PERMISSIBLE DOSES FOR CRITICAL TISSUES

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Abstract—If dose rates regarded as permissible for occupational exposure of different critical organs or body tissues need to be determined less in respect of any likely impairment of organ function at these dose rates than of the risk of neoplastic change or relevant genetic effects, the criteria on which such dose rates are determined ought to be related to any available quantitative information as to the sensitivity of the various human tissues and cell types to such changes. Possible bases for such comparisons are reviewed.

ONE of the most important functions of the International Commission on Radiological Protection, and certainly one of the most difficult, must be its assessment, quantitatively, of the maximum levels of dose or dose rate that can be regarded as permissible, but which should not be exceeded, under various particular circumstances of necessary exposure to ionising radiation. This judgement is of course central to all protection requirements. Yet it is doubly difficult to make if we need to envisage the possibility of occasional radiation damage even at the lowest doses and dose rates, since we must then review, not only the numerical level of risk from various possible injuries at low doses, but also the levels of risk that could be regarded as appropriate for various circumstances of occupational or other exposure. The first is a radiobiological judgement that has to be made in the absence, fortunately, of any direct statistical evidence as to the harmfulness to man of radiation at low doses or dose rates. The second is a sociological judgement as to the right criteria of safety and limitation of hazard, a subject on which the community offers remarkably little direct opinion, at least in the necessary quantitative terms, although it is evident in principle that risks should be minimized, or eliminated if practicable.

I believe that the Commission's recent Publication 9[1] will be of value in helping to keep these difficult and important questions in perspective; and that the report of a Task Group of its Committee 1,[2] on the problems of radiation risk evaluation, will be particularly helpful also for the light it throws on the available quantitative evidence, and on the degree of safety that is implied by particular dose limits. This report is one which appeared in the February number of *Health Physics*—so happily offered by the journal and by the Commission as a tribute to our distinguished colleague and friend, Rolf Sievert.

The necessary translation of recommended limits of dose rate into the corresponding estimates of body burdens, organ burdens or intake—building the bridge from rads to microcuries—has been a heavy and an equally difficult task, for which we all owe much to the President of the Association, Karl Morgan, for his chairmanship of the Commission's Committee on Internal Exposure. This essential task, of making the Commission's recommendations meaningful in terms of monitoring, of organ or body contents, of intakes or excretions, has been the harder because of the sparseness of metabolic data for many nuclides in man, even sometimes in mammals, and a wide field of investigation has to be kept continuously under review to strengthen the bases for the guidance needed on many different elements. The work of special task groups on particular tissues, for example recently on gut and on lung, and currently on bone, is also being of great value in defining the metabolic models which can be used to describe the behaviour

of radioelements in tissues, and to establish criteria for appropriate monitoring.

But all these recommendations on internal dose depend on a basic question which I would like to discuss briefly, since it is also one which requires to be kept under close review in the light of developing knowledge. When individual organs or tissues are exposed singly—owing to selective concentration of particular radionuclides in or near them—what dose rates for each tissue will ensure a degree of safety to the worker equal to that involved when *all* the organs or tissues are equally exposed at 5 rem/year?

This problem again is a difficult one to resolve in the necessary quantitative way. It obviously is less hazardous for the lung only to be exposed at 5 rem per year than for the lung and all other tissues to be exposed at this rate. The dose rate for the lung as critical organ alone should therefore clearly be higher than that for whole body radiation; but how much higher, and what should be the basis for deciding the ratio to be used?

On present criteria, the maximum dose rate for most organs in the body, if irradiated singly, is three times that for whole body irradiation, with the exception of a higher ratio for skin, bone and the thyroid of adults, and a lower one for gonads and red bone marrow. The use in this way of the same limit of dose rate for most organs would seem appropriate, in the absence of better information on the sensitivity of particular tissues, if we are essentially protecting against impairment of organ function, which might well depend on damage to enzyme systems or cell structures that were similar in different tissues; and the very proper present references to the importance of the different organs to the body health reflect the same concern with impairment of function.

It is becoming increasingly clear, however, that, at the low doses and dose rates involved in protection limits, the metabolic function of the organ as a whole will be essentially unimpaired, and the relevant risks to the exposed individual are of the possible occasional induction of malignant change in certain tissues—other changes contributing to life shortening being at present more uncertain in man although probably present. The risks to the individual's progeny will depend on mutations induced by irradiation of germinal tissues. And risks to a foetus would be added in exposure during pregnancy. If these are the hazards, what should be the criteria for setting up permissible doses to different critical organs or tissues?

The following three assumptions might be appropriate as a basis for setting the dose limits for individual body tissues, if irradiated singly, in relation to that adopted for uniform whole body exposure.

Firstly, that the hazard of whole body irradiation is simply the total of the hazards of the radiation of its constituent tissues. This will clearly be untrue at high doses, when the probability of the development of somatic or genetic change in an individual would be affected by the possibility of his earlier death from another somatic effect, or perhaps from effects of radiation on the function of particular tissues or from more subtle effects on endocrine or other forms of co-ordination. At the low doses, and presumably the low probabilities of somatic effects, that apply for permissible dose limits, however, it seems likely to be a reasonable approximation.

Secondly, that within the range of doses or dose rates applicable to permissible dose limits, the frequency of harmful effects is about proportional to the dose or dose rate. This again will not apply for certain (e.g. some chromosomal) changes, or perhaps if high dose limits were postulated for relatively insensitive tissues, or for locally high dose rates associated with non-homogenous dose distributions. It has however been rather widely postulated for protection purposes and might be assumed as an approximation within the range of dose rates involved.

Thirdly, that dose limits for individual tissues, when irradiated singly, or for the whole body, when uniformly irradiated, are set so that the risk from any of these modes of exposure is equal in magnitude. This has never been formally stated as the basis for different tissue dose limits and there are obvious difficulties in assessing the weight to be attached to different risks such as of disease in the exposed individual or in his descendents, fatal and non-fatal disease, or malignancies occurring

after short or long latency. The general aim of an equally high degree of protection for different forms of exposure, however, seems basic.

If these three assumptions are accepted as criteria for reviewing dose limits for critical tissues, I think that the first problem, setting aside for the moment the rather special question of foetal irradiation during a pregnancy, must be to consider the relative total importance of the somatic effects in the individual exposed and the genetic effects in his progeny. To pose a definite question: if a population of a million people of all ages were exposed to one rad of whole body radiation, how would the total of resulting cases of leukaemia, other malignancy or other somatic effect in those exposed compare in importance with the total of all injuries resulting from genetic damage?

This question can of course never be answered by any simple quantitative comparison, between say the number of deaths caused in the exposed individuals and the number of deaths or severe disabilities induced in their descendents. Some opinion must however be expressed, or will be implied, in any attempt to allocate dose rates for different tissues and for the whole body—even though the opinion may simply be that the sum of genetic damage is at present judged likely to be about equal to—or to be several times as important as—the sum of the somatic damage.

Examination of the "Risk Report" indicates that the receipt of one rad by a million people might result in of the order of 50 to 100 fatal malignancies. This number of effects would be increased if non-specific ageing effects were important in man. It would be very much reduced if the dose response relationship in man were quadratic rather than linear.

The same population exposure might result in of the order of 10 seriously defective offspring in the first generation from point mutations, and probably a substantially larger number from chromosomal aberrations. It is indicated that the total number of defects in all generations might reach several hundreds, but should not exceed several thousands even if every point mutation was equivalent to a major defect.

Any comparison of the somatic and genetic impact of radiation is thus beset at present by great quantitative uncertainties, as limiting as those involved in judging the importance of the different types of effect; and either somatic or genetic damage might involve total frequencies of major effects of some hundredths of one per cent per rad. If estimates of the type and frequency of all induced genetic effects led to the opinion that these had an importance equal to that of all induced somatic effects, then strictly the limiting dose rate for the gonads alone should be twice that for whole body radiation: and a gonad dose rate of 10 rem per year would correspond with the whole body rate of 5 rem per year if the hazard from each form of exposure were to be kept to an equally low level. Or if the genetic effects were judged to be more important than the somatic ones, the dose rate for gonads alone should be correspondingly closer to that for whole body radiation.

We may, I think, approach the dose limits for other tissues in a similar way. Suppose for a moment that non-specific ageing effects were unimportant compared with the induction of fatal malignancies, and that leukaemia formed one third of all the latter—again, broadly, on the basis of the Risk Report. If so, and if somatic and genetic effects were held to be equal in importance, the effects of whole body radiation would be due—as to one half to the gonad irradiation, and as to one sixth (one third of the remaining half) to irradiation of the bone marrow, if this is regarded as the critical tissue for induction of leukaemia. If then the whole body rate was 5 rem per year, that for gonads alone should be 10 rem per year and for bone marrow alone 30 rem per year. Clearly one could extend this type of argument with increasing information. If for example the thyroid and the pancreas were each responsible for one third of the remaining malignancies, the dose rates for these tissues, if irradiated alone, should be 45 rem per year—the dose rate for any particular tissue being inversely related to the risk per unit dose for that tissue, at least to levels at which a linearity of dose effect relationship might be assumed.

These values of course are quoted merely as illustrations of the way in which the increasing amounts of quantitative information that are

becoming available on radiation effects will need to be kept in review to ensure that protection criteria are properly related to current knowledge. The next few years are likely to see some clarification of the estimated relative frequencies of genetic and somatic effects; of the relative importance of malignant and other somatic changes; of the greater or less sensitivity of different tissues to malignant change. Already an approximate comparison can be made as to the sensitivity to induction of malignancies in the foetus and in the adult, so that some estimate could be made of relative total risk for different dose rates in the pregnant and non-pregnant individual. When the causes for any non-malignant life-shortening become clearer, we shall be better able to judge of the relative importance of the irradiation of such tissues as muscle or fat in which tumour induction seems likely to be of insignificant probability.

What I have discussed is simply a personal view of emerging information which may in the future alter somewhat, even if perhaps not greatly, the relative importance attached to the irradiation of different tissues—although the present criteria for some tissues may prove to be unduly restrictive. And it is stimulating to see in the scientific programme of this Congress so many papers on subjects which bear upon our advancing knowledge of the types and importance of the hazards with which the Commission is concerned in its protection recommendations and with which we are all involved in our development of protection procedures: the cells which are most sensitive; the dose rates which are of greatest importance; the localization of nuclides within the body, within the tissue or within the cell which are of highest significance; and the techniques of monitoring which can ensure the fullest and most reliable protection. I am sure that there will be the greatest value in this Congress's review of the means of achieving effective radiation protection and of the problems and difficulties which arise in the very varied fields of protection which we will have under discussion.

REFERENCES

1. Recommendations of the International Commission on Radiological Protection (Adopted September 17, 1965). *ICRP Publication* 9. Pergamon Press, 1966.
2. Evaluation of risks of radiation. *Health Physics*, **12**, 239 (1966).

DISCUSSION

M. GIUBILEO (*Euratom*):

1. La ICRP pensa di includere le dosi ricevute per scopi medici nella dosimetria generale dell'individuo?

2. Ritiene attuale considerare il midollo osseo come organo critico per la leucemia in base alle acquisizioni recenti sulla patogenesi periferica della leucemia?

E. E. POCHIN:

1. I believe that one should base one's procedure on the view that, if any radiation exposure may involve some element of risk, the risk should be justified by the need for the exposure. Levels of occupational exposure should correspond to a degree of safety appropriate to good industrial practice, and would not be influenced if a worker additionally required a radiological examination of which the necessity should also justify any risk involved. If the risks of radiation are regarded, at these dose levels, as being additive, the permissible occupational exposure should, on this basis, be no more affected by the need for a radiological examination than, for example, by the need for a surgical operation.

2. I would certainly agree that one cannot exclude the possibility that leukemia might be induced solely by irradiation of the blood, the lymph glands or other tissues, or that irradiation of part of the red bone marrow may be less important than irradiation of all of it. I think that one should, however, regard the red bone marrow as a "critical tissue" for leukemia induction, and that permissible doses for the marrow should be set with this in mind.