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HAZARDS OF RADIATION

We practise our art in an age of unprecedented technological advance. We use tools in Medicine for the effects of which we must hold ourselves responsible. Each use of a method for diagnosis or treatment must be a matching of its relative advantages and disadvantages, both to the individual and to the community. Such a matching can be based only on facts and knowledge; and yet much of the time our judgment is expressed in terms of possibilities, probabilities, and statistical significance. In no field is this more evident than in the use of *x* rays. The most recent report of the U.N. Committee on the Effects of Atomic Radiation[1] has brought home to us once more the need to understand all that is known, and to realize that which is not known, about the effects of ionizing radiation. In particular we should heed the warning[1] that "it is prudent to assume that some genetic damage may follow any dose of radiation, however small."

With the discovery of *x* rays over 60 years ago, and the development of nuclear energy, Medicine was presented with a powerful tool for both diagnosis and treatment. But it was evident from the earliest work that damage and even death could result from *x*-ray exposure. Ionizing radiation, whether it is in the form of *x* rays, α, β, or γ rays, whether from outside or inside the body, has the potential for producing biological damage. The quality of the damage is independent of the physical character of the radiation, though the amount of damage produced is dependent on the character of the radiation, the dose, the rate at which the dose is given, as well as the physiological condition of the tissues exposed. In man the injury produced is either somatic (i.e., injury suffered by the individual himself exposed), or genetic damage, resulting from gonad exposure, which can be handed on to the next and subsequent generations. Acute somatic damage is produced only after relatively large doses have been given over a short period of time, and is not seen below a "threshold" dose. Recovery from the acute effects, or exposure to lower doses, may result in long-term somatic effects, of which leukaemia and other forms of cancer are the most publicized form. For some of these long-term effects there may be no "threshold" dose.

With this knowledge in mind, what then is the problem? The controversy arises first on the extent of the damage produced by low doses of radiation; and, secondly, on the justification of this damage in terms of advantage. The first is a problem for technical resolution; the second, for enlightened social decision. Both the M.R.C. report[2] of 1960 and the recent United Nations report[3] call for more investigations in the fields of ignorance to clarify the first issue; but it is only application of these findings which can help us to resolve the second. It will be many years before we have a clear-cut technical resolution, but recent work indicates that as our knowledge increases so does our awareness of the deleterious effects of even low doses of radiation.

What is meant by a low dose? We are each of us exposed to radiation from natural sources of about 100 mrad per year. This figure varies by 20% from place to place in the British Isles. It is approximately the same whenever we consider the dose to the bone-marrow, significant as a somatic target; or to the gonads, significant as the genetic target. It is very roughly estimated that this level might be producing about 10% of some of the neoplastic diseases which occur naturally—e.g., leukaemia—as well as 10% of the new mutations added to the pool of genetic damage. On this estimate, and on a linear type of dose-response relationship, can be based our decision on whether additional radiation exposure is justified either to an individual or to a population in the light of the risk involved. So far as the genetic effects are concerned, and this is reaffirmed in the recent report, any additional radiation exposure increases the risk of genetic damage in the population, and the genetically significant exposure of the population must be kept to a minimum.

What is this minimum? After the warning to the medical profession inherent in the 1956 M.R.C. report it became evident that with improved techniques it is possible to utilize *x* rays fully in medicine without increasing the genetically significant dose. These findings were confirmed in the Adrian Report, which showed the advantages which could be gained

[1] *The Times*, September 10, 1962.
[2] Medical Research Council 2nd Report. *The Hazards to Man of Nuclear and Allied Radiations*, 1960. H.M.S.O. Price 7s. net.
[3] The Report of the United Nations Scientific Committee on the Effect of Atomic Radiation, 1958 and in press.
[4] James T. Duhig and Monica Rifaat, *The Effect of Small Doses of Tritiated Thymidine on Leukaemic Lymphocytes*, 1962, Second International Congress of Radiation Research. Abstr. p. 47.
[5] Dougherty, Thomas F., *Comparison of Carcinogenesis by Single Injection of Five Radionuclides*, 1962. Second International Congress of Radiation Research. Abstr., p. 47.
[6] MacMahon, B., *J. nat. Cancer Inst.*, 1962, **28**, 1173.
[7] Stewart, A., Webb, J., Giles, D., and Hewitt, D., *Lancet*, 1956, **2**, 447.
[8] —— —— and Hewitt, D., *Brit. med. J.*, 1958, **1**, 1495.
[9] See *Brit. med. J.*, 1960, **1**, 1492.
[10] ibid., 1959, **1**, 1232; 1960, **2**, 1720.
[11] ibid., 1955, **1**, 775; 1956, **1**, 1472; 1961, **1**, 41, and **2**, 875.

by improving radiological technique. Thus minimum can mean that level which allows the use of radiation without unnecessary exposure. For those occupationally exposed to radiation a different criterion has been used, and a so-called "permissible" level has been established. With increasing knowledge of the effects of radiation, the limit of this "permissible" dose has been decreased from 100 rads/year in 1928 to 15 rads/year in 1947, and more recently to 5 rads/year. The general population "permissible" dose is 10% of this. Similar reductions have been made in the maximum permissible concentration in foodstuffs —for example, strontium-90, 100 $\mu\mu$g. Sr^{90}/g. calcium in 1957 to 33 $\mu\mu$g. Sr^{90}/g. calcium in 1960. This trend of increasing caution with increasing knowledge is likely to continue.

Two recent papers[4 5] have indicated damage from dose levels of internal emitters below those previously considered to be harmful. In one study with strontium-90 on dogs it is concluded that "if the present trend continues osteosarcoma may appear at maximum permissible concentration levels towards the end of the beagle life-span of about 20 years." The significance of such a finding in relation to man's life-span of about 70 years should be carefully considered. Even those working in the radiological field have underestimated the biological effect of the radiations from isotopes incorporated into cells as labels. Even the tracer doses of tritiated thymidine incorporated in the nucleus of leukaemic lymphocytes increased their ability to induce leukaemia.

If these data seem remote from an application, data are being presented in the clinical field which must bring the consideration of the use and abuse of radiation home to each of us. In a life governed by the statistics of road accidents, smoking, drugs, and food additives, we are as individuals becoming inured to these warnings. But the possibility of affecting an unborn child is a different matter, for it threatens the survival of the species. Only a detailed and careful study of the data can help us to reassure those who are fearful of our practices in relation to radiation. The data are summarized in a recent paper by Brian MacMahon,[6] where he discusses the possible effects of radiation on the foetus. In this, a study of the late effects of prenatal exposure, and in other studies, there has been demonstrated the high susceptibility of the foetus. The most radiosensitive period probably occurs from conception through about day 38, immediately after implantation. After day 38 higher doses are needed to produce overt abnormalities. It is now believed that 40 rad to the human embryo before day 28 may produce serious abnormalities, but at any time during the first forty days neurological damage could result from *x*-ray exposure. For these reasons it is advised that pelvic *x*-irradiation should be discouraged except during the nine days after the onset of a regular menstruation. This is a simple precaution which could well be instituted more widely in practice.

The genetic consequence of foetal irradiation also presents a problem different from the adult. The damage produced in a primordial germ cell of a 32-day-old human embryo probably gives rise to damage in thousands of cells of the adult gonad, so that the effect of exposure could well be carried to all its surviving progeny. The real controversy still arises over the effects on the foetus of low doses within the diagnostic range. Alice Stewart[7] and her colleagues reported in 1956, and confirmed in 1958,[8] a higher frequency of prenatal *x*-ray exposure in those children dying of leukaemia or other forms of cancer than in the control group. Since then several independent studies have either confirmed or contradicted these findings. The problem is that the relative risk might be so small that only very large statistical studies could demonstrate the presence or absence of an effect. Seven reports have not found a statistically significant excess of cancer mortality in relation to prenatal *x*-ray exposure, but none was large enough to have demonstrated a risk of less than 50%.

MacMahon's study of 734,243 children indicates a cancer-mortality rate 40% higher in those prenatally *x*-rayed than in the non-*x*-rayed population. The relationship held for three major diagnostic categories —leukaemia, neoplasms of the central nervous system, and other neoplasms. The mean dose to the foetus was of the order of 2,000 mrems, given at one time—that is, 20 times the background level spread out over a year. From these figures it can be estimated that the doubling dose for these late somatic effects in the foetus is of the order of 6 rads, about one-fifth of that estimated by the United Nations Committee as the doubling dose for similar effects in the adult.

Thus, after 60 years or more of using *x* rays we are still being presented with data warning us to exercise caution. And yet we must realize that ionizing radiations have proved, and will continue to prove, to be one of the most important tools in the advancement of science and medicine. An appreciation is needed in each of us of its potential for good, matched with its skilful use and recognition but not fear of its hazards.

Nevertheless, the urgent warning coming this week from the United Nations report repeats the alarm signal shown in Britain by the Medical Research

Council in 1956 and again in 1960. The Veale Committee,[9] also in 1960, concerned with reducing all sources of radiation hazard, called for the training of medical officers of health and general practitioners in radiological protection; and advocated routine training of all other users of ionizing radiation in hospitals, from senior physicians and surgeons to junior medical and nursing staff. The Adrian Committee,[10] dealing with hazards from medical radiology, showed in 1959 and 1960 that if the techniques of radiology were raised to the standard of the 25% of British hospitals with the lowest "dose" of radiation we could gain all the advantages of the medical use of *x* rays and at the same time cut down by half the amount of radiation given to the population as a whole. How much longer must these warnings be repeated before remedial action is fully carried out? The remedies are known and simple. The effect of damage from radiation is cumulative. The recommendations of the various authoritative committees referred to above, and reinforced many times in leading articles,[11] in the *B.M.J.*, should be carried through to completion as soon as possible.

NEW IDEAS ON INTUSSUSCEPTION

In adults laparotomy almost always discloses a cause for intussusception—usually a benign polyp or a pedunculated carcinoma. In children on the other hand an obvious cause is found in less than 2% of cases,[1 2] while the very number of theories explaining the aetiology of intussusception in childhood testifies to our real ignorance of its origin. That the symptoms can also be puzzling is illustrated by the letters in our correspondence columns this week following on the recent case reports by R. P. Cumming.[3]

Any watertight theory of aetiology has to answer some perplexing questions. Why is intussusception noted especially in well-nourished children? Why is the age incidence so sharply restricted to children under 2 years—and especially between 3 and 6 months?[4] And why is its anatomical site almost entirely in the region of the ileocaecal valve? W. S. Perrin and E. L. Lindsay commented on the prominence of the Peyer's patches in the terminal ileum,[5] and noted that it was abruptly reduced after the first year of life. Furthermore it has been pointed out that the age incidence of intussusception is also that of the gastro-intestinal upsets which are often associated with teething and beginning supplementary feeding.[6] By analogy with adults therefore it was suggested that intussusception was caused by inflamed ileal lymphoid tissue acting as a foreign body; and that localization to the ileocaecal region was brought about by the prominence of the lymphoid tissue, the narrowness of the lumen of the caecum, and the laxity of the mesentery at this age. There are several observations supporting this theory. First, intussusception is more frequent in some years and in certain months than in others, which fact suggests an infective cause in some cases. Secondly, contrary to some accepted teaching, low-grade fever is not infrequent[4]—and may indeed have been responsible for a delay in diagnosis before admission. Thirdly, at operation the lumen of the terminal inch of ileum is often apparently totally occluded,[6] while several workers have found enlarged mesenteric lymph nodes in almost every case.[1 7] In some instances histological proof of lymphatic hyperplasia has also been obtained.[7] Lastly, the bowel has frequently been noted to be hyperactive.[8] Until recently, however, two facts have seemed to be irreconcilable with an infective aetiology: first, the frequent absence of any signs of infective illness (except fever),[4] and secondly the failure to recover organisms from bacteriological culture of mesenteric glands.[9]

The discovery of viruses which cause localized lymphadenopathy suggested a possible causal role in "non-specific" mesenteric adenitis and acute intussusception. J. G. Ross and his colleagues in Sheffield[10 11] and P. S. Gardner[12] in Newcastle upon Tyne found evidence of concurrent adenovirus infection in cases of intussusception though they considered that a virus infection was unlikely to be the only cause. Three papers in this week's *Journal* both endorse and supplement these conclusions. On p. 700 Dr. T. M. Bell and Mr. J. H. Steyn report the results of virological studies in mesenteric adenitis and intussusception. Over a 15-month period virus was isolated from the mesenteric lymph nodes in 11 out of 17 cases of intussusception and 11 out of 31 cases of mesenteric adenitis; in five cases viruses were isolated from the lymph nodes of 50 control subjects—a statistically significant difference. Furthermore serological tests indicated a recent or concurrent infection with an adenovirus or an enterovirus in 16

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4 Morrison, B., and Court, D., ibid., 1948, **1**, 776.
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7 Richardson, L. A., *Lancet*, 1961, **1**, 563.
8 Hadfield, J., ibid., 1961, **1**, 166.
9 Strang, R., *Scot. med. J.*, 1957, **2**, 425.
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11 —— —— and Zachary, R. B., ibid., 1962, **2**, 221.
12 Gardner, P. S., *Brit. med. J.*, 1961, **2**, 496.
13 Court, D., and Knox, G., *Brit. med. J.*, 1959, **2**, 408.
14 Smith, I. McD., ibid., 1960, **1**, 551.