Comments on the Proposed Change in RBE



A. There is no conflict which will be resolved by the proposed change.

It is well known[1,2] that the RBE depends on species, end-point, quality of the radiation, dose rate, fractionation of dose, general conditions of care and housing, etc. Without specification of these and other conditions of the experiment, the RBE will continue to be at best a vague and erratic concept. The imprecision is so great that nowhere in the literature does there seem to be any attempt to give it a precise meaning.

The usual form of the definition features a ratio:

$$\text{RBE} = \frac{\text{Dose of baseline radiation required for effect}}{\text{Dose of other radiation required for equal effect}} . \qquad (1)$$

It is clear that in nearly all the experiments involving mammals the dose pattern is not uniform even to within 5% or often to within 10%. Thus it is not clear what dose is to be used in the ratio. Is it the average dose in the entire animal? This would not seem to be the significant parameter in cases where a single organ is involved. If the maximum doses are used, this ignores radiosensitivity of particular tissues as well as synergistic effects. Since the RBE is known to be dose-rate dependent[1,2] and since the radiation field is frequently not constant in time, it is necessary to specify whether the total dose over the entire exposure period is to be used or some average dose, or a maximal dose rate over a shorter period. For example, consider the case of occupational exposure. If 0.1 μc of $Ra^{226}$ is accepted as a permissible skeletal burden and the permissible bone burden of the γ-emitting boneseeker $Sr^{85}$ is set at 120 μc, i.e.,

$$120\ \mu c = 0.1\ \mu c \times \frac{11\ \text{Mev/disintegration of } Ra^{226} \times 10\ \text{RBE for } \alpha}{0.091\ \text{Mev/disintegration of } Sr^{85} \times 1\ \text{RBE for } \gamma} ,$$

the comparison is really made on the dose rate at the end of a 50-year exposure period. The RBE that should be used would be one relevant to this type of exposure, and the doses used in (1) should be these maximal dose

1. K. C. Bora, Factors Affecting the Relative Biological Efficiencies of Ionizing Radiations. Progress in Nuclear Energy, Series VI, Biological Sciences, (Pergamon Press, 1959) pp 278-299.
2. J. B. Storer, P. S. Harris, J. E. Furchner, and W. Langham, The Relative Biological Effectiveness of Various Ionizing Radiations in Mammalian Systems, Radiation Research 6, 188-288 (1957).

rates at the end of the period. In short, the significance of the RBE as defined by (1) is inescapably connected or determined by the use that is to be made of it. If the RBE is to be used in comparing maximal dose rates, then it must be determined on the basis of the ratio of such maximal dose rates. Conceivably, an RBE determined on the basis of total dose might give a quite erroneous comparison.

It would seem that most scientists concerned with these problems have realized that the RBE is essentially an imprecise concept, and they have not attempted to give it great precision. It can be argued that in making it precise we destroy its usefulness. If species, dose rate, dose distribution, and every condition of the experiment other than radiation quality must be identical, we have a direct experimental determination of the level of effect for the required conditions of exposure, and no comparison is necessary to determine the effects of the given exposure. To be useful the RBE must be applied in slightly different situations, and in most of these situations the differences are of a kind which are known to affect the value of the RBE.

It does not appear that the distinction proposed by the ICRU will greatly clarify matters. Unless they are willing to forego further consideration of "the RBE for $\alpha$ radiation" and other such oversimplified phrases, the RBE will remain as imprecise as before. If the profession is willing to be more specific and only consider "the RBE for $\alpha$ radiation in human bone with end-point bone carcinoma at some time during 50 years of exposure at a dose rate and distribution comparable to that due to ingestion of $Pu^{239}$ at a constant rate of 13 mc/day during this period, exposure to begin at age 18, and other conditions to be typical of normal life for industrial employees," then the concept will be more nearly precise, although there does not seem to be any possible way of determining its value. The Main Commission of ICRP has, in fact, indicated this meaning of their RBE values without the pedantic meticulousness of the above phraseology (see Report of Committee I, 1954, pages 18-19) by saying that they apply to "all conditions of external exposure, all tissues, and effects of interest. etc." There is no conflict of such an RBE being assumed to be 10 and

having an RBE of 2 "for $\alpha$ radiation in rat bone with end-point bone carcinoma at some time during two years of exposure at a dose rate and distribution comparable to that due to ingestion of $Pu^{239}$ at a constant rate of 1/mc/day, etc., etc." Thus there is a conflict only if the assumption is made that there is an RBE for a particular quality of radiation which is independent of practically all other conditions of the experiments envisaged. The ICRP has not made this assumption but has selected values which, in the considered judgment of its members, represent acceptable approximations to these unknown RBEs. In the reference cited sanction is given to the use of any well-established relevant value which can claim general acceptance among those competent to judge.

If a relative hazard factor is adopted, this will resolve none of the above questions. This concept will involve all the above difficulties and conceptually can be distinguished from an RBE only with great difficulty. We did not adopt a new name for the unit of length to be used on the face of the moon opposite to us when we had no practicable way of measuring heights and distances there. The fact that we cannot determine RBE factors for conditions typical of occupational exposure is not altered by changing the name. We still have to use our best estimates, or guesses, of their value if we wish to base predictions and permissible levels on comparisons of doses.

B. Whatever change is made should be made only after careful consideration of the influence it may have on future developments.

If the concept of a hazard factor is introduced as distinct from the RBE, this will probably emphasize the point of view already voiced in some quarters that the permissible levels are, in fact, not scientifically determined but are only expressions of the personal views of the members of the Commission. Undoubtedly there is an element of judgment and of personal values underlying the "weighing of risks and benefits" which underlies the decision to adopt a given standard, say 0.1 $\mu$c of $Ra^{226}$ as standard of comparison for dose to bone. However, it is doubtful if the members of the Commission envisage this personal element as extending to the details of the calculations on which comparisons are based. Perhaps it is inescapable

that some value judgments are involved in deciding to accept a certain level of risk, but the comparison of biological effects due to specified conditions can be largely divorced from such considerations. Under specified conditions, a bone burden of 0.1 μc of $Ra^{226}$ is more carcinogenic than a bone burden of 0.04 μc of $Pu^{239}$ or it is not. Admittedly the answer, or relevant potency, is not known with any great precision, but it seems more in accord with usual scientific practice to use the best estimate experts can supply for the purpose in question, rather than seek to introduce a new concept which can scarcely be distinguished from that formerly used. The "best estimate for the purpose" is not necessarily the most accurate estimate from an objective point of view. The experts may choose to be "conservative." The more or less open admission that the Commission is not using scientifically validated data even in the details of its calculations is an unfortunate implication to suggest and is probably unwarranted. The estimates of these RBEs by the Commission are probably as good "for the purpose intended" as are most other criteria used in toxicology. There is no data known to us which suggests the contrary and much which suggests that these are conservatively appropriate estimates.

In the present ICRP publications fixed values of RBE are given which are suitable and generally applicable to internal dose calculations. These values are RBE = 1 for x, $\gamma$, $e^-$, $\beta^{\pm}$ (except in the case when $E_{Max} \leq 0.03$ Mev, and then RBE = 1.7) RBE = 10 for $\alpha$ and RBE = 20 for heavy recoil ions. For external sources of radiation values of RBE are given as a function of LET and these values were used by one of us (W. S. Snyder) to calculate the values of maximum permissible flux for fast neutrons for incident energies ranging ~~from 0.01 to 20~~ Mev. There is no great difficulty in theory or in practice in the application of these values to cases of chronic exposure and when more reliable data is available the above values will most certainly be revised. However, it is evident from experiments that the RBE for the general radiation syndrome is not necessarily the same as the RBE for more specific effects such as the weight loss of the gonad or the weight loss of the thymus. It appears likely that the RBE for many types of damage from exposure to neutrons or $\alpha$ radiation is considerably less for acute than

for chronic exposure. Nevertheless such generalizations must be made with caution because the RBE for cataract formation decreases with the dose rate. Even in the most elementary concept or basic experiment, when the dose rate is kept constant and the only variable is the energy of the monochromatic radiation, e.g., $\alpha$ particles impinging on a thin film of biological media, the RBE for each type of damage to the media probably increases as the incident energy increases beyond zero or finally reaches a maximum and then decreases with further increase in incident energy.

More serious and more subtle developments are likely to occur if the proposed change is made. The Commission is aware that particulate energy in bone for all radionuclides except $Ra^{226}$ is weighted with a "relative damage factor n" which is taken as 5. In some cases, such as $Pu^{239}$, this is truly a nonhomogeneity factor, and in other cases such as $Sr^{90}$ it must be termed a "relative damage factor" since the dose distribution due to $Sr^{90}$ is almost certainly more nearly homogeneous than the dose pattern due to $Ra^{226}$. This factor, in the case of $Sr^{90}$, rests on a rather direct experimental determination of the relative hazard of $Ra^{226}$ and $Sr^{89}$ as carcinogenic agents in bone. Whether this factor really corrects the high RBE of 10 for $\alpha$ radiation, or whether the lower, more uniform dose from $Sr^{90}$ irritates more cells while the more spotty dose due to $Ra^{226}$ kills the cells near to the "hot spots" (and thus wastes some of its energy on dead cells), or whether some other explanation is correct is not demonstrated. The factor stands as a "relative hazard factor" based on a fairly direct experimental comparison. Yet no parameter used in the current scheme of internal dose is less understood or requires more elucidation. It seems logical and tempting to adopt a "relative hazard factor," say H, and let it carry the burden of all such factors that are currently used. But if this is done the factor can hardly be determined by edict, or "legislation," without considerable repercussions. Thus, if we were to adopt H, and if H is to be defined as the factor by which energy of a given kind is to be weighted, and if for $\beta$ rays H is taken to be one while for $\alpha$ radiation H is taken as 10, then the permissible body burden of $Sr^{90}$ which is now 2 $\mu$c would become 10 $\mu$c based on a direct comparison of average doses to bone.

At present we have too little quantitative information on the dose distribution due to $Ra^{226}$ and too imprecise knowledge of the "significant volume" to make the comparison on any other basis.

While the n factor is probably the most important of these "relative damage factors" now used, there are others which might be included in this category. For example, $\alpha$ energy in the gastrointestinal tract is weighted by a factor of 0.01 since only a small fraction of the $\alpha$ energy penetrates the mucosal layer. This can be rationalized by deciding that the mucosal layer is not a body tissue of concern. However, this factor will appear in the computation of effective energy and might be included in a "relative hazard factor." It is apparent the factor will have to be carefully and precisely defined, and if it is to include all "weighting factors" that are used in computing effective energy, it must be carefully considered in individual cases and not "legislated" in uniform fashion without regard to organ, effect, condition of exposure, dose rate, other associated tissue irradiated, specific ionization, etc.

A more serious situation confronts us in the problem posed by the lymph nodes. Data accumulated during the past few years indicate that for inhalation of Pu and other heavy elements the lymph nodes may be the site of maximum concentration. A recent autopsy of one worker at Los Alamos revealed the concentration in the lymph nodes was some 20 times the concentration in the lungs and about 80 times the concentration in bone. Animal studies support this finding, although the quantitative dependence on particle size, etc., is not yet clearly established. At present the lymph nodes would be classed among the "other organs" for which the Commission recommends a dose limit equivalent to 15 rem/yr or 0.3 rem/wk. If this limit is to continue and if the RBE or relative hazard factor of 10 is to be used for $\alpha$ radiation, then the MPC values of $Pu^{239}$ will be lowered considerably. The question was raised at the Munich meetings as to whether the Commission might wish to consider RBE values which took into account organ specificity as well as quality of radiation, but it was decided to defer any present action or discussion of this question until adequate consideration could be given to all facets of the problem. Thus

if a relative hazard factor is to be defined, and if the Main Commission is to fix its value, the matter should be given very careful consideration. The question of appropriate dose limit and of relative hazard factor are almost inextricably interrelated. It is quite feasible to have a blanket limit of 0.3 rem/wk for all organs and end-points considered if the Commission wishes to recognize the organ and effect specificity of a suitably defined relative hazard factor. Thus the Commission must be precise in defining it, or its dose limits become almost meaningless, and it would be unwise to assume that the definition can ignore real differences in radiosensitivity of different tissues, dependence on end-point, etc.

This note is not intended to urge any particular action at this time, but rather to urge that the results of the present ballot should be sent to the members and that they should carefully reconsider the entire question. If a relative hazard factor is defined, its definition should be carefully scrutinized to see what effect this will have on present concepts, and if values are assigned, these should be carefully checked to see what effect they have on the present methods of arriving at operational values. It may be that the ICRP, like the NCRP in the USA, will find the question so involved that special consideration by a separate group is advisable. Only by very careful action can we be reasonably sure we will not have to retreat from an untenable position which was hastily assumed or arrived at by ballot without giving adequate consideration to all the many dependent variables.

W. S. Snyder
K. Z. Morgan
December 11, 1959