayed effects; all that can be said with certainty is that it would be small.

The Early Effects of Exposure to Radiation

43. The following description of the effects of a single heavy dose of gamma rays to the whole body is based on observation of the bomb-victims in Nagasaki and Hiroshima. It must be repeated that, in peacetime, exposure at this level could result only from an accident which would rarely, if ever, occur and that, even then, only those in the immediate vicinity of the disaster would be affected.

Effects of heavy dosage

44. The first effect of exposure of the whole body to a heavy dose of gamma rays of the order of 500 r is a sensation of nausea developing suddenly and soon followed by vomiting and sometimes by diarrhoea. In some people, these symptoms develop within half an hour of exposure; in others, they may not appear for several hours. Usually, they disappear after two to three days. In a small proportion of cases, however, the symptoms

persist; vomiting and diarrhoea increase in intensity; exhaustion, fever, and perhaps delirium follow; and death may occur a week or so after exposure.

45. Those who recover from the phase of sickness and diarrhoea may feel fairly well, although examination of the blood will reveal a fall in the number of white cells. Between the second and fourth weeks, however, a new series of ailments, preceded by gradually increasing malaise, will appear in some of those exposed. The first sign of these developments is likely to be partial or complete loss of hair. Then, from about the third week onwards, small haemorrhages will be noticed in the skin and in the mucous membranes of the mouth, which will be associated with a tendency to bruise easily and to bleed from the gums. At the same time, ulceration will develop in the mouth and throat, and similar ulceration occurring in the bowels will cause a renewal of the diarrhoea. Soon, the patient will be gravely ill, with complete loss of appetite, loss of weight, and sustained high fever. Feeding by mouth will become impossible, and healing wounds will break down and become infected.

46. At this stage, the number of red cells in the blood is below normal, and this anaemia will increase progressively until the fourth or fifth week after exposure. The fall in the number of white blood cells, noted during the first two days after exposure, will have progressed during the intervening symptomless period, and will by now be reaching its full extent. The changes in the blood-count seriously impair the ability to combat infection, and evidence from Nagasaki and Hiroshima shows that infections of all kinds were rife among the victims of the bomb. Many of those affected die at this stage and, in those who survive, recovery may be slow and convalescence prolonged; even when recovery appears to be established, death may occur suddenly from an infection which in a healthy person would have only trivial results.

Effects of lighter dosage

47. The radiation effects described above are the most severe which can follow a single whole-body dose of 500 r of gamma rays and still allow some hope of survival; but at least half of a population so exposed would die. With smaller doses, fewer people would develop symptoms, and the illness would become correspondingly less severe; thus, with a dose of 100 r, not more than about 15 per cent of the exposed population would be affected, the illness would be comparatively mild, and very few, if any, would die.

Effects of exposure to 'fall-out' in the vicinity of an explosion

48. The radiations considered above have been those occurring within one minute of the detonation of a nuclear weapon. These radiations have been called the 'prompt' radiations to distinguish them from those emitted by the radioactive dust, or fall-out, which settles over a wide area in the vicinity of an explosion. The fall-out may itself be active enough to cause radiation illness of a type similar to that described above and, in addition, it may contaminate and damage the skin with which it comes in contact.

49. Following the firing of a thermonuclear weapon in the region of the Marshall Islands, the fall-out on one island was so heavy that it was compared to snow, and the inhabitants received an estimated average whole-body dose of 175 r. This fall-out did not cause any deaths, but it did produce a mild illness with early sickness and diarrhoea, a fall in the number of cells in the blood, loss of hair, and some ulceration of the skin contaminated by radioactive material. The skin lesions, caused largely by the higher local

dose of beta-radiation emitted by the fall-out, appeared about two weeks after exposure on those parts of the body which had not been protected by clothing, and took the form of spotted areas of increased pigmentation, from most of which the skin peeled off as if it had been sunburnt. In about 20 per cent of cases, deeper ulceration of the skin occurred but all wounds healed satisfactorily.

Relationship between dose and incidence of effects

50. For the purposes of assessing risk and defining standards of safety, it is necessary to know the nature of the relationship between the dose of radiation and the effect induced. This relationship may be a simple linear one in which the incidence of the particular disease increases strictly in proportion to the dose received, or it may be a curvilinear one in which, with each successive and equal increment in dose, the incidence increases not by an equal but by a progressively greater amount. All the evidence suggests that the relation between dosage and radiation effects occurring within a few weeks of exposure is of the latter type, and that the curve shows a 'threshold' level, implying that a certain quantity of radiation must be exceeded before these particular effects are produced.

The Delayed Effects of Exposure to Radiation

51. Delayed effects of radiation which have been observed locally in tissues heavily irradiated are atrophy and fibrosis of the skin and underlying soft tissues, and sudden breakdown or necrosis of tissues such as bone and cartilage. In rare instances cancer has subsequently developed in the damaged tissues. Cataract has occurred if the lens of the eye has been irradiated. The delayed general effects of radiation which are known, are the development of severe anaemias and leukaemia; in addition, evidence is beginning to accumulate from observations made on animals that irradiation may cause some shortening of the normal life-span. In our report we have dealt in considerable detail with leukaemia, because experience in Japan following the atomic bomb explosions in 1945, and the results of our own investigation on the incidence of leukaemia among irradiated patients, have provided more precise information on the effects of different levels of exposure than is available for any other of the delayed effects.

52. The knowledge that long-term effects may be produced by radiation is in itself an insufficient basis for assessing the risk that any of them will develop as a result of a particular dose. For this purpose, it is necessary to estimate, from national mortality statistics, the incidence of the condition in the absence of exposure to radiation additional to that from natural sources, and then to compare this figure with the incidence of the same condition in a population that has been exposed to radiation. If an increase is demonstrated, the frequency with which the condition develops at different levels of radiation dose must be determined, and the relationship between the dose and the incidence of the disease must be evaluated. Only then is it possible to assess the hazards, if any, associated with the different uses of radiation.

INDUCTION OF LEUKAEMIA

53. Leukaemia is a disease in which uncontrolled over-production of the white blood-cells occurs. It is at present invariably fatal, although some forms may run a protracted course over many years. Several kinds of leukaemia are described according to the type of cell mainly affected. Usually, there is an increase in the number of the affected cells in the blood, associated with the appearance of immature forms of the cell in question. In some cases, however, the numbers in the blood may fall below normal.

through failure to liberate the cells from their site of formation in the bone marrow; the disease is then known as aleukaemic leukaemia.

54. In many countries the death rates from leukaemia have shown a steady rise in recent years. In 1920 the crude annual death rate from this condition for both sexes in England and Wales, for example, was 11 per million persons; in 1954 it was 49 per million. Some of this rise has undoubtedly been due to an improvement in diagnosis but it seems probable that this is not the whole explanation and that, for a reason as yet unknown, there has been a real increase in the national death rate from leukaemia.

55. It is known that leukaemia may be induced in animals as a result of exposure to radiation. Case reports have appeared from time to time of patients who have developed leukaemia after exposure to radiation for the treatment of various diseases, and there have also been a number of reports of radiologists dying from leukaemia. Such isolated reports do not of themselves prove that the relationship is one of cause and effect, but the matter has now been put beyond doubt by a series of recent observations on the incidence of leukaemia under conditions in which an estimate could be made of the degree of exposure to radiation.

Leukaemia following a single exposure: atomic bomb explosions

56. The most recent information, for which we have to thank the United States National Research Council, covers all cases of leukaemia recorded by the Atomic Bomb Casualty Commission in Nagasaki and Hiroshima between January, 1947, and August, 1955. Vital statistics allow an estimate to be made of the number of cases of leukaemia that would have been expected to occur over a similar period in a Japanese population not exposed to radiation from the bombs but otherwise comparable to the surviving populations of Nagasaki and Hiroshima. Calculations have been made for the combined totals of the survivors of the explosions in both cities (Appendix A).

57. During the eight years from 1947 to 1954, about 25 deaths from leukaemia would have been expected in an unexposed Japanese population of the same size and having the same age and sex distribution as the combined populations of survivors from both cities. Over the same period, however, 91 proven and 14 suspected cases have been recorded among those present at the time of the explosion and still resident in one or other city at the time of diagnosis. The difference between the expected and the observed number of cases is so great that it is most unlikely to be due to chance.

58. The difference between the numbers expected and those observed becomes even greater if the most heavily irradiated survivors are considered separately. Only for Hiroshima are adequate details available of the distances from the centre of the explosion at which the individual survivors had been exposed. In the absence of radiation, it is unlikely that even one case would have occurred among the number of survivors less than 1,000 metres distant, yet 15 cases have been found. Further, there is a much higher incidence among those who developed the early acute illness than among those who had, at the most, only mild symptoms.

59. An examination of the incidence of leukaemia in relation to the distance from the explosion has been made for the survivors in Hiroshima, where the concentric distribution of the radiation was not affected to the same degree as in Nagasaki by the irregular distribution of the radio-active fall-out. The dose from the prompt radiation decreases as the distance from the explosion increases. In survivors who were 2,000 metres distant

or more, the incidence during the period January, 1947, to August, 1955, was about 2 cases in every 10,000 persons. Among those between 1,500 and 2,000 metres distant, the incidence was about 3 to 4 cases per 10,000 persons, and for those at the shorter distances of between 1,000 and 1,500 metres and under 1,000 metres it was respectively about 28 and 128.

60. To make an accurate estimate of the relationship between the dose of radiation and the incidence of the disease, one would have to substitute doses expressed in roentgen units for the distances from the centre of the explosion. It has not been possible to obtain reliable estimates of these doses, which should include not only the contribution from the gamma rays but also that from the neutrons emitted by the explosion and that from the radioactive fall-out. Tentative estimates of the gamma ray dose received by people standing in the open can be made from the information published in 1950 by the United States authorities in 'The Effects of Atomic Weapons'. These estimates suggest that the dose at under 1,000 metres would not be less than 1,400r, and at 1,250 metres about 350r. At 1,750 metres it would be about 50r, and at 2,000 metres about 8r. As a dose of 1,400r or more would kill everyone exposed to it, survivors who were within 1,000 metres of the explosion must have been heavily protected. An unknown proportion of the survivors at all the other distances must also have been protected to some extent because they were either indoors or, if outside, shielded by buildings. For this reason, it is not possible to indicate with any great confidence the average levels of dose received by survivors at different distances from the bomb and, in view of the uncertainty about the actual doses received by the exposed population, one cannot infer with certainty whether the relationship between dose and the incidence of leukaemia is a curvilinear or a linear one.

61. For the Japanese cases which occurred up to the end of 1954, the average length of the period between exposure to the bomb and the first appearance of symptoms was about 6 years. It is clearly important to determine whether there has been any tendency for cases to occur less frequently in subsequent years. The morbidity rate has therefore been examined year by year in both Hiroshima and Nagasaki, and it has been found that the recorded incidence has remained approximately constant in Hiroshima in the period 1948 to 1954, and in Nagasaki in the period 1950 to 1954 (Appendix A). This finding suggests that there is no sharply-defined peak year of occurrence, but that with this type of exposure the incidence of leukaemia rises, after a variable latent period, and then remains approximately constant up to at least the ninth year.

Leukaemia following repeated exposures : radiotherapy

62. Before 1955, there had been a report of leukaemia developing in two patients given X-ray treatment for ankylosing spondylitis. In 1955, two further publications directed attention to this possibility, and another reported the occurrence of leukaemia in young children who had been given X-ray treatment to the chest in infancy for suspected enlargement of the thymus gland. In an attempt to obtain further evidence on the occurrence of leukaemia as a delayed effect of irradiation, and in particular on the relationship between the dose received and the incidence of the disease, we have sponsored a survey of patients treated for ankylosing spondylitis with radiation.

63. Ankylosing spondylitis is a disease which affects chiefly the joints of the spine, and to a less extent other joints, particularly those of the pelvis and the shoulders. It usually starts in early adult life and is about six times more frequent in men than in women. It causes severe pain and reduced mobility and, unless treatment is given, the affected joints may gradually lose their freedom of movement and the back become progressively stiffer. In

severe cases all spinal movement is lost, chest expansion is greatly diminished, and the movements of other major joints restricted. The popular description, 'poker back', is a very apt one.

64. Some patients with this condition are benefited by X-ray treatment, which is given to relieve pain and increase mobility and which may permanently halt the progress of the disease. As treatment usually takes the form of irradiation of the whole spine in one course of radiotherapy, it involves exposing a large section of the body directly to the X-rays. In some patients one course of treatment does not suffice, and further courses have to be given, either to the spine or to the major joints, or to both. Indeed, this group of patients was chosen for our investigation because the treatment is so extensive that it more nearly approaches whole-body irradiation than that given for any other non-malignant condition.

65. An analysis has been made of the hospital records of between 13,000 and 14,000 patients, all of whom had been treated with X-rays at some time during the twenty-year period 1935 to 1954. Thirty-eight of these patients developed leukaemia, an incidence of only about one-third of one per cent; yet calculations based on the national death rates over the same period show that even this low incidence is about ten times greater than would have been expected in the absence of irradiation. The possibility of such a difference being due to chance is so remote that we shall ignore it.

66. Caution is necessary, however, in interpreting this finding. It is not possible to conclude immediately that the increased number of deaths from leukaemia is related to the X-ray treatment, in the way that the increased death rates among previously healthy people in Hiroshima and Nagasaki can be attributed to exposure to the radiations from the bombs. The possibility has to be considered that death from leukaemia would, even in the absence of treatment by irradiation, be a more frequent occurrence among sufferers from ankylosing spondylitis than among the normal population, or alternatively that ankylosing spondylitis in some way increases a patient's susceptibility to irradiation.

67. By courtesy of the Ministry of Pensions and National Insurance, it has been possible to examine the records of a group of about 400 male patients with ankylosing spondylitis who had never at any time been treated with X-rays. The fact that no increased incidence of leukaemia was found in this group suggests that ankylosing spondylitis does not of itself predispose a patient to the development of leukaemia. To confirm this point, it would be necessary to examine the records of a much larger group of unirradiated patients; X-ray treatment is, however, so widely used for ankylosing spondylitis that it may be difficult to do this.

68. Clear evidence was, however, found in our main investigation for the existence of a relationship between the dose of radiation and the incidence of leukaemia. The dose was estimated in two different ways, firstly by calculating the total amount of energy absorbed in the whole body, and secondly by calculating the dose of radiation received in certain parts of the bone marrow. The first method demonstrated a curvilinear relationship between the incidence of leukaemia and the radiation dose, whereas the second method resulted in a linear relationship. Fortunately, over the range of doses likely to be met with in ordinary civil conditions, the difference between the two results is negligible. The theoretical implications of the two possible relationships are, however, very different and important and point the way to considerable future research. The data upon which the findings are based are summarised in Appendix B.

69. The average length of time between the first exposure to X-rays and the diagnosis of leukaemia was about six years. This period cannot be directly compared with that observed in the Japanese cases, as many of the patients had had several courses of radiation before leukaemia was diagnosed, and it is not known which particular course was the effective one or whether all the courses may not, to some degree, have affected the development of the disease. Nevertheless, it may be concluded from both series of cases that the latent period for radiation-induced leukaemia is shorter than for radiation-induced cancers.

Leukaemia following chronic exposure

70. We have no precise knowledge of the incidence of leukaemia under conditions of chronic exposure. It has been reported that, relative to the numbers at risk, there are about nine times as many deaths from leukaemia among American radiologists as among other American physicians. This figure is based on a study of the obituary notices published in the Journal of the American Medical Association from 1929 to 1948, in which both the professional occupation and the cause of death are usually reported. In about a quarter of the notices, however, the cause of death was not reported and thus a bias may have been introduced into the results of the study. A review of all the published papers on this subject shows that there may well be an increased death rate from leukaemia among American physicians as a whole, compared with the general population, and in particular among American radiologists, but it is not possible to estimate the extent of the increase with any certainty.

General conclusions on the induction of leukaemia

71. The results of the investigations carried out by the Atomic Bomb Casualty Commission in Japan, and of our own study of the occurrence of leukaemia in patients with ankylosing spondylitis, leave no doubt that ionizing radiations can induce leukaemia in man, and that the average latent period between exposure and the development of the disease is only a few years. In neither of these situations were the conditions of exposure similar to those of persons engaged in work associated with a possible radiation hazard. Those exposed occupationally tend to receive radiation in small doses over long periods, and it is not yet known whether the dose-response relationship based on short periods of heavy exposure is directly applicable to such conditions.

INDUCTION OF CANCERS

72. The evidence for the induction of cancers by radiation consists chiefly of reports of the occurrence of cases under circumstances which make it reasonable to suppose that some at least were radiation-induced, and of the apparently increased frequency of a particular type of cancer, itself rare in the normal population, in persons exposed to heavy doses of radiation. Most of the information comes from the case-records of patients treated with radiotherapy and from those of workers in certain special occupations who in the past received very heavy doses of radiation in the course of their work. It is noteworthy that tumours following radiotherapy tend to develop in tissue already severely damaged by radiation, and that, compared with leukaemia, a much longer period—up to 20 years or more—usually elapses between the first exposure to radiation and the clinical appearance of the disease.

Cancer of the lung

73. The mines of Schneeberg and Joachimsthal are rich in a variety of ores and, since the latter part of the last century, pitchblende, an ore containing radium and other radioactive elements, has been extensively worked there. It had long been known that the miners were liable to die in middle-life from a respiratory disease locally named 'mountain sickness'. It is now recognised that this condition is one of cancer of the lung and it is generally accepted that there is a strong connexion between the excessive mortality from this disease and the high radioactive content of the air of the mines. Investigations have suggested that, up to 1939, nearly one-half of the miners who had died had contracted lung cancer.

74. The first decay-product of radium is a gas, radon, which in its turn disintegrates, giving rise to a series of products, all of which are solids. Radon, being a gas, diffuses through the rocks containing the radium ore, and escapes into the atmosphere of the mines. The inhalation of radon is known to constitute a serious hazard, and the International Commission on Radiological Protection has advised that the concentration of this gas in the inspired air should not exceed 0.0001 microcuries per litre. A series of measurements of the radon content of the air of the mines, made between 1924 and 1939, showed that the concentration of radon must then have been on the average about thirty times greater than the maximum permissible level since laid down. The serious hazard incurred in breathing such an atmosphere comes, not only from the radon itself but also from its solid daughter-products which, being attached to dust particles in the atmosphere, may be retained in the chest and may irradiate the tissues of the lungs for long periods.

75. The average latent period for the induction of lung cancer in these miners was about 17 years, and calculations have shown that the dose to the lungs during this period would have been equivalent to about 1,000 r. This calculation assumes that the radiation dose is spread evenly over the lungs, but it may well be that some areas of the lung, depending on the sizes of the radioactively-charged dust particles which are inhaled, may be subjected to doses of more than 10,000 r over a whole working life. It is consistent with other knowledge that tumours could be induced under these conditions, particularly when it is remembered that radium itself and many of its daughter-products emit alpha particles with high biological efficiency.

76. The only conditions in which an increased incidence of lung tumours has been observed in association with radiation are those in which there is an increased risk of inhaling radon and the other daughter-products of radium. In theory, however, the inhalation of radioactive material in particulate form, either as a result of fall-out from nuclear weapon explosions or in the vicinity of nuclear reactors, could lead to the accumulation of a high radiation dose within the lungs. Such particles would not be uniformly distributed within the lungs but would tend to aggregate on discrete small areas of the bronchi, which would thus be subjected to a high radiation dose, with the result that in the long run lung cancers might be produced in some people. In this country appropriate measures are always taken to eliminate the hazard in the vicinity of nuclear reactors, and it would be extremely unlikely to occur as a result of fall-out except in conditions of actual warfare. There is no evidence that external irradiation by X- or gamma rays can cause lung tumours in man.

Cancer of the bones and joints

77. Radium and the daughter-products of thorium, when assimilated into the body, tend to be held for long periods of time in the bones where, if

in sufficient concentration, they may give rise to local destruction and disease. A number of artificially produced radioactive isotopes, of which the most important are strontium and plutonium, also show this predilection for bone. Radioactive strontium exists in several forms, one, strontium 89, having a half-life of 53 days and another, strontium 90, of 28 years, while the half-life of plutonium 239 is about 24,000 years. A warning of the potential danger from these artificial elements is given by past experience of the effects of the natural elements radium, mesothorium and radiothorium after they have gained entrance to the body and become fixed in bone (Appendix N).

78. Our knowledge of these effects comes mainly from the case-records of former workers in the luminising industry and of a group of patients given radium compounds internally in the course of treatment. Stringent controls are now enforced in the luminising industry to protect the workers, and the prescription of radioactive substances for treatment has been controlled by legislation.

79. Since 1925 there have been many reports of illness and death occurring among a group of workers engaged in the painting of watch and clock dials with luminous paint, most of whom had been in the industry during the period from 1916 to 1924. Luminous paint is compounded of zinc sulphide and radium, and, formerly, varying mixtures of radium, mesothorium and radiothorium were also used. It was customary for dial painters to apply their paint with fine brushes, the points of which they 'tipped' between their lips before painting. In this way they swallowed radioactive material, some of which became lodged in the skeleton. If large amounts were swallowed, death sometimes occurred, within about three years, from severe anaemia, haemorrhages, and infections, particularly of the bones of the jaw. Those who had ingested smaller quantities of paint often developed cystic and necrotic changes in the bones which might cause 'rheumatic' pains or fractures. Occasionally, these changes progressed and cancer of the bones appeared. Such tumours usually developed more than fifteen years after the first exposure to the hazard.

80. Similar effects have occurred in patients given radium compounds internally for the treatment of mental disease or for various rheumatic and other affections, and in people who, for quasi-medicinal reasons, have consumed large amounts of 'radioactive water'. In animals strontium 90 has been shown to produce similar biological effects.

81. It is possible to estimate the amount of radium in the body of a living person, if there is good evidence that no other radioactive element is present in addition to the normal components of the body. Measurements carried out on those who have been exposed to unknown mixtures, such as luminous compounds, are difficult to interpret. So far, no person is known to have developed radiation-induced bone cancer who had less than 3·6 microcuries of radium in his body, unless either mesothorium or radiothorium was also present; the lowest radium content, in the presence of one or other of these elements, has been 0·52 microcurie at the time of appearance of the tumour. On the other hand, it seems certain that early non-cancerous cystic changes in bones have developed with a body-content of as little as 0·4 microcurie of radium alone. These amounts of radium are to be contrasted with the maximum permissible level for body radium, which, as laid down by the International Commission on Radiological Protection, is 0·1 microcurie.

82. Bone cancer has also been reported after the use of X-rays in the treatment of non-malignant bone tumours and some infections. Such cancers have occurred only after very heavy doses of radiation and have originated

in the area of the body treated. The risk of the development of bone cancer at the levels of X- or gamma radiation experienced under modern occupational conditions is insignificant.

Cancer of the skin

83. Cancer of the skin was the earliest form of radiation-induced tumour to be described in man. Radiation dermatitis of the hands, forearms and face was common among the early radiologists and radiological technicians, and cancer often occurred in the damaged skin. By 1911 no fewer than 54 cases had been described; the occurrence of these tumours diminished as radiologists learned to take the necessary precautions.

84. Since the early part of the century, records have accumulated of the occurrence of skin cancers following X-ray or radium treatment. In some instances, these tumours have followed the injudicious use of X-rays for mild skin affections, or even for the removal of facial hair. The latent periods have usually been long, ranging in a recently reported series of 13 cases from 12 to 56 years, with an average of 33 years. Although it is usually impossible to make any accurate retrospective assessment of the doses of radiation received, the severity of damage to the skin suggests that, in these cases, they must have been of the order of several thousands of roentgens.

Cancer of the thyroid gland, the pharynx and the larynx

85. A number of cases of cancer of the thyroid gland have been reported among children, some years after they had been given X-ray treatment for conditions including suspected enlargement of the thymus gland, bronchitis, infected tonsils and adenoids, and enlarged glands in the neck. In many instances, the children were less than one year old when irradiated. In a series of cases irradiated for suspected enlargement of the thymus gland, the average latent period between irradiation and the establishment of the diagnosis of cancer of the thyroid gland was only about 7 years. Perhaps the most important feature of these cases is the comparatively small dose of radiation responsible for induction of the tumour, in contrast to the large doses associated with the induction of cancer in adults; cancer of the thyroid gland has developed in a child after a recorded dose as low as 250 r. It is possible that hormonal factors may be involved in addition to the direct effect of irradiation.

86. A few reports have drawn attention to the development, many years later, of cancers of the pharynx and larynx in patients who have had X-ray treatment for such conditions as tuberculous glands of the neck. The latent period is long, averaging about 20 years, and periods of more than 30 years have been recorded. In most cases, the irradiation was given in the early days of radiotherapy and there is practically no information available about the size of the radiation doses that were employed.

EFFECTS ON THE BLOOD OTHER THAN LEUKAEMIA

87. Observations have shown that a fall in the numbers of red cells, white cells and platelets in the blood may occur in persons exposed to radiation in the course of their work. There is little direct information on the dose-response relationships, but it seems possible that, even with whole-body doses of gamma rays as low as 1 r per week, slight changes can occur in the white-cell count of especially susceptible people. Certainly, with doses much in excess of 1 r per week, a general depression occurs in the white blood cell count. A reduction in the numbers of red cells and platelets may occur at a later stage, and in some persons continued exposure may lead to severe degrees of anaemia.

Aplastic anaemia

88. If not detected in time, radiation-induced anaemias may endanger life, particularly when the red bone-marrow is itself so severely damaged that the red-cell deficiency cannot be made good by the production of new cells; this condition is known as 'aplastic anaemia'. The diagnosis is not easy to make, and the condition can easily be confused with aleukaemic leukaemia unless a full examination of the bone marrow is carried out. This diagnostic difficulty was encountered during the investigation of leukaemia among patients treated with X-rays for ankylosing spondylitis. Particular attention was paid to deaths reported as being due to aplastic anaemia but, when these cases were fully investigated, evidence was found that a number were, in fact, aleukaemic leukaemia; eventually, only four deaths could with any certainty be ascribed to aplastic anaemia out of a total of some 50 deaths from leukaemia, aplastic anaemia and allied diseases combined. Similarly, only six cases of aplastic anaemia were reported from Nagasaki, compared with over 40 cases of leukaemia in the same city. It seems clear, therefore, that aplastic anaemia is a rarer delayed effect of radiation than leukaemia.

INDUCTION OF CATARACT

89. The term 'cataract' implies an opacity in the normally transparent lens of the eye, varying from a tiny granule which does not cause any definite impairment of vision, and which may disappear, to a large plaque resulting in blindness. It has been known for some time that exposure of the eye to X-rays can lead to cataract formation, but the large doses which appear to be necessary for its induction are only likely to occur under very unusual conditions. For all practical purposes, therefore, the production of cataract by X-rays is not an occupational hazard, although it was discovered in 1948 that the condition had developed among a group of physicists exposed to neutron irradiation during the operation of a cyclotron.

90. In the following year there were reports from Japan of an increased incidence of cataract in the populations of Hiroshima and Nagasaki. The extent of the increase cannot be determined with precision, but it is significant that, of 98 cases of cataract among survivors of the Hiroshima explosion, 85 occurred in persons who were within 1,000 metres of the centre of the explosion and would thus have been subjected to neutron- as well as gamma-irradiation. Confirmatory evidence of the high dosage which they had received is provided by the fact that most of them had suffered epilation of the scalp and that two subsequently developed leukaemia.

EFFECTS ON THE SKIN OTHER THAN CANCER

91. In the paragraphs dealing with the induction of skin cancers by irradiation, it was noted that cancers develop mainly in skin which has been subjected to such heavy doses of radiation as to be obviously damaged. Most of our knowledge of the less serious delayed effects on the skin has been obtained from observation of the results of therapeutic irradiation with X-rays, during which the skin may be exposed to large doses of radiation directed to underlying tissues. With doses of 1,500 r or more, a certain amount of permanent skin-damage is likely to occur, but it will not be particularly severe unless a large area has been irradiated. Larger doses, however, say of 4,000 r or more, are often followed by obvious skin-damage, the texture becoming thinner, and the surface being usually covered with dilated blood vessels. In such cases, the skin may be very sensitive and prone to infection, and it is in this type of damaged skin that radiation-induced tumours are most likely to develop.

92. The hair follicles and glands of the skin may also be affected by radiation. A dose of the order of 300 to 400 r will cause temporary loss of hair, and with higher doses, perhaps 700 r or more, hair-loss may be permanent. It is a common finding that, owing to the destruction of the sweat glands, heavily irradiated skin permanently loses its ability to sweat. After doses of the order of 1,500 r, the sebaceous glands are destroyed and the skin loses its normal greasy texture.

EFFECTS ON THE KIDNEY AND LUNG

93. It has been reported that therapeutic doses of X-rays to the region of the kidneys may affect their function and lead to the development of high blood pressure which may prove fatal. The damage described has followed the treatment of certain rare tumours with large doses of radiation and it is unlikely that such effects will occur under other conditions of exposure. It has also been reported that pneumonitis, sometimes fatal, has followed radiotherapy directed towards the chest.

SHORTENING OF THE LIFE-SPAN

94. A number of reports based on observations made on animals suggest that exposure to ionizing radiations may lead to a reduction in the expectation of life. No evidence has yet been published that this occurs in man.

The Effects of Exposure to Radiation during Pregnancy

Abortion and stillbirth

95. After heavy doses of radiation, a pregnant woman may miscarry or give birth to a stillborn child. Information from the Atomic Bomb Casualty Commission shows that in Hiroshima and Nagasaki there were higher abortion and stillbirth rates among pregnant women near the explosion than among those at greater distances. Of 98 pregnant women in Nagasaki who were within 2,000 metres of the centre of the explosion, about 23 per cent of those who had severe radiation illness miscarried, in comparison with only about 4 per cent of those who did not develop any severe illness, and with about 3 per cent of women who were between 4,000 and 5,000 metres distant. It is apparent that abortion and stillbirth as a result of irradiation during pregnancy do not constitute a problem unless the dose of radiation is large.

Effects on the children of women irradiated during pregnancy

96. There is considerable evidence, both from the case records of patients treated with radiotherapy and from reports published by the Atomic Bomb Casualty Commission, that heavy irradiation of pregnant women can lead to the birth of children who are either abnormal at birth or who later develop in an abnormal way. The case records of women therapeutically irradiated during pregnancy describe a number of different developmental abnormalities in their children, the most striking of which is the condition known as 'microcephaly'; one such case was found during the course of our investigation of patients treated by X-rays for ankylosing spondylitis. The underlying cause of this condition is a partial failure of the development of the brain, as a result of which the head is smaller than that of a normal baby. All grades of the condition exist, ranging from the most severe, in which the child usually has to be maintained in a mental institution, to others in which there is only slight impairment of development and mental powers.

97. There are published records of eleven mentally-retarded children in Nagasaki and Hiroshima who were exposed before birth at a distance of between 700 and 1,200 metres from the centre of the explosion. Ten of the mothers of these children suffered acutely from the effects of radiation, and the eleventh probably did so. The head circumferences of all eleven children were appreciably less than those of unirradiated Japanese children of the same age-group and, in the cases among Nagasaki children, smaller than those of children exposed before birth at distances of between 4,000 and 5,000 metres from the explosion, where the dose of prompt radiation would have been less than 1 r. The evidence from Hiroshima suggests that children irradiated between the twelfth and eighteenth weeks of intra-uterine life are more likely to develop microcephaly than children irradiated either before or after this period.

The Effect on Fertility of Exposure to Radiation

Permanent sterility

98. It is well-established that irradiation may reduce the fertility of men and women, and even render them permanently sterile. In men, a single dose of 500 r to the testes would probably produce permanent sterility. The dose to the ovaries likely to produce the same result in women would depend to some extent upon the age of the woman concerned; a woman nearing the end of her reproductive life would require a smaller dose, about 300 r, than a woman in her early reproductive years. These levels of dose are so high that, if they were received in the course of whole-body irradiation, the individual would develop the early acute illness already described. It is extremely unlikely, therefore, that permanent sterility would be induced in any one accidentally exposed to a large whole-body dose of radiation, unless the acute illness had been manifest.

99. Under modern conditions of occupational exposure, for example among radiologists and radiographers, there is no evidence of any impairment of fertility. Furthermore, there is no suggestion that female radiographers suffer from radiation-induced menstrual disturbances which might be accompanied by diminished fertility.

CHAPTER IV

THE GENETIC EFFECTS OF RADIATION

Introduction

100. Nowhere in our report have we been more conscious of the difficulties of the task which we have undertaken, and of the limitations of the knowledge at our disposal, than in considering the genetic effects of radiation. The established scientific evidence in this field provides but an insecure basis on which to frame answers to the many important questions that are now being asked. Consequently we have been forced to make many assumptions of questionable validity and our conclusions must be regarded as provisional and treated with a measure of reserve. An essential part of future studies will be the collection of more detailed vital statistics. Moreover, it must be realised that genetic studies inevitably tend to be slow and that sufficient knowledge on which to base firm conclusions will be accumulated only after many years of intensified fundamental research.

The Material Basis of Heredity

101. In man and other sexually reproducing animals, every individual arises from a single living cell, which is formed by the fusion of two germ cells, an egg cell from the mother and a sperm cell from the father. Soon after it is fertilised, the egg cell divides into two; each of these divides again, to give a total of four, and this process is repeated until there are enough cells to give rise to all the organs and tissues of the body, among them the sex glands from which in time new germ cells will be formed.

Chromosomes and genes

102. Each cell contains within it a nucleus whose essential component is a number of microscopic thread-like structures, the chromosomes. These are aggregates of sub-microscopic particles—the genes—which determine the hereditary nature of the individual. The total number of genes in a cell is not known with any accuracy but it is certainly high, perhaps thousands or even tens of thousands in a human cell. Each chromosome carries a large number of them arranged in order along its length, so that each gene has its own special place, or locus, in a particular chromosome.

Cell division

103. The nucleus of each human germ cell carries 24 chromosomes, all of them different from one another. When egg and sperm come together, their nuclei also fuse, so that the fertilised egg contains a nucleus carrying 48 chromosomes constituting 24 pairs. The members of a pair, derived one from the mother via the egg and one from the father via the sperm, normally correspond to each other both in the gene loci which they carry and in the order in which these loci are arranged. When the fertilised egg, or any later cell in the body, is about to divide, a replica is first formed of each of the 48 chromosomes. This makes it possible for the two cells so produced to receive sets of chromosomes exactly like each other and like those of the parent cell. The cell divisions immediately preceding the formation of germ cells, however, follow a somewhat different pattern, which

results in the egg or sperm receiving only one member of each pair of chromosomes; thus the number that the egg or sperm contains is reduced to 24.

Gene mutation

104. In the normal course of events, each cell possesses a set of genes identical with those of the cell from which it is derived. Occasionally, however, a sudden change occurs in a gene, which is converted into a slightly different form. The altered form of the gene is spoken of as a new allele and the process of change is known as mutation. Once such a mutation has occurred, the gene is reproduced and passed on in the new form at all subsequent cell divisions. Thus, each locus can come to be represented in the population by a number of these variants or alleles.

Homozygotes and heterozygotes

105. Having but one chromosome of each kind, the germ cell carries only one allele at each gene locus, whereas the body cells, with a pair of each kind of chromosome, carry two alleles. These two alleles may or may not be exactly the same. An individual bearing two identical alleles is said to be homozygous at that particular locus; one with two different alleles is said to be heterozygous at the locus. A homozygous individual clearly must have received the same allele from each of his parents and he will pass it on to all his offspring. A heterozygous individual must have received different alleles from his two parents, and he will on the average pass on one of the two to half his offspring and the other to the other half. This sorting out of the genes when they are distributed to the offspring of a heterozygote is a direct result of the halving of the number of chromosomes during germ cell formation and is known as segregation.

Gene reassortment

106. If an individual is heterozygous for two or more loci, the process of segregation will result in his genes being reassorted into new combinations in his offspring. Thus, in the process of reproduction, the various alleles at the different loci are continually being reassorted into an immense variety of combinations, with the result that each person has a particular hereditary constitution not exactly like that of anyone else. Each of us is, in fact, genetically unique, with the exception of identical twins, who are produced when the fertilised egg—very early in its development—splits into two parts each of which gives rise to a complete individual.

Dominant and recessive alleles

107. Some alleles produce a noticeable effect only on those individuals who are homozygous for them. Such alleles and the characters which they determine are spoken of as recessive. Other alleles have some effect even when the individual is heterozygous, and the characters which these determine are described as dominant. Among the numerous genes which have been studied in man and other animals, all gradations are known between the extremes of fully recessive alleles, which have no effect at all on the heterozygote, and fully dominant ones which have as strong an effect on the heterozygote as on the homozygote.

108. A dominant allele which is being transmitted in a family will be manifest in every generation unless it dies out. A recessive allele, on the other hand, can be transmitted to later generations by an individual who shows no sign of carrying the allele in question. The character produced by such

a gene will appear from time to time in the population, in families where both parents carry the gene; this is especially likely to occur where there is a marriage between cousins.

Sex-linked genes

109. There is a special category of genes whose transmission is connected with the determination of sex. The sex of an individual is determined by one particular chromosome pair. In the female, both chromosomes of the pair are similar; in the male, one is of another type. Thus, the structure of the female sex chromosome pair can be represented as XX , that of the male as XY . Genes carried on these chromosomes are said to be sex-linked, but the Y chromosome, having few gene loci, has little effect on most hereditary characters. If a male contains an abnormal allele on his X chromosome, he will show its effect, even if the same allele situated on one of the two X chromosomes of a female would be recessive. If a recessive sex-linked gene is uncommon, it will occur only very rarely on both the X chromosomes of a female and the characteristics it produces will therefore not often be found in females. They will be commoner among males, who will be affected whenever their single X chromosome contains the allele. The apparently normal females can, however, transmit the chromosome carrying the affected gene to the next generation, and so act as carriers of the abnormality. The classical example of this type of condition is the disease haemophilia, which appears in males but is transmitted by apparently normal females.

Continuous variation

110. Not all gene differences have effects which are sufficiently distinct to be recognised by their segregation among the members of a family. As can be seen in human stature and intelligence, for example, some characteristics vary by continuous gradations over a wide range which is regarded as normal. Such characters are believed to be controlled by the combined action of a large number of genes, the effects of which are supplementary and each so small that they are not individually distinguishable.

Causes of mutation

111. Reference has already been made to the process of mutation by which one allele changes into another. We do not know all the factors which cause mutation. It is believed to be due sometimes to chance disturbance of the complex molecules which constitute the genes, and sometimes to external influences such as certain chemicals or natural background radiation. We shall discuss later the extent to which naturally occurring mutations are likely to be attributable to background radiation, but from observation of organisms other than man it is known that other causes can be important. Present evidence suggests that mutations, whatever their origin, are for the most part random changes not specifically related to the nature of the stimulus or to the needs of the individual.

Mutation rate

112. So far as is known, all genes are subject to mutation, and, over the population as a whole, mutation is continually occurring at a definite but very low rate (Appendix C). Factors influencing mutation increase the rates at which the genes change; they do not produce changes of a novel type. Most genes, if not all, are susceptible to such factors, though some may be affected more readily than others. No methods are yet known for stimulating the mutation of only one particular gene, or even of a small selected group of genes.

Mutation and natural selection

113. The hereditary variation found in human or other populations is the result of mutations which occurred in past generations. New alleles which cause abnormalities harmful to those who possess them tend to be eliminated from the population. Thus, a new dominant allele causing death before the reproductive age, or for some other reason preventing the individual from leaving descendants, is eliminated in one generation. Those with less drastic effects are eliminated with a speed related to the severity of the handicap which they impose. Recessive alleles, which give rise to harmful conditions only when they are in the homozygous state, are also eliminated, but very slowly, since the allele can continue to exist or to spread in the heterozygous state without contributing any significant handicap to the perpetuation of the line. Thus, in the case of both dominant and recessive harmful alleles, natural selection is constantly operating towards their removal from the population. Equally, it will operate even against genes whose effects are valuable to the individual during his own lifetime, if they reduce his chances of leaving offspring.

114. For alleles which increase the chances of leaving offspring the situation is the reverse. Those individuals in which these effects are manifest are more than ordinarily likely to propagate their kind, so that their descendants tend to become the predominant type. Many, but perhaps not all, of the genes which tend to increase fertility will also have effects which are useful in other ways to the individual in whom they are manifest; they can be considered as generally advantageous.

115. Between these clear-cut examples there are genes with every gradation of effect. The manifestations of genetic abnormality in the individual may vary from the trivial to the disastrous. The action of some genes is delayed until after the end of the reproductive period of life and they are therefore largely immune from the eliminating influence of natural selection. There are genes which are harmful whether the individual carrying them is homozygous or heterozygous; there are others which are advantageous to heterozygotes and harmful to homozygotes. The relative prevalence of any particular allele, in any particular population, can be understood only in the light of the relationship between the environment and the advantages or disadvantages of the condition to which the allele gives rise.

Genetic equilibrium

116. As natural selection is constantly operating towards the elimination of harmful genes from the population, the incidence of the conditions to which they give rise would steadily decrease, were it not that they are being replenished by the occurrence of new mutations. Their frequency will therefore tend to reach the level at which their loss by selection is balanced by new mutation. A state of genetic equilibrium has then been reached. This is the situation with regard to many of the more harmful abnormalities in man, the incidence of which remains relatively steady in the population despite the failure of those affected to leave normal numbers of offspring.

The general effects of increasing mutation rates

117. The above considerations suggest the broad qualitative effects which can be expected to follow an appreciable increase in mutation rates. At this present time, the advantageous alleles that have appeared in the past are already widespread and will have become part of the normal constitution of the population. An increase in the rate at which they are produced can therefore have little effect. The harmful alleles, on the other hand, have been restricted to a low incidence by the operation of natural selection. A

significant increase in the rate at which these are produced will therefore have a more easily detectable effect. The general inference is that increasing the mutation rate in a human population would have a relatively much greater effect upon the incidence of harmful than upon that of harmless or of advantageous hereditary traits.

Mutation and the adaptability of populations

118. Mutation provides the means by which the human race, through hundreds of thousands of years, has successfully adapted itself to its environment. There is no reason to believe that this adaptation has proceeded by sudden and conspicuous changes in human characteristics. The consensus of opinion is that evolution has occurred by a succession of small variations from the average, which conferred a slight but eventually important advantage in relation to the trend of environmental change. It is the existence of this galaxy of hereditary traits, varying only slightly from the accepted normal, that has conferred adaptability upon the human race. The recurrence of a small but steady incidence of harmful mutations is the price that has to be paid for this asset.

The Genetic Effects of Radiation : Basic Principles

119. There is as yet little direct information about the genetic effects of ionizing radiations on man and, for reasons which we examine later, the few observations that have so far been made present many difficulties of interpretation. We have therefore to rely on information obtained from experiments on other organisms. The experimental evidence is itself incomplete and largely derived from observations on forms of life other than mammals, but a general picture is beginning to emerge which appears to be consistent for the organisms which it has been practicable to study. The question arises, however, to what extent it is justifiable to draw inferences concerning man from the reactions of remote organisms observed under the artificial conditions of laboratory experiment. Since the genetic mechanism in man is the same as that in other animal and plant species, and since the animals and plants that have been studied all show the same type of genetic response to ionizing radiations, it would be unreasonable to suppose that the response in man will do other than follow the same general pattern. On the other hand, we do not think that conclusions derived solely from observations on other organisms offer a secure basis for quantitative estimates concerning man and, except where we have explicitly stated the contrary, we have not used them for this purpose.

Effects of radiation on germ cells

120. Ionizing radiation will have genetic consequences only in so far as it affects any of the germ cells or the cells ancestral to them in the reproductive organs. It may then have one of three results: the affected cells may die, their chromosomes may be broken, or the genes may be caused to mutate.

121. Death of a germ cell, or indeed of any cell ancestral to it, can have no genetic consequence, because this very death will terminate the lineage of cells to which it belongs.

Chromosome structural change

122. Chromosome breakage may also lead to death of the cell lineage. Broken chromosomes may fail to reunite or they may join up to give new forms of chromosomes which are incapable of passing through the process of cell division in the normal way; either of these circumstances leads to

subsequent death of the cell lineage. If the damage occurs in an immature germ cell in the sex gland, the cell lineage will usually die before mature germ cells are formed, and there will be no genetic consequences. If it occurs in a mature germ cell which later participates in fertilisation, the ensuing embryo will usually die early in gestation, and the ultimate genetic effects will be minimal.

123. Chromosome breakage may, however, have a different outcome if the fragments reunite in new patterns which are capable of passing through cell division. The resulting kinds of structurally changed chromosomes may be transmitted to apparently normal offspring, and at least one type of change will manifest itself by the occurrence of repeated abortions or malformations among the descendants of the irradiated individual. Experiments on mammals indicate that this inherited effect will appear only if conception takes place within a few months of irradiation.

124. Such structural changes of the chromosomes are induced especially by large single doses of radiation, for example heavy doses of X-rays or the prompt radiation from atomic bombs. They are induced only rarely by long-continued exposure to low-intensity X- or gamma radiation, although relatively small doses of neutrons or alpha particles are more effective in bringing them about.

125. Although they may cause partial sterility or abortion in their carriers, major structural changes of the chromosomes do not as a rule bring about other kinds of abnormality in individuals bearing them. For this reason, and also because of their low rates of spontaneous occurrence and induction by chronic irradiation, and of the probability of their having an adverse effect on fertility, chromosome structural changes are likely to be of comparatively little importance among the radiation hazards to man.

Induced gene mutation

126. The third and, from the genetical point of view, the most important effect of exposing germ cells to additional radiations is the induction of increased gene mutation. Since all germ cells from time immemorial have been continuously exposed to some radiation from natural sources, it would be surprising if exposure to additional radiation were found to induce any novel types of mutation. The results of experiment support this view: the types already known recur, but at an enhanced rate.

Proportionality of induced gene mutation to additional radiation

127. There is no known threshold for the induction of gene mutations by radiation: that is to say, any additional exposure, no matter how small, must be expected to raise the mutation rate, if only by a minute amount. Furthermore, to judge by our experience up to the present, it is probably true that the rise in the rate of mutations is directly proportional to the amount of additional exposure. This law is known to hold good, for such organisms as have been studied, when the radiation dose is fairly high. It is also known to hold good for the induction of one class of lethal genes in the fruit-fly, *Drosophila melanogaster*, by X-ray doses as low as 25 r. In this chapter of our report we are chiefly concerned with doses well below this level; but, for the present, there does not appear to be sufficient evidence to warrant the assumption that there is any real departure from this law even at the lowest doses, and proportionality has therefore been accepted as the basis of what follows.

Accumulated dose to germ cell lineage

128. Cells arise only from pre-existing cells. Mature germ cells are produced from a line of ancestral immature cells which have been present at every instant during the individual's life, from conception onwards. It will be remembered that mutated genes reproduce themselves as faithfully in a cell lineage as do the normal genes from which they arise. In consequence, the mutated genes arising throughout a germ cell lineage will be accumulated in the mature germ cell, and a given radiation dose will therefore have the same order of effect whether it is given over a short or a long period of time. In other words, long continued exposure to low-intensity radiation induces as much gene mutation as a single exposure to high-intensity radiation, provided that the total dose is the same. Experiments have shown that this probably remains true even when the dose is split into a series of small fractions, and no matter what interval elapses between the separate irradiations. Thus, in contrast to most other types of biological response to radiation, damage to the genetic material cannot be repaired and the effect from repeated exposures is cumulative.

Genetically effective dose to a population

129. This cumulative effect of radiation indicates that the genetic effects of exposure will depend on the ages of the individuals exposed as well as on the dose they receive. If, for example, all are past the reproductive age, the genetic effects will be nil; if they are younger, the possible number of offspring they may have is of importance. The age distribution of those exposed is therefore an important factor to take into account when estimating the consequences to future generations of additional radiation.

The Effects of Increased Mutation Rates on the Incidence of Disease in Human Populations

130. In approaching the problem of making some quantitative assessment of the genetic effects of radiation upon a human population, we have been very conscious of the inadequacy of the evidence in two essential respects. First, we do not know the dose of radiation required to double the mutation rate of any specified human gene; secondly, there is reason to suspect that the radiosensitivity of human genes may vary considerably, so that it could be very misleading to treat them as an approximately uniform group which would respond to any particular dose of radiation with a standard increase in mutation.

131. It is, however, possible to give a general idea of the effects of an increase in the mutation rate of particular human genes without raising the question of dose or degree of uniformity in sensitivity to radiation. We have therefore taken selected examples of diseases in which genetical factors are known to play an important part, and have attempted to assess the effects in a human population of doubling the spontaneous mutation rates of the genes concerned, without specifying the agent or agents causing this increased rate of mutation.

132. The role of heredity in the production of disease ranges from that of a predisposing to that of a preponderating cause. Thus, there is some evidence that heredity is a factor influencing susceptibility to tuberculosis; but this could be of no significance unless the individual were infected with tubercle bacilli. On the other hand, achondroplasia, a form of dwarfism, is probably determined entirely by genetic factors, in the sense that no known modification of the environment can prevent its appearance in those who possess the necessary gene.

133. In making our assessment we have confined our attention to those conditions which impose a significant handicap and which are determined, entirely or to an important extent, by hereditary factors. To put it another way, our object has been to give an assessment of the social load that would be imposed upon a population, like that of this country, by increasing mutation rates. We propose to consider two possible situations: first, when the mutation rate of every gene concerned is supposed to have been doubled in one generation only, thereafter reverting to its former level, and secondly when the rates having been doubled remain at that new level generation after generation.

THE EFFECTS OF DOUBLING MUTATION RATES ON DISEASES DUE TO A SINGLE GENE

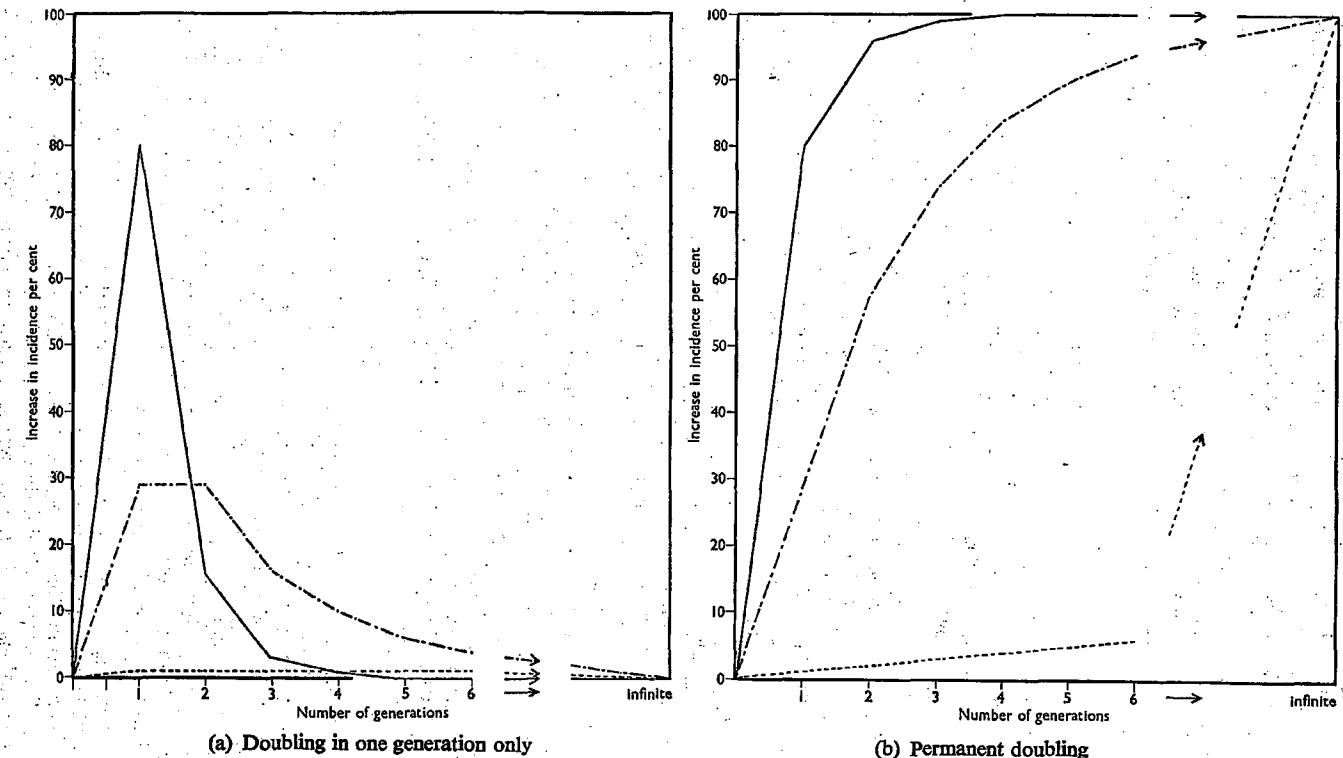
134. For abnormal genes with effects which are masked in any way, either by normal alleles—as in recessive traits—or by the influence of environment, mutation has less immediate or less apparent consequences than for genes with effects which are directly manifest, as in dominant traits. Severely disabling dominant diseases reveal the results of recent mutation most readily. Sex-linked traits show a less rapid response. The effects of genes which produce recessive traits are masked until two genes come together in the homozygous state; hence, the results of their recent mutation will be less noticeable, although in the course of time their full effects will appear. Where a gene is common and mainly benign, but can occasionally cause disease, the results of its recent mutation will be scarcely detectable.

135. The effects which might be expected to result from an increase in mutation rates can most easily be calculated for diseases known to be caused by single genes (Appendix D). For this purpose we need to know what proportion of cases in a given generation is due to recurrent fresh mutation. The incidence of the particular disease in the population must be ascertained; so must its mode of inheritance (dominant, partially recessive, recessive or sex-linked), the degree to which it handicaps or favours the affected individuals—as shown by their length of life and reproductive capacity—and the modifying effect, if any, of environmental factors. This information is available for only a relatively few conditions and much more research will be required before we can feel reasonably confident in making estimates for groups of diseases. To illustrate the different types of effect, we have chosen three examples about which we have some fairly accurate information.

(i) *A dominant trait*

136. Achondroplasia (chondrodystrophy) is a dominant form of dwarfism. Although there are many clinical types, it will be assumed for the present purpose that the condition is due to a single gene with a manifestation which is independent of environmental factors. The incidence at birth, according to Danish estimates, is one in 9,400. Biological fitness is greatly reduced on account of high stillbirth rates and also, in adult life, on account of low fertility, especially of females. The chance that an affected individual will have offspring is estimated at only 1 in 5. The majority of cases are believed to arise through fresh mutation.

137. Doubling the mutation rate of the causal gene for one generation would produce an 80 per cent increase in the incidence of the condition in the first generation, that is the incidence at birth would rise to nearly one in 5,000. The excess would, however, rapidly disappear and within five or six generations the incidence would return to normal (Fig. 1a). If the



Key:
 Achondroplasia (dominant) ———
 Haemophilia (sex-linked) - - -
 Phenylketonuria (recessive) ·····

FIG. 1. The effects of doubling the mutation rates for three hereditary conditions, expressed as the percentage increase in incidence (Appendix D, Table 2D).

mutation rate were permanently doubled, the incidence would rise to a level close to double the present figure (i.e. 100 per cent increase) within three or four generations (Fig. 1b).

(ii) *A sex-linked trait*

138. The term haemophilia covers a group of sex-linked traits in which there is impairment of blood clotting. For the present purpose it will be assumed that all severe cases are caused by abnormal alleles at a single locus. The incidence is at least 1 in 12,000 of the male population at birth and the chances that an affected male will survive and have descendants is about one in eight. Females carrying the abnormal gene are healthy and have normal chances of reproduction. Doubling the mutation rate for one generation would produce a 29 per cent increase in incidence in the following generation, that is, the incidence would rise to about 1 in 9,300. In the next generation this level would be sustained but thereafter it would sink back moderately quickly towards the previous level (Fig. 1a). If the mutation rate were permanently doubled, the incidence would rise to 90 per cent above the previous level in about six generations, and thereafter slowly approach the point where the incidence was doubled (Fig. 1b).

(iii) *A recessive trait*

139. Phenylketonuria is an example of a deleterious recessive trait associated with severe mental deficiency. Its incidence in the population at birth is about 1 in 40,000 and, although the early mortality is not high, the chance that an affected person will have offspring is practically nil. A doubling of the mutation rate in one generation would cause an increase of one per cent in the incidence of the disease in the first generation. If allowance were made for the effects of inbreeding, a further small increase would be predicted sometime after the second generation and this would be followed by a very slow return to the previous level (Fig. 1a). The response to a permanent doubling of the mutation rate would be a slow rise by almost equal increments. It would take more than 50 generations of 30 years each to increase the incidence by 50 per cent, and many more to approach an increase of 100 per cent (Fig. 1b).

THE EFFECTS OF DOUBLING MUTATION RATES ON BROAD GROUPS OF DISEASES

140. The three examples given above illustrate the kind of result to be expected from doubling the mutation rates of genes representing each of the three classical types of genetical effect. A large number of dominant, sex-linked and recessive diseases are known; many of them are rarities but together they may account for a relatively large proportion of serious hereditary disability in the population. However, to give an idea of the extent of the problem of hereditary disability, and the total results of doubling the mutation rates of the genes which are responsible, common categories of illness must be considered. Our information, from the genetical point of view, is unfortunately not often precise and, in addition, the effects of genes are in many cases modified by environment. Mental diseases and mental deficiency, when taken together, account for nearly half the hospital beds provided in this country and are the most extensive inclusive category in which hereditary causes are known to be important. We shall first consider severe mental defect and then the two main types of mental illness.

(i) *Severe mental defect*

141. The incidence in the population of cases of severe mental deficiency which survive has been estimated to be about 1 in 500. It is higher than this at birth but subsequently reduced by the heavy mortality in early life. Beyond

this, there are grossly affected individuals, many with malformations of the nervous system, who are stillborn or who do not survive early infancy but who would have been mentally defective had they lived; the incidence of such cases is at least 1 in 200. The number of cases of severe defect at all ages surviving in England, Wales and Scotland may be nearly 100,000. The fact that not far from 30,000 hospital beds are provided for these cases indicates the extent of the medical care required.

142. In this broad category of disease, conditions with dominant inheritance include epiloia (sebaceous adenoma with tuberose sclerosis), several types of acrocephaly, hypertelorism and neurofibromatosis. In such diseases, many of the severely affected cases, say one half, can be attributed to recurrent fresh mutation. Doubling of all the mutation rates, for one generation, would have a large effect in the subsequent generation, and a permanent doubling of the mutation rates would soon permanently double the incidence. We may suppose that diseases such as these, collected together, form four per cent of all surviving cases of severe mental defect, as shown in Table 1. If all mutation rates were doubled, this would add 50 per cent to the numbers of these cases in the first generation, that is to say, two new cases in every 100 in the whole category, an increase which would mean a thousand extra cases requiring medical care.

TABLE 1

Effect of doubling mutation rates of genes concerned with severe mental deficiency : cases per generation classified according to probable causation

Type of Diagnosis	Probable causation	Surviving cases of severe mental deficiency under present conditions (i)* (ii)†	Increase in first generation if mutation rates are doubled (i)* (ii)†
Acrocephaly ...	Dominant gene ...	4·0 2,000	2·00 1,000
Epiloia ...			
Neurofibromatosis ...			
<i>et cetera</i> ...			
Micropthalmos ...	Sex-linked gene ...	0·5 250	0·15 75
Gargoylism ...			
<i>et cetera</i> ...			
Amaurotic idiocy ...			
Cerebral diplegia ...			
Phenylketonuria ...	Recessive gene ...	40·0 20,000	0·40 200
'True' microcephaly ...			
<i>et cetera</i> ...			
Mongolism ...	Environmental influence plus common genetical susceptibility ...	12·5 6,250	?+ ?+
Others ...	Miscellaneous, including birth injury and infection ...	43·0 21,500	?+ ?+
All ...	—	100·0 50,000	3·0 1,500 (approximate figures)

* (i) percentages based upon all cases in the category.

† (ii) numbers which would occur in a generation of 20 million births.

143. A few rare diseases causing severe mental defect are known to be due to sex-linked genes, for example one type of microphthalmos and one type of gargoyleism (Hurler's syndrome). The contribution of this group to the total number of defectives is small and can hardly exceed half of one per cent of severe cases. Nevertheless, for the reason given above, diseases of this kind must be due to genes with significant mutation rates: if these rates were doubled in one generation, the incidence at birth of the diseases would be increased by nearly one-third, as in haemophilia. After a doubling of the mutation rates in one generation, there would be an increase of 0·15 per cent in the total number of cases of severe mental defect, or 75 extra cases requiring medical care.

144. Other important known genetical causes of mental defect are recessive conditions, such as the two kinds of amaurotic idiocy, phenylketonuria, cerebral diplegia, and 'true' microcephaly. Known conditions caused in this manner account for 20 per cent of low grade mental defect and the same type of causation may easily account for twice as much as this. The case frequency of these traits individually is low, that is about one in 40,000 in the population at birth; about 20 conditions of this type are already known and perhaps another 20 may exist undetected. Since these diseases are all very deleterious, so that those affected scarcely ever have offspring, it is generally accepted that the genes causing them arise continually by spontaneous mutation. As previously explained, the reason for this assumption is that the incidence in the population can only be maintained if loss of genes through failure of reproduction is balanced by an equivalent appearance of new mutations. From this consideration the mutation rates can be estimated for these recessive traits but the method is indirect and the results are imprecise; they are likely to be too high. A doubling of mutation rates in one generation would cause a one per cent increase in the incidence of each lethal recessive trait the original incidence of which is one in 40,000. If 40 per cent of severe mental deficiency were determined in this manner, doubling mutation rates would cause an increase of 0·4 per cent in the whole category or 200 extra cases requiring medical care.

145. The problem of mongolism, a disease responsible for between 10 and 15 per cent of all cases of severe mental defect living in the population, requires separate consideration. There is strong evidence of a genetical element in the causation but maternal age is also a very significant factor. The hereditary predisposition must be very common and only harmful in exceptional circumstances. Although a slight increase in incidence might be expected as a result of doubling mutation rates, the nature of the predisposition is so imperfectly understood at the present time that it does not seem useful to make a numerical estimate for this condition.

146. As shown in Table 1, 43 per cent of the cases are not yet accounted for. Among these, there must be a large group in which injury or infection is the main cause, perhaps 15 per cent of all cases of severe mental defect. A still larger number are of quite unknown origin, although genetical factors may have some influence. Furthermore, there may be a residual proportion of cases due to relatively common genes, acting either singly or in combination with one another, on which the effect of increased mutation could be appreciable. It is impossible to make quantitative predictions about mutation for this group with unknown causation but the number of cases ordinarily caused by fresh mutation must be very small.

147. The conclusion is that, after doubling the mutation rates, an overall increase of three per cent in the category of low grade mental deficiency in one generation is possible; in a generation of 20 million births the known

surviving cases would number 50,000 and an increase of three per cent would mean 1,500 additional cases requiring care. If the mutation rate remained permanently doubled, the incidence in the population would, on the most pessimistic assumptions, eventually, after very many generations, double also and twice as much medical care would accordingly be needed.

(ii) Mental illness

148. Current theories concerning the genetical factors underlying mental illness imply that a small but substantial proportion of cases must owe their origin to the recurrence of mutations. This is almost certainly true for Huntington's chorea, a rare dominant disease. For the common disease groups, schizophrenia and manic-depressive reaction, the situation is less clear. According to figures for 1954, there were approximately 63,000 cases of schizophrenia and 31,000 cases of manic-depressive reaction under hospital care in England, Scotland and Wales. Since these diseases account for about half of all mental illness, it may be worthwhile to attempt a rough estimate of the effects of changing mutation rates upon their incidence.

149. Theoretically, any genes responsible for conditions, like mental illness, which lower biological fitness to a marked degree would have been eliminated from the population, or would have become very rare, unless they had been continually replaced by fresh mutation. However, there are uncertainties about the relevant facts concerning the genetics of schizophrenia and manic-depressive reaction. First, the incidence of these diseases in the population is not accurately recorded; secondly, the biological fitness of predisposed and even of affected individuals has not been fully investigated; thirdly, the nature of the genetical contribution is known only by surmise; and, fourthly, nothing definite is known about possible compensating mechanisms which might, if they existed, make unnecessary the assumption of gene replacement by spontaneous mutation.

150. Calculation, on the basis of elementary and simplified assumptions about gene action, leads to the conclusion that doubling the mutation rate might have the effect of raising the incidence of schizophrenia by a factor of one per cent and of manic-depressive reaction by a factor of 1·4 per cent in the first generation. It is not possible to estimate the number of extra hospital beds which this proportional increase in frequency of genetical predisposition would imply. We can, however, obtain an idea of the expected number of extra chronically incapacitated patients from the calculations set out in Appendix E. The total number of such cases which would appear among the first generation of 20 million births after doubling mutation rates would be 200 schizophrenics and 200 manic depressives. The number of extra patients needing psychiatric care at one or other time during their lives, on account of these genetical predispositions, would be from 5 to 10 times as great. A permanent doubling of mutation rates would have in each succeeding generation an effect similar to that in the first generation. Thus, over a very long period of time, the number of cases would slowly increase until the limiting value of twice the initial number was approached.

(iii) Blindness

151. A frequent cause of severe disability is blindness. The extent of the morbidity is shown by the fact that every year, in England and Wales, 12,500 new cases of blindness are registered. These include cases of developmental abnormality, tumours, metabolic diseases and the results of injury and infection. The genetical background is extremely varied but at least half of the hereditary cases can be attributed to single genes, often recessive like those causing retinal degeneration, though a few are dominant like that for

retinoblastoma; some are known to be sex-linked. High myopia is believed to have a complex genetical background. The important cases from the present point of view are those with onset in early life and about three-quarters of all such cases of blindness are thought to be hereditary. About 300 children between the ages of 0 and 15 years are registered as blind annually. Severe cases in the causation of which mutation is likely to play an important part will mostly be in this group which includes aniridia, microphthalmos and retinoblastoma. The mutation rates for these dominant diseases are listed in Appendix C. Assuming that these figures apply to England, Wales and Scotland, we can estimate that, in one generation of 20,000,000 births, there would be 80 cases of aniridia, 80 cases of microphthalmos and (using the mean of three estimates) 560 cases of retinoblastoma due to spontaneous mutation in ordinary circumstances. These numbers would be almost doubled if the mutation rates were doubled for one generation. If the mutation rates were permanently doubled, this increase would be continued until the total incidence of these diseases was doubled, as was calculated for achondroplasia.

152. Numerous cases of blindness due to recessive conditions are known, and some have sex-linked inheritance. Figures for the incidence of these traits are not well enough established for the effects of doubling mutation rates to be estimated.

(iv) Neonatal deaths, stillbirths and congenital malformations

153. An increase in mutation rates would be expected to have an effect upon the abortion, stillbirth and neonatal death rates and upon the incidence of congenital malformations. These deaths and malformations are known to be caused in large part by the environment of the unborn child, which may be affected by illnesses and other conditions in the mother. Many may be due to single recessive genes, some to chromosome abnormalities and others are known to be caused by immunological incompatibility between mother and foetus. For these reasons we have not found it possible to make detailed calculations of the kind used above for other conditions, but it is certain that the total effects of doubling mutation rates in one generation would be slight. Observations on these foetal conditions in actual circumstances where the mutation rates might have been increased have been made on human populations and are discussed below in paragraphs 162 to 170.

THE OVERALL LOAD OF ILLNESS IMPOSED BY DOUBLING ALL MUTATION RATES

154. We have expressed the opinion that, from the standpoint of the social load imposed, mental diseases constitute the most important single category of disease which is determined to a marked degree by heredity and which is serious, in the sense both of being highly harmful to the individual and of making heavy demands on medical resources. We are aware that this is only an opinion and that others may have different views. We believe, however, that it will be conceded by all that the mental diseases contribute a very substantial proportion of the total number of those suffering from serious hereditary disorders. It seems reasonable, therefore, to suggest that the total increase in the social load due to serious hereditary illness of all kinds, which would follow doubling all mutation rates, would be unlikely to exceed more than a few times the estimates we have given for mental defect and mental illness combined.

155. Hereditary diseases are sometimes thought of as incurable, and it is true that present knowledge provides no grounds for believing that cures will

be found for some of the grosser forms. With the advance of medical science, however, it has become possible to alleviate many hereditary conditions or even to maintain the affected patients in good health. A classical example is diabetes mellitus, into the causation of which a hereditary factor enters in many cases. Before the discovery of insulin, the majority of diabetics were destined for invalidism or premature death. Now with its aid they live essentially normal lives. With further advances of medical knowledge, it may be expected that an increasing number of hereditary conditions will be brought into this category, and thus the load of suffering from illness of this kind be reduced. It should be realised, however, that the preservation of those afflicted by hereditary conditions will increase their chances of having children and so lead to an increased prevalence of the condition in the population and with it an increased need for medical services.

156. From the point of view of the long-term effects on the population, it must be remembered that, even though most of the new recessive alleles produced by an increase of mutation rates will not meet a like partner in the first generation after they are produced, and will therefore remain concealed, they will still exist in the population. They will in fact persist until, at some later time, two carriers of like genes happen to mate. The recessive effects will then become manifest in some of the children of such matings. If such genes are harmful, these affected children will produce fewer offspring than the normal, so that there will be a reduced chance that the genes will be passed on to later generations. In this way mutated genes can eventually die out. The extinction of the gene will have been brought about, however, only by the failure of some affected individual or individuals to reproduce at the normal rate, a circumstance which may sometimes be merely unfortunate but in other cases may be the expression of a hereditary defect which causes great suffering. Thus, if the mutation rate is increased, and a crop of newly mutated recessive genes produced, they will continue to cause harmful effects for many generations.

The Effects of Increased Mutation Rates on Hereditary Traits showing Continuous Variation about the Normal

157. Although in any human population we can find individuals who are physically, biochemically or mentally abnormal in a relatively gross way and whose abnormality can be traced to single gene differences, most of the variation between human beings is not in fact of this kind. Even in that greater part of the population which we should describe as normal, no two individuals are alike: they vary by imperceptible gradations over a wide range in respect of many characters such as physique, general well-being, life-span, intelligence and so on. Some of the variation is hereditary but some is due to differences in environment—in the circumstances under which the individual lives and has grown up. The hereditary portion of this variation is believed to be due to the combined action of many genes which supplement one another in producing their effects. These genes cannot be distinguished one from another, and their effects have therefore to be measured in a way differing from that used where a gene has consequences sufficiently drastic for it to be followed as a separate entity. The importance of heredity in such cases is expressed by estimating the proportion of the variation which is traceable to gene effects. The properties of the system of genes are inferred from observations on the amount of this variation which is shared by relatives and on the change in the proportion from generation to generation. In particular, the effect of mutation will be measured by the increment it adds to the variation in each generation.

158. One difficulty should be observed at the outset. The success of this method of approach depends on the ability to measure separately the proportions of the variation attributable to the combined effects of the genes, and the proportion attributable to environmental factors external to the individual. Even in animals and plants, under the conditions of controlled experiment, this is not always easy. In man, whose parents give him not only his genes but also the home and environment in which his early and most formative years are passed, the separation of hereditary and environmental effects is always extremely difficult. Observations on, for example, children brought up by foster parents are of some assistance; but, even so, the conclusions at which we have been able to arrive must be regarded as rough estimates and treated with due caution.

159. Genetic theory leads us to expect that, since mutation brings new gene differences into the population, the basic effect of an increase in the mutation rate will be to increase the variation shown by these characters, that is to raise the numbers of the more extreme types at the expense of the more central, average individuals. Very little information is available, however, even from experimental animals and plants, about the magnitude of the effect to be expected. Such few observations as we have (Appendix F) suggest that in any generation the variation due to new mutation is but a small fraction of the heritable variation observable, and, of course, a still smaller fraction of the total variation, which includes that due to the environment. Indeed, the available data would lead us to expect that hundreds of generations of mutation would be needed to build up the variation which is seen in a human population. A doubling of the mutation rate for a few generations would therefore be expected to have only the most trivial effect on the variation in such characters, and even a persisting doubling of the mutation rate would take very many generations to approach its full effect, which at most would be to double the variation.

The distribution of intelligence

160. The effect on the distribution of intelligence—or, more accurately, of the score in intelligence tests—of an increase in the hereditary variation, such as would be expected to result from a raised mutation rate, is considered in Appendix G. Extensive studies have been made of the intelligence score and something is known about its distribution in the population and the extent to which it is inherited. Increase in the variation, that is in the spread of the distribution, will lead to an increase in the numbers both with markedly low and markedly high scores. Furthermore, the more extreme the class under consideration, the greater the increase in its numbers relative to the overall change in the variation. Thus, from the table in Appendix G, it will be seen that a doubling of the heritable variation could lead in the long run to nearly a tripling of the numbers falling short of an intelligence score of 70 and conventionally regarded as requiring special schooling. On the assumption that the average score did not fall, a corresponding increase would be expected in those with the high scores of over 130.

161. The increase in the two extremes of the distribution may, however, not be symmetrical. Evidence from experimental organisms shows that, where a character has been subjected in the past to much selection in a particular direction, new variation is likely to produce a disproportionately large increase of the more extreme types in the direction opposite to that towards which selection has been pushing the character. This would still be true when the variation is being increased by irradiation. It seems probable, in the light of man's evolutionary history, that he has been subjected to fairly

intense natural selection for increased intelligence. It might therefore be expected that an increase in the variation, resulting from a raised mutation rate, while leading to some increase in the fraction of those who are highly intelligent, would lead to a greater—perhaps much greater—increase in the other extreme fraction with low intelligence. In addition to the calculation which assumes that the average intelligence score remains constant and so assumes symmetrical increases at the two ends of the distribution, Appendix G. includes a calculation which assumes an asymmetrical effect, the overall average of the population falling but the proportion of children of grammar school ability remaining constant. The disproportion in the increase of the low end of the distribution is of course increased, a doubling of the variation raising the proportion with a score of less than 70, perhaps by as much as four or five times. It should be remembered, however, that these calculations apply to the situation when the increase in variation has reached its full extent. We have already seen that such data as are available suggest that a permanent increase in the mutation rate would take hundreds of generations to produce its full effects on hereditary variation.

Observations on Populations Exposed to Radiation

162. An alternative approach to the problem before us, and one which in addition might provide direct evidence of the relation between the dose of radiation and increased incidence of hereditary traits in man, is to observe the effects on human populations which have been exposed to ionizing radiations. Three such studies have been carried out, two on American radiologists and the other on the Japanese populations who were in Hiroshima and Nagasaki at the time of the atomic bomb explosions. For various reasons, the evidence from each is inconclusive, even that from the extensive study by the Atomic Bomb Casualty Commission in Japan.

Possible indicators of change in mutation rates

163. Among the possible indicators of a change in the mutation rate are changes in the sex ratio at birth, the congenital malformation rate, the stillbirth rate, the neonatal death rate, the weight at birth, the weight at nine months, and measurements of the head and body. Changes in the sex ratio may be used as an indicator of genetic damage. The inheritance of abnormal genes in the sex chromosomes has been considered in relation to haemophilia. Experimental observations have shown that abnormal genes which kill the infant long before birth can be carried on the sex chromosomes and there is reason to believe that this may be true in man. Such genes will necessarily disturb the sex ratio at birth; mothers with such mutations will have too few sons, and, in rare cases, fathers too few daughters.

164. It is known, from both human and experimental evidence, that genes can produce abnormalities which are evident at birth. Estimates of the congenital abnormality rate vary with different observers from just over one per cent to about six per cent, owing to lack of agreement on what shall be reckoned an abnormality as well as to real differences in populations with respect both to their environments and to the frequencies of the causal genes. Further, genes are not the only cause of such abnormal conditions. Both clinical and experimental evidence suggests that maternal ill health, particularly infectious disease and malnutrition during pregnancy, can produce them. There is no definite information as to what proportion of cases of malformation should be attributed to the effects of single genes; nor are the forms of inheritance understood.

165. The stillbirth and neonatal death rates are also influenced by a variety of factors. The evidence that abnormal genes can play a part is based

partly upon experimental genetics and partly upon investigations of family histories. On the evidence available at the present time, it is difficult to estimate the extent of the part played by genetical causes.

Genetic studies on radiologists

166. The evidence provided by the studies of congenital abnormalities in the offspring of American radiologists is inconclusive for two reasons. First, no measurements were made of the radiation doses which were received by the radiologists in the course of their work and it is virtually impossible to deduce these in retrospect. Secondly, the data were obtained by postal questionnaire, to which only three-quarters of the radiologists replied and little over half the other specialists who were used as a control group. Whether those who chose to answer were representative of the total is open to question. As the magnitude of the effects observed was small (slight rises in the incidence of twinning, foetal death and congenital malformation), one cannot exclude the possibility that the increases were due to statistical bias in the data rather than to the radiation exposure, or alternatively that statistical bias in the other direction may have partly concealed a somewhat larger increase than was observed.

Studies on Japanese populations

167. The Atomic Bomb Casualty Commission's genetic study was much more extensive. An attempt was made to assess the prompt radiation dose received by each individual; and in each city those remote from the burst constituted a control population with which to compare those close to it. More than 80,000 subsequent pregnancies were followed, and a third of the children were re-examined at nine months of age.

168. The final report on the genetic programme of the Atomic Bomb Casualty Commission has not yet been published; but through the courtesy of the United States authorities, and especially of Dr. James V. Neel and Dr. William J. Schull, we received copies of the draft and are permitted to refer to it. The data present many difficulties of interpretation for several reasons. First, the radiation dose was not known with any accuracy. Second, the parents with different degrees of exposure were not entirely comparable in various characteristics, such as maternal age at birth of the child, to which the congenital malformation rate is related; for this reason, even if there were no effect due to exposure, the children of the highly exposed parents would be expected to differ in their congenital malformation rate from those of the slightly exposed. Complex statistical procedures are necessary to allow for this. Even more open to error is the comparison between the children of exposed parents and those of parents who were entirely unexposed. The latter group of parents included immigrants from other cities or from rural areas after the time of the bombing, and some who were away from home at the time, and the effect of these factors on, say, the congenital malformation rate is quite unknown. Thirdly, the number of people who survived high exposures was not large and therefore there were comparatively few births in this group; estimates of the incidence of congenital malformations and other abnormalities are consequently of low statistical precision, being open to relatively large disturbances through the operation of chance. Fourthly, only small effects would be expected in any given generation, even if the mutation rate had been raised many times.

169. Any opinion on a report which is still only in draft must be regarded as provisional. In our view, however, the data suggest an effect of the bomb radiations on genetic factors in prenatal survival, as shown by the sex-ratio at birth. The evidence for this effect is not highly significant statistically

and any change which was induced in the sex-ratio is unlikely to have exceeded 2 per cent per 100 r exposure of one parent. This appears to be the only positive conclusion that might perhaps be drawn but it is possible, for several of the measurements, to set upper limits to the changes that might have occurred without being detected. From the nature of the evidence a possible doubling, but not more than doubling, of the congenital malformation rate, or a 50 per cent rise in the stillbirth rate, following exposure of one parent to 200 r, might have escaped detection.

170. Although it was possible to set an upper limit to the increase in sex-ratio, congenital malformation rate and stillbirth rate, we were unable to do so for the increase in mutation rates of the genes responsible. For this purpose it would first be necessary to know what proportion of prenatal death or malformation is in ordinary circumstances due to newly mutated genes and what proportion to genes already present in the population. We cannot, therefore, derive from the Atomic Bomb Casualty Commission's data any estimate of the mutation-rate-doubling radiation dose for man.

The Radiation 'Doubling Dose' for Human Mutation Rates

171. At this stage it becomes necessary for us to attempt to give a quantitative estimate of the magnitude of the effect of any given dose of radiation on the mutation rate in human populations. This is an extremely difficult task, since not only have we as yet too little precise information on which to base an accurate estimate, but also it is by no means simple to know in what terms the effect should best be measured.

172. We have seen that all genes mutate spontaneously. The spontaneous mutation rate (s) of any particular gene can be considered to be made up of two parts: some of its mutations (x) will be provoked by the naturally occurring radiation, while others (y) will be due to other influences, so that $s = x + y$. It would be easy to find a theoretically adequate measure of the effect of increased radiation on mutation, if all mutations were caused by radiation of some kind, y would then be zero; and, since we have seen (paragraph 127) that radiation-induced mutations increase in simple proportion to the amount of radiation, it follows that, if the amount of radiation were doubled, the mutation rate would be doubled also, and so on. We could express the effect of increased radiation in terms of the 'doubling dose', that is the quantity of radiation required to double the spontaneous mutation rate. It is clear that the doubling dose under these circumstances would be equal to the naturally occurring radiation.

173. However, as we shall see later (paragraph 178), there is good evidence that in the few well-studied animals spontaneous mutations are not due solely to radiation, and therefore we cannot safely assume that y is zero. The situation would remain fairly simple, provided x and y were always in the same proportion, so that we could assume that a certain constant fraction of the spontaneous mutations of each gene is caused by natural radiation; but this also seems unlikely to be the case. Older parents have accumulated higher doses of radiation than younger parents; if all genes were equally sensitive to radiation, the frequency of all new mutations should then show the same increase in the children of older fathers as in the children of older mothers. It is found, however, that for some human genes, but not for others, the increase is more marked in children of old fathers than in those of old mothers. This fact suggests that the genes which exhibit this relationship to paternal age differ from other genes in that their mutation is dependent in an important way on something other than radiation, perhaps on the number

of cell divisions since conception, which is much greater for sperm than for eggs. There is also some evidence from experiments on flies and other organisms, in which high doses of radiation were employed, that certain genes are more radiation-sensitive than others. In view of these facts, it is only safe to assume that the same may be true of human genes, and that for each gene the spontaneous mutation rate is built up of both an x and a y fraction, which do not always bear the same proportionate relation to each other.

174. If this is so, an amount of extra radiation which will double the mutation rate of the most radiation-sensitive genes will have a much smaller effect on the more radiation-tolerant ones. It is then impossible to give any one figure which will measure the effect of radiation on the whole set of genes. However, in practice we still know so little about human mutation rates that we can, provisionally, make some simplification of the theoretical considerations. We can attempt to assess the effects of increased radiation in terms of that dose of radiation which will double the spontaneous mutation rate of an adequate and representative sample of the most sensitive genes. This would be a minimum estimate of the doubling dose. By 'adequate and representative' we mean that we must consider a sufficient number of the more sensitive genes to get examples of all the different kinds of genetic effects. Fortunately there is no reason to doubt that, if one considered a fairly large number of the most radiation-sensitive genes, they would contain examples of genes with all possible kinds of effect. We shall assume that this is indeed so, and, further, that there are sufficient genes with roughly the same degree of radiation-sensitivity for us to employ the concept of a representative doubling dose of radiation of the kind which we have been discussing.

175. The attempt to estimate a figure for the minimum representative doubling dose in man is beset with many difficulties. We have as yet no useful direct evidence. The only data which might provide information about actual increases in human mutation following irradiation are those from the investigations of the results of the atomic bombs in Japan, and those on the offspring of radiologists, and, as we have already seen (paragraphs 162-170), in neither is the material sufficient to lead to any firm conclusions. At the present time, therefore, we are driven to making indirect estimates.

176. Perhaps the most firmly based line of argument towards an indirect estimate is one which leads us to an assessment of a minimum figure above which the doubling dose must almost certainly lie. Let us suppose that all human spontaneous mutations are radiation-induced; then, provided the mutation rate increases in direct proportion to the radiation, the doubling dose would be the same as the quantity of natural radiation received. The only way of escape from this argument would be by the supposition that for human genes the mutation rate is not directly proportional to the radiation, but that they are comparatively insensitive to small doses up to the level of natural radiation, and relatively much more sensitive to doses slightly greater than this. There is no evidence in any other animal for such an effect, but a few experiments in plants, the results of which are not entirely consistent, have suggested an effect of this kind, though only a slight one. It therefore seems safe to argue that, even under the most pessimistic assumption that all human spontaneous mutations are induced by radiation, the doubling dose could not be less than the normal amount of natural radiation. It will be seen, in the chapter on exposure levels, that in this country, over a period of 30 years this amounts to about 3 r to the reproductive organs. We may therefore take this figure as the lower limit of our estimate.

177. The next step is to try to determine whether the actual value of the doubling dose is quite near this limit or considerably above it. There are several ways in which we can proceed. We may first ask whether the Japanese data are compatible with a doubling dose as low as 3 r, or whether, if the value were as low as that, one would have to anticipate rather striking effects in place of the almost complete absence of definitely significant results which was actually observed. Calculations show that, if some more or less plausible assumptions are made, the absence of definitely recognisable effects in the Japanese data does not contradict a doubling dose as low as 3 r, although it is of course more easily accounted for if the real doubling dose is considerably higher.

178. Our lower limit for the doubling dose was based on the supposition that all spontaneous human mutations are caused by radiation. If natural radiation accounts for something less than 100 per cent of spontaneous mutations, then this lower limit would be raised accordingly. In experimental animals, one can determine what fraction of spontaneous mutation is due to radiation by measuring the effects of several different large radiation doses and extrapolating the results to the naturally occurring dose. Even among experimental animals, it is only for fruit flies that we yet have sufficient information to do this with much confidence. It turns out in this case that natural radiation accounts for only about one ten-thousandth (0.0001) of their spontaneous mutations. In trying to extend this result to man, we have to take into account two considerations. The first is that the longer the time elapsing between the conception of an individual and his reproducing, the greater the dose of radiation he will accumulate. The second is that, if the genes are equally radiation-sensitive in two species, the fraction of the spontaneous mutation induced by natural radiation will be smaller if the spontaneous rate is large than it would be were the spontaneous rate small. If one compares the lengths of the pre-reproductive periods of man and flies one finds that man has time to accumulate about 1,000 times as much radiation as the fly. We are much less certain about the comparison of their spontaneous mutation rates, since figures for man are not available for many loci (Appendix C). However, estimates have been made that the human mutation rate is probably about five times as great as that in flies. We should then find that the fraction of the human spontaneous rate due to radiation can be estimated at $1,000/5$ times the fraction which holds for flies, i.e. 200×0.0001 , or about 2 per cent.

179. The argument given above is based on the hypothesis that the sensitivity of human genes to radiation, that is the mutation rate induced per roentgen, is the same as it is in flies. As has been repeatedly pointed out, we have no definite evidence about the radiation-sensitivity of human genes, by which this assumption could be checked. The mouse is the only mammal for which we have any evidence on the radiation-sensitivity of genes. The induced mutation rates for a small number of genes have been roughly measured for this species. The experiments suggest that its genes are about ten times as sensitive as fly genes; but it should be noted that this figure depends very largely on only one of the seven genes tested. However, in order to be cautious we may make the hypothesis that mouse genes are ten times as sensitive as fly genes, and that human genes are similar to mouse genes. According to this hypothesis, we must increase our estimate of the fraction of human spontaneous mutation rate due to radiation by ten times, from 2 per cent to 20 per cent.

180. According as we suppose the radiation-induced fraction of the spontaneous mutation rate of man to be 20 per cent or 2 per cent, we arrive

at estimates for the doubling dose that are five or fifty times the naturally occurring radiation, that is 15 r or 150 r. It must be pointed out, however, that the calculations which have just been given have involved a number of quantities which are still only imperfectly known; for instance, the spontaneous mutation rates of flies, mice and particularly men. One cannot therefore, on this basis, absolutely exclude the possibility that the doubling dose may actually lie somewhat below 15 r.

181. Various other theoretical methods have been suggested for utilising the data about experimental animals to calculate a doubling dose for man. They all lead to values within the same rather wide range as we have just reached. Moreover, they all involve even more conjecture about quantities on which we have little precise information, such as the comparative numbers of gene loci in man and other animals. We shall not attempt to summarise them here.

182. There is another rather different type of approach to the problem; that is, to compare the values of the minimum representative doubling dose in the animals and plants for which we have the most reliable data (Appendix H). They mostly run from about 25 r upwards, many of them being between 25 and 60 r. Only a few types of organisms have yet been studied in detail, but taken as it stands this evidence would suggest that all doubling doses lie in about the same range, and it is therefore possible that man's may do so too. It is unfortunate, though easily understandable, that none of the fully investigated organisms has a lifetime comparable in length to that of man, and this suggests the necessity of caution in applying the results to man. But one might expect, *a priori*, that evolutionary processes would have acted to reduce the radiation sensitivity of the genes of organisms with long pre-reproductive periods, so that they would have higher doubling doses. Thus, this line of approach would lead us to expect the human doubling dose to lie above 25 r.

183. The discussion in the last few paragraphs has been given at some length in order to bring out the great uncertainty of our present knowledge of the doubling dose for most human genes. Mustering all the arguments at our disposal, we can only come to the conclusion that it almost certainly lies above 3 r, but that it may be as much as 150 r or even more. Any statement which goes beyond this can only be phrased in terms of probabilities, and depends on a judgment made by balancing all the different lines of argument against one another. In this tentative fashion, we should advance the view that there is little likelihood that the representative value lies between 3 r and 15 r; and that, although we cannot exclude the possibility that for some human genes the doubling dose may be less than 30 r and for others more than 80 r, the best estimate which we can make, in the light of present knowledge, is that the representative value lies between 30 r and 80 r.

184. It remains to consider what dangers would arise if we have, for lack of adequate information, materially over-estimated the value of the doubling dose for human genes. Even if we suppose that it is actually as low as the minimum that we can reasonably entertain, namely 15 r, it is extremely improbable that in times of peace the whole population, or a large fraction of it, will receive an additional dose of this magnitude from industrial or other sources. We need not therefore anticipate any general danger. There may, however, be small groups of people, for instance those employed in certain industrial processes or receiving medical treatment involving X-rays, who may be exposed to doses near the representative doubling dose. Have they grounds for fearing any disastrous effects on their descendants? In the first place, it is obvious that if, for reasons of age or other considerations, they do

not reproduce after the period of exposure, no genetic effects at all will eventuate. If they do reproduce, there are two aspects to be considered: the effect on their immediate offspring and the effect on their later descendants.

185. We shall consider first the immediate descendants. It has been calculated on theoretical grounds that at the present time, without any additional radiation, approximately one human germ cell in ten (10 per cent) carries a new mutation. The great majority of these are recessive, and only very rarely have an effect on immediate offspring. Probably not more than one in a hundred is a dominant, the action of which will be seen in the next generation. Thus, a doubling of the mutation rate might lead to an increase of one in a thousand (0·1 per cent) in the numbers of harmfully affected children in the next generation. This must be compared with the present chance that the children born in a family will be congenitally defective. At present, about four per cent of all babies are stillborn or die shortly after birth, while another two per cent survive but are malformed; and in addition a considerable number in later years develop diseases or abnormalities in which hereditary constitution is a preponderating cause. Thus a doubling of the mutation rate in one parent would only add to the chance of producing a defective child an additional 0·1 per cent, above the present level of about seven to eight per cent.

186. A more realistic estimate of individual genetical risk can be obtained from the figures given in paragraphs 141 to 150. For example, the ordinary risk that any pair of parents will produce an imbecile or an idiot—that is a case of severe mental defect—which survives, is about one in 500. The increased proportional risk for parents in both of whom mutation rates have been doubled is three per cent; this means that the risk of their having a child with severe mental defect which survives is one in 485. If only one parent is affected, the risk would be increased by a factor of 1·5 per cent, so that the chance would then be about one in 493. Similarly, the risk of producing psychotic offspring might be increased by a factor of one per cent if mutation rates were doubled in both parents and by half this amount if only one was affected. The likelihood of miscarriage, stillbirth, or foetal malformation would probably be even less increased; compared with the changes in incidence which occur, for example, at different maternal ages or between the first and later births, these alterations would be inappreciable. The risks of occurrence of specific dominant or sex-linked traits, such as those listed in the table of human mutation rates (Appendix C), would indeed be proportionately much more markedly affected; but, because of their rarity, the risks of these abnormalities are ordinarily considered negligible for the individual and, even after being nearly doubled, they would remain so.

187. In ordinary circumstances, if a parent carries any given allele, the chance that one of his offspring receives it is one in two; a grandchild has one chance in four of receiving it and a great-grandchild has one chance in eight. The same rule applies to an allele which has arisen by fresh mutation in the parent. Thus it follows that the extra risk of disability, which applies to the children of an individual who has been exposed to doses of radiation causing mutation, will be halved in each subsequent generation of his offspring, provided that the level of mutation rate in the rest of the population has not also been raised. Moreover, it must be remembered that under natural conditions every human being already carries a certain number of harmful recessive genes, the results of spontaneous mutation in the past. There is therefore no reason why an individual in whom the mutation rate has been doubled, or increased by some similar figure, need fear that he runs an appreciable risk of founding a 'bad line' of descendants.

188. One may conclude that, if a relatively small group of prospective parents receives a doubling dose of radiation, no noticeable effects will be produced either on their immediate offspring or upon their descendants. For levels of radiation up to the doubling dose, and even some way beyond, the genetic effects of radiation are only appreciable when reckoned over the population as a whole and need cause no alarm to the individual on his own account.

CHAPTER V

EXISTING AND FORESEEABLE LEVELS OF EXPOSURE TO RADIATION

Introduction

189. Throughout the whole of his evolutionary history man, like all living organisms, has been exposed to small but variable amounts of ionizing radiation from his natural surroundings. To these he has now added similar radiations from his own inventions. In their biological action these differ but little from each other, and all must be taken into account when assessing the present hazards from ionizing radiation. We shall first consider those inescapable radiations which come from the natural background and, thereafter, those which are derived from sources controllable by man.

190. It will be clear from an earlier chapter of this report that relatively heavy doses of radiation are required to impair the health of the individual and such doses are rarely associated with the ordinary circumstances of civilian life. The use of radiation for medical purposes or occupational exposure to sources of radiation may be associated with the possibility of high doses, but every precaution is taken to safeguard the patient, and the employee is protected by nationally and internationally recognised recommendations which limit the doses received occupationally to levels considered to be safe.

191. On the other hand, our knowledge of the genetic effects of radiation is less precise and it is believed that doses of radiation which have no known effects on the health of the individual may be of genetic consequence. Doses received from all sources, however small, have therefore to be assessed in the light of their possible genetic implications. It has been seen that ionizing radiation can have genetic consequences only in so far as it affects the reproductive organs—the gonads—and it is thus the dose received by the gonads up to the end of reproductive life which must be estimated in all cases. At the levels of dose with which we are mainly concerned, the genetic effects of radiation can be calculated only in relation to the population as a whole. It is therefore in terms of the total gonad dose* to the population that the following estimates of the exposures from various sources have been made.

Radiation from Natural Sources

Cosmic radiation

192. Cosmic radiation reaches the earth from interstellar space. The atmosphere surrounding the earth has substance and acts as a filter, absorbing almost all the dose to which otherwise we should be exposed. In general, the longer their path through the atmosphere, the more the radiations will be attenuated; thus, the dose at sea level is less than that at high altitudes.

* The total gonad dose has been calculated on the basis of the considerations set out in paragraph 129.

193. Cosmic radiation has several components—protons,¹ fast and slow mesons,² electrons³ and neutrons⁴—which differ in their relative contribution to the natural background of radiation according to the altitude; at sea level the most important are mesons, electrons and neutrons. Mesons and electrons are considered to be, for equal physical doses, of about the same biological effectiveness as gamma rays. Fast neutrons and protons of high energy may be several times more damaging to the individual but are less likely to induce gene mutation. Neglecting this possible variation in effectiveness and assuming equal biological efficiency for all the particles, one derives a dose at sea level equivalent to 0.028 r per annum from cosmic radiation. Virtually all of this is highly penetrating radiation and can be assumed to irradiate the whole body, including the gonads, almost uniformly.

Terrestrial radiation

194. A few of the naturally occurring elements, particularly the heavy elements, are radioactive, thorium and uranium being the chief primary sources. These two elements are only feebly radioactive and each has a half-life measured in many millions of years. Each atom, in its radioactive disintegration, is transmuted to a daughter atom which is also radioactive and which in turn disintegrates to another radioactive atom, the process being continued until ultimately a non-radioactive stable atom of lead is formed. All the daughter elements decay much more rapidly than the original parents, thorium and uranium, and many of them emit gamma rays as well as nuclear particles in their disintegration.

195. Thorium and uranium are almost universally distributed in trace quantities in rocks and soils, areas of granitic rock usually having higher concentrations than sedimentary rock. Occasionally, the concentration is considerably greater than normal, sufficient to make the area worth mining, but even in these rich lodes it is usually only of the order of one per cent or less.

196. As a consequence of the presence in many soils of the radioactive daughter products of uranium and thorium, emission of gamma rays occurs widely over the land surfaces of the earth. Brick and stone necessarily contain traces of these radioactive substances and, inside houses built of such materials, radiation is added from this source. On the other hand, substantial structures of brick and stone offer slight shielding from cosmic radiation.

197. The amount of radiation contributed from the earth and from buildings varies from place to place even in the same country and any average figure can be only an approximation, but 0.078 r per year would perhaps be representative of the amount received inside buildings on the surface of the body by the inhabitants of this country. The corresponding figure in the open would perhaps be 0.048 r per year. Measurements show that about 37 per cent of the dose of gamma rays is absorbed superficially and filtered off before reaching the internal tissues and organs: allowing for this and esti-

¹ Protons are nuclei of hydrogen atoms and carry a unit positive charge. Fast moving protons are a minor component of cosmic rays at ground level. Neutron radiation also ejects protons from hydrogenous material.

² Mesons are unstable particles with masses intermediate between those of electrons and protons. Energetic mesons constitute the main component of the more penetrating cosmic rays.

³ Electrons are the smallest constituent particles of atoms. The electron carries the elementary negative charge of electricity. It has a positively-charged counterpart of equal mass called the positron. The soft or less penetrating component of cosmic rays consists essentially of positrons and electrons and about an equal number of gamma rays.

* Neutrons, see Chapter II, paragraph 19.

mating the amount of time that a person spends in the open, the average dose to the gonads of persons in this country from external gamma radiation is estimated to be 0·043 r per year.

Atmospheric radon

198. One of the decay products of uranium is radon, a gas which diffuses out of the earth and buildings and from minerals such as coal. In general, its concentration in the atmosphere is extremely low, about 0·3 of a micro-microcurie* per litre of air, but in cities such as London, where much coal is burnt, it may sometimes reach ten times this amount. In these circumstances, the dose of gamma rays from the further disintegration-products of radon may almost equal the dose of radiation from cosmic sources. The average dose to the gonads from this source, however, probably does not exceed 0·001 r per year from the atmosphere and an approximately equal or slightly greater amount from the gas absorbed into the body from the lungs.

Radioactive constituents of the body

199. Among the normal constituents of the body are the elements carbon and potassium, each of which has a radioactive isotope occurring naturally as a minute fraction of the total element. The radioactive isotope potassium 40 forms 1/8000 of natural potassium and emits both beta particles and gamma rays. An average value for the potassium content of the body is 0·21 per cent by weight, and measurements suggest that the figure for the gonads does not differ greatly. Calculation on this basis gives an estimated dose to the gonads of about 0·02 r per year. Naturally occurring radioactive carbon, carbon 14, constitutes one part in a million millions (10^{12}) of natural carbon; it emits only beta particles. Taking body tissue to be 18 per cent carbon, one derives a dose from this source of about 0·001 r per annum to the gonads.

Total gonad dose from natural sources

200. Information on the total dose to the gonads from natural sources of radiation is summarised in Table 2. It will be seen that, from all sources, the total is roughly 0·1 r per annum, or about 3 r per generation of 30 years (Appendix J).

TABLE 2

Estimated dose rates to gonads from natural sources of radiation

Radiation source	Estimated average dose rate to gonads in roentgens per year
<i>External radiation</i>	
Cosmic rays (sea level)	0·028
Gamma rays from the earth	0·043
Radon in air	0·001
<i>Internal radiation</i>	
Potassium 40	0·020
Carbon 14	0·001
Radon and decay products	0·002
Total	0·095

* $\frac{1}{1,000,000,000,000}$ of a curie.

Radioactivity in bone

201. Within the body, radioactivity is probably highest in bone. The naturally occurring radioactive heavy elements are contaminants of food and water as well as of soil and they and their disintegration products, of which radium is the most important biologically, are absorbed to a very limited extent from the gut. The body removes them from the circulation and stores them in bone. In this way the radioactivity of bone builds up gradually throughout life but there is no evidence that the rather higher doses in bone compared with other tissues are deleterious. Table 3 gives the estimated doses to bone from these sources.

TABLE 3

Estimated radium content and radiation dose rates to bone-cells

Geographical conditions	Estimated radium in skeleton at age 35 in micro-microcuries	Dose rate to bone-cells in equivalent roentgens per year		
		radium	external sources	total
Average areas	60	0.037	0.08	0.12
Active areas (See Appendix J)	1,100	0.37	0.18	0.55

Radiation from the Appurtenances of Civilisation

202. Since the discovery of X-rays and radioactive materials man has adopted them increasingly for certain of his needs. In medicine they now provide invaluable, and often irreplaceable, aids to diagnosis and treatment. They are also used extensively in industry and in the amenities of modern civilised life. It is necessary, therefore, to assess the dose that these developments contribute above that received from the natural surroundings.

Diagnostic X-rays

203. For some time it has been realised that by far the largest contribution is made by diagnostic X-rays. Continuing efforts are therefore being made to assess the dose of radiation given to the whole population in this way. The problem of accurate assessment is beset with difficulties and at present any estimate must be based upon very imperfect data. The two basic requirements and the best means of fulfilling them from available figures are as follows:

- (i) *The number of radiological examinations made annually, subdivided according to the sex and age of the persons examined and the part of the body under examination.* It is possible to make from published figures a reasonable estimate of the total number of X-ray examinations made within the National Health Service. A minimum figure for the year 1955 would be 12,200,000. To this must be added an unknown but relatively small number for hospitals outside the National Health Service and for private practice. This number has been estimated at rather less than half a million, giving a total of 12,650,000.

The division of this very large figure into sex, age and type of radiological examination has been made on the basis of information supplied by five hospitals only and covering some

21,000 patients (two London teaching hospitals and three others). While there are certainly differences between these hospitals, they are not so wide as to make an approximate calculation unwarranted. The sample has therefore been accepted as representative.

A very important source of radiation to the gonads is provided by radiological pelvimetry, which measures the size of the pelvic outlet of the woman in relation to the actual or potential size of her infant; a second important source is X-ray examination of the abdomen in pregnancy. Information of the frequency with which such examinations are made has therefore been specially sought from a rather wider group of nine hospitals. On the assumption that these are representative, the results have been applied to all live births occurring in hospitals in England and Wales.

In addition to the 12,650,000 X-ray examinations already mentioned, certain others are undertaken for special reasons and these bring the estimated total during 1955 up to nearly 18,000,000. The additional examinations include mass miniature radiography, dental radiography, and examinations of service personnel and mineworkers, but each of these types of examination represents a relatively unimportant source of radiation to the gonads and the effect of any error in estimating their contribution will be slight in relation to the total.

- (ii) *The average dose to the gonads—male, female and foetal separately—produced by the diagnostic irradiation of each separate part of the body.* For the purposes of calculation the figures used, which cover X-ray examinations of 24 different parts of the body, have been derived almost entirely from one London teaching hospital where careful measurements have been made and precautions taken to restrict the irradiation of the gonads to the lowest possible level. They are therefore almost certain to be minimum figures. It should be realised that with the X-ray tube only slightly misaligned the dose may sometimes be multiplied many times.

204. Bringing together these two sets of figures—the estimated numbers and ages of persons irradiated and the estimated average gonad dose delivered to them with specified examinations—leads to two important general conclusions. It shows, first, that almost the whole population dose is accounted for by a relatively few sites of examination, principally the hip, the lumbar spine, the lower abdomen and the pelvis. The far more frequent examinations of chest, head and limbs make relatively unimportant contributions. Secondly, according to the present calculations, the amount of radiation reaching the reproductive organs of the people of this country through diagnostic radiology is as much as 22 per cent of that derived from natural sources. Indeed, in view of the minimum figures adopted in these calculations, the contribution of diagnostic radiology may well be very considerably higher than 22 per cent. It undoubtedly forms the most important source of man-made irradiation and its application has been steadily increasing in recent years (Appendix K).

Radiotherapy

205. At present there is little information about the contribution to the population dose from therapeutic irradiation. Although its main use is for patients with malignant disease, the majority of whom are beyond the child-bearing age, some younger patients are treated for non-malignant conditions such as ankylosing spondylitis. Less penetrating X-rays are widely used in the treatment of a large number of diseases of the skin, and the artificially

produced radioactive element iodine 131 is now being administered for hyperthyroidism.

206. It is as yet not possible to state a figure for the population dose to the gonads from this source of radiation. Rough assessments would suggest that it is considerably less than the dose from diagnostic radiology but probably greater than that from any other source. The problem is one upon which research is required.

X-ray fluoroscopy for shoe-fitting

207. X-rays are used commercially for fitting shoes but, with modern equipment and good practice, it appears that the number of machines in operation would probably deliver not more than 0·1 per cent of the dose to the gonads received from natural radiation.

Luminous watches and clocks

208. Watches and clocks with luminous dials depend for their luminosity upon the rays from radium or other radioactive material used in the paint. Measurements and calculations suggest that the average wrist-watch contains about one-fifth of a microcurie of radium. A calculated dose to the gonads from wearing such a watch is about 0·01 r per year.

209. From the information given by the trade, it can be deduced that there are in use about three million men's watches and about a million women's and children's watches with luminous dials. In addition, there may be about ten million luminous alarm clocks. On this basis it can be estimated that the population dose from this source is about one per cent of the natural background.

Television sets

210. Cathode-ray tubes for television sets are capable of causing the production of X-rays. In general, however, the operating voltages are comparatively low and the X-rays are readily absorbed by the walls of the tubes and by protective screens. It can be estimated that the population dose from this source is at present much less than one per cent of the dose received from natural radiation.

Cosmic radiation in aircraft

211. Since the amount of radiation from cosmic sources is greater at high altitudes, the doses received by persons in aircraft have been investigated and the population dose calculated. The additional dose averaged over the whole population is at present insignificant compared with that received from the natural background.

Occupational Exposure to Radiation

Medical and industrial workers

212. Men and women have been exposed to ionizing radiation in the course of their occupations for over half a century. In the early years after the discovery of X-rays and radioactive materials many suffered injury, but safe practices have gradually been elaborated and standards of safety laid down. In this country since 1921 the British X-ray and Radium Protection Committee, and later the Medical Research Council's Committee on Protection against Ionizing Radiations, have considered the available information and made periodic recommendations on occupational exposure levels. Equivalent levels have been advocated by the International Commission on Radiological Protection.

213. Control of radiation exposure may be effected in two ways. In the first, the intensity of radiation in the vicinity of the source is measured at frequent intervals and, provided that the intensities are always below those levels accepted by international agreement as being without danger, no separate check is required on the exposure of the individual. In the second, the doses actually received by the individual are recorded, usually by means of a photographic film which he carries and which blackens on exposure to radiation, so allowing the dose received, if any, to be estimated. For twenty years the National Physical Laboratory has provided a service whereby such films are issued on demand and subsequently read. The worker and his supervisor can thus keep a check on the doses received to ensure that the accepted weekly levels of dose are not exceeded.

214. The provision of film badges has now been taken over by the National Radiological Protection Service which serves the majority of people known to be occupationally exposed, other than those employed by the Atomic Energy Authority or in the many hospital departments which process their own films. The Service will be available to those employed in the many and increasingly varied industrial applications of ionizing radiation as well as to research laboratories.

215. The available records have been sampled and analysed to assess the total dose from these sources to the population but, as precise records are not available from all branches of industry, the contributions from some sources are estimates only. It has not been possible to make as accurate an assessment as for the employees of the Atomic Energy Authority because the number, sex and ages of those exposed are not known with any precision and the monitoring, when carried out, is not as complete.

216. On the basis of figures from the hospitals which make use of this service, it has been roughly calculated that about 60 per cent of the medical workers at risk are women; in industry and research, women constitute only 15 per cent. It is estimated that in total about 14,000 people are employed, of whom half are women. After allowance for the fact that in women radiation is more completely absorbed before it reaches the gonads, it is estimated that the average gonad dose for both men and women would be about 2.5 r per year. Because the ages are not known with precision, it is not possible to make an accurate estimate of the genetic dose to the population as a whole, but after making certain assumptions we have reached a figure from this source of 1.6 per cent of natural background radiation (Appendix L).

Atomic Energy Authority employees

217. The Atomic Energy Authority now employs about 7,000 people who are exposed or potentially exposed to radiation in the course of their work. All employees liable to be exposed wear film badges that are examined weekly or monthly, and the sex and age of each individual are known. Thus it has been possible to calculate, with considerable accuracy, the doses received by the employees in relation to their expectation of parenthood. The average dose to the Authority's employees from all occupational sources of radiation is 0.4 r per year. The results of personnel monitoring show that in all recent years no employee has had an average weekly dose exceeding the maximum permissible and that about 90 per cent of the persons exposed to radiation averaged less than one-tenth of the maximum permissible weekly dose. It has been estimated that the gonad dose averaged over the population as a whole is about 0.1 per cent of the natural background.

Contamination of the World by Fall-out from the Explosion of Nuclear Weapons

218. Nuclear weapons differ in their construction and size and the same type of weapon can be detonated in different ways—under water, on land or in the air. These variations lead to differences in the radioactive dust produced, in its distribution and in the rate at which it falls out from the atmosphere on to the earth. Except in the immediate vicinity of a nuclear weapon explosion, the ionizing radiations to be considered arise from radioactive particles.

Radioactive fission products

219. Radioactive fission products, formed when the atoms are split, become mixed with the vapourised material from the bomb and with any earth, water or debris caught up in the explosion. Large particles fall quickly and are deposited close to the site of explosion; small particles are carried up with the hot gases to heights which vary with the power of the explosion. They subsequently travel in air streams for considerable distances and times, depending on the size of the particles and the height to which they were carried.

220. The particles reaching this country from the distant explosion of a typical nuclear weapon detonated over land are spherical in shape and consist of fused silica and metallic oxides impregnated with fission products. The vast majority are smaller than 0.001 of a centimetre in diameter. Particles from the thermonuclear tests in the Pacific atolls differ, in that they consist of calcium oxides or carbonates from coral and are irregular in shape. Both varieties are radioactive.

221. Different types of weapon produce a similar mixture of fission products in slightly different proportions, but the overall rate of decay of radioactivity is almost the same in all types. The total radioactivity decays to one-tenth of the original level for each seven-fold increase of time in days, as measured from the moment of detonation; thus, if the radioactivity is one unit on the first day after detonation, it is 1/10 unit at seven days, 1/100 unit at 49 days, and so on.

222. At the time of atomic explosions some normally stable elements may become radioactive by virtue of the capture of neutrons. Such induced activities are for all practical purposes short-lived and therefore of little importance when long-term hazards are being considered.

223. Since January 1951, continual watch has been kept by the Atomic Energy Authority on the radioactive fall-out reaching this country from nuclear devices exploded in other parts of the world. The activity in rain water at selected sites is recorded continuously. In addition the atmosphere is sampled daily by the collection of dust on a cylindrical filter through which about 1,500 kilogrammes of air are passed, and the radioactivity of the filter papers is determined (Appendix M).

Radioactivity in air

224. When the ordinary type of atomic bomb is exploded in Nevada, the dust-cloud rises to a height of about 40,000 feet. It then travels eastwards with the winds which prevail at that height and diffuses both vertically and laterally. It may or may not pass over this country on its first circuit round the world; if it does so, it will usually appear about 5 days after the explosion. The cloud continues circling the earth, and peaks of activity can be detected over any particular place in its path at about monthly intervals. The total radioactivity per unit volume of air falls progressively with time

owing to decay of the radioactive elements, to increased spread of the cloud and to deposition on the surface of the earth; approximately half the available material is deposited every 22 days.

225. Clouds from thermonuclear explosions behave differently because of the far greater height, approximately 100,000 feet, to which the debris is carried. Diffusion downwards from the stratosphere is a very slow process, and months after a thermonuclear test explosion most of the radioactive debris is still at these great heights.

226. Dust clouds from distant tests passing on the first circuit over this country are usually too high to impart measurable activity to air at ground level. Subsequently, at the peak periods, concentrations are in the region of five radioactive disintegrations per minute per cubic metre (dpm/m^3) of air. From April, 1952, to December, 1955, the mean concentration of activity from all bombs exploded in that period was $0.5 dpm/m^3$. The corresponding average activity from naturally occurring radon decay products in the air was measured at one of the sampling stations and found to be $130 dpm/m^3$. The debris from the thermonuclear tests in the Pacific in 1954, much of it by now already decayed, has mostly still to come down, but it is not expected to exceed $0.1 dpm/m^3$ in the next few years. The dose to a person fully exposed to air with a radioactivity of $0.5 dpm/m^3$ has been calculated to be one millionth of a roentgen per year.

Deposited radioactivity

227. The radioactive fall-out is cleared, sooner or later, from the air by deposition. Rain contains the bulk of deposited activity and continuing measurements have been made since 1951 of the radioactivity of rain water collected from specially treated roofs. Any radioactive dust deposited on the roofs in spells of dry weather is washed off and included with the next sample of rainwater. From these measurements the amount of radioactivity deposited per square mile can be determined for each explosion.

228. The dose that a man standing in the open in this country would receive from the deposition of radioactivity from all bombs so far exploded has been estimated. It has been assumed that all the radioactivity remains on the surface of the earth and that none is lost, as we know some will be, by drainage and weathering. Including all ordinary atomic bombs exploded before December, 1955, and calculating all the radioactivity which they have contributed and will contribute over the next 50 years, it is found that the total dose which a man continuously out of doors, night and day, would receive is $0.005 r$. To this dose from ordinary atomic bombs must be added the dose from thermonuclear weapons. For these latter the dose from the radioactivity still to be deposited is more important. It can be estimated that the accumulated dose from thermonuclear weapons is 0.002 to $0.003 r$ with another $0.027 r$ still to come.

Total radioactivity from weapons already exploded

229. All these doses together add up to about $0.035 r$ from weapons already exploded. This is a maximum dose. The loss of radioactivity from weathering has not been taken into account, nor has the protection afforded by buildings in and around which most people in this country spend a large part of their lives. It would be realistic to divide the dose by three for weathering and by seven for protection afforded as a result of time spent in houses. The average inhabitant of this country may therefore receive in the next 50 years between 0.001 and $0.002 r$ from this fall-out, or 0.02 to 0.04 per cent of the radiation that he will receive during the same period from natural surroundings.

230. If the firing of both types of bomb were to continue indefinitely at the same rate as over the past few years, there would be a build-up of activity gradually reaching a plateau in about a hundred years time which, on the same basis of calculation, would give the average individual a dose over a period of 30 years of 0.026 r or about 0.9 per cent of what he would receive in the same period from natural sources.

231. The most impressive feature of these figures for exposure from fall-out is the very great effect of a very few thermonuclear explosions. This is not surprising since their power is measured in equivalents of millions of tons of TNT compared with the thousands of tons for atomic bombs. If the rate of firing this type of weapon increases, the radiation exposure will be altered proportionally.

SPECIAL HAZARDS FROM RADIOACTIVE FISSION PRODUCTS

Particulate contamination

232. The total radioactivity in the air from fall-out is measured daily, and determinations are made of selected individual radioactive substances. The activity will arise from particles which may be inhaled into the lung. It can be calculated, however, that not more than one or two particles of the more highly active substances are breathed by any person in the course of a year (Appendix M). Although the radioactivity of these particles is minute, it is concentrated in a few million-millionths of a cubic centimetre (10^{-12} c.c.) and the possibility of their creating a hazard must therefore be considered. The International Commission on Radiological Protection has concluded that the critical volume of tissue to be taken into account is of the order of one cubic centimetre, which is a larger volume than could be heavily irradiated by a few such radioactive particles. It seems unlikely that particulate contamination of the air from the fall-out from test explosions would constitute a problem in ordinary civilian life.

233. Radioactive material from the air is deposited and accumulates on the ground where it may contaminate drinking water and agricultural crops. After deposition it becomes possible to make routine measurements of the present concentration of the more dangerous radioactive substances. By December, 1955, this concentration amounted to 0.011 curie of strontium 90 and 0.0002 curie of plutonium 239 per square mile. The continuing fall-out from explosions which have already taken place will cause a rise, to a maximum by about 1965, of around 0.045 curie of strontium 90 per square mile. These figures should be viewed against the background of the fact that the top one foot of soil has always contained on the average about one curie per square mile of the equally, if not more, dangerous naturally occurring radium.

Strontium 90

234. From the point of view of general contamination of the world, the hazard from deposited strontium 90 might, according to present ideas, be greater than that from external radiation, since strontium, like radium, is ordinarily retained in the body and deposited in bone. The average concentration of radioactive strontium in rain water over a period of three years ending December, 1955, was 1.7 micro-microcuries per litre and, since most water passes through soil before being drunk, the activity reaching human beings through drinking water is extremely small.

235. Strontium 90 is deposited on herbage and soil and is then absorbed into plants. Man and animals consuming the leaves of plants will therefore receive strontium 90 in food as well as in water. The hazard is greater for

grazing animals than for man, since animals may crop herbage from wide areas of contaminated pasture. Man, moreover, relies for his food more on grains and roots, which are not sites of concentration of strontium, and on animal produce from which the animal has removed most of the strontium to its bones. Cows' milk contains strontium, but fortunately the cow in its metabolic processes secretes calcium into the milk in preference to strontium.

236. The importance of radioactive strontium, compared with other long-lived fission products produced by exploding nuclear weapons, derives from four factors; its relative abundance among the fission products, its facility for following calcium through the human food chain, the ease with which it is absorbed, and the fact that, once absorbed, it is stored for long periods in the bones of the body. In bones it forms more or less localised deposits which, judging by animal experiments and according to analogy with the action of radium compounds on human subjects, can if present in sufficient amounts give rise to bone tumours or, by irradiating the neighbouring bone marrow, to aplastic anaemia or leukaemia. There is evidence that the young are more susceptible to its action than adults. Such measurements as have been made of strontium 90 in human bone suggest that the highest levels are at present about a thousand times less than is considered permissible for those occupationally exposed.

Plutonium

237. Plutonium 239, another very long-lived radioactive element, is also a potentially dangerous contaminant since, like strontium, it is deposited in bone. The amount of activity from plutonium in fall-out is small relative to that of strontium 90, its solubility is low, and less than one-tenth of one per cent of the amount taken by mouth is absorbed. The hazard from plutonium in fall-out debris is thus very small.

Caesium

238. Very sensitive methods of measuring the radioactivity of the human body have now been developed and, on the records obtained in recent months, there has been some indication of gamma radiation suspected to be due to the long-lived fission product caesium 137. Although it is not possible yet to identify with certainty the source of this radiation, calculations have been made on the assumption that it is due to this isotope. Caesium is not concentrated in any particular organ of the body and, on the basis of present information, is unlikely materially to affect the figure given above for the dose from the fission products deposited on the ground.

Other important isotopes

239. Of the other elements in mixed fission products strontium 89 and barium 140 behaves similarly to strontium 90; iodine 131, which is easily absorbed, is highly concentrated in the thyroid gland. These three isotopes, having half-lives which are only a matter of days, are of very little significance in relation to the long-range fall-out from atomic bombs, since most of their radioactivity will have decayed before they are deposited. In relation to the heavily contaminated areas within a few hundred miles of the explosion of a thermonuclear bomb, however, they will be of great importance.

TOTAL GONAD DOSE FROM MAN-MADE SOURCES OF RADIATION

240. Information on the total dose to the gonads from man-made sources of radiation is summarised in Table 4, the dose from each source being expressed as a percentage of the dose received from natural sources. It will be seen that the total dose amounts to approximately 25 per cent of that already received from the natural background.

TABLE 4

Summary of estimated population doses of radiation to the gonads expressed as percentages of natural background

Source of Radiation	Approximate dose to gonads as a percentage of natural background
Natural background	100
Diagnostic radiology	at least 22
Radiotherapy	?
Shoe-fitting	0·1
Luminous watches and clocks	1
Television sets	much less than 1
High altitude flying	insignificant
Occupational exposure:	
Radiology and Industry	at least 1·6
Atomic Energy Authority	0·1
Fall-out from test explosions	less than 1

Nuclear Warfare

241. Atomic bombs were developed for their capacity to create blast, which was the chief cause of casualties at Hiroshima and Nagasaki. The additional effects of the detonation of a nuclear weapon are due to the release of other forms of energy—heat and ionizing radiation. The ionizing radiations produced by the weapons are the new feature of military operations. Of the prompt radiations, produced at the moment of explosion, neutrons are the direct result of the process of nuclear fission. Gamma rays are also a by-product of fission but most of these are produced immediately after the detonation by the enormous quantities of radioactive fission products. The rapid ending of the gamma-flash at ground level after an explosion is due partly to the ephemeral nature of the radioactivities of many of the fission products and partly to the very rapid removal of the debris in the up-draught of hot gases.

242. The effective range of the prompt ionizing radiations from an ordinary atomic bomb explosion is less than that of the thermal radiation, and at Hiroshima and Nagasaki the range within which death and severe injury from ionizing radiations were encountered was about one mile, as compared with up to three miles for severe flash burns and five miles for indirect blast effects.

243. The notable feature of the ionizing radiations is that, in contrast to the heat rays, they are very penetrating. Clothing which may be adequate to shield the body from heat flash is 'transparent' to these rays, and even four inches of concrete transmit half the radiation at a distance of one mile from the atomic bomb burst. Thus, at ranges relatively close to such a weapon, people in stoutly constructed buildings might survive the effects of the heat and blast waves but suffer from the damaging effects of the penetrating gamma rays and neutrons.

244. From the comparative ranges of the heat flash and ionizing radiation it will be seen that distance is a factor of great importance. With gamma-rays, as with heat, the intensity falls in proportion to the square of the distance and is diminished by an attenuation factor. It is unlikely that the prompt radiations from thermonuclear weapons would be relatively more significant than those from atomic weapons. The hazard from radiation is

therefore only one of the immediate effects of nuclear weapon explosions, and a relatively minor one in a holocaust. Its particular importance lies in the delayed and distant effects, which arise from the radioactive fission products.

245. At Hiroshima and Nagasaki the atomic bombs were exploded high in the air so as to obtain the maximum effects from blast. Virtually all the fission products were therefore carried up with the hot gases and must have been enormously diluted before being deposited gradually round the world. However, some did fall to earth locally and presumably contributed to the delayed effects recorded by the Atomic Bomb Casualty Commission.

246. When bombs are exploded in or near the surface of the ground or near the surface of water, much debris highly contaminated with fission products is flung into the air and the large particles are deposited more or less locally. Some of intermediate particle size is carried by the local winds and gradually diffuses and settles down-wind. The best known phenomenon of this character following a test-explosion arose from the thermonuclear device exploded on 1st March, 1954. According to the Press release in February, 1955, of the United States Atomic Energy Commission, the area over which fission products settled to give a radiation dose which might well have been lethal to a man unable to take shelter was about 7,000 square miles. Over a considerably larger area, conditions in the open would have been hazardous to man and beast. The size and shape of these lethal and hazardous areas will vary with the conditions of the explosion and of the local meteorology. Nevertheless, the inferences are plain: weapons such as these can be devastating, not only locally over areas measuring hundreds of square miles, but in their more distant effects, which may occur over thousands and tens of thousands of square miles.

CHAPTER VI

ASSESSMENT OF THE HAZARDS OF EXPOSURE TO RADIATION

247. We have reviewed the effects of radiation both upon the exposed individual during his own lifetime and upon his descendants. It is now necessary to relate these effects to dose levels, and to attempt to assess the consequences of exposure to those levels of radiation which now occur or might conceivably come about in the future.

248. It will be recalled that human beings have always been exposed to radiation from outer space and from traces of radioactive materials in their surroundings and in their own bodies. The problem is, therefore, to assess the effects of any additional radiation to which they are or may be subjected, rather than to define a new experience. Our ignorance of the results of exposure to radiation is great and much intensive research is required in many fields; but the naturally occurring background of radiation to which mankind has long been adjusted can be taken with some confidence as a safe standard of reference, whether we are considering irradiation from outside the body or from radioactive materials taken into the body and stored, temporarily or permanently, in its tissues.

Differences between individual and genetic effects

249. Different considerations enter into the assessment of the significance of any particular level of exposure, according to whether we are concerned with effects on the individual or with genetic effects. In respect of the effects on the individual, we are concerned with doses received throughout the whole of life. In respect of genetic effects, however, we are concerned only with doses to the gonads received up to and during the reproductive period of life. In this country the average age of mothers conceiving children is about 28 years; of fathers, two to four years older. We have therefore taken the period of 30 years to represent the average length of time during which the germ cell lineage of the human population is effectively exposed to radiation. From a genetic point of view, any exposure to radiation after reproduction has ceased is irrelevant, since any mutations produced will not be passed on to future generations.

250. The second important difference relates to the accumulation of the effects of exposure on separate occasions. The genetic effects of radiation are cumulative; a mutation persists once it has been produced in a germ cell lineage, and to this are added any further mutations that are induced in the same reproductive cells. Since dose and effect are proportional, we are concerned, from the genetic point of view, with the total dose of radiation which has been accumulated up to any particular time in the reproductive period of life.

251. The position with regard to the effects of successive doses on the individual is incompletely known. It is certain that a dose of radiation which would produce acute effects if given as one single exposure may produce no similar effects if spread over a longer period. Moreover, if a sufficient period has elapsed after recovery from the acute effects, the individual may again recover from a further exposure which produces acute symptoms. Uncertainty

arises in relation to some important delayed effects of radiation where, in view of the results on the increased incidence of leukaemia in repeatedly irradiated cases of ankylosing spondylitis, we must now entertain the possibility that repeated exposures to radiation may combine to produce certain irreversible changes in the tissues exposed.

Dosage and Effects on the Individual

Acute effects

252. The effects which appear within the first 48 hours are seen only as a result of accidents and in those within a short distance from an atomic bomb explosion, or occasionally after exposure to the heavy doses of radiation which may be necessary in the treatment of serious illnesses by radiotherapy. They are, therefore, not important in ordinary civilian circumstances.

253. The same considerations apply to the acute effects on the blood occurring up to two months after exposure to a single dose or to a few heavy doses of radiation. Similar effects occurring later can, however, be produced by doses of radiation, given continuously or repeated at short intervals, which would not be sufficient to produce any symptoms in the first few hours. Formerly, it was thought that continuous exposure to 1·0 r per week would produce no effects on the blood but, after some individuals were found to be affected by this dose, the figure recommended by national and international bodies as the maximum permissible level was reduced to 0·3 r per week.

Delayed effects

254. Of the delayed effects, the one about which we have most information is leukaemia. It also appears to be the most easily induced and seems, at present, to be the most important as far as radiation of the whole body is concerned. We have therefore taken the incidence of leukaemia as a measure of the doses of radiation that are capable of producing delayed effects. The statistical evidence indicates that an increased incidence of leukaemia can be demonstrated after exposure to doses of radiation which might, in exceptional circumstances, be met with in civil life. For example, after either a single exposure of 200 r, or a few exposures which in total amount to 200 r, there is a noteworthy increase in the small chance of developing this disease. What we do not know for certain is whether there would be an increase if a total dose of 200 r were spread over many years. Be this as it may, however, any risk that there may be from such a dose appears to be within the range of risks of other kinds commonly incurred in industrial and professional life.

255. We consider, therefore, that an individual could, without feeling undue concern about developing any of the delayed effects, accept a total dose of 200 r in his life-time, in addition to radiation from the natural background, provided that this dose is distributed over tens of years and that the maximum weekly exposure, averaged over any period of 13 consecutive weeks, does not exceed 0·3 r. We recommend, however, that the aim should always be to keep the level of exposure as low as possible.

Internal radiation

256. The problem of irradiation by radioactive materials taken into the body is in some ways a more complex and difficult one. The material is often concentrated in a particular tissue, such as bone, where it may give rise to malignant change. Owing to the short distance that the rays from a particular concentration of radioactive material can penetrate the tissues, the dose of radiation is extremely variable from place to place in the body.

Nevertheless, on the basis of the known levels of external radiation that can be tolerated, and of experience gained from the accidental ingestion of substances such as radium, 'permissible' levels of exposure for a large number of radioactive isotopes have been agreed. No single level that comprehends them all can be given, since each isotope emits its own characteristic amount and type of radiation, dies away at its own rate, and is absorbed and excreted at a rate dependent on its chemical form and its method of entry into the body. However, it has now been possible to estimate for many different isotopes the concentrations that it is safe to accumulate.*

Dosage and Genetic Effects

257. Our conclusion in the chapter on genetics was that 'For levels of radiation up to the doubling dose, and even some way beyond, the genetic effects of radiation are only appreciable when reckoned over the population as a whole and need cause no alarm to the individual on his own account'. In other words they are essentially problems for society as a whole, to be assessed in terms of the load of medical care that may, in different circumstances, be imposed on the population.

258. In ordinary circumstances only a small fraction, perhaps one or two per cent, of the hereditary abnormalities which appear in a generation can be attributed to fresh gene mutations. For the offspring of any given parents the risk from increasing the mutation rate is very slight. Nevertheless, if the whole of a large population is exposed to enough radiation appreciably to affect mutation rates, an increase even in this small fraction may add up to a large number of new cases. However, it is only if members of an irradiated group or their descendants intermarry over several generations, and do not mate with the unirradiated population, that there is likely to be a disproportionately greater manifestation of hereditary defects among the descendants. Such an extreme degree of inbreeding is unlikely to occur. A fraction of the community can, therefore, without significant genetic risk to their progeny or harm to the population as a whole, receive doses of radiation which would be likely to have serious effects if applied to the whole population (see paragraphs 185-187).

259. From the genetic point of view, we have therefore to consider radiation dosage under three headings:

- (i) The dose which the individual can accept without undue concern about its possible effects on his own progeny.
- (ii) The dose which can be accepted by a fraction of the population whose occupation exposes them to more than the dose of radiation received by the ordinary member of the community.
- (iii) The dose which can be accepted by the whole population.

Dose to the individual in relation to genetic effects

260. We have concluded that doses up to, and somewhat beyond, the 'doubling dose' need cause no undue concern to the individual as regards his own offspring. Further, we gave reasons for believing that the values for the doubling dose of radiation for human genes may be, in general, in the range of 30 r to 80 r. We consider, therefore, that an individual could

* Precise data for a large number of isotopes are given, for example, in the Recommendations of the International Commission on Radiological Protection (1955) (*Brit. J. Radiol.*, N.S., Suppl. No. 6).

reasonably accept a total dose to the gonads of not more than 50 r from conception to the age of 30 years, in addition to that received from the natural background. There will be no undue risk to the offspring of parents over this age provided the rate of exposure laid down in paragraph 255 is not exceeded.

Dose to occupationally exposed groups

261. Similar considerations apply to groups of the community whose occupation exposes them to more than the usual dose of radiation. Provided that such groups do not in aggregate total more than one-fiftieth of our population, we consider that all their members could each safely receive a total gonad dose of up to 50 r from conception to the age of 30 years, in addition to that received from the natural background.

Dose to the whole population

262. In the chapter on genetics we tried to give an indication of the load on the community that might be imposed by a doubling of mutation rates. It will be generally agreed that such a load should not voluntarily be accepted. In relation to genetic changes in the whole population, the significant figure is the total gonad dose of radiation which is received by all those capable of reproduction. A relatively high dose to a fraction of the population can only be offset by a correspondingly low dose to the remainder. If, therefore, we are to contemplate the possibility—and the necessity to develop the beneficent uses of atomic energy and ionizing radiations forces us to do so—that a significant fraction of our population may in future be allowed to receive doses of radiation of a similar order to the doubling dose, then it becomes additionally important to ensure that the dose of radiation to the rest of the community shall be held at the lowest possible level.

263. In view of the inadequacy of present knowledge, however, we do not feel justified in naming any specific figure as a limit for the average exposure of the whole population. It is nonetheless highly desirable that such a figure should be named as soon as possible and we understand that the International Commission on Radiological Protection has this matter under consideration. In the meantime, we feel bound to state our opinion that it is unlikely that any authoritative recommendation will name a figure for a permissible radiation dose to the whole population, additional to that received from natural sources, which is more than twice that of the general value for natural background radiation. The recommended figure may indeed be appreciably lower than this; and we consider that those on whom rests the responsibility for authorising the development and use of sources of ionizing radiation would be well advised to keep this possibility in mind.

The Hazards from Radiation

264. In the light of these general criteria, we may now proceed to examine the various hazards, actual and potential, to which the population in a country like our own may be exposed in consequence of the increasing use of ionizing radiation. In doing so, it will be necessary to distinguish between the hazards of peacetime experience and those which may be encountered in war.

PEACETIME HAZARDS

265. The development of modern civilisation has led to the increasing use of processes which produce radiations. Its future progress will come to depend, to an ever increasing extent, upon their further exploitation in power production, in industry, in medicine and in agriculture, as well as in basic

scientific research. It would be impossible to abolish their use without denying ourselves services upon which we have already come to rely; and, in the future, nuclear energy will constitute a major, if not the most important, physical factor upon which our civilisation will depend. In assessing the hazards consequent upon its use, it is therefore necessary to maintain a sense of perspective and to weigh, as society has done in the case of steam-power, electricity and the internal combustion engine, the risks entailed against the advantages to be gained from the employment of this newer source of power. The risks are twofold: those to the individual and those to the population as a whole. In regard to the former, we may indicate our own assessment by saying that, in view of the small numbers likely to be employed in atomic power production and of experience already gained in the effectiveness of protective methods, it seems probable that a given amount of power might be made available to the community at a smaller cost in accidents, illness and disability than that involved in present methods of mining and power production. The novel aspect of the situation lies in the possible genetic risk to the community as a whole. The considerations which we have put forward suggest that, although this is at present small and seems unlikely ever to be large, it is potentially important. We propose now to indicate the relative hazards of particular uses and to point out where and how these may be expected to increase or should be curtailed.

266. In the chapter on exposure levels, the contributions of the various man-made sources of ionizing radiation to the total exposure were expressed as percentages of the radiation received from natural sources; and it was shown that today the population of this country receives, from man-made sources, a dose of radiation equivalent to at least one-quarter of that from the natural background. In itself this figure, which amounts to less than 1 r over a period of 30 years, can give rise to no immediate apprehensions; but its significance should not be disregarded. From the point of view of population genetics, all extra radiation is undesirable, and it is at least a portent that, in the half century following the discovery of ionizing radiation, man has increased his exposure levels by about 25 per cent. It does not therefore seem to be too early to suggest where the use of ionizing radiation might be restricted.

Medical diagnostic radiology

267. The greatest contribution in this country to the increased exposure to radiation comes from medical diagnostic radiology, the application of which has been steadily increasing in amount and scope in recent years. A large proportion of the genetically significant dose derived from diagnostic radiology is contributed by relatively few types of examinations, of which fluoroscopic and radiological examination of the female pelvis, and examinations of the hip joint and lumbar spine in males, are important examples. Clearly, the small genetic risk to the community and to individuals must be weighed against the possible great advantage and even necessity of the radiological examination to the particular patient. The final decision must be made on medical grounds. There can, however, be no doubt that the risk could in many instances be reduced, not only by a reduction of the actual number of examinations carried out on young people, but also by the use of modern methods of X-ray examination and by strict limitation of the X-ray beam to those parts of the body which have to be exposed. From the point of view of the dose distributed over the population as a whole, and from the point of view of the special risks to individuals associated with examinations involving heavy exposure, we are of the opinion that the time has arrived for a review of present practice in diagnostic radiology.

Radiotherapy

268. The dangers associated with the heavy exposures employed in radiotherapy are well recognised, and the illnesses for which it is used are usually so serious that the risks can be fully justified. In addition, many of the patients treated for cancer are of an age when the genetic risk will be small. Nevertheless, treatment by radiotherapy of certain non-malignant conditions, particularly in children, could with advantage be reconsidered from the point of view of reassessing the risks entailed against the benefits conferred.

269. The increasing use of therapeutic amounts of radioactive isotopes must also be carefully assessed and controlled, although at the present time the total used is probably of little practical significance from a genetical point of view. Should, however, their use become widespread in relation to common diseases of early or middle life, they might make a significant contribution. The risks from the use of 'tracer' amounts of radioactive substances in diagnosis and investigation are at present very small.

Occupational exposure : Atomic Energy Authority employees

270. For a number of years the main group of persons exposed to radiations were workers in the X-ray and radium departments of hospitals. Later, this experience was supplemented by careful observations of those employed in atomic energy projects and the various atomic industries. We have already seen that, as a result of all this experience, the maximum permissible level of radiation for workers was fixed at 0.3 r per week, and this figure is still regarded as a satisfactory working level provided that it is not maintained for years on end. There is, however, no large factor of safety in this figure and, as we have seen above, other limitations are needed for those exposed over very long periods of time. The excellent practice of the Atomic Energy Authority, now the main industrial employer of persons occupationally exposed to radiation, is shown by their record that the average exposure of their employees is less than half a roentgen yearly, and that their contribution to the population gonad dose is only about 0.1 per cent of that contributed by the natural background. These, however, are average doses; but, even if one takes the maximum exposure of those employees engaged in special tasks, this has only occasionally and for short periods approached the maximum permissible dose of 0.3 r per week. In view of the expected development of atomic energy as a source of power, this evidence of the awareness of the risk, and of the care with which it is being met, gives justifiable grounds for reassurance:

Radioactive effluents

271. Concern has been expressed about the possible emission from some nuclear reactors of radioactive particulate matter, which on inhalation might lodge in the lungs and give rise ultimately to cancer. This possible risk is well recognised and has been effectively dealt with.

272. Similar concern has been felt about the disposal of radioactive wastes. It is true that the amounts of radioactive material involved are formidable, but by treatment, by long-term storage to allow of decay, by concentration to relatively small bulk and subsequent burial in sealed containers or disposal in the depths of the ocean, there seems no reason to doubt that this problem can continue to be solved. In this country strict control of the hazard is exercised by legislation.

Occupational exposure : hospital employees

273. The handling of large quantities of radioactive isotopes in the treatment and investigation of patients in hospitals raises many difficult problems

but, with adequate care and training of the workers concerned, experience shows that the doses received can be kept down to one-tenth or less of the maximum permissible levels.

274. In this country a code of practice, formulated by the Ministry of Health on the advice of the Medical Research Council, has been drawn up for the National Health Service. This lays down the relevant permissible levels of exposure as well as giving instructions and suggestions for the implementation of these in practice.

Other industrial employees

275. The control of radiological hazards in non-atomic industry will be more difficult to codify owing to the wide variety of circumstances in which ionizing radiations are used. Measurements of the doses received by many workers are made periodically, but it is difficult to avoid the impression that industrial personnel are, in general, less aware of the hazards of radiation than those engaged in the fields of medicine and atomic energy. The record of the Atomic Energy Authority shows the standard that is attainable and the practicability of being satisfied with nothing less.

Definition and review of safety standards

276. All these problems are under close and continuous scrutiny. Expert national committees, notably those of the Medical Research Council and Ministry of Health, work in close conjunction with international bodies such as the International Commission on Radiological Protection (itself associated with the World Health Organization), so that a wealth of experience is brought to bear on all these problems, and the standards of safety are under constant review.

Miscellaneous sources of radiation

277. There are several other sources of radiation which at present contribute only very small amounts but which cannot be disregarded. The practice of routinely examining the feet by X-rays when fitting shoes is of dubious value and, in view of the possibilities of multiple exposures to children, may even be dangerous. On the basis of avoiding any unnecessary exposure, it is in our view hardly justifiable. We hope that the procedure will be abandoned, except when prescribed for orthopaedic reasons.

278. The contribution of radiation from watches and clocks with luminous dials is also small but real. The main hazard is to workers in the luminising industry but the risk from the widespread use of such instruments is not entirely negligible. We recognise that there are circumstances which require the use of instruments with self-luminous dials. For the majority, however, there is no such necessity and their wider use constitutes an avoidable, if small, risk which could be minimised for all concerned if the amount of radioactive material in these instruments was reduced to the lowest possible level.

279. It has been recognised that television sets give rise to very small amounts of X-rays, but at the present time radiation from this source does not constitute either a personal or a significant genetic hazard. This applies to domestic sets working at normal operational voltages but, near special types of high voltage projection equipment used commercially, the radiation may reach significant levels, although it is improbable that in practice any operator would be appreciably exposed. Nevertheless, the possibility of television equipment giving rise to radiations should be borne in mind when

considering the design and operation of such instruments. So far as sets used by the general public are concerned, most of the radiation is normally absorbed in the apparatus itself and is insignificant at the usual viewing distances.

Test explosions of nuclear weapons

280. It is impossible to explode a nuclear weapon without liberating radioactive matter into the atmosphere. As described in the chapter on exposure levels, the radioactive material diffuses all over the world and in the course of time is gradually deposited on the surface of the earth and comes into contact with human beings. Continuation for an indefinite time of testing at the same rate as over the last few years would gradually increase the contamination of the atmosphere, until in about 100 years time the average individual in this country would receive a dose of external radiation to the gonads of 0.026 r in 30 years of his life, an amount which represents only one per cent of that received from the natural background. The individual and genetic effects of such a dose of external radiation would be insignificant.

281. Account must be taken, however, of the particular hazard from radioactive strontium in the fall-out. The maximum permissible level of strontium 90 in the human skeleton, accepted by the International Commission on Radiological Protection, corresponds to 1000 micro-microcuries per gramme of calcium. But this is the maximum permissible level for adults in special occupations and is not suitable for application to the population as a whole or to children with their greater sensitivity to radiations and greater expectation of life. It is known that radiostrontium is more heavily concentrated in the bones of young than of adult animals, and the few measurements on human bones indicate that at the present time those of children contain about ten times the concentration found in those of adults. We consider, therefore, that the maximum allowable concentration of radiostrontium in the bones of the general population, with its proportion of young children, should not be greater than 100 micro-microcuries of strontium 90 per gramme of calcium.

282. In this country, measurements on human bones of the radiostrontium content, derived from the nuclear explosions that have already occurred, show that the irradiation from this source is now reaching about one-thousandth of the maximum permissible occupational level; and calculation of the fall-out likely to come, if the present rate of firing continues, suggests that this level may be increased ten-fold in the course of several decades. The present level would produce no detectable increase in the incidence of ill-effects. It is evident, however, that we are now accumulating radiostrontium at an appreciable rate and that a close watch will need to be kept on this increase.

283. In the light of knowledge at present available, we should feel that immediate consideration were required if the concentration in human bones showed signs of rising greatly beyond one-hundredth of that corresponding to the maximum permissible occupational level.

284. We are well aware of the inadequacy of our knowledge of the biological effects of radioactive strontium and of the urgent necessity to obtain further information. Nevertheless, recognising all the inadequacy of our present knowledge, we cannot ignore the possibility that, if the rate of firing increases and particularly if greater numbers of thermonuclear weapons are fired, we could, within the life-time of some now living, be approaching levels at which ill-effects might be produced in a small number of the population.

PEACETIME HAZARDS: GENERAL CONCLUSIONS

285. The general conclusion to be drawn from a consideration of the hazards inseparable from the application of ionizing radiations in peacetime is that at present there is no cause for alarm; but that, as all such radiations are potentially dangerous, their use should be the subject of constant and close scrutiny, and that adequate justification should be required for their employment on however small a scale. There is a limit to the amount of radiation which any population or any individual can accept and we cannot afford to expend, without careful forethought, the margin which is now available to us.

WARTIME HAZARDS

286. We have given a brief résumé of the effects of nuclear warfare. From this it will be seen that there are three broad categories of effect: those within the range of the actual explosion, those within the contiguous area in which radioactive fission products settle, and world-wide effects due to the contamination of the atmosphere.

287. Within close range of the explosion, nuclear radiations are but one element in the destructive effect. Blast and heat would be of major and probably of more immediate importance in producing casualties but survivors, unless heavily sheltered, would have been exposed to such an intensity of radiation that they would be at risk of developing each and all of the effects that we have described.

288. Explosions of atomic weapons always give rise to radioactive fission products, the heavier particles of which settle in the vicinity. With a ground burst of a thermonuclear weapon, the area of intense fall-out may cover hundreds of square miles. Within this area, those who were not in shelter, and did not remain under cover until the radioactivity of the fall-out had decayed substantially, would be exposed to intensities of radiation sufficient to produce the effects described in all grades of severity. Outside this area, there would be another zone, measured in thousands of square miles, where significant intensities of radiation would occur and where a proportion of those exposed would be at risk of serious consequences.

289. It must be emphasised that these doses, from the point of view both of the individual and of the general population, are several thousand times greater than those we have considered as possible peacetime hazards.

290. The importance of the effects of atomic warfare which would be relayed through contamination of the atmosphere to parts of the world remote from the actual conflict, would depend upon the number and type of bombs exploded. Given a sufficient number of bombs, no part of the world would escape exposure to biologically significant levels of radiation. To a greater or less degree, a legacy of genetic damage would be incurred, and an increased incidence of delayed effects on the individual would probably be induced. Although it is difficult to imagine the general occurrence of radiation intensities which would eliminate the entire human race, atomic warfare on a large scale could not fail to increase for many generations the load of distress and suffering that individuals and all human societies would be called upon to support.

CHAPTER VII

SUMMARY

291. The future development of civilisation is bound up with the exploitation of nuclear energy. Its use, like that of other sources of energy, entails risk, but the risk is controllable and, within limits, can be accepted. It is the scale and not the nature of the hazard that is new, for human populations have always been exposed to natural radiation of low intensity. (Paragraphs 1-14.)

THE NATURE OF RADIATION AND ITS ACTION ON LIVING CELLS

292. Ionizing radiations are so described because they cause the formation of electrically charged particles, ions, in the matter through which they pass. The common types of penetrating radiation are X-rays, gamma rays, alpha and beta particles, and neutrons. Alpha particles cannot penetrate tissue beyond a fraction of a millimetre but gamma rays, and X-rays produced by extremely high voltages, can traverse the whole body. (Paragraphs 15-20.)

293. The biological effects of radiation are related to the intensity of radiation and to the period of exposure. The basic unit of radiation dosage which has been generally used is the roentgen (r). All living tissue can be killed if exposed to sufficiently high doses of radiation. The effects of dosages below those which damage tissues irretrievably may be modified by processes of healing, so that the response to a dose of radiation which is spread over a long time may be much smaller than, or quite different from, the response which would occur if the same dose were given in a very short time. This does not apply to the important type of genetic effect, called gene mutation, produced by the irradiation of reproductive cells, the consequences of which are cumulative and irreversible. (Paragraphs 21-27.)

THE EFFECTS OF RADIATION ON THE HEALTH OF THE INDIVIDUAL

Sources of information

294. Our knowledge of the effects of ionizing radiations on human beings comes from four main sources: from the uses of X-rays and radium in the treatment of disease, mainly of cancer; from a study of the occupational hazards of medical radiologists, workers in the luminising industry, and miners of radioactive ores; from a study of the victims of atom bomb explosions; and from experiments on animals. (Paragraphs 28-34.)

The harmful effects of radiation on man

295. Almost all the effects of ionizing radiation on tissues are essentially deleterious. The benefits to the individual patient of the eradication of a malignant tumour by radiotherapy result from selective damage to the tumour cells. The nature and severity of radiation injury is determined by the type and dosage of radiation received, the part and extent of the body irradiated, the length of the period of exposure, and the age of the persons exposed. The harmful effects may be classified into those which develop within a few weeks of exposure, and delayed effects which may not make their appearance until many years after exposure. (Paragraphs 35-42.)

Effects occurring within a few weeks of exposure

296. The effect of exposing the whole body to a single dose of gamma radiation of the order of 500 r is such that all the persons so exposed would develop acute illness and at least half would die. In civil life, exposure to such a dosage could occur only under the most exceptional circumstances. With smaller single doses, for example of 100 r, not more than 15 per cent of an exposed population would suffer acute illness and very few, if any, of those affected would die. After a single dose of 50 r, acute illness would be very rare. The relationship between the dose of radiation received and the effects that may be produced within a few weeks of exposure is not one of strict proportionality; with each successive and equal increment of dosage the response increases by a progressively greater amount, at least until very large changes have been produced. (Paragraphs 43-50.)

The delayed effects of radiation

297. Delayed effects of exposure to radiation may occur at any time after the end of the second month. Disorders of the skin and underlying soft tissues and of bone may occur and there may be subsequent development of cancer. Cataracts, severe anaemias and leukaemia have been caused and there is evidence from animal experiments that exposure to radiation may cause death at a prematurely early age. (Paragraphs 51-52.)

Leukaemia

298. Leukaemia is a disease in which there is an uncontrolled over-production of white blood corpuscles. Experiments on animals have shown that the incidence of leukaemia is increased by irradiation. Clear evidence that the same is true of man comes from two main sources: a study by the Atomic Bomb Casualty Commission of the incidence of leukaemia in Hiroshima and Nagasaki, and a survey under our sponsorship of the incidence of leukaemia among patients treated by radiation for ankylosing spondylitis. (Paragraphs 53-55.)

299. Ninety-one proven and fourteen suspected cases of leukaemia have been recorded in Hiroshima and Nagasaki between 1947 and 1954 among those present at the time of the explosion and still resident in the cities; the expected incidence in an unexposed but otherwise comparable population is twenty-five. The difference is greater than would be attributed to chance. Moreover, there was a much higher frequency of occurrence among those who had developed early acute radiation illness and among those who had been nearer to the centre of the explosion. The latent period, that is the average length of the period between the explosion and the first appearance of symptoms of leukaemia, was about six years. The evidence suggests that with this type of exposure to radiation the likelihood of developing leukaemia, after its initial rise, remains approximately constant up to at least the ninth year. (Paragraphs 56-61.)

300. Ankylosing spondylitis is a disease in which the joints, particularly those of the spine, progressively lose their freedom of movement. In the treatment of this condition very extensive areas of the body are exposed to irradiation. The records of between 13,000 and 14,000 patients, who had been treated with X-rays between 1933 and 1954, have been studied. Up to 1955, thirty-eight of these patients developed leukaemia, an incidence which, although only about one-third of one per cent, is about ten times greater than the normal expectation. No increased incidence of leukaemia was found among 400 patients who had not been treated by irradiation, but the number is too small to exclude completely the possibility that ankylosing spondylitis

may of itself predispose its sufferers to leukaemia; nor can the possibility be excluded that these patients are more liable than the average person to develop leukaemia after irradiation. Nevertheless, there is clear evidence of a correspondence between the dosage of radiation received and the incidence of leukaemia. The average length of the latent period between the first exposure to X-rays and the diagnosis of leukaemia was about six years.

(Paragraphs 62-69.)

301. The conditions of exposure to radiation in Hiroshima and Nagasaki, and in the treatment of ankylosing spondylitis, are not comparable with the irradiation in small doses over long periods which might be received by persons engaged in work with a possible radiation hazard. Some evidence has been presented suggesting an increased death rate due to leukaemia among radiologists but our knowledge of the occurrence of leukaemia under conditions of chronic exposure is too scanty to allow any reliable conclusions to be drawn.

(Paragraphs 70-71.)

Cancers

302. Two characteristics of cancers induced by radiation are noteworthy: the tendency of tumours to arise in tissues already severely damaged by radiation, and the long latent period, twenty years or more, before they appear.

(Paragraph 72.)

303. A study of the pitchblende miners of Schneeberg and Joachimsthal suggests strongly that inhalation of the radioactive gas radon may lead to cancer of the lung. The latent period has been put at seventeen years and the dosage to the lungs over that period at about 1000 r and in some parts of the lung much higher. In theory, the inhalation of radioactive particles in the fall-out from atomic explosions or in the vicinity of nuclear reactors could also lead to cancer of the lung, but the former hazard is extremely unlikely in peacetime, and steps are always taken to ensure that the latter does not occur.

(Paragraphs 73-76.)

304. Radium, mesothorium, plutonium and radioactive forms of strontium are accumulated by and retained in bone. Until the enforcement of stringent controls, cancer of bone occurred among workers in the luminising industry as a result of swallowing radium-containing paint. The latent period was more than fifteen years.

(Paragraphs 77-82.)

305. Cancer of the skin was the earliest form of radiation-induced tumour to be described in man. By 1911, before the adoption of modern safeguards, fifty-four cases had been described among the pioneers of radiology. The doses of radiation which have led to the formation of skin cancers must have been several thousand r.

(Paragraphs 83-84.)

306. Cancer of the thyroid gland in children has been a sequel to irradiation of the neck for enlargement of the thymus gland. This form of cancer is distinguished by its short latent period (about 7 years) and the comparatively low dosage of radiation required to induce it. However, it is not unlikely that other factors are involved here in addition to the direct effect of irradiation.

(Paragraphs 85-86.)

Other delayed effects

307. A fall in the number of red cells and white cells in the blood may follow exposure of the whole body to even moderate doses of gamma radiation. If not detected in time a condition known as aplastic anaemia may occur.

(Paragraphs 87-88.)

308. Cataract formation is known to have been caused by neutron irradiation, but for all practical purposes the production of cataract by X-rays is not an occupational hazard. (Paragraphs 89-90.)

309. Delayed effects of radiation on the skin extend from a temporary loss of hair after local dosages of 300r-400r to severe and permanent damage after local exposure to single dosages of 1500r or more, or to repeated doses totalling 4000r or more in a number of weeks. It is in the skin damaged by these higher doses of radiation that tumours, when they occur, are most likely to develop. (Paragraphs 91-92.)

310. Miscarriage and stillbirth may be a consequence of irradiation during pregnancy, but they do not constitute a problem unless the dose of radiation is large. A number of different developmental abnormalities have been described in the children of women treated by irradiation during pregnancy, the most conspicuous defect being microcephaly, a partial failure of the development of the brain. Eleven cases so classified are recorded in children irradiated before birth in Hiroshima and Nagasaki.

(Paragraphs 95-97.)

THE GENETIC EFFECTS OF RADIATION

311. The assessment of the genetic effects of ionizing radiations is subject to special difficulties. We believe that we have formed as fair an assessment as is possible in the light of present knowledge, but our conclusions must be regarded as provisional. (Paragraph 100.)

The material basis of heredity

312. The physical determinants of heredity are genes, carried on chromosomes in the nuclei of cells. Chromosomes are present in pairs; one member of the pair is of maternal origin, the other of paternal origin. There are twenty-four pairs of chromosomes in human beings; the number of genes is not known, but may well be many thousands. (Paragraphs 101-103.)

313. The two genes which occupy corresponding positions on the two chromosomes of a pair are spoken of as alleles of each other. Alleles of different kinds arise by the process of mutation and are thereafter reproduced faithfully in their altered form. (Paragraph 104.)

314. Some genes produce the same effect whether they are paired with like or with unlike alleles. Such genes, and the characters they determine, are described as dominant. Other genes produce a noticeable effect only when paired with similar alleles; these, and the characters they determine, are described as recessive. There is every gradation between these two extremes. A recessive gene can be transmitted in a family by an individual who gives no signs of carrying it. (Paragraphs 105-108.)

315. Sex difference is determined by a special pair of chromosomes, and the genes carried on these chromosomes are said to be sex-linked. (Paragraph 109.)

316. So far as is known, all genes are subject to mutation, and mutation occurs spontaneously all the time at a very low rate. Factors influencing mutation appear to affect only the frequency with which it happens. New alleles of harmful effect are eliminated by natural selection until equilibrium is reached with the rate at which they are introduced by fresh mutation. Recessive alleles are eliminated much more slowly than dominant alleles. (Paragraphs 111-118.)

Basic principles of the genetic effects of radiation

317. There is little direct knowledge of the genetic effects of ionizing radiations on man, but with certain reservations it is justifiable to draw upon our knowledge of the effects of radiation on other organisms.

(Paragraph 119.)

318. Ionizing radiations have genetic consequences only in so far as they affect the reproductive cells or the cells ancestral to them in the reproductive organs (gonads). Two kinds of effect may have genetic consequences: the chromosomes may be damaged or the genes may be caused to mutate more frequently. Chromosome changes of the kind that can persist are only rarely produced by long continued exposure to X-rays or gamma rays of low intensity. They are likely to be a comparatively unimportant radiation hazard.

(Paragraphs 120-125.)

319. It is the frequency of gene mutation that is increased by radiation; there is no evidence and little likelihood that radiation produces entirely new kinds of genes. The rise in mutation rate is probably directly proportional to the amount of additional exposure to radiation, and any additional exposure, however small, must be expected to raise the mutation rate, if only by a minute amount.

(Paragraphs 126-127.)

320. Damage to genetic material is cumulative and irreparable. Long continued exposure to radiation of low intensity induces as much gene mutation as a single exposure to an equal dosage of radiation of higher intensity.

(Paragraph 128.)

321. The age-distribution of those exposed to radiation has an important bearing on the future consequences of its effects. The genetic consequences of the irradiation of individuals beyond the age of reproduction are of course nil.

(Paragraph 129.)

Effects of increased mutation on the incidence of disease in human populations

322. The role of heredity in the production of disease ranges from that of a predisposing to that of a preponderating cause. The effects which might be expected to result from an increase in mutation rates can most easily be calculated for diseases known to be caused by single genes, but for relatively few such diseases have we sufficient evidence of the kind upon which such a calculation must be based.

(Paragraphs 130-135.)

323. Achondroplasia, haemophilia, and phenylketonuria have been taken as examples of diseases believed to be caused by single genes. If the mutation rates of these genes were to rise to, and remain at, twice their present values, the incidence of the diseases for which they are responsible would ultimately, though at very different rates, rise to nearly twice their present frequencies. Calculations suggest that the incidence of achondroplasia, a dominant form of dwarfism, would rise 80 per cent above its present value in a single generation; haemophilia, a sex-linked disease, would take about six generations to rise by 90 per cent in frequency; and phenylketonuria, a recessive disease associated with severe mental deficiency, would take more than fifty generations to increase its frequency by one half.

(Paragraphs 136-139.)

324. Mental diseases, the most important single category in which hereditary causes are known to be important, account in all for nearly half the hospital beds provided in this country. There are grounds for believing that a doubling of the mutation rates of the genes concerned with their causation would, in one generation, increase the frequency of low-grade mental deficiency by three per cent, and of the two principal types of mental illness,

schizophrenia and manic depressive reaction, by about one per cent. If the mutation rates were to remain at twice their present values, the incidence of mental diseases might on the most pessimistic assumptions double also, but would only attain this value after very many generations.

(Paragraphs 140-150.)

325. When all serious illnesses with a hereditary element in their causation are taken into account, it is unlikely that the burden put upon society by a doubling of mutation rates would exceed by more than a few times the contribution made by the increase of mental disease.

(Paragraphs 151-154.)

326. It must be remembered that a harmful recessive gene gives no outward evidence of its presence until chance brings it together with another of its kind. The crop of newly mutated recessive genes caused by an increase of mutation rates could cause suffering over many generations.

(Paragraphs 155-156.)

Hereditary traits showing continuous variation about the normal

327. Most of the variation between human beings is not of the sharp kind that can be traced to the action of single genes. Characters such as physique, intelligence and length of life vary over a wide range by imperceptible gradations, and the hereditary portion of this variation is believed to be due to the combined action of many genes.

(Paragraphs 157-159.)

328. The basic effect of an increase in mutation rates upon such characters, here exemplified by scores in intelligence tests, will be to increase the numbers of the more extreme types at the expense of the more average individuals. A doubling of the mutation rates for a few generations would be expected to have only the most trivial effect upon their variation. The effect of a permanent doubling of the mutation rate would be, at most, to double the variation, and this would take hundreds of generations to achieve.

(Paragraphs 160-161.)

Observations on populations exposed to radiation

329. Three direct studies have been made on the children of human beings who have been exposed to ionizing radiations. Two, on the children of American radiologists, were for a variety of reasons inconclusive; the third is the extensive study made by the Atomic Bomb Casualty Commission on the children of those who were in Hiroshima and Nagasaki when the atomic bombs exploded. All three studies are limited to observations on the first generation, so that little genetic effect would yet have become manifest even if the mutation rate had increased.

(Paragraphs 162-166.)

330. The evidence assembled in the report of the Atomic Bomb Casualty Commission is beset by many difficulties of interpretation, but we believe that it reveals, in the children of those who were the more heavily exposed, a slight but significant change in the sex ratio at birth which might be due to genetic damage. From the nature of the evidence a doubling of the rate of incidence of congenital malformations, or a 50 per cent rise in the stillbirth rates, might have escaped detection if either had occurred. The evidence does not allow us to make any useful estimate of the radiation dose which doubles the mutation rate in man.

(Paragraphs 167-170.)

The 'doubling dose' in man

331. An assessment of the sensitivity of human genes to radiation is particularly difficult. Any such estimate should be based upon a sample of genes large enough to be representative of all the effects they exercise, for it cannot be assumed that all genes are equally radiosensitive, nor that the

proportion of the spontaneous mutation rate which can be attributed to natural radiations is the same for different genes. (Paragraphs 171-175.)

332. If all mutations were indeed due to radiation, then the dosage which doubled their frequency would be expected to be equal to that received from natural sources, namely, a dosage to the gonads of about 3 r in thirty years. The available evidence suggests, however, that the percentage of human mutations that are caused by natural radiation might lie between 2 per cent and 20 per cent, and if this is so the doubling dose will lie between 15 r and 150 r. (Paragraphs 176-181.)

333. The direct estimates which have been made of the doubling doses for a variety of plants and animals mostly run from 25 r upwards. It is true that none of the more fully investigated organisms has a lifetime comparable with man's, but there are theoretical grounds for believing that the organisms with the longer pre-reproductive periods might be expected to have the less radiosensitive genes. (Paragraph 182.)

334. The evidence at our disposal, though far from adequate, leads us to conclude that there is rather little likelihood that the real value for the doubling dose for human genes lies between 3 r and 15 r; and that, although we cannot exclude the possibility that for some human genes the doubling dose may be less than 30 r and for others more than 80 r, the best estimate that we can make in the light of present knowledge, is that the value in general lies somewhere between 30 r and 80 r. (Paragraph 183.)

335. Even if the doubling dose were as low as the minimum we can reasonably entertain, namely 15 r, it is extremely improbable that in times of peace more than a small fraction of the population could receive an extra dose of this size. The prevalence of naturally-occurring hereditary abnormalities is such that, if comparatively few individuals received such a dose, there would be no noticeable effect on their immediate offspring or on their descendants even over several centuries. For levels of radiation up to the doubling dose, and even some way beyond, the genetic effects of radiation are only appreciable when reckoned over the population as a whole, and need not cause alarm to the individual on his own account. (Paragraphs 184-188.)

EXISTING AND FORESEEABLE LEVELS OF EXPOSURE TO RADIATION

336. Doses of radiation which are of no known significance to the individual may have genetic consequences. Exposure levels must therefore be expressed in terms of the total dosage to the gonads received by the population as a whole during the period of reproductive life.

(Paragraphs 189-191.)

Radiation from natural sources

337. The natural sources of radiation are cosmic rays and the naturally-occurring radioactive elements. From all such sources an individual in this country receives, on the average, a total gonad dose of about 3 r over a period of thirty years. (Paragraphs 192-201.)

Radiation from the appurtenances of civilisation

338. Over the past sixty years man has made increasing use of X-rays and radioactive materials in medicine, industry, and ordinary civil life. The additional gonad doses received from these sources by people of this country are expressed as percentages of the gonad dose which they already receive from natural sources. (Paragraph 202.)

339. We have conducted a limited survey which suggests that the additional dose received from the various forms of diagnostic radiology may well

be higher than 22 per cent, the major amount of which is accounted for by examination of a relatively few sites of the body. The contribution made by the use of radiation in medical treatment cannot be accurately estimated; it is probably much less than that made by diagnostic radiology but greater than that received from any other artificial source.

(Paragraphs 203-206.)

340. Watches and clocks with radioactively luminous dials contribute about one per cent of additional radiation. X-rays from television sets account for much less than one per cent. The contribution from X-ray apparatus used in shoe-fitting is not likely to exceed 0·1 per cent. (Paragraphs 207-210.)

341. The contribution arising from the work of the Atomic Energy Authority is the most accurately known, and is about 0·1 per cent. A study of the records of the National Radiological Protection Service has put the contribution from other occupational sources at about 1·6 per cent.

(Paragraphs 212-217.)

Contamination of the world by fall-out from the explosion of nuclear weapons

342. Continual watch is kept by the Atomic Energy Authority on the radioactive fall-out reaching this country from nuclear devices exploded in other parts of the world. From the bombs exploded up to the present time, the population of this country may expect to receive, over the next fifty years, additional radiation amounting to between 0·02 per cent and 0·04 per cent of the radiation which will be received over the same period from natural sources. (Paragraphs 218-229.)

343. If the firing of bombs were to continue indefinitely at the same rate as over the past few years, radioactivity would gradually accumulate to a level at which an inhabitant of this country would receive an average dose of 0·026 r over a period of thirty years, or about one per cent of that which he would receive in the same period from natural sources.

(Paragraph 230.)

344. The contribution to this figure from thermonuclear explosions, relative to their numbers, is very great. If the rate of firing of weapons of this type increases, exposure to radiation will be significantly raised. (Paragraph 231.)

Special hazards of radioactive fission products

345. It is unlikely that the inhalation of radioactive particles present in the air as a result of fall-out would constitute a problem in ordinary civil life. (Paragraphs 232.)

346. The deposition of radioactive strontium is probably a greater hazard, because it is soluble and, if ingested, is deposited and retained in bone. Measurements which have been made of radioactive strontium in bone show that the highest levels are at present about a thousand times less than is considered permissible for those who are occupationally exposed.

(Paragraphs 234-239.)

Atomic war

347. Atomic bombs were developed for their capacity to create blast, but for persons exposed in the open the heat flash is equally to be feared. The ionizing radiations produced immediately after explosions have a much greater penetrating power than the heat rays, but the range at which they cause death or immediate injury is somewhat less. The hazard from radiations is therefore only one of the immediate effects of atomic explosions. Their peculiar danger lies in their distant and delayed effects.

(Paragraphs 241-246.)

ASSESSMENT OF THE HAZARDS OF EXPOSURE TO RADIATION

348. An attempt is made to assess the medical and genetic consequences of exposure to radiation at the levels of dosage which occur now or which might conceivably come about. The naturally occurring level of radiation can be accepted as a standard of reference, because it is a level to which mankind has long been adjusted. (Paragraphs 247-248.)

349. In considering the genetic effects of radiation, we are concerned with the sum, over the whole population, of the total gonad dose received by its members from conception until the end of reproductive life. (Paragraphs 249-250.)

350. In considering the effects of radiation upon the individual, we are concerned with his whole span of life, and with the rate at which the radiation is received as well as with its total dosage; and we must have regard to the possibility that the severity of the effects produced by radiation may increase in more than equal proportion to the dosage that is received. (Paragraph 251.)

Dosage and effects on the individual

351. The acute effects of radiation which appear within two months of exposure to a single dose or a few heavy doses do not enter into ordinary civil calculations; nor is it feared that they may be produced by repeated exposures to doses that do not exceed 0.3 r per week. (Paragraphs 252-253.)

352. Of the delayed effects of irradiation of the whole body, leukaemia is probably the most easily induced. We consider that an individual could, without feeling undue concern about developing any of the delayed effects, accept a total dose of 200 r in his life-time, additional to that received from the natural background, provided that this dose is distributed over tens of years and that the maximum weekly exposure, averaged over any period of 13 consecutive weeks, does not exceed 0.3 r. We recommend, however, that the aim should always be to keep the level of exposure as low as possible. (Paragraphs 254-255.)

Dosage and genetic effects

353. The genetic effects of radiation are essentially problems concerning the future welfare of the population as a whole. (Paragraph 257.)

354. It follows from the nature of the genetic effects of radiation that a small fraction of a population can, without harm to its members, receive dosages of radiation which would be likely to have serious genetic effects if applied to the population as a whole. We feel that an individual, considered as such, can accept a total gonad dose of not more than 50 r, from conception until the age of thirty, additional to that received from the natural background, without undue concern for himself or his offspring, but that the number of such individuals should not exceed one-fiftieth of the population as a whole. (Paragraphs 258-262.)

355. Our present knowledge does not justify us in naming any specific figure as a limit for the average dose of radiation which might be received by the population as a whole. It is highly desirable that such a figure should be named as soon as possible; and we understand that the International Commission on Radiological Protection has this matter under consideration. In the meantime, we feel bound to state our opinion that it is unlikely that any authoritative recommendation will name a figure for permissible radiation dose to the whole population, additional to that received from the natural background, which is more than twice that of the general value for natural background radiation. The recommended value may, indeed, be appreciably lower than this. (Paragraph 263.)

The peacetime hazards from nuclear radiation

356. Nuclear energy may become the principal source of power. So far as its use affects the small numbers likely to be employed in its production, we believe that nuclear energy might make power available at a lower cost in accidents, illnesses and disability than that incurred in connexion with other sources of power. What is novel in the use of nuclear energy and the other, increasing, uses of processes producing radiations is the genetic risk to the community as a whole. The risk from civil usage is at present small, and seems unlikely ever to be large; but from the point of view of population genetics all possible extra radiation should be avoided, and it is not now too early to suggest where we might restrain its use.

(Paragraphs 265-266.)

357. With regard to occupational exposure we consider that the record of the Atomic Energy Authority shows the standard that is attainable and the practicability of being satisfied with nothing less. (Paragraphs 270-276.)

358. We consider that the time has come for a review of present practice in diagnostic radiology, and of certain uses of radiation in the treatment of non-malignant conditions, particularly in children. Among the less important sources of radiation, we hope that the use of X-rays in shoe-fitting will be abandoned except when prescribed for orthopaedic reasons; that watches and clocks with radioactively luminous dials will be confined to necessary uses; and that the X-ray hazard from television tubes, at present negligible, will be borne in mind if special types of high voltage equipment come to be widely used.

(Paragraph 267-269 and 277-279.)

Test explosions of nuclear weapons

359. The genetic effects to be expected from present or future radioactive fall-out from bombs fired at the present rate and in the present proportion of the different kinds are insignificant. They might not be so, if present rates of firing were increased and particularly if a greater number of thermonuclear weapons were tested.

(Paragraph 280.)

360. So far as radioactive fall-out may affect the individual, we believe that immediate consideration would be required if the concentration of radioactive strontium in bone showed signs of rising greatly beyond that corresponding to one-hundredth of the maximum permissible occupational level.

(Paragraphs 281-284.)

Wartime hazards

361. The area in which a greater or lesser proportion of those exposed would be at serious risk from the radioactivity released by the ground burst of a thermonuclear weapon is measured in thousands of square miles. If a sufficient number of nuclear weapons were exploded, no part of the world would escape biologically significant degrees of exposure or the load of distress and suffering to individuals and society which such exposure would entail.

(Paragraphs 286-290.)

CHAPTER VIII

CONCLUSIONS

362. On the basis of the considerations in this report we feel justified in drawing the following conclusions in relation to the use of ionizing radiations in peacetime :

1. Limitation of the use of all sources of radiation

Adequate justification should be required for the employment of any source of ionizing radiation on however small a scale.

2. Dose levels to the individual

(a) In conditions involving persistent exposure to ionizing radiations, the present standard, recommended by the International Commission on Radiological Protection, that the dose received shall not exceed 0·3 r weekly, averaged over any period of 13 consecutive weeks, should, for the present, continue to be accepted.

(b) During his whole lifetime, an individual should not be allowed to accumulate more than 200 r of "whole-body" radiation, in addition to that received from the natural background, and this allowance should be spread over tens of years; but every endeavour should be made to keep the level of exposure as low as possible.

(c) An individual should not be allowed to accumulate more than 50 r of radiation to the gonads, in addition to that received from the natural background, from conception to the age of 30 years; and this allowance should not apply to more than one-fiftieth of the total population of this country.

3. Dose level to the population

Those responsible for authorising the development and use of sources of ionizing radiation should be advised that the upper limit, which future knowledge may set to the total dose of extra radiation which may be received by the population as a whole, is not likely to be more than twice the dose which is already received from the natural background; the recommended figure may indeed be appreciably lower than this.

4. Fall-out from test explosions of nuclear weapons

(a) The present and foreseeable hazards from external radiation due to fall-out from the test explosions of nuclear weapons, fired at the present rate and in the present proportion of the different kinds, are negligible.

(b) Account must be taken, however, of the internal radiation from the radioactive strontium which is beginning to accumulate in bone. At its present level, no detectable increase in the incidence of ill-effects is to be expected. Nevertheless, recognising all the inadequacy of our present knowledge, we cannot ignore the possibility that, if the rate of firing increases and particularly if greater numbers of thermonuclear weapons are used, we could within the life-time of some now living, be approaching levels at which ill-effects might be produced in a small number of the population.

5. Recommendations regarding specific uses of radiation

(a) All sources of radiation, both medical and industrial, should be under close inspection, in order to ensure that the high standards of protection now

attainable against the absorption of ionizing radiations, and against radioactive materials, are generally observed. Those using radiations should be instructed in the precautions to be taken, and no unnecessary or unauthorised person should be allowed to engage in such occupations. A personal record, not only of doses of radiation received during occupation but also of exposures from all other sources, such as medical diagnostic radiology, should be kept for all persons whose occupation exposes them to additional sources of radiation.

(b) Present practice in medical diagnostic radiology should be reviewed, with the object of clarifying the indications for the different special types of examination now being carried out and defining more closely, both in relation to the patient and to the operators, the conditions which should be observed in their performance.

(c) The uses of radiotherapy in non-malignant conditions should be critically examined.

(d) The small amounts of irradiation from miscellaneous sources, such as X-ray machines used for shoe-fitting, luminous watches and clocks, and television apparatus, should be reduced as far as possible.

6. Collection of vital statistics

As an essential basis for future studies of the genetic effects of radiation, further data are required on the genetic structure of human populations; to this end, there is an urgent need for the collection of more detailed information, when births, marriages and deaths are registered.

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APPENDIX A

The Incidence of Leukaemia among the Survivors of the Atomic Bomb Explosions at Hiroshima and Nagasaki

Information concerning the cases of leukaemia which are known to have occurred among the survivors of the atomic bomb explosions at Hiroshima and Nagasaki has been supplied by the Atomic Bomb Casualty Commission of the National Research Council of the U.S.A. By the end of August 1955, the diagnosis of leukaemia had been confirmed in 125 patients; in all these cases blood smears and, when necessary, bone-marrow and autopsy material, had been examined by a member of the Commission's staff. In 18 other cases, the diagnosis was suspected but the evidence was less conclusive; and in a further 5 the diagnosis was still under review.

Sixty-one of the confirmed and four of the suspected cases occurred among persons resident in Hiroshima at the time the diagnosis was made, and it is possible to relate these cases to the numbers of persons who survived the explosion and who were recorded as residing in the city subsequently. The incidence of leukaemia among survivors at various distances from the hypocentre of the explosion is shown in Table 1A. The incidence was substantially higher among those who were close to the hypocentre than among those who were more distant from it—128·0 per 10,000 among those less than 1,000 metres away, against 1·6 per 10,000 among those more than 3,000 metres away. Separate incidence rates for persons at each distance who showed major radiation symptoms shortly after the explosion and for persons who did not show such symptoms have been published by Moloney and Kastenbaum (1955).

TABLE 1A

The incidence of leukaemia among survivors of the Hiroshima atomic bomb explosion exposed at various distances from the hypocentre; persons subsequently resident in Hiroshima City only

Distance from hypocentre at time of explosion (m.)	No. of survivors on 1.10.50*	No. of cases of leukaemia		Incidence per 10,000 persons (total cases)
		Confirmed	Suspected	
Less than 1,000 ...	1,250	16	0	128·0
1,000–1,499 ...	10,350	28	1	28·0
1,500–1,999 ...	18,450	6	1	3·8
2,000–2,999 ...	30,350	7	0	2·3
3,000 or more ...	37,700	4	2	1·6
All distances ...	98,100	61	4	6·6

* The numbers of survivors have been rounded off to the nearest 50. The estimates differ slightly from those published by Moloney and Kastenbaum (1955) in accordance with data provided by the Atomic Bomb Casualty Commission.

Comparable figures are not available for the incidence of leukaemia in the unexposed population of the rest of Japan, but since leukaemia is invariably fatal it is reasonable to use mortality figures to provide an estimate of the incidence of the disease which might have been expected if no explosion had

taken place. National mortality figures are, however, based on the causes of death given on death certificates, and they are not necessarily suitable for comparison with figures obtained after an intensive search for cases and after the submission of each case to expert clinical scrutiny. In fact, the use of national mortality data is justified only by the fact that the number of deaths attributed to leukaemia among survivors who were 2,000 metres or more from the hypocentre and who cannot have received more than very small amounts of radiation, is close to the expected number calculated on the basis of these data. Table 2A therefore presents for comparison the numbers of cases of leukaemia known to have occurred during the eight years from 1947 to 1954 among residents of Hiroshima who survived at different distances from the hypocentre, and the numbers of deaths from leukaemia which would have been expected in a similar period among populations of the same size and the same sex- and age-distribution, subjected to the age- and sex-specific mortality rates from leukaemia observed in the whole of Japan in 1952. It can be seen that the observed incidence among survivors who were less than 1,000 metres from the hypocentre is 100 times greater than the mortality which would have been expected.

TABLE 2A

A comparison between the observed and the expected incidence of leukaemia among survivors of the Hiroshima atomic bomb explosion exposed at various distances from the hypocentre; persons subsequently resident in Hiroshima City only

Distance from hypocentre at time of explosion (m.)	No. of cases with onset in the 8-year period 1947-54		No. of deaths expected among the survivors in an 8-year period*	Ratio of total cases observed to expected
	Confirmed	Suspected		
Less than 1,000 ...	15	0	0.15	100.0 : 1
1,000-1,499 ...	28	1	1.32	22.0 : 1
1,500-1,999 ...	6	1	2.33	2.6 : 1
2,000-2,999 ...	6	0	3.96	1.5 : 1
3,000 or more ...	4	2	4.83	1.2 : 1
All distances ...	59†	4	12.59	4.7 : 1

* Calculated from the Japanese mortality data for 1952. In calculating the numbers of expected deaths, certain assumptions had to be made about the rate of change of the numbers of survivors in the different age groups, and the figures must be regarded as approximate estimates.

† Two cases referred to in Table 1A are omitted, since the onset of symptoms in one patient was in 1955 and in another patient, who died in April 1955, the date of onset is unknown; the latter patient was exposed at a distance of 2,400 metres from the hypocentre.

The data available for survivors of the Nagasaki explosion are less detailed than those for survivors of the Hiroshima explosion. Altogether 32 confirmed cases and 11 suspected cases are known to have occurred among survivors who subsequently resided in Nagasaki. Of these, 32 and 10 respectively occurred during the eight years 1947-54, and the corresponding total number of deaths which might have been expected in that period on the basis of the national mortality data is approximately 12.3.

Table 3A shows the year of onset of the disease for each of the 108 cases which have occurred among the survivors resident post-war in Hiroshima or Nagasaki, together with estimates of the annual incidence rates. The rates in

the first two years may be under-estimated, since medical organisation was incomplete at that period; in 1953 and 1954 they are almost certainly under-estimated since new cases continue to be discovered and some of the patients give histories of one or more years' duration. The data provide no evidence of a sharp peak in incidence at any particular period after the explosion, nor any clear indication that the incidence has yet begun to diminish by the end of the ninth year.

TABLE 3A

The incidence of leukaemia in different years among survivors of the Hiroshima and Nagasaki atomic bomb explosions; persons subsequently resident in Hiroshima City and Nagasaki only

Year of onset	No. of cases at Hiroshima		No. of cases at Nagasaki		Incidence per 10,000 persons (total cases)		
	Confirmed	Suspected	Confirmed	Suspected	Hiroshima	Nagasaki	Hiroshima and Nagasaki
1946 ...	0	0	0	1	0·0	0·1	0·05
1947 ...	3	0	2	0	0·3	0·2	0·3
1948 ...	7	3	2	1	1·0	0·3	0·7
1949 ...	5	0	1	2	0·5	0·3	0·4
1950 ...	6	1	5	1	0·7	0·6	0·7
1951 ...	11	0	7	3	1·1	1·0	1·1
1952 ...	11	0	6	2	1·1	0·8	1·0
1953 ...	10	0	2	1	1·0	0·3	0·7
1954 ...	6	0	7	0	0·6	0·7	0·7
Part 1955 or date unknown	2	0	0	0	—	—	—
All years	61	4	32	11	6·6	4·5	5·6

Reference

Moloney, W. C. and Kastenbaum, M. A. (1955). Leukemogenic effects of ionizing radiation on atomic bomb survivors in Hiroshima City. *Science*, 121, 308.

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APPENDIX B

Leukaemia and Aplastic Anaemia in Patients Treated with X-rays for Ankylosing Spondylitis

(*A summary of the findings of the investigation sponsored by the Medical Research Council Committee reporting on the hazards to man of nuclear and allied radiations*)

The investigation had two main objectives: first, to see whether the incidence of leukaemia and of aplastic anaemia was abnormally high in patients treated with X-rays for ankylosing spondylitis; and second, if the incidence of those conditions was found to be raised, to determine the quantitative relationship between incidence and dose of X-rays.

RESULTS

The incidence of leukaemia and aplastic anaemia

The case records of 13,352 patients (11,287 men and 2,065 women) were studied; these patients had been treated at 81 radiotherapy centres and sub-centres during the period 1935-54 inclusive. Slightly fewer than half of them were known to have been alive in 1955 or to have died earlier; the remainder were lost to follow-up at various dates between 1935 and 1954. They had therefore been under observation for periods of between one and twenty years, with an average for the whole group of just under five years.

49 of the patients studied were found to have developed leukaemia, aplastic anaemia, or myelofibrosis (a condition considered to be possibly a variant of leukaemia), and, of these, 46 had died by the end of 1955; 28 of them were certified as having died from leukaemia, 13 from aplastic anaemia and 1 from myelofibrosis. Three other patients with leukaemia and 1 with aplastic anaemia were found, who had been certified as having died from other causes.

With the co-operation of the Registrars-General, special efforts were made to recognise all patients in the series who had died of leukaemia or aplastic anaemia. The great majority of such cases have probably been traced despite the incomplete follow-up, but there is reason to believe that a few more might be revealed if the follow-up could be made complete.

The numbers of deaths from leukaemia and aplastic anaemia which could be expected under normal conditions were calculated from the national death rates for those diseases in the general population; they have been estimated as 2.9 and 0.3 respectively up to the end of 1955, but these estimates are certainly too high, as they are based on the assumption that all the patients untraced in 1955 were, in fact, alive at the end of 1955. In the compilation of the numbers of observed deaths from leukaemia and aplastic anaemia for comparison with these figures, only deaths *certified* as due to these conditions could be used, since the figures for expected deaths are based on death-certificate data. Thus enumerated, the numbers of observed deaths from leukaemia and aplastic anaemia are respectively 28 and 13. The differences between the observed and expected deaths are highly significant for both diseases.

Three of the observed cases of leukaemia died within the first year, and in these cases it was assumed that leukaemia was already present at the time of first treatment. If these 'co-existent' cases, and the corresponding expected mortality in the first year after treatment, are omitted, the observed and expected numbers of deaths from leukaemia for 1935-55 are 25 and 2·4 respectively.

Clinical review of cases

All the relevant data for each case were reviewed, and it was concluded that many of the patients certified as having died of aplastic anaemia had, in fact, been suffering from aleukaemic leukaemia. The diagnosis of aplastic anaemia was substantiated in only 4 cases and it was, therefore, not possible to examine the relationship between the incidence of this condition and the dose of X-rays received.

The relationship between the incidence of leukaemia and the X-ray dose.

This relationship has been determined for male patients only, in order to avoid difficulties introduced by the possibility of there being a sex-difference in susceptibility to leukaemia; the 3 'co-existent' cases were excluded, and there then remained 37 cases of leukaemia for study.

Details of X-ray treatment were obtained from the case records for 1,878 men, a sample of approximately 1 in 6 of the whole group of 11,287 male patients. The X-ray dose was expressed in two ways. By the first method, the total energy absorbed in the whole body was calculated, and expressed in megagramme-roentgens (Mgm.r.); by the second, the maximum dose in the spinal marrow was determined and expressed in roentgens (r)*. The number of man-years at risk following each level of dose, calculated by each of the two methods, was estimated for the whole group of male patients and was related to the number of cases of leukaemia. The results of these calculations are given in Tables 1B and 2B, which show the crude incidence rates per 10,000 men per year at all levels of dose.

TABLE 1B

The numbers of male patients developing leukaemia and the crude incidence rates after different doses of radiation (measured by the total amount of energy absorbed by the whole body)

	Amount of treatment: whole-body integral dose (Mgm.r.)						
	0	Less than 7·5	7·5-14·9	15-22·4	22·5- 37·4	37·5- 52·4	52·5 or more
Number of men developing leukaemia ...	—	1	9	9	10	4	4
Crude incidence per 10,000 men per year ...	0·5†	0·7	4·7	5·1	11·3	22·6	60·2

* For the second method extensive measurements were made on a 'phantom' man.

† The rate given for 'no treatment' has been estimated from the national vital statistics for all forms of leukaemia, and weighted to allow for the fact that not all the patients in the series were certified as dying from leukaemia. If lymphatic leukaemia is excluded (as may be more appropriate) the rate is 0·3.

TABLE 2B

The numbers of male patients developing leukaemia and the crude incidence rates after different doses of radiation (measured by the maximum amount received at a point in the spinal marrow)

	Amount of treatment: maximum dose to the spinal marrow (r)						
	0	Less than 500	500 to 999	1,000 to 1,499	1,500 to 1,999	2,000 to 2,749	2,750 or more
Number of men developing leukaemia ...	—	2	8	8	8	6	5
Crude incidence per 10,000 men per year ...	0.5*	2.2	4.1	4.2	11.3	13.0	17.6

* The rate given for 'no treatment' has been estimated from the national vital statistics for all forms of leukaemia, and weighted to allow for the fact that not all the patients in the series were certified as dying from leukaemia. If lymphatic leukaemia is excluded (as may be more appropriate) the rate is 0.3.

CONCLUSIONS

Deaths from leukaemia have been found to be greatly increased among the patients studied, and it is believed that this increase is the result of exposure to X-rays; the possibility that sufferers from ankylosing spondylitis are unusually sensitive to the action of X-rays cannot, however, be excluded.

Both methods of estimating the dose show a relationship between the crude incidence of leukaemia and the dose of X-rays, with an increase in the incidence over the whole range of dose studied. With neither method is there any evidence of a threshold below which no increase in incidence is produced. Both sets of results, therefore, suggest that even very small amounts of radiation will have an appreciable effect if given to a large enough population. The method based on calculation of the whole-body energy absorption, however, shows a disproportionately greater increase at high levels of dose, whereas that based on calculation of the spinal-marrow dose shows a simple proportional increase at all levels of dose. It is of considerable importance to determine the reason for this discrepancy. If the true relationship is of the curvilinear type suggested by the first method, it remains a theoretical possibility that very small doses (which could not be tested in the investigation) will have no leukaemogenic effect at all; but such a possibility can almost be ruled out if the relationship is linear.

A full account of the investigation will be published by H.M. Stationery Office as a report in the Medical Research Council's Special Report Series.

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APPENDIX C

The Spontaneous Mutation Rate in Man

In certain circumstances the spontaneous mutation rate of human genes, expressed as the number of mutations per locus per generation, can be estimated with a fair degree of reliability. A direct count of cases due to fresh mutation can be made for a gene which has a dominant effect. This number can also be directly inferred for sex-linked traits shown only in the male. If the incidence of a trait in the general population is known, the mutation rate can be determined from the proportion of cases due to fresh mutation.

When the effects of a gene are very disadvantageous a different line of argument can be used, even though the gene may not be fully manifest in the heterozygous state. The principles on which the indirect estimation of mutation rates can be made were laid down by Haldane (1932), and they are used in the formulae given in Appendix D. The assumption is made that the human population is in a state approaching genetical equilibrium; it is supposed that disadvantageous genes could not have persisted in the population unless their extinction by selective mortality were balanced by the recurrence of mutation.

In the case of dominant or sex-linked characters associated with very high mortality, the direct measurement of mutation rate can be supplemented by the indirect argument. Estimates which are entirely indirect are untrustworthy, but they have been made for a variety of genes recognised only by their recessive effects. One difficulty with recessive traits is that allowance has to be made for the effects of inbreeding. Another likely source of error is that genetical equilibrium can be maintained not only by mutation but also by a slightly advantageous effect in the heterozygote. Hence, indirect estimates are likely to be too high.

There is a further general difficulty; this arises from uncertainty as to whether or not a single locus is involved in determining the trait under consideration. Mutations at two or three loci might produce similar characters; this apparently occurs in haemophilia and also in achondroplasia. In these circumstances any estimate of mutation frequency, direct or indirect, based upon accepting one locus as the hereditary cause of the trait, would be too high by a factor depending upon the frequencies of the component causal genes.

Estimates of mutation rate in man are given in Table 1C. Those for dominant traits are based upon the direct method, though they can all be indirectly supported; the estimates for sex-linked genes are calculated indirectly, but are supported by direct observation of pedigrees almost certainly containing freshly mutated genes; those for recessive traits are all indirectly estimated.

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TABLE IC
Estimates of the spontaneous mutation rates of some human genes

Trait		Mutation frequency of the causal gene (per million per generation)	Region	Source	Date
Name	Mode of inheritance				
Epiloia (tuberose sclerosis)	Dominant	8	England	Gunther and Penrose	1935
Achondroplasia ...	Dominant	45	Denmark	Mørch	1941
Aniridia ...	Dominant	.5*	Denmark	Møllenbach	1947
Microphthalmos (without mental defect)	Dominant	5	Sweden	Sjögren and Larsson	1949
Retinoblastoma ...	Dominant	15	England	Philip and Sorsby	1947
		23	U.S.A.	Neel and Falls	1951
		4	Germany	Vogel	1954
Partial albinism (with deafness)	Dominant	4	Holland	Waardenburg	1951
Haemophilia (severe type)	Sex-linked	20 32 27	England Denmark Switzerland and Denmark	Haldane Andreassen Vogel	1935 1943 1955
Muscular dystrophy (Duchenne type)	Sex-linked	95	U.S.A.	Stephens and Tyler	1951
		45 43	N. Ireland England	Stevenson Walton	1953 1955
Albinism ...	Recessive	28	Japan	Neel <i>et al.</i>	1949
Ichthyosis congenita ...	Recessive	11	Japan	Neel <i>et al.</i>	1949
Total colour blindness ...	Recessive	28	Japan	Neel <i>et al.</i>	1949
Infantile amaurotic idiocy	Recessive	11	Japan	Neel <i>et al.</i>	1949
Amyotonia congenita ...	Recessive	20	Sweden	Böök	1952
True microcephaly ...	Recessive	49	Japan	Komai <i>et al.</i>	1955
Phenylketonuria ...	Recessive	25	—	(Appendix D)	—

* This estimate differs by a factor of 2 from that given by the author, but it is based on the author's material.

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APPENDIX D

Calculation of the Quantitative Effects of Spontaneous and Induced Mutation Rates in Diseases Caused by Single Genes

In order to estimate the quantitative effect of doubling the mutation rate or of raising it by any given factor, it is necessary to calculate the proportion of cases of the disease in question in each generation which can be attributed to spontaneous mutation. This can be done by using the indirect method of calculating mutation rate; the steps in the argument are set out in Table 1D. The abnormal allele is represented by **a**, and the normal by **A**.

TABLE 1D

Calculation of the number of cases due to spontaneous mutation in diseases caused by single genes

Steps in the calculation	Dominant trait		Sex-linked trait		Recessive trait	
	Formula	Example: achondroplasia	Formula	Example: haemophilia	Formula	Example: phenylketonuria
1. Sex affected ♂ or ♀	♂ or ♀	—	♂	—	♂ or ♀	—
2. Genotype responsible for the disease	Aa	—	a	—	aa	—
3. Frequency of genotype in population (where q is the frequency of a)...x	2q	1/10,000	q	1/12,000	q^2	1/40,000
4. Comparative loss of fitness associated with the genotype	(1-F)	4/5	(1-F)	7/8	(1-F)	1
5. Mutation rate of A to a per gene per generationm	q (1-F)	40×10^{-6}	q (1-F)/3	24×10^{-6}	$q^2 (1-F)$	25×10^{-6}
6. Proportion of genotypes (or cases of the disease) due to fresh mutation in each generationd	(1-F)	4/5	(1-F)/3	7/24	2q (1-F)	1/100
7. Frequency of abnormal genotypes due to fresh mutation:						
(i) in each generation of birthsx × d	2m	80×10^{-6}	m	24×10^{-6}	2mq	0.25×10^{-6}
(ii) among 20×10^6 births (♂ and ♀) over a period of 30 years ...	$40m \times 10^6$	1,600	$10m \times 10^6$	240	$40mq \times 10^6$	5

In this table three hereditary diseases, achondroplasia, haemophilia and phenylketonuria are used to show the methods applicable respectively to dominant, sex-linked and recessive traits determined by single genes. For the present purpose the population is assumed to be in genetical equilibrium; the loss due to unfitness of genotypes is balanced by recurrent natural mutation. The figures for achondroplasia are derived from Mørch (1941); in Step 3, 1/9,400 has been rounded off to 1/10,000. For haemophilia the figure (7/8) in Step 4 has been taken from Andreassen (1943) and that in Step 3, (1/12,000), agrees with estimates by Haldane (1935). The figures in Steps 3 and 4 for phenylketonuria are derived from Jervis (1939) and Munro (1947). Doubling the spontaneous mutation rate on one occasion would increase the frequency of each disease by a proportion, shown in Step 6, in the next generation.

The results given in Step 7 (ii) in Table 1D apply only to the first generation after doubling. The quantitative effects in subsequent generations can be ascertained by substituting appropriate new incidence figures and repeating the steps of the calculation. Calculations made by this method and extended to cover six generations yield the results shown in Table 2D; the theoretical limiting values obtained after an infinite number of generations are also given. The results are shown graphically in Fig. 1 (p. 32). Two situations are considered: (a) the effect of a single doubling of mutation rates in one generation, and (b) the effect of permanently doubling the mutation rate.

TABLE 2D

The effects, expressed as the increase in incidence per hundred cases, of doubling the mutation rates, (a) in one generation only, and (b) permanently, for three hereditary traits

(a) *Doubling in one generation only*

Number of generations	Increase in incidence per hundred cases		
	Achondroplasia (Dominant)	Haemophilia (Sex-linked)	Phenylketonuria (Recessive)
0	0	0	0
1	80	29	1
2	16	29	1
3	3	16	1
4	1	10	1
5	0	6	1
6	0	4	1
Infinite	0	0	0

(b) Permanent doubling

Number of generations	Increase in incidence per hundred cases		
	Achondroplasia (Dominant)	Haemophilia (Sex-linked)	Phenylketonuria (Recessive)
0	0	0	0
1	80	29	1
2	96	58	2
3	99	74	3
4	100	84	4
5	100	90	5
6	100	94	6
Infinite	100	100	100

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APPENDIX E

Estimate of the Incidence of Cases of Schizophrenia and Manic Depressive Reaction due to Spontaneous Mutation

The calculation of (d), the proportion of cases which can be attributed to fresh mutation in each generation, for the conditions discussed in paragraphs 148–150, can be set out as shown in Table 1E.

TABLE 1E

Calculation of (d), the proportion of cases due to fresh mutation in each generation, in schizophrenia and manic depressive reaction

Steps in the calculation	(i) Schizophrenia		(ii) Manic depressive reaction	
	Formula	Example	Formula	Example
1. Sex affected ♂ or ♀	♂ or ♀	—	♂ or ♀	—
2. Genotype responsible for predisposition to the disease ...	aa	—	Aa	—
3. Frequency of genotype in population (where q is the frequency of a) x	q^2	1/100	2q	1/200
4. Comparative loss of fitness associated with the genotype ...	(1-F)	1/20	(1-F)	1/70
5. Mutation rate per gene per generation m	$q^2 (1-F)$	1/2,000	q (1-F)	1/28,000
6. Proportion of predisposed cases due to fresh mutation in each generation d	$2q (1-F)$	1/100	(1-F)	1/70

(i) Schizophrenia

This is a type of mental disease which has its onset at about the age of 30 years on the average. There are many degrees of severity, and males are more often affected than females. The genetical predisposition occurs in subjects who are, according to Kallmann (1938), homozygous for a specific recessive gene; it has an incidence of about 1/100 in European populations (Fremming, 1947). On the basis of a rough survey of hospital data, it is assumed here that only one-tenth of predisposed subjects become chronically incapacitated. Neglecting sex differences, the fertility of these incapacitated patients is reduced by 1/2 (Essen-Möller, 1935). The total loss of fitness of predisposed genotypes is thus $1/10 \times 1/2 = 1/20$. It follows that $d = 2q(1-F) = 1/100$, as shown in Table 1E. In a generation of 20×10^6 births the number of incapacitated people would be 20,000, of whom 200 would be cases due to fresh mutation.

(ii) Manic depressive reaction

This is a type of mental disease with mean age of onset at about 40 years. There are many degrees of severity, and females are more often affected than males. The genetical predisposition, which is commonly believed to depend upon a dominant gene (Marrell, 1951), has a frequency in the population of about 1/200; Mayer-Gross, Slater and Roth (1954) quote 0·35 per cent for Scotland and 1 per cent for Sweden and Denmark as the total morbidity risk of affective psychosis. The incidence of chronic breakdown among those who are predisposed can be estimated at one-seventh and, for such incapacitated patients, fertility is reduced, according to observations by Essen-Möller, by a factor of 1/10. Hence the total loss of fitness for predisposed genotypes is $1/7 \times 1/10 = 1/70$. It follows that $d = (1-F) = 1/70$. In a generation of 20×10^6 births there would be 14,000 people incapacitated, of whom 200 would be cases due to fresh mutation.

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APPENDIX F

The Effect of Changing the Mutation Rate on Characters Showing Continuous Variation about the Normal

Member genes of a polygenic system cannot be followed as individuals in our observations. We must therefore measure mutation by the increment it adds to heritable variation, instead of measuring it by the frequency of change, as is done in the case of individually traceable genes.

The increment added to the variance per generation has been estimated for spontaneous mutation in two hair characters in *Drosophila* (Clayton and Robertson, 1955; Durrant and Mather, 1954; Paxman, 1955). Technically this is a difficult operation, but the estimates agree surprisingly well for each character when allowance is made for various possible sources of bias. The two characters agree, also, in showing an increment of about 1×10^{-8} of the amount of heritable variation estimated by Clayton and Robertson to be present in a normal population of *Drosophila*. The estimate may easily be too small by a factor of 2 or 3, but seems unlikely to be out by a factor of 10. This finding suggests that the relation between the amount of heritable variation in a population and the mutation rate is roughly linear, and certain theoretical considerations point the same way. It also shows that a marked increase in the mutation rate for a few generations would have only a trivial effect on the heritable variation of the population, and that, even with a persistent increase, the new equilibrium showing the full effect of the raised mutation rate in raising heritable variation would take very many generations to achieve.

Clayton and Robertson also record the result of irradiating the adults of each generation with an X-ray dose of 1,800 r. The increment added in each generation to the heritable variation available to selection was about ten times the spontaneous increment. Thus the dose which doubles the effect of spontaneous mutation would be some 200 r as measured by this criterion. But the new heritable variation available to selection in these experiments seems to have represented only about one-sixth of all the new heritable variation as measured directly by the increase in phenotypic variation. If we take the overall total therefore, 200 r must have produced about six times the spontaneous increment, so that the doubling dose becomes just over 30 r. This is more in keeping with the figure obtained from lethal mutation, though it might have been expected that the polygenic figure would be higher, not lower, than the monogenic, because of the way in which mutations can balance one another's effects in a polygenic system. It would, in any case, be unwise to place great confidence in these calculations, both because other experiments of the same kind have given results even more difficult to assess, and because doses as heavy as 1,800 r produce so many lethal mutations and so much structural change in the chromosomes that the polygenic effects may well be quantitatively distorted.

In attempting to extrapolate from these findings to the effects of irradiation in natural, including human, populations, two points must be borne in mind. Firstly, the flies which yielded these observations were from inbred lines, so that any mutation in the polygenic system would add its quota to the increase in variation. In a natural population, however, variation is already present, and mutation from one allele to another, where both already exist

and are not uncommon in the population, could add little if anything to the variation. Only mutation in genes whose alleles are rare or absent in the population will contribute materially to an increase in variation, and the contribution will fall off as the alternative alleles become more common. So if most of the member genes of a polygenic system are already varying, mutation will add correspondingly little to the total variation. On the other hand, if, as seems likely, many of the genes which can prospectively contribute to the variation of a polygenic system are not doing so because only one allele is present or at least common, new mutation increases the number of loci contributing to the variation which will then increase correspondingly. The roughly linear relation between mutation and variation suggested by the experiments is thus to be regarded as a maximum effect, the closeness of approach to it depending on the initial conditions of variation prevailing in the population in question.

The second point concerns the properties of heterozygotes. The linear relation would cease to hold if there were any innate advantage of individuals heterozygous for the genes over others homozygous for them. A situation analogous to balanced polymorphism would then arise, and at equilibrium the heritable variation would become independent of mutation rate. No such heterozygotic advantage was detected in the variation arising by mutation, even though Paxman made a special search for it; nor is it likely on general grounds. Such an advantage must, however, remain as a possible, even if unlikely, additional reason for regarding a linear relation as representing the maximum, rather than the regularly realisable, effect of mutation on variation in populations such as those of man. In other words a permanent doubling of the mutation rate would not be expected to do more, and under some circumstances might do less, than double the heritable variation in the population.

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APPENDIX G

The Effect on the Distribution of Intelligence of Increasing the Heritable Variation

Under conditions of natural selection the effect of raising the heritable, and hence the total, variation of expression of a character, some particular expression of which is the fittest, must in general be to lower the average fitness in the population; though where the mean departs widely from the most advantageous expression of the character the fitness of selected groups might be raised. Furthermore, where all expressions of the character may be displayed, the overall fall in fitness must be directly related to the increase in variation. A fall in fitness is not, however, to be translated directly into social load when we are considering the consequences of raising the heritable variation in such a character as mental capacity in man.

The intelligence score of an individual is derived from his performance in a series of tests, and the frequency distribution obtained from a population must therefore reflect the structure of the tests. The distribution obtained is generally treated as being normal, but in fact certain disturbances occasionally appear, and they seem to be of a type which no simple transformation or statistical adjustment can remove. It is very likely that such discrepancies spring from innate features of the test, and they should not, in any case, be allowed to obscure the essentially normal nature of the distribution. Normality will in fact be assumed in the following discussion. It is considered that by avoiding the use of very narrow ranges and, more particularly, by discussing relative rather than absolute effects, broadly valid conclusions should be attained.

I am informed by Professor F. A. Peel of the Department of Education in the University of Birmingham, that in educational discussions the distribution of intelligence scores is taken as normal and is standardised to a mean of 100 with a standard deviation of 15. The scores have been found to approximate to I.Q.'s as measured by the original tests, and are commonly referred to as 'I.Q. scores'. In these terms, Professor Peel further informs me, children with an I.Q. of less than 70 are generally regarded as educationally sub-normal and as requiring education in special schools; those with an I.Q. of between 70 and 80 are regarded as needing special teaching in ordinary schools; and those with an I.Q. of over 115 as being of grammar school quality. These figures are to be taken only as general guides since they are applied neither rigorously nor uniformly throughout the country.

For information and advice on the estimation of the heritable variation in respect of I.Q., I am indebted to Dr. J. A. Fraser Roberts. Sibs show a correlation close to 0.5 in this character. Data on parent-offspring relations are less full, but suggest a similar figure, so that there is no good reason to postulate any over-dominance or heterozygous advantage. Taken on their face value, such figures would indicate virtually complete genetic determination, but there is strong assortative mating in respect of this character and there is also the effect of a common home environment to be taken into account in assessing the genetic meaning of these familial correlations. Observations on twins and foster children would seem to indicate $\frac{1}{2}$ as the fraction of variation which is heritable. However, lest this should be an over-estimate, parallel calculations have been made, assuming fractions of $\frac{1}{2}$ and $\frac{1}{4}$ as likely to straddle the true situation. Should even the figure of $\frac{1}{2}$ be too high the effect of increasing the heritable component would be correspondingly smaller. Assortative mating has been disregarded, as we may

reasonably assume that its incidence would not be affected by alteration in the amount of heritable variation, so that its relative effect would remain the same.

Calculations have been made of the effects of raising the heritable variation (V_H) to 1.25, 1.50 and 2.00 times its present value, assuming that environmental variation (V_E) remains unaltered. Thus, taking V_H to be $\frac{1}{4}$ of the total variation (V_T) we have:

$$V_H = \frac{1}{4} V_T = \frac{1}{4} \times 15^2, \text{ and}$$

$$V_E = V_T - V_H = \frac{1}{4} \times 15^2,$$

so that doubling the heritable variation would give us the new total:

$$V'_T = V_E + 2V_H = (\frac{1}{4} \times 15^2) + (2 \times \frac{1}{4} \times 15^2) = 1\frac{1}{4} \times 225 = 393.75$$

and the new distribution of I.Q. would have a standard deviation of 19.84, the mean remaining at 100. The proportion of individuals expected to have, for example, an I.Q. of less than 70 can then be found as the area in the tail of the distribution cut off by the ordinate falling short of the mean by a normal deviate of $\frac{30}{19.84} = 1.512$.

The results of this and similar calculations are shown in Table 1G, where they are expressed as values relative to the proportion calculated as falling into corresponding classes with the distribution as it is now assumed to be. Thus the assumed present distribution ($\bar{x}=100, s=15$) gives 2.27 per cent of individuals with an I.Q. of less than 70. With the heritable fraction at $\frac{1}{4}$ of the total and doubled, 6.53 per cent fall below a score of 70, making a relative value of $\frac{6.53}{2.27} = 2.88$. In other words, on these assumptions, doubling

the heritable variation would nearly treble the number of children with an I.Q. of less than 70 (i.e. those needing to be taught in special schools, as judged by a common convention of today). In addition to the relative changes in the numbers with an I.Q. of less than 70, figures are also given for those in the classes with I.Q. less than 75 (a figure sometimes taken to indicate the need for special schooling), I.Q. between 70 and 80 (special teaching), and I.Q. over 115 (grammar school).

TABLE 1G

The effects of raising the heritable variation on the frequencies of different intelligence groups

Intelligence group	Present proportion per cent of population (assuming a normal distribution)	Assumed present heritable fraction	Factor of increase relative to present proportion with heritable variation raised to:					
			(constant mean)	(falling mean)	1.25	1.5	2.0	
I.Q. < 70	2.27	$\frac{1}{4}$			1.31 1.46	1.62 1.94	2.26 2.88	3.24 4.51
I.Q. < 75	4.78	$\frac{1}{4}$			1.22 1.32	1.42 1.63	1.82 2.17	2.50 3.24
70 < I.Q. < 80	6.85	$\frac{1}{4}$			1.09 1.13	1.16 1.22	1.27 1.33	1.59 1.75
I.Q. > 115	15.87	$\frac{1}{4}$			1.09 1.13	1.17 1.24	1.30 1.42	1.00

In these calculations the variance has been assumed to change without alteration of the mean, so that the proportion of high I.Q. increases with the proportion of low I.Q. A further calculation has been made in which, as the variance increases, the mean is allowed to fall so as to keep constant the proportion with I.Q.'s of over 115. This is intended to illustrate the kind of result which would be obtained if mutation were preponderantly, but not wholly, degradatory. The relative changes for doubled heritable variation on this assumption are also shown in the table.

It should be remembered that these changed proportions would be achieved by corresponding increases in the mutation rate, only when equilibrium had been reached or at least closely approached, that is to say, after very many generations.

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APPENDIX H

The Doubling Dose of Radiation for Various Plants and Animals

In paragraphs 171-182 we were concerned with finding some quantitative measure of the effectiveness of radiation in causing mutations, with the purpose of using this estimate to establish maximum levels of exposure which are genetically tolerable. In this context, one must be particularly careful not to under-estimate the effects of radiation. In order to express its influence in terms of a 'doubling dose', we should try to arrive at a figure for the lowest dose of radiation which changes mutation in a way which is effectively equivalent to a doubling of the mutation rates of every gene. For those genes with very low spontaneous mutation rates a doubling of the rate will be relatively unimportant. Among the genes with relatively greater spontaneous mutation rates, some may be more sensitive to radiation than others. What we need to estimate is the dose of radiation which doubles the mutation rate of a sample of these more sensitive genes sufficiently large to be physiologically representative of mutations in general. This might be called a 'minimum representative doubling dose'.

After pointing out (paragraph 176) that this can scarcely be less than the naturally occurring dose of radiation, we discuss the possible modifications of this bedrock minimum in terms of an argument which was originally largely due to J. B. S. Haldane (1948). This consists of an attempt to estimate the fraction of the spontaneous mutation rate in man which can plausibly be attributed to natural radiation. The argument proceeds by analogy with the conditions in other organisms, and particularly those in the fruit-fly (*Drosophila*) and the mouse.

In *Drosophila*, suppose that:

f =the fraction of spontaneous mutations due to natural radiation,

r =the rate of natural radiation (in r per day),

m =the rate of mutation induced by 1 r,

s =the spontaneous mutation rate,

t =the average age at reproduction (in days).

Then we shall have:

$$f = \frac{m r t}{s}$$

Similarly if capital letters represent the same factors in man, we shall have

$$F = \frac{M R T}{S}$$

Now the spontaneous mutation rate and the rate of induced mutation (s and m) are much better known for flies than for man (S and M). Thus, the procedure is to arrive at F by first finding as good a value as possible for f and then modifying this according to the relation,

$$F = f \times \frac{M R T s}{m r t S}$$

In his original presentation of the argument, Haldane adopted for f a value (0.001) which had been calculated by D. E. Lea (1946). However, it has recently been pointed out (Spiers, 1956) that Lea based his calculation on an estimate of natural radiation of 2.2 milliroentgens (mr) per day, which is about eight times greater than that accepted at the present time (paragraph 200). The value for f has to be reduced accordingly. For the sake of simplicity we have taken it as 0.0001 (paragraph 178), although this may be a slight underestimate.

This value for f is based on an estimate of 0.15 per cent sex-linked lethals. Lea argues, in agreement with other authors who have considered the matter, that there may be about 1,000 genes capable of mutating to sex-linked lethals in *Drosophila*; his value for the spontaneous mutation rate can therefore be expressed as 1.5×10^{-6} per locus. The statement (paragraph 178) that the human spontaneous mutation rate is probably about five times as great as this is based on the observation that the mutation rates of several human genes are around 10 per million per generation (cf. Table 1C).

The opinion (paragraph 179) that mouse genes are more sensitive to radiation than those of *Drosophila* (i.e. have a higher value for m) is based on the work of W. L. Russell (1954). It is disputed by some authors; but if one adopts it, and takes it to suggest the hypothesis that human genes are also more sensitive, the result is to increase the value of F , and thus to lower the estimate of the minimum representative doubling dose. In order to be as cautious as possible, we have therefore adopted these assumptions.

The estimate (paragraph 185) that one human germ cell in ten carries a new mutation is a minimum figure arrived at in calculations by H. J. Muller (1950, 1954).

Some typical figures for doubling doses derived from experiments on plants and animals are given in Table 1H. These figures are open to a wide margin of statistical error, as the number of spontaneous mutations was always small; in most instances values smaller or larger by a factor of 2 are not excluded.

There have been many other reports of experiments in which mutations were induced by ionizing radiations, especially in plants and lower organisms; however, in the great majority of these, either the control series was too small for any spontaneous mutation to be observed, or the apparent mutants found were not confirmed by genetic test. The figures quoted here are probably representative.

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(a) Text

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TABLE 1H

Some typical figures for the doubling dose of radiation in various higher organisms

Group	Genus and species	Cell stage irradiated	Genes studied	Doubling dose (r)	Source of information (see list of references)
Plant	<i>Zea mays</i>	Pollen	Four recessive visibles ...	28	No. 1
	<i>Oenothera organensis</i> ...	Pollen	Self-incompatibility ...	60	2, 3
	<i>Prunus avium</i> ...	Pollen	Self-incompatibility ...	60	2, 3
Insect	<i>Drosophila melanogaster</i> ...	Spermatozoa ...	Sex-linked lethals ...	50	4
	<i>Drosophila melanogaster</i> ...	Spermatozoa (aged) ...	Sex-linked lethals ...	140	5, 6
	<i>Drosophila melanogaster</i> ...	Spermatogonia ...	Sex-linked lethals ...	8	7
	<i>Drosophila melanogaster</i> ...	Oocytes and oogonia ...	Nine recessive visibles ...	390	8
	<i>Drosophila melanogaster</i> ...	Spermatozoa ...	White eye ...	60	9
	<i>Mus musculus</i>	Spermatogonia ...	Dominant visibles, semi-steriles, sex-linked lethals	50	10
Mammal	<i>Mus musculus</i>	Spermatogonia ...	Seven recessive visibles	50	11, 12

(b) *Table 1H*

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APPENDIX J

The Dose of Radiation Received in Human Tissues from Natural Sources

All living organisms absorb ionizing radiation from sources which are either present in their environment or incorporated in their own tissues. The most important 'external' radiations are cosmic rays and the radiations arising from elements of the uranium and thorium series present in the earth or the air and from the potassium 40 content of the earth and of vegetable matter. The 'internal' irradiation arises chiefly from the potassium in tissues, but there is also a small contribution from carbon 14 and in some cases soft tissues within bone receive radiation from very small amounts of radium present in the skeleton. Radon in the atmosphere, besides contributing its quota to the external radiation, may also add to the internal dose, by access of the radioactive material to the tissues via the lungs. Because alpha rays and beta rays are so readily absorbed, even by the elements of low atomic number which comprise the soft tissues, the dose from external sources may be regarded as entirely due to cosmic rays and gamma rays. The dose from internally absorbed radioactive materials, however, arises in large measure from beta rays and, when present, from alpha rays.

The radiation dose to human tissues from this normal background is small compared with doses known to cause immediate somatic change, and its significance is presumably to be sought in possible long-term effects; of these the genetic and carcinogenic actions of ionizing radiation would appear to be the most likely. The critical tissues considered in this appendix are, therefore, the gonads and the osteocytes of the Haversian systems in bone. An estimate of the dose to these tissues is made as far as present data allow, and although this is attempted for a number of different localities, it must be emphasised that knowledge of the basic data is far from complete.

All doses are expressed as soft-tissue doses in rads, and where calculations have involved the quantity 'W,' the energy per ion pair formed in air, a value of 34 eV has been taken as representative of recent experimental determinations of that constant.

SOURCES OF EXTERNAL RADIATION

Cosmic rays

The cosmic ray ionization intensity in air at sea-level (and geomagnetic latitudes above 41° N) has been variously quoted in the literature over a range of from 1.5 to 2.8 ion pairs/cc/sec. The differences have arisen largely in the interpretation of high-pressure ionization-chamber measurements, and the correct method of analysis appears to be that used by Clay and his co-worker (1938), and re-examined and supported by further experiments by Burch (1954). The mean of three values given by these workers and corrected to ionization in free air is 1.92 ions/cc/sec. Converting this value to a tissue dose gives:—

$$\text{cosmic ray dose-rate to soft-tissues} = 0.028 \text{ rad/year}^*$$

This dose-rate applies to any soft tissues in the body, including the gonads and osteocytes, and is typical for most locations at the earth's surface above latitude 41° N. It may be some 20 per cent less in basements of tall buildings, which absorb the 'soft' cosmic ray component; but any considerable

* 1 rad corresponds to a dose of about 1.07 r in soft tissues.

reduction in dose-rate will only occur in deep underground situations. At a height of 10,000 ft. the cosmic ray dose-rate is increased by a factor of 3 or more, but it will be seen later that cosmic rays contribute only a fraction of the total tissue dose, and that, in consequence, the tissue dose-rate at this height might be only some 40 per cent greater than at sea-level.

The dose-rate of 0.028 rad/year is less than the figure 0.035 rad/year, given, for example, by Libby (1955). For the reasons given above, the lower figure appears to be the correct one and is retained in the present analysis. It is a matter of some discussion whether or not the small component of slow particles in cosmic radiation has a higher R.B.E. than the fast-meson component, the R.B.E. of which has been taken as unity. Some mutations are reported as being less effectively produced by heavily ionizing particles; in a few other cases the R.B.E. for heavy particles has been found to be in the region of 5. In the extreme case, the slow-particle component would not appear likely to add as much as 0.01 rad/year to the effective cosmic ray dose. On the other hand, some shielding of the soft gamma ray component of the cosmic radiation by building structures occurs, which reduces the dose below the unshielded value. It would seem best, in view of this and the possible effect of a higher R.B.E., to accept the unshielded value of 0.028 rad/year as the best estimate for sea-level and latitudes above 41° N.

Local gamma rays

Under most conditions of life, gamma radiation from local surroundings is responsible for the greater fraction of the external radiation dose. Measurement of this contribution, however, has been made in comparatively few places.

Some measurements of local gamma ray dose-rates in Leeds and Aberdeen (Spiers and Griffith, 1956) are summarised in Table 1J. The results cover only limited types of situation, but the concordance between the dose-rates in brick and concrete buildings, whether in Leeds or in Aberdeen, suggests that they may be fairly representative of the dose-levels in areas which are not specially radioactive and in buildings not made of granite. The dose-rates in Leeds determined with a lightly shielded counter, are about 20 per cent higher than the background measurements previously reported, but this effect was shown to be due to the difference in shielding in the two measurements. The results in Table 1J represent the local gamma ray dose-rates under conditions of light shielding.

TABLE 1 J

*Measurements of local gamma ray dose-rates in Leeds and Aberdeen
(Spiers and Griffith, 1956)*

Type of building (or "out-of-doors")	Location	Local gamma ray dose-rate (rad/year)
I. All granite	(a) Aberdeen—laboratory	0.107
	(b) Aberdeen—bell tower	0.099
	(c) Aberdeen—entrance hall	0.101
II. Brick and concrete	(a) Aberdeen—rooms on various floors	0.073
	(b) Leeds—room in hospital building...	0.081
	(c) Leeds—single-storey laboratory ...	0.080
	(d) Leeds—various rooms in house ...	0.077
III. Out-of-doors	Leeds—garden of house II(d) above ...	0.048

Sievert and Hultqvist (1952) and Sievert (1955) have reported measurements of the total 'cosmic ray plus gamma ray' background in Swedish houses and in out-of-door situations. Some of the Swedish results are given in Table 2J where an allowance has first been made for the cosmic ray fraction and the residual ionization converted to tissue dosage. The mean dose-rates recorded were based on measurements in about 70 houses. Variations in dose-rate were most marked in Type 3 houses where, in some, values 50 to 100 per cent above the mean in Table 2J were recorded.

TABLE 2J

Measurements of the total 'cosmic ray plus gamma ray' background in Swedish houses and in out-of-door situations in Sweden (Sievert and Hultqvist, 1952; Sievert, 1955)

Situation		Gamma rays only (ions/cc.sec.)	Mean dose-rate (rad/year)
Indoors, centre of room	Wooden houses	4.0	0.059
	Brick and concrete houses (Type 1)	6.2	0.091
	Brick and concrete houses (Type 2)	6.5	0.095
	Brick and concrete houses (Type 3)	14.8	0.216
Outdoors	Stockholm streets	5.8	0.085
	Over igneous rocks	3.9 to 8.3	0.06 to 0.12
	Over clay	3.4	0.05

The local gamma ray dose-rate can also be estimated approximately at some places in South-west England from geiger-counter recordings reported by Peirson (1951). Taking the counting rate given by Peirson for a 'normal' background situation, and allowing for the cosmic ray fraction, a counting rate of about 1.3 cts/min. per cm² of projected cathode area is deduced for this 'normal' local radiation. Assuming an over-all efficiency of the counter assembly of 0.6 per cent, and a mean gamma ray energy of 1 MeV, a gamma ray flux is deduced which corresponds to a tissue dose-rate of 0.05 rad/year, a figure reasonably in accord with measurements in Leeds and in Sweden away from areas of high radioactivity. Applying the same analysis to the recorded counting rate in St. Ives and its neighbourhood, the local gamma ray dose-rate is deduced as approximately 0.25 rad/year. Great accuracy cannot be claimed for this estimation in view of the assumptions made, but it is of the same order as the values given in Table 2J for areas of known high radioactivity in Sweden. Dose-rates of 0.3 rad/year and over have been reported in some parts of Cornwall (Wood and Willey, 1954).

Atmospheric radon

Radiation from the break-down products of atmospheric radon also add to the external gamma ray dose. This effect may be expected to be small under most conditions, but so far no measurements have been made to distinguish its contribution from that of gamma rays from the solid surroundings. Peirson and Franklin (1951) have calculated that at ground level an atmospheric radon content of 3×10^{-18} c/l produces a gamma ray flux of the order of 10 quanta/cm²/min. Taking a mean energy of 0.8 MeV for radium B and C gamma rays, the tissue dose-rate for this flux is 0.0022 rad/year. Anderson, Mayneord and Turner (1954) have reported levels of atmospheric radon in London (in May 1953) which averaged $2-3 \times 10^{-12}$ c/l, and under these conditions the external gamma ray dose from atmospheric radon is of the order 0.02 rad/year—a contribution of nearly the same magnitude as that due to cosmic rays.

SOURCES OF INTERNAL RADIATION

Potassium 40

The following data have been used in the calculation of the dose-rate from the potassium content of the body:—

Mean potassium content of body	= 0.215 per cent
Specific β -activity of K	= $27.4 \beta^2/\text{sec./g. K}$
Specific γ -activity of K	= $3.5 \gamma/\text{sec./g. K}$
Mean β -ray energy of K 40	= 0.605 MeV
Mean γ -ray energy of K 40	= 1.46 MeV

Because the mean range of the beta particles of potassium 40 is only some 2 mm, the dose-rate in a given organ is determined mainly by its own potassium content. In the absence of precise values for the potassium content of the gonads, the mean for the whole body, derived from Shohl's data (1939) is adopted. The total tissue dose-rate derived from the energy released per g. of tissue, is then:—

$$\text{tissue dose-rate due to K} = 0.018(\beta) + 0.002(\gamma) = 0.020 \text{ rad/year.}$$

In relation to this calculation there may be doubt as to the precise value for the potassium content of the gonads. So far it has only been possible to make flame-photometric measurements on tissues taken from two post mortem examinations. The results, obtained through the kind co-operation of Dr. F. M. Parsons of the Urological Department of the General Infirmary at Leeds, are as follows:—

<i>Case and age</i>		<i>Potassium content (mg./100 g.)</i>	<i>Sodium content (mg./100 g.)</i>
A. 67 yr. (testes)	...	(i) 190	205
	...	(ii) 240	172
B. 28 yr. (ovaries)	...	(i) 188	200
	...	(ii) 197	204

Three results are concordant and one (Aii) is suspect in that the sodium value is so low. They suggest, however, that no great error is being made in assuming an average potassium content of 0.215 per cent, as given by Shohl. The tissues were taken from the central parts of the gonads, and the potassium content should be representative of the average value over dimensions of a few mm. of the tissues containing the germ cells.

Carbon 14

Carbon in living systems contains approximately 1 part carbon 14 in 10^{12} , and has a specific beta ray emission of 0.2 beta particles per sec per g. carbon, with a mean energy of 0.053 MeV. Taking the carbon content of tissue as 18 per cent, the energy deposition due to the carbon 14 amounts to a tissue dose-rate of only 0.001 rad/year.

Radon and its disintegration products

An estimation of tissue dose arising from the inhalation of air containing radon can be made if, in the absence of complete information on all the factors concerned, some simplifying assumptions are made. The concentration of radon in the atmosphere is regarded as uniform, and it is assumed that the break-down products (radium A, B, C and C²) are in equilibrium with the radon and are uniformly suspended in the air. The calculation is then made in two parts: (1) for a steady level of radon (plus disintegration

products) in body-tissues via the blood in contact with the radon in alveolar air, and (2) for a steady intake into the lungs of the disintegration products formed in the air.

The solubility of radon in water at 37° C. is 0·17, and in fat the figure is about five times higher. If the concentration of pure radon in alveolar air is C , and is regarded for the moment as free of disintegration products, the concentration of radon in the 50 kg. of aqueous tissue will be 0·17 C and that in the 10 kg. of fatty tissue will be 0·85 C , giving a mean for the whole soft tissues (63 kg.) of 0·27 C . This level of radon in the tissues is maintained, and hence it will maintain its disintegration products in equilibrium with it. Taking the effective disintegration energy of the series as 20 MeV, and assuming an atmospheric radon content of 3×10^{-18} c/l (as above) the energy deposition per g. of tissue corresponds to a dose-rate of only 3×10^{-5} rad/year, mainly of alpha radiation. Using an R.B.E. of 10 to enable this alpha dose-rate to be added to the beta and gamma dose-rates already calculated, the tissue dose-rate for the dissolved radon is 3×10^{-4} rem/year.

The dose-rate from the disintegration products formed in the atmosphere and subsequently inhaled can be calculated on an assessment of the fate of the products retained. If the products are insoluble in body fluids, little if any irradiation of the gonads could occur from inhalation; if soluble, a fraction of the retained products (the retained fraction in lungs and respiratory tract is 75 per cent, I.C.R.P., 1955) would be generally disseminated in the bloodstream. The calculation has been based on the assumption that 20 per cent of the inhaled disintegration products are effective in irradiating general body-tissues, and an exact formula has been used in calculating the equilibrium energy dissipation. The total dose-rate to soft tissues due to the inhalation of air containing 3×10^{-18} c/l of radon plus disintegration products is then 1·9 millirem per year.

The total dose-rate to soft tissues due to the inhalation of air containing 3×10^{-18} c/l of radon plus disintegration products might be expected, therefore, to be about 0·0022 rem/year. At the radon concentration of 3×10^{-12} c/l reported by Anderson *et al.*, (1954) for London air the dose-rate thus calculated would be 0·022 rem/year, i.e. a figure comparable with the cosmic ray background.

Total dose-rate to the gonads

Before summarising the total gonad-dose from all sources the effect of body-shielding on the local gamma ray dose should be considered. Measurements have now been made of this shielding factor by using a water-filled tin model. A thin-walled tube was fixed in the trunk so that a small geiger-counter could be positioned at the site of an ovary. The counter was placed

TABLE 3J

The screening factors for local gamma rays: horizontal, sitting and standing postures

Position of model	Screening factors for local gamma rays			
	Female	Mean	Male	Mean
Horizontal	0·52		0·67	
Sitting	0·58		0·70	
Standing	0·59	0·56	0·72	0·70

Mean factor for both sexes 0·63

outside the trunk to assume representative positions for the testes. Measurements were made in a laboratory (site IIIb in Table 1J) where the background was known to be steady. The cosmic ray response of the counter was allowed for by measurements made inside a cubicle shielded by a minimum thickness of 9 in. of steel. The screening factors for horizontal, sitting, and standing postures are given in Table 3J.

The correction for the cosmic ray component inside the building could only be estimated approximately, but if this were in error by as much as ± 100 per cent it would produce errors in the screening factor of not more than -8 or $+4$ per cent. In the male, the factor varies with the position assumed but by not more than ± 8 per cent. The average ratio for the two sexes should not be in error, therefore, by as much as ± 10 per cent.

Summary of dose-rates to the gonads

Table 4J summarises dose-rates which may be regarded as typical for regions in this country and possibly elsewhere, where the local rock radioactivity is not specially high, and the buildings are of brick or concrete construction not incorporating specially radioactive materials such as granite or granite chips. In arriving at the dose-rates a gonad shielding factor of 0.63 has been assumed, and the local gamma ray dose is averaged for an assumed 8 hours* out-of-doors and 16 hours indoors.

TABLE 4J

Dose-rates to the gonads for a region of 'normal' ground radioactivity

Radiation source	Dose to gonads per year (rad)
<i>External irradiation</i>	
Cosmic rays (sea level)	0.028
Local gamma rays (Leeds, 78 millirad/year indoors ... 48 millirad/year out-of-doors) ... } ...	0.043
Radon in air, 3×10^{-13} c/l	0.001
<i>Internal irradiation</i>	
Potassium 40	0.020
Carbon 14	0.001
Radon + disintegration products, 3×10^{-13} c/l ...	0.002
Total dose per year	0.095†
Dose to age 30 years	2.85†

† Includes allowance for the R.B.E. of the alpha radiation where present, and therefore also expresses the gonad-dose in rem.

Table 5J illustrates an attempt to assess the gonad-dose to populations in three different localities and in different types of building. Estimates are given for two radon-in-air concentrations but it is not known whether levels as high as 3×10^{-12} c/l persist for long periods.

It should be noted that higher dose-rates and greater differences between localities could be obtained by taking the extreme values observed in some of the Stockholm and Aberdeen sites, but an attempt has been made to assess as far as possible the conditions affecting large numbers of people. Thus, because even agricultural workers spend probably 8 hours per day or more

* This is a maximum figure and is probably an over-estimate.

TABLE 5J

Assessment of the gonad-dose to populations in three different localities and in different types of building

Location	Type of building	Dose to gonads (rad per year)*	
		Radon 3×10^{-13} c/l	Radon 3×10^{-12} c/l
Leeds	Brick	0.095	0.125
Aberdeen	Granite	0.108	0.138
Stockholm	Wood houses ... Type 2 houses ... Type 3 houses ...	0.095 0.109 0.160	0.125 0.139 0.190

* Gonad shielding factor, 0.63; exposure, 8 hours out-of-doors and 16 hours indoors.

in a brick house, their gonad-dose is not very different from that calculated for a Leeds town-dweller. The body-shielding factor of 0.63 considerably reduces the difference otherwise apparent in situations of differing local radioactivity.

DOSAGE IN BONE

Consideration should be given to the problem of dosage in bone from natural sources, in order that the significance of the ingestion of bone-seeking radioactive isotopes may be properly assessed. The dose-rate to osteocytes has been estimated, therefore, by a summation of the dose-rate from sources external to the bone and that from radium deposited in the skeleton itself.

Dose from sources external to bone

The dose-rates to osteocytes from the sources considered above will not be very different from the tissue doses already calculated. The dose-rate from potassium 40 will be less, because the potassium content of the bone is only about one-quarter of that for the body as a whole. The dose-rate from inhaled atmospheric radon and its products may also be expected to be greatly reduced, because even if the radioactive content of an osteocyte from these sources were the same as that deduced for soft tissues, the alpha particles would leave only a small fraction of their energy in the osteocyte itself. The reduced dose-rate to osteocytes for the conditions assumed in Table 4J might be put at about 0.08 rem/year.

Dose from radium in bone

The most likely value for the radium content of the skeleton for a region not exceptionally high in radioactivity would appear to be the mean content of 1.2×10^{-10} g. measured by Hursh and Gates (1950) for subjects in Rochester, New York, U.S.A., where the radium content of drinking-water is given as 0.6×10^{-16} g./cc. If the skeletal radium is proportional to the radium level in drinking-water, the measured level of 1.1×10^{-15} g./cc for tap water in St. Ives (Gleuckauf and Jacobi, 1953) would imply a body radium content of 2.2×10^{-9} g. Swedish waters are known to have very much higher radium contents, implying body radium contents approaching 10^{-7} g., but measurements of body gamma ray emission by Sievert (1953) do not suggest radium contents of this order. In fact a cross-check in 1953 between Sievert's apparatus and one in Leeds indicated that measured activities of persons not occupationally exposed to radium salts were about the same in Stockholm

and Leeds. These measurements, however, do not exclude small skeletal-radium burdens of the order of 5×10^{-9} g.*

A mean radium-burden of 10^{-10} g. has been taken as typical for a region not specially radioactive, and a mean burden of 10^{-9} g. of radium for an active region like St. Ives. Using methods similar to those given by the author elsewhere (Spiers, 1953) the mean dose-rates to osteocytes have been estimated as in Table 6J.

TABLE 6J
Estimation of the mean dose-rates to osteocytes

Conditions	Ra in skeleton (g.)	Dose-rate to osteocytes (rem/year)		
		Ra	External sources	Total
Not specially active region, e.g. Leeds 3×10^{-13} c/l radon in air	10^{-10}	0.037	0.08	0.12
Active region 3×10^{-12} c/l radon in air	10^{-9}	0.37	0.18	0.55

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F. W. SPIERS

* Recent work in America and in Germany has confirmed the value for the skeletal-radium burden as about 10^{-13} g., and suggests that burdens greater than 10^{-9} g. are unlikely.

APPENDIX K

The Genetically Significant Radiation Received from Diagnostic Radiology

The total number of X-ray examinations performed per annum

Information under this head relating to the National Health Service has been obtained from the Annual Reports of the Ministry of Health. Other information was supplied by the Services, other Government departments, and various bodies which undertake diagnostic examinations.

Hospitals operating under the National Health Service are responsible for by far the biggest proportion of the X-ray diagnostic work carried out in this country. Total figures for the number of X-ray examinations performed at these centres are available for the years 1951 and 1952; for the years 1953 and 1954 however the only information given is the number of 'units of work done'. Between 1951 and 1952 the number of examinations carried out under the National Health Service (Table 1K) increased by 13·2 per cent, and between 1953 and 1954 by 10·9 per cent. It has, therefore, been assumed that the mean of these figures, 12 per cent, would fairly represent the increases for 1952-53 and 1954-55. The number of examinations carried out in 1954 was estimated by applying to the number of 'units of work done' the ratio derived from the previous year's figures, i.e., that 1 examination equals 1·8566 'units of work done'. The figure for examinations performed in 1955, estimated on the assumption that the trend shown in the previous years continues, is, therefore, approximately 12,200,000.

TABLE 1K

The number of X-ray examinations per year carried out at National Health Service hospitals : 1951-55

Year	Number of 'units of work done'	Number of examinations
1951	—	7,738,389*
1952	—	8,756,643*
1953	18,214,310*	9,810,365†
1954	20,201,177*	10,880,506‡
1955	—	12,189,801†

*From the Annual Reports of the Ministry of Health.

†Obtained by adding 12 per cent to the figure for the previous year (see above).

‡Obtained by applying to the number of 'units of work done' the ratio derived from the previous year's figures, i.e. that 1 examination equals 1·8566 'units of work done'.

This total refers only to National Health Service hospitals. It has been assumed that hospitals outside the Health Service undertake 3 per cent of this number of examinations, i.e., 350,000, and that private medical practice accounts for a further 100,000 examinations. It is further assumed that the distribution between types of examination and sex and age of the patients examined is sufficiently similar to justify the final total of 12,650,000 being treated as a single group.

The gonad dose per examination

The values used in the calculations for radiation dose to the reproductive organs are listed in Table 2K. They are based almost entirely on the work of Stanford and Vance (1955). These workers made careful measurements on more than 1,500 patients, largely at one hospital. For males, the measuring instrument was placed close to the testes; for females, at a point on the skin over the ovaries. A subsidiary experiment on six cadavers gave the ratio of ovary-dose to surface-dose to be expected for the different kinds of X-ray examination; it did not, however, give any indication of the dose received by the reproductive organs of a foetus. Accordingly, where the site of examination is remote from the pelvis of a pregnant woman, the dose to the foetal gonads is taken to be the same as that to the mother's ovaries; where the child is in the direct beam, however, the dose has been estimated from the information given by Stanford and Vance. For salpingography and pelvimetry, the doses used are the lowest that have been published in this country. In the case of pelvimetry, it is assumed that three films are taken in each examination, although many hospitals take more. The dose for salpingography is as reported by Barnett and Bewley (1955) and that for the foetal gonads in pelvimetry by Stanford (1951).

It must be emphasised that the doses quoted in Table 2K are those produced by the techniques and methods of only one hospital; further, this hospital is one where particular care is taken to reduce the gonad doses to the minimum.

TABLE 2K

The dose of radiation received by the gonads in the course of X-ray diagnostic examination of various parts of the body

X-ray examination	Dose (mr) received by the gonads		
	Male	Female	Foetal
Head ...	0.8	0.2	0.2
Teeth	4.75	0.8	0.8
Shoulder	0.22	0.03	0.03
Arm, hand	0.26	0.05	0.05
Rib, sternum	0.48	0.16	0.16
Chest—large film	0.36	0.07	0.07
"—mass miniature radiography	0.25	0.15	0.15
"—special*	37	5.4	5.4
Barium: swallow and meal	20	9	9
enema	40	20	20
Abdomen	69	200	580
Cholecystogram	1.8	15.6	15.6
Pyelogram	486	1,290	3,210
Bladder	279	690	2,610
Pelvis	1,100	210	800
Hip, femur	710	210	800
Leg, foot	3.5	0.6	0.6
Spine—cervical	1.74	0.18	0.18
"—thoracic	22	15	15
"—lumbar	129	713	713
Lumbosacral joint	22	220	1,540
Sacro-iliac joint	129	713	2,700
Salpingogram		1,700	
Pelvimetry		1,280	2,680

* An average value for bronchography, tomography, etc.

TABLE 3K

*The genetically significant radiation resulting from diagnostic radiology:
England and Wales, 1955*

Examination centres	Type of examination	Males		Females		Foetal gonads
		Examinations as per cent of total*	Dose as per cent of total†	Examinations as per cent of total*	Dose as per cent of total†	Dose as per cent of total†
Hospitals	Head	3.9	0.1	3.4	n‡	n
	Teeth	0.2	n	0.3	n	n
	Shoulder	0.8	n	0.6	n	n
	Arm and hand	4.8	n	4.3	n	n
	Rib and sternum	0.4	n	0.1	n	n
	Chest—large film	11.8	0.1	12.5	n	n
	" —special	0.4	0.2	0.8	n	n
	Barium swallow and meal	2.6	0.4	1.6	0.1	n
	" enema	0.5	0.2	0.7	0.1	n
	Abdomen (including obstetric)	0.6	1.1	1.1	4.0	6.4
	Cholecystography	0.2	n	0.4	n	n
	Pyelography	0.7	3.0	0.6	10.7	2.3
	Bladder	0.1	0.1	0.1	0.4	0.4
	Pelvis	0.7	7.4	0.7	2.3	0.7
	Hip, femur	1.4	19.2	1.4	3.8	0.2
	Leg, foot	5.0	0.4	3.9	n	n
	Spine—cervical	0.4	n	0.7	n	n
	" —thoracic	0.5	0.1	0.6	0.1	n
	" —lumbar	1.4	2.6	1.4	10.8	0.7
	Salpingography	—	—	0.1	1.1	—
	Pelvimetry	—	—	0.1	3.0	15.6
	Total	36.4	34.9	35.4	36.4	26.3
	(Re-allocation of the foetal dose)s		13.5		12.8	
	Total		48.4		49.2	
General Dental Service	All types	1.8	0.1	3.0	n	n
Armed Services	" "	3.4	2.2	0.1	0.1	
Mass	" "	10.8	n	8.3	n	
Miniatu re Radiography	" "	0.2	n	—	—	
National Coal Board	" "	0.5	n	0.1	n	
Others	" "					
	Total	53.1	50.7	46.9	49.3	

* i.e. of the total of all X-ray diagnostic examinations in England and Wales, 1955.

† i.e. of the total of all genetically significant radiation received from X-ray diagnostic examinations in England and Wales, 1955.

‡ n = negligible (i.e. below 0.1 per cent).

§ Allocated between the sexes in the sex-ratio at birth, 1 : 1.059.

Classification of examinations by sex and age of patient and by type of examination

Information as detailed as this is not readily available in many hospitals. It has, however, been obtained for 2 London teaching hospitals, 2 general non-teaching hospitals in the Greater London area, and a children's hospital. In the few cases where appreciable discrepancies exist, weighting was in favour of the non-teaching hospitals. Information on the number of pelvimetry and obstetric abdomen examinations carried out was obtained from 9 hospitals, 5 of them outside London. Apart from these two types of examination, the number of unborn children exposed to radiation was calculated from the number of women of childbearing age examined.

Detailed results

The results of the calculations on the genetically significant radiation received from diagnostic radiology are given in Table 3K. The number of examinations has in each case been expressed as a percentage of 17,650,000, the estimated total number of X-ray examinations of all kinds performed in England and Wales in 1955. The doses received, weighted according to the age of the patients exposed, are expressed as percentages of the total genetically significant dose from diagnostic radiology in England and Wales in 1955.

For comparison, the genetically significant radiation dose from natural radiation has been similarly calculated. Dose rates of 0.10 rad per year for males, and 0.09 rad per year for females have been assumed, and weighted according to the ages of the population as a whole. The total radiation received from diagnostic radiology is found to be 22 per cent of that received from natural radiation by the whole population, and is in addition to it.

Strictly, these figures apply only to England and Wales, but there is no reason to think that the corresponding figures for Scotland and Northern Ireland will be greatly different. Each approximation in the calculation has, however, been estimated on the low side. According to the calculations based on the present sample, therefore, the value of 22 per cent should be regarded as a probable lower limit rather than as an estimate. A realistic estimate of the radiation contribution from diagnostic radiology might be considerably greater than this figure.

A more detailed presentation of the subject than is possible here has been prepared and is to be published shortly (Osborn and Smith, 1956).

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S. B. OSBORN

APPENDIX L

The Contribution of Occupational Exposure to the Genetically Significant Dose of Radiation

In order to calculate the amount of radiation contributed to the total gonad-dose by occupational exposure, it is necessary to know (a) the number of persons, distributed by sex and age, who are exposed to radiation in the course of their work, and (b) the average gonad-dose received per person exposed. Accurate information on these points is lacking at the present time, and the following estimate is based on the best available data.

An estimate of the average gonad-dose per worker can be made by analysing the data obtained by the radiation monitoring service operated at one time by the National Physical Laboratory and now by the Radiological Protection Service; this service measures the occupational exposure to radiation for workers in the fields of medicine, research and industry, excluding the Atomic Energy Authority. It is a voluntary service and its coverage is incomplete, since many organisations, particularly hospitals, carry out their own monitoring, and there are undoubtedly others where no monitoring is done. However, the average dose recorded by the N.P.L. Service is a low one, and all the available evidence suggests that the doses recorded by the self-monitoring organisations are of a similar order. In these circumstances it has been assumed that the data obtained by the N.P.L. Service are applicable to all workers, except dentists in private practice; analysis of these data gives the figure of approximately 50 mr per week, or about 2.5 r per year, as the average gonad-dose for both males and females in all occupations.

Practically no information is available about private dentists and their assistants, but it is clear that, taking into account the number and type of examinations involved, their exposure risk is very much less than that of radiologists and radiographers; given reasonable care, the average gonad-dose they receive will be considerably lower than the figure of 2.5 r per year just quoted.

Besides those persons actually working with irradiating equipment, there are large groups of people, for example nurses in hospitals, who are exposed to some extent as a result of their work-places being near a source of radiation. These people are not regarded as being radiation workers and are not monitored; their total number however, greatly exceeds that of the radiation workers, and although the average doses are very low, the aggregate dose is undoubtedly significant.

From the Annual Reports of the Ministry of Health, it would appear that there are at present about 9,000 persons, excluding private dentists, occupationally exposed in the medical field; and it is estimated from information supplied by the Factory Department of the Ministry of Labour and National Service that there are about 5,000 persons occupationally exposed in the field of industry and research. This total of 14,000 persons is divided roughly equally between the sexes, and these are the people to whom the figure of 2.5 r per year is considered to apply. Thus, the gonad-dose received per year by this group as a result of occupational exposure, is 17,500 r to each sex. In order to allow for the group of workers exposed at a low level mentioned

above, it is considered advisable to increase this aggregate dose by about 50 per cent, i.e. to 25,000 r per year, for each sex; and a further 1,000 r should be added for each sex to cover the doses likely to be received by those private dentists who possess X-ray equipment, and by their assistants. The final total, which, it will be appreciated, is a very rough estimate, would then be 26,000 r each for males and females.

There is, unfortunately, no precise information about the age-distribution of these groups, and the best assumption that can be made at the present time is that the females are all below the mean age of reproduction (for women, about 28 years) and that the males are evenly distributed between the ages of 18 and 60 (mean age of reproduction about 32 years).

The total number of females below the age of 28 in the United Kingdom is 10×10^6 . Each of these women receives a gonad dose from natural radiation of about 0·1 r per year, so that the total dose-contribution from natural radiation to this part of the female population is 10^6 r per year. Hence, at the present time, the occupational dose adds about 2·6 per cent to the genetically significant dose of natural radiation received by the female population.

For males in the United Kingdom, the population is about 5×10^6 between the ages of 18 and 32, and about 9×10^6 between the ages of 32 and 60. Only the dose-contribution for workers aged up to 32 is effective, so that the occupational exposure of genetic importance for male workers is about 9,000 r per year. The total number of males in the United Kingdom below the age of 32 is about 12×10^6 , so that this section of the population receives a total dose from natural radiation of $1·2 \times 10^6$ r per year. Thus, the occupational dose constitutes an addition of about 0·75 per cent.

Accordingly, in the United Kingdom the occupational contribution to the genetic dose from all sources except the Atomic Energy Authority is 26,000 r per year for females and 9,000 r per year for males, i.e. 35,000 r per year in all. The dose of natural radiation received by females up to the age of 28 is about 10^6 r per year, and by males up to the age of 32, about $1·2 \times 10^6$ r per year, making a total of $2·2 \times 10^6$ r per year. Hence, on the basis of the assumptions made, the occupational dose adds about 1·6 per cent to the genetic dose received by the population from natural radiation. It is to be noted that the contribution from the Atomic Energy Authority, reported by Farmer (1956), is 0·09 per cent.

I should like to thank Dr. G. H. Aston of the National Physical Laboratory and Mr. K. L. Goodall of the Factory Department, Ministry of Labour and National Service, who supplied some of the information on which the above estimates are based.

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E. E. SMITH

APPENDIX M

The Long-range Fall-out from Nuclear Test Explosions

This appendix summarises the data available on the radiation dose to human beings resulting from the fall-out from distant nuclear explosions. Continuous measurements have been made since 1951 by the Atomic Energy Research Establishment, Harwell, of the deposition on the ground of fission products from distant nuclear explosions. Measurements have also been made of the activity in the air at ground level in the United Kingdom, and on several occasions the variation of activity with height has been explored in the atmosphere up to 50,000 ft. (Stewart, Crooks and Fisher, 1955).

Diffusion and deposition of dust clouds from nuclear explosions

The dust cloud from a weapon in the 'nominal' size-range generally remains within the troposphere, reaching a maximum height of some 25–40,000 ft. when exploded in the middle latitudes. This part of the atmosphere is comparatively turbulent, and as the cloud travels downwind it diffuses both laterally and vertically and contaminates the lower atmosphere across a broad front at great distances. The dust is ultimately removed from the atmosphere by washout in rain-water and by direct deposition on to surfaces. Measurements made in the United Kingdom have shown that the former is the more important process and that the latter can be neglected in comparison; this conclusion however is not necessarily true close to the test site, where gravitational deposition may be an important factor. The United Kingdom measurements have also shown that, on the average, one half of the fine dust from the smaller type of nuclear explosion is removed from the atmosphere by rain-water in a period of 22 days. Deposition of the dust cloud from such explosions is therefore effectively complete within 3 months of the time of burst.

The behaviour of the clouds from explosions in the megaton class is markedly different. These clouds penetrate into the stratosphere, and may reach heights of the order of 100,000 ft. Diffusion is a very slow process in the stratosphere, and material returns to the lowest layers of the atmosphere at a much slower rate than in the case of the smaller type of explosion: a significant fraction of the dust generated may remain in the stratosphere for years after the weapon is exploded. Systematic surveys of the radioactive content of the air at various altitudes, taken in conjunction with fall-out measurements made at the same time, have shown that the dust from these tests was being deposited at a rate of between 10 and 20 per cent per year.

Measurement of airborne dust at ground level

The concentration of radioactive dust in the atmosphere has been measured routinely by drawing measured volumes of air through filters and counting the resultant beta activity on a suitable geiger-counter. Ground-level measurements made at Harwell since 1951 have shown that the activity present in air is of less biological significance than that deposited on the ground. The average level of activity from nuclear explosions has been found to be less than 1 per cent of that due to natural radioactivity in the air, and the maximum level has never exceeded that due to natural radioactivity. The measurements also show that over the past 7 years an individual in the United Kingdom might, on the average, have inhaled a total of 3.4×10^4 dpm of fission products, including 8.7×10^3 dpm of fresh fission-products

(measured at an age of 10 days) and including the particles of relatively high individual activity (Heard, 1956). The remaining 2.5×10^4 dpm consisted of particles of low activity, owing to their low specific-activity or prolonged radioactive decay whilst airborne. For comparison, the continuous occupational permissible breathing-level for strontium 89 dust is 1.3×10^6 dpm per day over a working life. Table 1M summarises information on the particles which might have been inhaled, deduced from the detailed 'particle-size and activity' analysis. Only particles in the high and medium specific-activity groups are considered; particles in the lower specific-activity groups are of less individual importance.

TABLE 1 M

Estimate of the probable number of radioactive particles in the high and medium specific-activity groups, inhaled by any given individual in the United Kingdom over the past seven years

Particle size (μ)	High specific-activity		Medium specific-activity	
	Probable number inhaled	Total activity per particle* (dpm)	Probable number inhaled	Total activity per particle* (dpm)
1-2	7	5.4×10		
2-3	1	2.5×10^2		
3-6	0.5	1.4×10^3	112	
6-9	0.07	6.6×10^3	14	66
9-12	0.01	1.8×10^4	3	180

* Immediate half-life = 6 days.

The particles carry fission-product beta activity which decays approximately inversely with time, and the activities quoted in Table 1M are those at 10 days after burst. The only significant alpha activity in the particles is that of plutonium. The activity of a 10 μ -particle may vary from about 4 disintegrations per day to extremely low levels. The mean concentration of this alpha activity in the ground-level air over the period has been 2×10^{-17} μ c per cc compared with the occupational maximum permissible limit of 2×10^{-12} μ c per cc (International Commission on Radiological Protection) for breathing insoluble plutonium dust over an occupational lifetime.

Measurements of deposition

Measurements of the deposition of the activity have been carried out at Milford Haven and at Chilton, near Harwell, since 1951, and in New Zealand since February 1955. In the current system, rain-water falling on a 12×10 ft. polythene roof is passed through a cylindrical esparto-grass filter and is collected in a tank. The beta activity of the dried filter is measured by mounting it co-axially over a calibrated cylindrical geiger-counter. Samples of the filtered rain-water are evaporated and counted on the same counting system, so that a correction can be made for the solubility of the radioactive material. This measurement is made only periodically, since experience has shown that the solubility of material from any particular bomb-series does not vary significantly with age, and it is possible to use a mean figure.

The daily deposition records at Chilton and Milford Haven are generally similar, although they occasionally differ markedly in detail. All daily deposits

of surface activity greater than 5 mc per sq. mile observed between February, 1951, and December, 1955, have been arranged in groups, and the frequencies of occurrence of the various groups are given in Table 2M.

TABLE 2 M

The range of values of all daily deposits of surface activity greater than 5 mc per sq. mile, observed at Chilton and Milford Haven between February, 1951 and December, 1955

Range of values of deposited activity (mc per sq. mile)	Frequency of occurrence	
	Chilton	Milford Haven
5- 25	83	76
26- 50	9	5
51-100	3	1
101-150	3	—
151-200	1	—
201-250	—	1

The highest daily deposit at the sites was 190 mc per sq. mile at Chilton and 240 mc per sq. mile at Milford Haven; these occurred about the same time in heavy rain, some 5 days after the explosion of a weapon in Nevada in the autumn of 1951. The highest deposition in a single day from a thermonuclear weapon test was 25 mc per sq. mile at Chilton and 100 mc per sq. mile at Milford Haven.

The dose from deposited radioactivity

The gamma ray dose to human beings from each individual deposition of fission products has been calculated. Little difficulty has been experienced in dealing with the fission products from individual test series in which all the explosions take place within a period of a few weeks, or in interpreting the data when a series of nominal-bomb tests takes place in an atmosphere previously contaminated from thermonuclear tests; the difference in the time-scales of the deposition processes and in the decay-rates of the samples can be used to separate the components. The major difficulty arises when the stratosphere is contaminated with the fission products from thermonuclear tests widely separated in time. If, as we believe, the fine dust in the stratosphere is deposited at a rate of only 10-20 per cent per year, then it can be shown that more than 90 per cent of the integrated dose per generation is due to the single isotope, caesium 137.

The gamma ray dose from each individual deposition of fission products has been calculated, initially for the idealised case of an individual standing on an infinite flat plane. A protection factor of 3 has then been introduced to take account of the material which is washed into drains or is otherwise removed from the topmost layer of the earth's surface; this factor is believed to be conservative, since about one-half of the material already deposited has been found to be soluble in water. An additional factor of 7 has been allowed for the shielding provided by buildings* against the gamma rays from fission products; this figure has been derived from measurements carried out

* It is perhaps noteworthy that the reduction in dose from this cause is much less than the enhanced dose received from the gamma radiation from the natural radioactivity of the building materials (see Appendix J).

at the Atomic Energy Research Establishment with the gamma rays from cobalt 60, and is based on the assumption that the average individual spends 2½ hours daily out-of-doors.

The individual doses have been summed, and the total external dose to be received by the average inhabitant of the United Kingdom due to material deposited on the ground from bombs exploded before 31st December, 1955, is estimated to be 1·7 mr. About 75 per cent of this dose is associated with material which has yet to be deposited ; the dose due to bomb dust suspended in the air near ground level is negligible by comparison. It has also been estimated that if the various types of weapon continue to be fired at the present rates for an indefinite period, the ultimate dose per individual per generation of 30 years will be 26 mr ; this level will be reached in approximately 100 years.

Very sensitive methods of measuring the radioactivity of the human body have been developed in recent years, and there has been some indication, on the records obtained in recent months, of the presence of a 0·6 MeV gamma ray, which is suspected to be due to the fission-product caesium 137 arising from the fall-out ; it is not yet possible, however, to identify this radiation rigorously. The radiation has been observed qualitatively on body-monitoring records obtained at Harwell, and has been reported in some detail in progress reports from the Argonne National Laboratory in the United States. The highest body-activity detected so far in the United States is found to be 4×10^{-8} μc . This activity would, if maintained, produce a total-body irradiation of 0·6 millirad per year, or about 1/30 of the dose due to the naturally-occurring isotope potassium 40 in the body. The caesium activity in the body may be expected to fluctuate in step with the rate of fall-out, if the biological half-life is about 20 days as suggested by the International Commission on Radiological Protection, and if this activity in human bones arises from the direct contamination of herbage ; in this respect the caesium differs markedly from the strontium 90, which is cumulative. From the quantities expected in the fall-out and from the chemical and metabolic properties of this isotope, the caesium 137 in the human body due to uptake from food and water is unlikely, on the basis of present information, materially to affect the dose, calculated above, from the fission products deposited on the ground.

The accumulation in the human body of strontium 90 from fall-out

The rate of deposition on the ground of strontium 90 in the fall-out has been measured by radiochemical analysis and, since the spring of 1954, has been found to be approximately 6 mc per sq. mile, per year. The total at 31st December, 1955, was 11 mc per sq. mile. From the measurements of activity in the upper air, it is anticipated that the total from bombs already fired will rise in about 10 years to a maximum of approximately 45 mc per sq. mile. Should the various types of explosion continue at the present rates, the accumulated deposition is likely to rise to an equilibrium value of about 500 mc per sq. mile in about 100 years' time.

Because of its similarity to calcium, strontium is found to follow this element in the human food-chain. Measurements have accordingly been made of the strontium 90 activity per g. of calcium in samples of vegetation and soil from a number of locations in the United Kingdom (Bryant and Chamberlain, 1956). Using refined radiochemical techniques and anti-coincidence counting procedures, the activity per g. of calcium has also been measured in the bones of yearling sheep, in samples of milk, and in human bones. The representative figure for the strontium 90 activity of vegetation in the autumn of 1955 was about 35 $\mu\mu\text{c}$ per g. of calcium. The corresponding representative

figure for sheep bones was 14 μc per g. of calcium but in a few mountain pasture areas, values up to ten times higher have been recorded.

The maximum activity found so far in the limited number of human bone-samples in the United Kingdom is 1.2 μc per g. of calcium in the skeletons of one-year-old children. Adult bones show lower activities, ranging from 0.05 to 0.2 μc per g. of calcium. These levels may be compared with the maximum permissible level for strontium 90 in the body for occupational workers, recommended by the International Commission on Radiological Protection, which corresponds to about 1,000 μc per g. of calcium. The average radiation dose to the bone from a level of 1 μc per g. of calcium would be about 3 millirem per year, and may be compared with the dose to the bone from the background level of radium in the average person in this country (10^{-10}c), which is about 37 millirem per year, and from natural gamma radiation, which contributes about a further 80 millirem to the bone (see Appendix J).

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W. G. MARLEY

APPENDIX N

An Attempt to Estimate the Hazard from the Ingestion of Strontium 90

During the last fifty years, information has been accumulating about the induction of cancer in man and various species of animals by ionizing radiation and radioactive substances. Much of the evidence is qualitative and we have still very little reliable quantitative information on which to assess hazards.

The main risk from the absorption of bone-seeking isotopes is the delayed production of changes in bone, sometimes followed by osteogenic sarcoma, as well as blood changes consequent upon effects in the bone marrow.

The best human evidence is from the clinical investigation of patients to whom radium salts were administered for therapeutic purposes some twenty-five to thirty years ago, supplemented by earlier studies on industrial workers including those who ingested radioactive luminous paint. One of the most characteristic features of the production of malignant tumours of all kinds by ionizing radiations and radioactive materials is the very long latent period, often in the region of twenty years.

From a consideration of all the available evidence, the maximum permissible level of radium permanently incorporated into the skeleton has been fixed by the International Commission on Radiological Protection for persons occupationally exposed as 0.1 microcurie. From a comparison of the toxic effects of strontium 90 as compared to radium in animal experiments, the corresponding maximum permissible level for strontium 90 has been fixed at 1.0 microcurie. It must be appreciated that the biological effects of the radium and its breakdown products are probably largely due to alpha particles, whereas strontium 90 with its associated yttrium 90 emits only beta radiation. These differences in the energies and nature of the radiations, as well as differences in the patterns of distribution of the radioactive materials in the bone itself, probably cause the differences in biological effects. Strontium behaves chemically very similarly to calcium in bone formation and it is therefore natural to associate the two elements. The maximum permissible level of strontium 90 in the human skeleton corresponds to 1,000 micro-microcuries of strontium 90 per gramme of calcium in the skeleton, and it is this concentration which determines the dose level.

However, this maximum permissible level has been fixed for a group of adults educated in relation to the risks, under medical supervision, and working under carefully controlled conditions.

It is well-known that growing bone takes up more of the bone-seeking isotopes such as strontium 90, and concentrates them in the rapidly growing portions of the bone. It is also well known that rapidly growing tissues, such as those of children, are often particularly radiosensitive. We must also conclude from the available evidence that the damage produced by radioactive materials in bone is an integrated effect over the whole time and dose of the radiation. Since the radioactive half-life of strontium 90 is long (28 years), any material incorporated during childhood has a longer time to act than material taken up in later life. The danger is a little mitigated by the fact that radioactive strontium may not be retained in bone for as

long as radium. The biologically effective half-life of strontium 90 together with its daughter product yttrium 90 has been estimated by the International Commission on Radiological Protection as 2,700 days.

Another factor which suggests caution is that it is well-known that the irradiation of tissues in inflammatory conditions is more likely to induce tumour formation than the irradiation of normal tissues, and such conditions are more likely to occur in the whole population than in the specially selected occupational group.

It is difficult to fix precisely the lowest level at which tumour formation and other effects have occurred, owing to the fact that in many instances the material ingested by the worker or patient has been an unknown mixture of mesothorium and radium, and this uncertainty complicates the estimation of dose since the rates of decay of these substances are very different (mesothorium 6.7 years half-life and radium 1600 years).

Examination of the results of ingestion of radium by humans makes it clear that in the fixing of the maximum permissible level there is no great safety factor involved. A suggestive destructive lesion (in the dentine of the teeth) has been observed in a patient who carried a body burden of approximately 0.15 microcurie of 'radium' (probably a mixture of radium and mesothorium). Of 44 patients investigated by Looney *et al.*, 36 had body burdens of 0.4 microcurie or more; clinically recognisable, but not malignant, bone lesions were observed in 32 of these. The lowest level of pure radium producing a bone sarcoma in this series was 3.6 microcurie. Sarcomata were seen in five other patients included in this study, but these patients may well have ingested a mixture of radium and mesothorium. Among these five, the lowest level associated with the production of a tumour was 0.52 microcurie of 'radium' (mixture).

If we assume, in accordance with the agreed international recommendations, that 1 microcurie of strontium 90 carries the same risk as 0.1 microcurie of radium, then with all these considerations in mind, it would be unwise to fix the maximum allowable concentration of radioactive strontium in the bones of the general population, with its proportion of young children, at more than one tenth of the level agreed for occupationally exposed persons. That is, the maximum allowable concentration should not be more than 100 micro-microcuries of strontium 90 per gramme of calcium.

As we consider the possible effects which might be produced at lower dosage levels (that is, below one tenth of the maximum permissible level) our ignorance increases still further and we can only rely upon extrapolation from limited animal experience. It is still not possible to give a certain quantitative answer to the question of the relationship between dose and the frequency of bone changes, induction of tumours, and other effects of the radiation. At very low dose levels the incidence is so small in animals that the existence of a threshold below which no effect occurs has been postulated.

It appears however that each unit quantity of radiostrontium absorbed by the bone confers a certain probability of bone-tumour formation, the tumour development time perhaps decreasing and the tumour incidence increasing with the dose. On the whole, the experiments seem in favour of a proportionality between the frequency of tumours produced in a given length of time and the amount of radioactive material in the body even at low dose levels.

If we again assume, in accordance with the agreed international recommendations, that one microcurie of strontium 90 carries the same risk as

0.1 microcurie of radium, and attempt in this way to estimate the effects at one-hundredth of the maximum permissible level, we provisionally conclude that the effects are unlikely to be detectable. Nevertheless, if the concentration in human bones showed signs of rising greatly beyond one-hundredth of that corresponding to the maximum permissible occupational level it would indicate the need for immediate consideration of the problem.

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