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Quantitative Risk in Radiation Protection Standards *

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Summary.

Although the overall aim of radiobiology is to understand the biological effects of radiation, it also has the implied practical purpose of developing rational measures for the control of radiation exposure in man. The emphasis in this presentation is to show that the enormous effort expended over the years to level quantitative dose-effect relations relationships in biochemical and cellular systems, animals and human beings, now seems to be paying off. The pieces appear to be falling into place, and a framework is evolving to utilize these data. Specifically, quantitative risk assessments will be discussed in terms of the cellular, animal and human data on which they are based; their use in the development of radiation protection standards; and their present and potential impact and meaning in relation to the quantity dose equivalent and its special unit, the rem.

Historical

Although harmful effects of radiation including carcinogenesis were appreciated from the earliest days, most emphasis was placed initially on short-term (early) effects. It was not until the 30's and 40's that the genetic and carcinogenic potential of "low-level" exposure began to be appreciated fully. In the context of radiation protection, quantitative risk was introduced in the mid-50's with the virtually-simultaneous publication of a British report on radiation effects (1), and the report of the Biological Effects of Atomic Radiation (BEAR) Committee of the American National Academy of Sciences (2). In the genetic section of the BEAR Committee report, quantitative assessments of the impact on human beings of given doses were made. The princi-

ples of dealing with a no-threshold situation, risk-benefit considerations, and "as low as reasonably achievable" were described explicitly. The risks of radiogenic cancer were not treated quantitatively to any degree until the late 1950's: the reports of UNSCEAR and of the ICRP in the late 1950's and 1960's (3,4) dealt extensively and quantitatively with mutagenic and carcinogenic risks. The BEIR (Biological Effects of Ionizing Radiation) Committee report in 1972 provided extensive estimates of both genetic and somatic effects of very low dose exposure (5).

The above estimates of effects were not translated directly into radiation protection practice for some time, although the estimated "risk coefficients" provided (the assumed slope of the dose-effect curve for exposed human populations) have been used extensively in the evaluation of risks from occupational and other exposure of individuals and populations. It is only quite recently (6,7) that the ICRP has outlined in some detail the role of quantitative risk in the radiation protection framework.

Limitations of Human Data for Risk Assessment

Central to the estimation of carcinogenic and genetic effects (risks) in man are dose-effect relationships, and their variation with dose rate. In Figure 1, incidence (see below for relationship between incidence of effect and risk) is plotted against dose, and typical data available on the human being (e.g., for human cancer from x- or gamma ray exposure) are represented as the hypothetical data points at relatively high doses, e.g., 100 or more rads. Of principal interest in the context of radiation protection is the very low dose (about 10 rads or less) region, in which no reliable data exist. Estimation of effect at these low doses thus must be obtained indirectly, and linear interpolation between background dose and incidence, and the data points at high

doses and dose rates (curve B, slope α_L in Figure 1) is frequently used for the purpose. This relationship is referred to as "linear, no threshold," and is to be contrasted with the curvilinear (curve A) relationship also shown in Figure 1. Much discussion centers around which (if either) function best represents the "true" relationship for human carcinogenesis. Obviously, the linear relationship predicts a greater degree of effect at low doses, than does the curvilinear function.

The low-dose part of curve A in Figure 1 in principle has the slope "α" in the formulation,

$$I = \alpha D + \beta D^2, \qquad (1)$$

(an additional "cell killing" factor would have to be introduced to characterize the higher dose regions of curve A).

in which I is the incidence of effect, D is dose and α and β are constants/ As shown below, this function appears to represent well a large amount of relevant data in "simple" cellular systems. Curve C approximates the slope obtained experimentally at low dose rates, i.e., if the doses represented by the three solid-circle "data points" were delivered at lower and lower dose rates, the data points would move downward and approach curve C. The limiting effect of lowering the dose rate would in principle be the superposition of curve C on curve D, the extension of the low-dose α_1 slope of curve A. Thus to a very large degree, the affect of lowering the dose or the dose rate is the same, and the two are often referred to as being interchangeable (i.e., departure from the linear, no threshold relationship and dose rate dependence are used interchangeably). The factor by which the linear, no threshold function may overestimate the effect at low doses and dose rates is the ratio of the slopes of curve B, to curve C (or ultimately, curve D). If the $\alpha D + \beta D^2$ model is used,

the ratio can be defined, at any given dose level, as the sum of the αD and βD^2 components, divided by the αD component. Much of the disagreement over the quantitative carcinogenic effects of low-LET radiation involves the most probable value of this ratio.

Dose-Effect Relationships in "Simple" Systems

Relationships among dose and dose rate can be evaluated most quantitatively in "simple" cellular systems, in which the effect of both variables can be studied in detail. The dose-effect curve for human chromosome damage is shown in Figure 2 is representative of a number of responses seen in cellular systems, and it corresponds to the $\alpha D + \beta D^2$ relationship described above. The similar dose-effect curve for the plant Tradescantia (spiderwort) will be used here, however, because of the wealth of highly-quantitative data available.

The basic Tradescantia data (8-11) are shown in Figure 3, in which the pink mutant events scored in the stamen hairs is plotted against dose. A log-log plot is used to make clear the extent and nature of the data at very low doses, i.e., below 10 rads. Obtaining these data points at low doses involves the scanning of approximately 300,000 stamen hairs, or several million individual cells, requiring several days of microscopic observation and a total of some two to three weeks of effort. Thus while the data (Figure 3) indicate clearly the proportionality of dose and effect at low doses, and the lack of a threshold, the frequency of the events is extremely low. The data up to about 100 or more rads can be represented well by the function $I = \alpha D + \beta D^2$, (the flattening of the curve due to "cell killing", obviously important at higher doses, is not considered here).

The effect of dose rate is seen in Figure 4, in which are shown on arithmetic coordinates (upper curve) essentially the same data shown in Figure 3. The two central curves with data points represent lower dose rates than used for the uppermost curve. The lower curve marked "X" represents the extension of the "αD" part of the low-dose curve in Figure 3, corresponding to curve C (and D) in Figure 1. The lowermost curve marked "γ" is analogous to the "X" curve in Figure 4, and is obtained experimentally if γ- instead of X- rays are used to determine the lower part of the curve in Figure 3. This substantial (factor of 2 or more) difference in the slopes of the X and γ curve, seen only in the lower "αD" portion of the overall X- or γ curves, is discussed elsewhere (12) and will not be dealt with here.

The effect of average dose rate (or exposure time) is seen in more detail in Figure-5 (11). A dose of about 80 rads was delivered at progressively lower dose rates. The effect/80 rads is seen to decrease progressively as the dose rate is lowered (exposure time lengthened), and the slope (effect/80 rads) is seen to approach asymptotically the (gamma) effect/rad at low doses, as seen in Figures 1 and 4. One can thus see that the lower limit of the effect per rad (slope) at very low doses, seen in the context of a full dose-effect curve (Figures 1 and 4) involving high doses and dose rates, is the same as the lower limit of the effect/rad (slope) using high doses delivered at low dose rates.

The linear and quadratic components of effect (Figures 1 and 4) are thus separable equally well, by lowering either the dose or the dose rate. The two components are shown separately in Figure 6. The "sub-effect" damage of the quadratic component can be repaired completely and at low dose rates is repaired completely before it can contribute to a visible lesion. The linear component

is without threshold and shows definite effects at small (fraction of a rad) or large doses, independent of dose rate.

These same dose-dose rate relationships are seen in studies on radiation-induced chromosome abnormalities in human cells in vitro (Figure 2 and Refs. 13-14), although the data are not as extensive as those given above for Tradescantia. Thus, for "simple" systems in which the number of cells showing a given effect can be scored, there is little question that the $\alpha D + \beta D^2$ formulation fits the data down to extremely small doses (i.e., there is no threshold), and that an effect at very low dose rates is definite and equal per rad to that of the "alpha component" seen at low doses.

Limitations of Cellular Models for the Intact Mammal

Although the types of damage to the genetic material discussed above and the $\alpha D + \beta D^2$ formulation most likely play a role in mutagenesis in animals and man (heritable mutations might be regarded as taking place in systems of essentially non-interacting cells), and perhaps in carcinogenesis (15-17), there is no assurance that dose-effect relationships for the more complicated end effect of direct interest, carcinogenesis, need follow the same type of function. For various reasons (e.g., multicellular basis for carcinogenesis, hormone and other influences, latent period perhaps exceeding remaining life span), the effect per rad at low doses and dose rates might well be less than expected from an $\alpha D + \beta D^2$ formulation, even if cellular damage of the types noted above were involved directly in the chain of events (18-22).

It is useful to consider the possible application of data from "simple" cellular systems to carcinogenesis in the intact mammal and man, and two papers (23,24) in particular represent useful contributions in this regard. It is pointed out (23,24) that the $\alpha D + \beta D^2$ model fits a large amount of data in in

vitro systems, and that a dose rate effect pertains. It is also noted that curvilinearity and a dose rate effect are also seen in carcinogenesis studied in animal systems, and that this factor, numerically, can be large. The application to man of these findings in animal systems is not accepted, however, on the basis that the mechanisms of carcinogenesis may well be different in animals and man. Values of α/β derived (Eq. 1) from in vitro genetic and cytogenetic effects on human chromosomes are then used to predict dose effect relationships for carcinogenesis in human beings. On the bases that "extrapolation" of human data to low doses is frequently carried out from dose levels of the order of 100 rads, and taking into account the "α/β" values of dose-effect curves for human chromosome abnormalities, it is concluded that the "linear, no threshold" assumption would be accurate within a factor of 2 for predictions at low dose and dose rates. This in vitro approach is thus considered to be better for prediction of dose-effect relationships in the intact human being, than are data derived on the directly-relevant endpoint, carcinogenesis, in other mammalian species, using the intact animal.

There are some specific uncertainties and difficulties with the arguments set forth, most referred to in the papers (23,24), that would argue against accepting this approach to prediction for human radiation carcinogenesis. Although direct causative relationships between the chromosome aberrations observable in surviving Japanese in Hiroshima and Nagasaki and carcinogenesis in these individuals have been sought, no definitive relationship has emerged (25,26). Persons having persistent radiation induced lesions in lymphocytes were found not to be at greater risk of developing malignancy than were persons without persistent lesions, and no karyotypic (chromosomal) abnormalities peculiar to A-bomb survivors have been noted in leukemic cells of exposed per-

sons. Perusal of α/β values provided (23,24), shows that genetic and cytogenetic endpoints, for both the mouse and for man, are highly variable but center around the value of 100. Thus one should be able to predict the same small "dose/rate effect" for the mouse, for carcinogenesis, as is predicted for man. This is contrary to extensive observations, however (see under "Animal Systems", below, in which dose rate effects by factors of 10 or more are observed). Thus while chromosome damage and cancer may well be related, the model appears not to have consistent predictive value for quantitative dose-effect relationships in carcinogenesis.

In summary of the data on "simple" systems, they provide models that, although useful as guides, can serve only as a framework for discussion of dose-effect, dose-rate relationships in more complex biological systems.

Animal Systems

Data on animal tumor systems shed considerable light on the question of dose and dose rate dependence and indicate that, although some broad generalizations are possible, the complexities make definitive statements difficult. Extensive data and summaries of relevant data are available (e.g., 5, 27-29), and no detailed treatment is attempted here. In Figures 7 to 9 are shown examples of dose-effect relationships under conditions of "high dose rate" and "low dose rate" (30). It is clear that a "dose rate effect" does obtain, i.e., the effect/rad is lower at low doses and dose rates. In some situations (Figure 10, ref. 27), the dose-effect curves appear to start out with a negative slope. These examples (and other data) indicate that the degree of effect differs among tumor systems, and within the same system but in different species. The overall statement can be made, however, that in general and apparently without exception the effect per unit of absorbed dose decreases as the dose rate decreases. The

degree to which dose and dose rate influence the effect per unit of absorbed dose, however, is highly variable among biological systems.

It is also apparent (Figures 7 to 10) that the degree of effect is difficult to quantify. The shape of the curves often is not simple or obvious, at either high or low doses and dose rates. The "low dose rate" curves may or may not appear to become linear at low-dose rates. There may be a clear cut dose rate effect even though the high-dose-rate dose effect curve cannot be shown clearly to depart from linearity. Many curves at high doses and dose rates flatten or decrease, an effect that is minimal or absent at low dose rates. Even a "reverse dose rate" effect may appear but this seems to be confined to certain tumors (thymomas, ovarian tumors) at high dose levels at which organ damage, instead of or in addition to cellular damage, is known to be, or strongly suspected of being necessary for the tumorigenic effect. The degree of "dose rate" effect depends on the precise temporal pattern of dose, e.g., low dose rate over a fraction vs. most or all of the life span; fractionation in large or small increments, closely or widely spaced; age of animals at time of dose delivery, etc.

Despite the above (and other) complexities, additional generalizations appear to be possible with respect to the degree of dose rate dependence. For some tumors, e.g., lung and breast, although there appears to be a dose rate effect, the function cannot be shown to depart appreciably from a linear, no threshold relationship (dose rate factor perhaps 2 or even less). Several tumor system responses, e.g., myelocytic leukemia, pituitary, uterine, harderian gland, appear to be approximated adequately by the $\alpha D + \beta D^2$ formulation, and both a "linear, no threshold" and pure dose squared function can be essentially excluded (dose rate factors perhaps 2 to 10 or more). Some tumors, e.g., ovary,

thymus, skin, appear to be described by a dose squared relationship (no detectable linear term), although a definite threshold seems more likely. "Dose rate factors" in the case of a threshold would have no meaning at the low doses of interest, since zero effect would be expected at any dose or dose rate below the "threshold".

Thus even for individual tumors it is difficult to arrive at a single number to indicate the extent to which dose rate may reduce the degree of effect. The factor might range from close to unity (little effect) to perhaps as much as 10 or more. It is even more difficult to arrive at a simple number that might apply to all tumors resulting from whole body exposure, although a factor of 5 has been given as an approximation (31). As a very rough estimate, most neoplasms would seem to be encompassed in the range of perhaps 2 to 10. A dose rate effect (factor of 3) has for many years been recognized explicitly by geneticists (5), in arriving at estimates of health consequences of radiation exposure.

The carcinogenic effects of radiation on man can be evaluated to a reasonable degree from an extensive body of data (5,27), and reasonable risk assessments can be made for exposures at intermediate to high doses of low-LET radiation, for a number of tumors. It is not possible to demonstrate from the data, however, that a dose magnitude or dose rate effect either does or does not exist (i.e. the uncertainty in the data is too large to prove or exclude either). Some data on the human being (female breast, thyroid; see References 5, 32 and 33) can be represented well by the linear, no-threshold relationship, but a quadratic relationship with a definite alpha term is not excluded by the data. Some "low dose rate" data on breast cancer from repeated fluoroscopic examination appear to yield risk coefficients similar to those obtained with ex-

posure at high doses and dose rates, but the uncertainties are large. Although these and other human data have been used as evidence that the linear, no threshold assumption may not be conservative (23,24), they are inadequate to allow a defensible characterization of the dose-effect relationship.

Spurred by Congressional interest, there has been a recent flurry of activity surrounding reports of excess leukemia in populations exposed previously in the relatively low dose and/or dose rate range, e.g., workers in national laboratories, workers in shipyards handling radioactive materials, and military men exposed during exercises involving atomic weapons. Perhaps most prominent has been the "Mancuso study" on national laboratory personnel. The preliminary reportedly-positive findings (34) have been seriously questioned (e.g., 35, 36). In summary, all of these claims are based on incomplete information, and although the circumstances must be investigated, it seems unlikely that they will represent a definitive contribution to the question of "low level" effects.

Also, extensive claims have been made (37, 38) about the presumed effects of diagnostic radiation, in utero and in the adult, based on reanalysis of large epidemiological studies done in the 1950's (39, 40). Neither the original authors nor the BEIR Committee (5) went beyond noting the positive correlations indicated by the results as well as the inconsistencies in the data and pointing out the need for additional confirmatory studies. The methodology used (37), and the conclusions, have been severely criticized (41).

Studies of thyroid tumors following scalp irradiation of children (42) have indicated that the "linear, no threshold" hypothesis may describe the effects. Although extensive efforts were made to reconstruct procedures and estimate doses, many uncertainties remain. Hence, while the data are not to be ignored, additional work is required.

Thus the data on human beings are not definitive and can be subject to different interpretations. Hence a strong consideration in determining the applicability of dose magnitude or dose rate factors in man is the use of animal data. Some previous Committees (27) have relied heavily on animal data to conclude that linear extrapolation should not be used for realistic estimation of consequences at low doses and dose rates. The BEIR Committee (5) on the other hand, relied principally on human data and provided estimates only on the basis of linear "extrapolation". The data on human beings were considered to be inadequate to show that a dose rate factor should be applied to human data, or conversely that it should not be applied. Animal data showing a dose magnitude and dose rate factor were not applied to man.

Although the NCRP and ICRP have used risk coefficients based on the "linear hypothesis" as an operational policy (6,43) and have stated that linearity may overestimate the true effect a low doses and dose rates for low-LET radiation, no factor has been introduced to take this into account quantitatively. A maximum factor of 5 was introduced as a realistic assessment in the context of a reactor safety study (31), to adjust for curvilinearity and dose rate factors. The move has been criticized (44).

In the human being, factors in addition to linearity and dose rate must be taken into account in risk assessment. The widely-used risk estimates based on linearity (5,27) are also based mainly on the absolute (vs. the relative) risk model, as well as on numerical estimates of the latent period and of the duration of the "plateau period" following exposure during which the incidence of tumors is greater than normal. There are continuing questions about these factors as well. The degree to which linearity overestimates depends not only on the relative size of the linear and squared contributions, but on the dose range

from which interpolation is carried out. It depends also on the degree to which the curve bends at higher doses due to "cell killing". These factors represent uncertainties in addition to the "linear, no threshold" question that must be taken into account in risk assessment.

In summary of the effects of low-LET radiation, important considerations in the quantitative estimate of risk of carcinogenesis in the human being are the related factors of the shape of the dose effect curve, the risk per rad at very low doses (about 10 rad or less) vs. higher doses, and the effect per rad of higher doses delivered at very low dose rates. Data on the human being, though extensive and adequate for quantitative risk estimation at high doses and dose rates, do not allow definitive conclusions on these factors. Data on "simple systems" of eukaryotic cells are represented well and in detail by a quadratic relationship with a definite linear term, and indicate that the linear no threshold, the pure dose squared and the threshold relationships are rare or essentially nonexistent. A dose rate effect is ubiquitous in animal tumor systems, but the extent varies widely among different tumors and species. Some data on carcinogenesis in mammals can be represented well by the "linear-quadratic" model, although the simple "linear, no threshold" and the pure dose squared, or more likely a threshold model may well apply in some tumor systems. Considerations and uncertainties in addition to curve shape and dose rate (e.g., the dose range from which interpolation is carried out, possible use of relative vs. absolute risk models, and longer plateau periods leading to changes in current "linearity" risk estimates) may tend to offset any credit that might be afforded by dose rate. Hence, while it is highly probable that dose rate does to some degree reduce the current risk estimates based on the linear, no-threshold assumption, it also seems probable that, at least for some time,

current carcinogenesis risk estimates based on proportionality (or close to it) probably will continue to be used as an approximation of the degree of risk associated with radiation exposure at very low doses and dose rates.

Quantitative Risk and Protection Standards: ICRP 26

Because quantitative estimates of radiation risks are becoming increasingly extensive and refined, and because of the tendency to refer to these estimates in the context of radiation standards, it is necessary to reexamine the framework of the standards in terms of suitability to accommodate the new quantitative information. Two recent ICRP documents (6,7) are quite significant in this regard because of the introduction of such risk estimates specifically into radiation protection. It is useful first to discuss the basic elements of, and the framework for a radiation protection system using quantitative risk (similar to that outlined on ICRP 26). The current radiation protection system is then discussed, followed by a summary of the changes that have been introduced (6,7), the relationship between risk and dose modifying factors, and some additional modifications in the ICRP system that might be considered.

In Figure 11 are shown the basic elements for a radiation protection system using quantitative risk. Central is a dose-effect (risk) curve, in this case for the "standard" low-LET radiation, for the effects of interest (total radiogenic cancers; plus genetic effects). Also shown is an "acceptable" total annual risk line, a level that cannot be determined on scientific bases alone (ICRP has determined this line by comparison with the amount of risk encountered in other "safe" industries). The intersection of these two lines must then fix the amount of dose that corresponds to the amount of acceptable risk, i.e., the annual upper limit absorbed dose in rads.

If the dose-effect curve has been quantified, (i.e., the slope in terms of risk/rad is known), then any incremental exposure in terms of absorbed dose is immediately translatable into an increment of absolute risk. One has the option of recording, summing and controlling incremental exposures in terms either of absorbed dose, or absolute risk.

Now consider a "non standard", or high-LET radiation, e.g., to fast neutrons, shown in Figure 12. One has two dose-effect curves, and the "acceptable risk" line is in fact an "isoeffect" or "isorisk" line that determines the annual limiting degree of effect for either type of radiation in a population, or the limiting risk for an individual in that population. As with the standard radiation, one can record and control incremental exposures by monitoring either the incremental absorbed doses, or the corresponding incremental risks. The incremental risks of exposure to the standard, and to the high-LET neutron radiations would be directly additive; the incremental absorbed doses would not because of the difference in slopes (risk/rad) of the dose-effect curves.

Because quantitative dose-effect curves for carcinogenesis were not available until recently, the option of exposure control by use of absolute risk was not available. Incremental absorbed doses of different radiations could not be added because of the different presumed risk values (effect, or risk/rad) of the radiations of different LET. Because one has two dose-effect curves and an "isoeffect" line (Figure 12), the RBE of the two radiations can be determined. This dimensionless ratio will "convert" a given absorbed dose of high-LET radiation into its "dose equivalent" (equivalent only in terms of effect, or risk) of the standard radiation, and the resulting increments of dose equivalent would then be additive. It was decided to introduce a new quantity "dose

equivalent" (designated H) as the physical quantity related to the radiation risk, with the special unit rem (the dimensions are the same as for absorbed dose, i.e., J/kg).

It is seen that the quantitative radiation protection system of dose equivalent and rem can be regarded as an administrative device designed to control and limit the absolute accumulated risk from incremental exposures to different radiations. With quantitative risk coefficients one can in principle do this directly by summing incremental risks. Alternatively, this can be done by summing increments of a surrogate for risk, e.g., dose equivalent in rem, that in principle can be evaluated in terms of absolute risk, if and when necessary.

Present System. The present (pre-Refs. 6 & 8) radiation protection system is described in basic outline by

$$H = DQN, \qquad (2)$$

in which H is the dose equivalent, D is the absorbed dose, Q is the quality factor and N is the product of other modifying factors (currently assigned a value of unity). The special unit of the physical quantity dose equivalent is the rem, and a dose equivalent of 1 rem equals 10^{-2} J/kg. The dose equivalent was introduced to "---provide a quantity that is related to the presumed radiation risk", such that, "---equal values of the product (of DQN) are postulated to correspond to equal radiation risk for any given target". The "critical organ" concept is used, and the annual exposure limit is 5 rem to the critical organs. No quantitative risk values enter directly into the limits established, and no level of "acceptable risk" is designated. For a number of years, however, quantitative estimates of genetic and carcinogenic (stochastic) effects per unit absorbed dose, estimated on the basis of the "linear, no threshold" hypothesis

and often taken to be upper limits for the risk at low doses and dose rates, have been available (4-6). It can be assumed that such risk estimates, applied to the annual 5 rads of low-LET radiation (5 rem), must have been deemed acceptable as an annual upper limit for occupational exposure. Thus historically a limiting physical dose equivalent, and by extension the risk associated with it, has been established, by virtue of "safe" usage over the years, as an acceptable upper limit.

While H is more closely related to risk than is absorbed dose, it is defined as a physical quantity and not as a measure or expression of risk. Thus, while QN (or Q, since N is unity) adjusts for differences in effect (risk) per unit of absorbed dose of different LET radiations for a given target, e.g., an organ or the summation of all organs (whole body), one rem to one organ or to the whole body does not necessarily indicate the same risk as one rem to another organ. Hence separate annual dose equivalent limits in rem are set for whole-body exposure, for some organs and for some forms of partial body exposure. Single-value reporting of summed exposures is usually given in terms of the "whole body" exposure only. Also, limits for some internal emitters may be given in terms of annual activity intake, activity concentration (e.g., μCi), instead of in terms of dose and dose equivalent. The organ exposures are not included in single-value summations of the total exposure. Hence no single value or summation of values of rem at present necessarily reflects the total risk incurred during the period of rem summation.

ICRP changes in present system. The most significant changes introduced by the ICRP (6,7) are the following: 1) the dose equivalent for uniform whole body exposure (H_{wb}) is related directly to the slope of the dose-effect curve for whole body exposure to the standard low-LET radiation. 2) A specific risk coefficient

value of 10^{-4}/person-rad (10^{-4}/?-rad) is attached to that slope i.e., 1 rem of H_{wb} is associated directly with a risk (detriment) of approximately 10^{-4} $?^{-1}$ (see ICR? 26 and 27 for precise meanings of detriment, harm, probability, risk, and the value of 10^{-4} $?^{-1}$ rem^{-1}). 3) A new approach to the determination of levels of "acceptable" annual risk for occupational radiation exposure is introduced, i.e., by comparison with the average risk experienced and accepted in a number of relatively safe industries. 4) The "critical organ" concept is abandoned in favor of the whole body concept, although dose equivalent for individual organs (H_T) is retained. 5) Instead of the system of separate annual dose equivalent limits for different organs or tissues, the inverse of those limits is provided as a series of weighting factors (w_T) to relate the risk of organ exposure to that of the equivalent whole-body exposure $H_{wb,e}$ (for which the risk is equal to the summation of the fractional, or w_T values of the separate organs, i.e., unity). Although the risks associated with one rem of H_T and H_{wb} are not equal and thus not additive, the portion of the annual limit $H_{wb,L}$ of 5 rem that may be received is restricted to 5 rem minus the summation of ($H_T w_T$) values received in the same year. 7) The fraction of the $H_{wb,L}$ limit of 5 rem that can be received is limited similarly to one minus the summation of individual internal nuclide exposures, each expressed in terms of the fraction of the annual limit of intake for the individual isotopes. Many of the changes are similar to those recommended earlier (45).

Thus for the first time in radiation protection the three basic elements of a health protection system for radiation exposure were made explicit (Figure 11), i.e., a) a dose-effect curve(s) for the potentially harmful agent(s), radiation(s); b) an "acceptable risk" level, and c) the annual absorbed dose

limit for that agent, determined from the intersection of the two curves. The ICRP has thus in effect reversed the historic process of setting dose limits. The risk coefficient of 10^{-4} P^{-1} rem^{-1}, for the carcinogenic and mutagenic (stochastic) risk of whole body irradiation from occupational radiation exposure was first established. The "acceptable risk" level, that cannot be determined on technical bases alone, was then arrived at in principle through a comparison with the levels of easily-identifiable serious risks that historically have been and are accepted in other "safe" industries (actually an average risk of 0.5 x 10^{-4} P^{-1} from the average annual occupational exposure of about 0.5 rem was noted to compare favorably with the average risk of 1 x 10^{-4} accepted in other industries, from which it can be inferred that the maximum acceptable annual risk level a associated with 5 rem, 5 x 10^{-4}/P, should also be acceptable). From these two values, of presumed actual risks per unit of exposure and acceptable annual risk, the D_{max} of 5 rad of low-LET radiation (5 rem) per year for whole body exposure was fixed (actually, the value so determined did differ, but not significantly, from the current value of 5 rem; hence no change was introduced). A useful addition would have been discussion of the limiting dose and risk to the individual vs. the range and average for the exposed population, and the relationships among them in establishing standards and controlling exposure.

Extension of the ICRP 26 system. In taking the several steps listed above, particularly by introducing the factor w_T and in abandoning the critical organ concept in favor of the whole body concept, the ICRP stopped just short of (but utilized the effect of) introducing a second factor w_T analogous to Q (w_T was used to limit exposure, but not as a dose modifying factor would be used; see above).

Had w_T been included as a factor, then Eq. (2) for incremental exposure to organ T could be rewritten,

$$H^*_{wb,e} = D_T\ Q\ w_T \qquad (3)$$

in which $H_{wb,e}$ is the effective whole body dose equivalent. For multiple-organ exposure (ultimate of which is whole body), the sum of w_T values (unity) is used. The Q is assumed to be the same for all organs. The risk associated with one rem of $H_{wb,e}$ is the same as that for H_{wb} 10^{-4} P^{-1}.

By the above approach the risk of partial body (organ) exposure is "normalized" to that of whole body exposure, and the "whole body" becomes incorporated into the "standard" (i.e., the "standard conditions" are then whole body uniform exposure to low-LET radiation). For example consider the whole body x-ray exposure to 1 rad, with a risk of 10^{-4}/P; an exposure of 1 rad of x-rays to organ T with a w_T value of 0.1, and hence a risk of 10^{-5}/P; and an exposure of 2 rads of neutrons (Q of 10) to organ T with a w_T of 0.1, and a risk of 2×10^{-4}/P. The respective dose equivalent values are 1, 0.1, and 2 rem. A dose equivalent of 1 rem in each case has the same associated risk value (10^{-4}/P), and the three values of rem and associated risk are additive for a total exposure of 3.1 rem, associated with a risk of 3.1×10^{-4} P^{-1}. Thus in going as far as the ICRP did and in the extension noted above, it is in effect recognized that dose equivalent should in principle take into account and reflect all factors associated with the risk of an exposure to an individual (i.e., different radiations delivered under different conditions of whole and

*It is evident that the use of "dose equivalent", factors to employ etc. must be in strict accordance with recommendations of the NCRP and/or ICRP. Hence $H_{wb,e}$ instead of H will be used here for possible extensions beyond present recommendations.

partial body exposure), and not just to one expression of radiation quality, LET.

Relationship between risk and dose modifying factors. It is useful to examine more explicitly the relationship that does or should exist between risk and dose equivalent. "Risk" of exposure is used here (see Ref. 6, for definitions) as the fraction of individuals in an exposed population that will die from a radiogenic cancer (could include genetic effects in offspring), which is also the probability p that an "average" individual in that population will die of radiogenic cancer. The "risk coefficient" is used as the slope of the dose-effect curve, or the effect (risk) per unit of absorbed dose (or per unit dose equivalent). The absolute risk (probability of effect) of a given exposure is the absorbed dose times the slope (the risk coefficient).

The dose equivalent H is clearly a physical quantity equal to the absorbed dose times one or more dose modifying factors (Eqs 2 and 3). Any of the dose modifying factors (e.g., Q) is usually taken as the ratio of the doses for equal biological effect, or, if the dose-effect curves are linear, the ratio of the risk coefficient for the test exposure condition, to that of the standard radiation and exposure condition. The dose-effect curves are usually assumed to be linear at the low doses of interest in radiation protection, and it seems likely that the assumption will continue to be made, for pragmatic if not for other reasons. Hence Eq. (3), for neutron exposure of target organ T, can be written,

$$H_{wb,e} = D_T Q w_T = D \frac{E_{wb,n}/D_{wb,n}}{E_S/D_S} \quad \frac{E_{pb,x}/D_{pb,x}}{E_S/E_S} \quad \text{---} \qquad (4)$$

where E is the effect or risk, and the subscripts n, wb, pb, x and s stand for high-LET (e.g. neutron) radiation, whole body, partial-body (organ), low LET (e.g., x-ray) and standard exposure, respectively. Note that the multipliers of D still represent dimensionless ratios, so that H remains a physical quantity with the same dimensions as absorbed dose.

Dose modifying factors in addition to Q and w_T might be employed, for still greater refinement of risk estimates, i.e., for macro dose inhomogeneities within organs, microscopic (many micron to millimeter dose) inhomogeneities. The ultimate of adding more factors would be estimates of the physical dose equivalent that reflect realistically the ratio of the risk of a given increment of absorbed dose, to the risk of the same dose increment delivered under a standard set of exposure conditions in which all factors included in Eq. (3) are unity. If the factors used are extensive and accurate enough, and if all of the factors are assumed to act independently as Q and w_T now are (ICRP 26, para. 104), then the product of all the factors in Eq. (4) must represent the ratio of the risk coefficient for the test radiation and exposure condition, to that of the standard condition.

Thus Eq. (4) could be rewritten,

$$H = D \frac{E_t/D_t}{E_s/D_s} \qquad (5)$$

in which E_t/D_t now represents the slope of the "actual" (observed) dose-effect (risk) curve for the test exposure, rather than the presumably-equivalent curve "synthesized" by use of several factors. The effective dose equivalent in rem for test exposure t is seen to be, in principle, D times the ratio of either 1) the risk coefficients for the test and standard exposure, 2) the respective

doses if the risk is held constant, and 3) the respective risks if the dose is held constant. Thus, in principle, dose equivalent and risk can be related specifically, and one can be derived from the other. In practice simplifications are of course necessary; hence usually dose equivalent would be expected to be related only approximately to risk.

If the dose effect curves (Eq. 4) are assumed to be linear, then the ratios of doses or of risks are equally valid to represent the ratio of the entire curves. If linearity is not known or assumed, it is equally invalid to generalize beyond a point determination of a ratio of either doses or risks, unless the functions describing the two curves are known or assumed.

Radiobiological considerations; direct risk vs. factors. Since $H_{wb,e}$ depends ultimately on risk coefficients that might also be used directly instead of H for practical radiation protection, it is necessary to examine and contrast the more radiobiological (as opposed to pragmatic) problems encountered in providing the necessary risk information for the two approaches. In perhaps oversimplified terms, the "direct risk" approach can be characterized as "situation specific", i.e., needed would be relatively large amounts of information (risk coefficients) in the form of charts or graphs, in which the specific exposure of interest (radiation type, "quality" in terms of either energy or LET, region of body exposed, specific isotope, etc.) would be found. A risk conversion factor would be provided, that would yield an absolute risk value associated with the measured or estimated "dose", in terms of either absorbed dose, another quantity (e.g., Ci/g, WLM) having a known or presumed relationship to absorbed dose, or in terms of mass. The increments of risk so determined would of course be additive.

The "factor" approach could be characterized as more generalized, i.e., a relatively small number of generalized "all purpose" factors (ratio of risk coefficients) would be provided that, when multiplied by the absorbed dose would provide additive increments of dose equivalent in rem. Hence absorbed dose must be known or assumed (e.g., Ci/g, WLM) etc. cannot be used or included in a single-number summation of total exposure or "risk"). The absorbed dose may have to be multiplied by more than one factor to obtain the $H_{wb,e}$.

The basic radiobiological risk data available are inadequate to develop either approach satisfactorily. Preference on purely radiobiological grounds would depend largely on 1) the degree to which dose-effect curves that apply to the single isolated variables implied by a factor (e.g., LET, degree of non-uniformity) can be developed, vs. the "situation specific" dose-effect curves in which several variables are known to be operative simultaneously, 2) the degree to which factors can be general in application (e.g., is the Q for one tumor in one organ, the same as that for another tumor in the same or another organ?), and 3) does the implied assumption (Eqs. 2 and 3) of the different factors acting independently in fact hold?

Although definitive evaluations of the above considerations are not available (specific studies of the problems have not been made), there is some relevant information. The RBE (on which Q is based in principle) is carefully defined in terms of its specificity to a given situation, casting doubt on its suitability for generalization. There is evidence that the RBE of neutrons for different tumors in the same irradiated human population may be appreciably different (32,46,47). The relationship between the amount and kind of tissue irradiated and the effect on (risk to) the individual is recognized widely as being neither constant nor simple. Most, if not all dose-effect curves for

human carcinogenesis, and certainly those for neutrons, include a "mix" of factors, i.e., there is a deviation from "whole body standard exposure" in terms of radiation energy, quality and dose distribution. With internal emitters, the situation is much worse because of shifting isotope location and hence of dose distribution in time and space. Hence it is difficult if not often impossible to determine a useful value of absorbed dose, let alone determine or apply a value of RBE (Q).

Hence the problems of attempting to derive and/or apply "pure" factors that in fact represent the risk variation as associated with that factor are large, and substantial simplification must be resorted to.

A number of the problems alluded to above in connection with the "factor approach" are also inherent in the "direct risk" approach; however many are or can be reduced appreciably in extent and severity. Key advantages with the "direct risk" approach include removal of the requirement to know or assume a value of absorbed dose, and the freedom (particularly with human data) to attempt to relate the actual risk per unit of "dose" as determined from one situation, to the probable risk in a similar but unknown situation, without having to employ or conform to intermediate stages of absorbed dose or factors that depend in principle on absorbed dose (this is in no way intended to imply that absorbed dose should not be used---it should be used whenever it can usefully be employed, and it must be used if factors are employed).

As brief examples of what is meant by the above statements, consider the Hiroshima neutron data. Dose-effect curves for several tumors can be determined, and "dose" is easily expressed in terms of kerma, entrance dose, "deep dose equivalent index", average dose, etc. (i.e., whatever the "user" health physics community finds most useful in practice). Hence risk/unit "dose" can be

obtained with some confidence, even at low doses. Extrapolation to the "dose"-effect curves expected in man for other-energy neutrons could be made by a knowledge of the changes in the markedly non-uniform dose distribution with energy, of the mix of organs exposed to different doses, and of the change in slope of the neutron dose-effect curve with neutron energy (not RBE related to x or γ rays) in animals (the change in degree of effect with neutron energy probably would be related more to changing depth-dose distribution, than LET). Contrast this approach with attempting to determine "RBE", for extrapolation to other circumstances. There is substantial question as to which dose parameter (e.g., average, midline, or entrance dose) should be used with such non-uniform exposure. There is also a question as to whether an RBE can be determined legitimately for one organ or for all collectively, because of the markedly non-uniform dose distribution within and across organs. The influence of radiation "quality" in terms of LET and RBE cannot be untangled from that of "quality" in terms of the energy spectrum and effect of dose distribution. Also, an RBE for man (related to x or γ radiation) cannot be determined satisfactorily at the low doses of interest because of the substantial uncertainty of the effects of low-LET radiation, and hence of the RBE as a function of dose. Pure "factors" would be extremely difficult to extract or apply.

A similar situation holds for internal emitters, for which there is a great deal of information in man. All of it is "situation specific", however, in that the effects of different "doses" are inevitably confounded by changes in the spatial distribution of dose with time. Hence absorbed dose and factors represent difficult or impossible intermediate steps, and the alternative of relating one known situation to another, and to unknown conditions directly and in terms other than absorbed dose and factors appears to have many advantages.

Use of factors vs. risk in radiation protection. Although H was extremely useful and indispensable prior to the use of quantitative risk, it must now be considered seriously if it is still necessary and/or desirable. The choices available include the following: 1) retain the present system, involving no direct use of quantitative risk. 2) Use the recently introduced ICRP approach. 3) Modify and extend 2 above, to make it a combined H-risk system and 4) go to a complete risk system.

Retaining the present system appears to be undesirable. It would be difficult to ignore or withdraw from the numerous risk estimates becoming increasingly available, and the associations extend between quantitative risk and the standards. The framework of the system as it stands will not accommodate adequately the quantitative concepts that have of necessity evolved with the introduction of quantitative risk.

The ICRP 26 system represents a substantial advance and is workable. It has introduced a number of accommodations to quantitative risk, but is not as complete and internally-consistent as it could be. It is unnecessarily complex, e.g., its aims in using w_T and the analogous approach for internal emitters could be accomplished more directly and simply.

A modified and extended ICRP 26 system would make it much more flexible and useful. Thus dose equivalent might be redefined to mean $H_{wb,e}$ (redesignate it to be simply H), i.e., include whole body as a part of the standard condition in the definition of $H_{wb,e}$. Dose equivalent as a physical unit would be retained, yet increments of all different types of exposure would be additive, and the summation of increments of $H_{wb,e}$ in rem, would be additive and readily translatable in terms of absolute risk.

A critical difficulty, however, lies with those internal emitters for which, because of spatial and/or time changes in the distribution of dose, a relevant value of absorbed dose cannot be estimated and hence the exposure is left in terms of activity per unit of exposure time (e.g., μCi/week). Because absorbed dose cannot be usefully calculated, dose equivalent as a physical unit cannot, strictly speaking, be estimated either. One could easily, however use direct conversion from a measurement other than absorbed dose (e.g., μc/g) to risk and hence to rem, with the implied assumption that the appropriate value of absorbed dose to a relavant tissue does exist in fact or in principle.

This "modified ICRP system" would be quite flexible and useful in the context of quantitative risk. Replacement of the current low-LET standard radiation with a specified fast neutron beam might be quite helpful.

In a <u>complete risk system</u>, the risk per increment of "dose" would be read directly from a series of dose-effect curves, for several radiations, for several energies and for whole and partial body exposure (Figures 11 and 12). Alternatively, tables of conversion factors F could be provided, to obtain risk from "dose" under different exposure (radiation type, energy, body region irradiated, etc). The "dose", however, could be in quantities other than absorbed dose, e.g., activity (μCi/g or μCi/cc), "working level months" (WLM). Conceptually, one could include the risk of non-radiation and non-radioactive toxins, in terms of amount (mass or volume) of exposure, or amount ingested or absorbed. In each case, the increments of risk so derived would be additive, including those from radiation and non-radiation exposures.

The advantages of going to a full-risk system as opposed to a strict "dose modifier" system are the following: 1) the risk of all incremental exposures (whole body, partial body, internal emitters) would be additive, and the summed

total would in principle reflect the total absolute risk incurred from all of the exposures, for the time period of summation. Thus the intermediate step of calculating (or assuming) values of absorbed dose could be bypassed, if indicated. 2) Records of exposure increments would be kept, in terms of absorbed dose (or other physical quantity used) as they now are, and as accumulated risk. 3) There would be no need for dose equivalent, rem, Q, any other possible factors, a standard radiation, or standard exposure conditions. 4) Since in either system (use of modifying factors vs. direct risk) the true risk must have been evaluated to accomplish the aims of either or both systems, the unnecessary additional step of providing generalized factors that are cumbersome to apply in the field would be avoided. 5) Changes in the evaluation of the risk of any radiation, high or low-LET, internal or external exposure, would be reflected in a change only in the risk coefficient for that radiation, and not for other radiations (as is usually the case when the various "factors" determining risk must be related to a "standard"). 6) The severe problems in evaluating and using Q at low doses and/or dose rates would be largely avoided.

The disadvantage is that of not having a physical unit for use in referring to the sum of multiple exposures. The dose equivalent in rem now allows this, but only under the limited conditions of presumed whole body external exposure, and exclusive of partial body or organ exposure, or exposure to internal emitters. Individual and summed exposure in the risk system could be referred to in terms of absolute risk values, or in terms of "risk units" (e.g., a risk of 10^{-4}/? could be defined as one "risk unit" (RU), or just "unit of exposure" (U)).

From the above discussion, it would appear that the present system, although quite workable in the absence of quantitative risk, falls short of accom-

modating adequately to quantitative risk. The new ICRP approach, particularly if modified and extended as suggested above, represents substantial advances. The full risk system appears to accommodate quantitative risk to the maximum extent and to allow maximum flexibility. It should be considered seriously for ultimate adoption, since the disadvantages do not appear to be serious. Only by use of quantitative risk can the more-defensible comparative (with other industries) approach to "acceptable" levels of radiation risk be used, to substitute for personal opinion and "usage".

Neutron Data from Hiroshima

A dose effect curve for neutron induction of leukemia, from Hiroshima, is shown in Figure 13 (47). Similar dose effect curves are becoming available for other individual tumors in Hiroshima, and for the total carcinogenic risk of fast neutrons (32,48-49). These data, though scanty, promise to have considerable significance not only in their own right, but for radiation protection in general.

The data represent the first dose effect curves available for an external beam of "high LET radiation" delivered to the "whole body" (the dose distribution is markedly non-uniform) of man. Hence there is now available some basis for direct comparison of high and low-LET radiation for the endpoint of overriding interest, carcinogenesis, for the species of interest, man. Prior to this the only data on high-LET radiation in the human being were derived from internal alpha emitters, and the comparison with external radiation is obviously difficult.

The curve (Figure 13) is consistent with a linear function. This may or may not be the true function, and the slope may decrease somewhat with increasing dose. There is little doubt, however, that the curve enters the ori-

gin with a positive slope, and there are data points at relatively low doses. Contrast this with low-LET radiation, for which a dose squared, or even a threshold function have not been ruled out.

Thus these data provide strong evidence against the existence of a threshold, at least for one radiation of considerable importance in radiation protection. Obviously, the absence of a threshold cannot be proved. The limits of uncertainty in this regard for the neutron curves, however, is less than that for low-LET radiation.

As a corollary to the above, the fast neutron data might then represent a better basis for the evaluation of the actual carcinogenic risk associated with the annual occupation limit of 5 rem. They would also provide an excellent (less hypothetical) basis for discussion of the level of risk that should be considered "acceptable". They would remove much of the uncertainty sometimes associated with the risk attached to low-LET radiation, i.e., a threshold for the high-LET radiation could not reasonably be defended.

For the above and other reasons, the neutron data from Hiroshima and Nagasaki must be extensively and even exhaustively evaluated with respect to dosimetry, data on individual tumors, and total carcinogenesis. The data also point up the importance of evaluating the role of nonuniform and partial body irradiation, in terms of their potential for carcinogenesis relative to that from whole body exposure.

Neutron Risk and Radiation Standards

The Hiroshima neutron data on leukemia in human beings, discussed above (Figure 13, Refs. 46-49) have been discussed in relationship to RBE and Q (46,47,50). The interpretations of the same data are quite different, however (46,47,49), and it is instructive to review the reasons for the differences.

Only the general approaches and the different conclusions (differences of about a factor of 10) will be discussed here. The actual risk coefficients for leukemia and their relationship to ICRP actual and "acceptable" risk are dealt with elsewhere (50).

The comparative neutron and gamma results of two sets of authors (47-49) are summarized in Table I, and presented graphically in Figure 14. The figure depicts the three dose-effect curves involved (neutron, n; gamma, linear no-threshold, γ_ℓ; and gamma quadratic, γ_q), and two possible "acceptable risk" lines, E and E/10.

One group of authors (48) concluded that the comparison gamma ray data could be fitted equally well with either the presently-assumed conservative linear, no-threshold function, or with a quadratic function (Table I, Figure 14). If the linear function for gamma rays is used for comparison, then an RBE of about 12 is obtained (Table I, and points a and b in Figure 14). This is very close to the current neutron Q of 10; hence the result is consistent with current assumptions on the relative and absolute carcinogenic potential of neutrons. Using a quadratic function with a small linear component for the gamma rays, a high RBE (or higher ~140) for neutrons could also be obtained. This clearly resulted, however, from the use of the quadratic function for the gamma rays as opposed to the current conservative assumption of the linear no threshold relationship. Thus any significance of the high RBE for radiation protection could be related only to the possibility of relaxing the exposure limits of the gamma rays (e.g., from 5 to 50 rads, from point b to point c in Figure 14). Using either assumption with respect to gamma rays, no radiobiological reason emerged from these authors' analyses (49) to suggest changing the current upper limit exposure level of neutrons from the current value of 0.5 rad per year.

Another group of authors (46,47) obtained the identical neutron and gamma coefficients (although only the quadratic function for gamma was used; Table I) as did the above authors, but reached startlingly different conclusions. They concluded that the hazard of neutrons is "unacceptably high" and that the annual neutron exposure limit (0.5 rads) is in need of downward revision with "some urgency" by means of an increase in the quality factor Q by a factor of about 10. It was added that ".....no changes seem necessary (in the limits for).....low-LET radiation, "which are conservative".

Some of the reasons put forth for the "unexpectedly high hazard" represent personal opinion related to the presumed level of absolute risk, and some are related to a comparison with the risk of gamma ray exposure. The opinion of an unacceptably high hazard derives from the extreme assumption that the individuals will be exposed to the annual dose limit. The evaluation can be criticized on the bases that competing risks are not taken into account (51); that RBE varies markedly among tissue types (52); /that average absorbed dose is used for the RBE determination; but that exposures are recorded in values closer to the kerma (51), and that average and not maximum dose, in effect, limits population exposure (6). Further discussion here, however, will be limited to these authors' (46, 47) perception of neutron risk relative to that of the comparison gamma radiation.

These authors (46, 47) used only the quadratic function for gamma rays, and elected to retain the annual limit of 5 rads for gamma rays. Thus, instead of placing the 5 rad limit for gamma at point b as had the previous authors (48), they chose to place it at point f, i.e., they assumed not only a different (quadratic) gamma dose-effect function, but also the different (E/10) "acceptable risk" level as well. Viewed from this vantage point (point f), it is then understandable why the neutron risk (0.5 rad, point a) was viewed as

"too high", with the suggestion that it be changed to 0.05 rad (point d). With the two changes (of "acceptable risk" level, and the gamma function to quadratic from linear), it then follows that the RBE would increase from about 10 to about 100.

As shown in the treatment of the data by the first authors (49), there is no radiobiologically-compelling reasons for the conclusions of the second authors (46, 47), i.e., there is no radiobiological reason given to change from either the linear to the quadratic function, or from the current risk level E to E/10, or both.

The full implications of the conclusions of the second authors (46, 47) are substantial. Although it is implied that only the neutron RBE need be changed and that no change in the gamma limit is required, clearly their recommendations would reduce the 5 rem/year exposure limit for all radiations, i.e., for alpha emitters, neutrons, x-rays, etc. More specifically with respect to gamma rays, had only one change (e.g., lower the acceptable risk level) been made, then the 5 rad (5 rem) gamma limit would have become 0.5 rad (0.5 rem). It is only by simultaneously changing the risk level and adopting the quadratic versus the linear no threshold gamma function, that the 5 rad gamma limit remains "unchanged". Currently it is not generally accepted, however, and it may well not be accepted, that a quadratic function should be adopted for gamma. If it is not, then the annual gamma limit of 5 rad (5 rem) would have to be reduced by a factor of 10, along with that for all radiations.

Hence, when viewed in its entirety in the context of the ICRP "acceptable risk" and actual risk framework, it becomes clear that the recommendations are much more extensive than a simple change in neutron Q. Rather, they represent

in effect a recommendation, not required on radiobiological grounds, that the current limit of 5 rem exposure for all radiations be reduced to 0.5 rem.

The above situation highlights the importance of, and the requirement for the ICRP move to establish a limit for "acceptable" risk for occupational radiation exposure by comparison with the risk now experienced in other "safe" industries. This approach goes far toward a desired goal, i.e., to remove the establishment of an "acceptable" upper limit of the risk of exposure from the realm of personal opinion, and to put such decisions on the defensible basis of being in line with widely-accepted practice in non-radiological occupations.

Figure 1

Schematic curves of incidence vs. absorbed dose. The curved solid line for high absorbed doses and high dose rates (curve A) is the "true" curve. The linear, no threshold dashed line (curve B) was fitted to the 3 indicated experimental points and the origin. Slope α_1 indicates the essentially-linear portion of curve A at low doses. The dashed curve C, marked "low-dose rate", slope α_{Ex}, represents experimental high-dose data obtained at low dose rates. This experimental low dose rate curve may in principle, at very low dose rates, approach or become indistinguishable from the extension of the solid curve of slope α_1, the dashed curve D labeled "limiting slope (α_1), low-dose rate" in Figure 1.

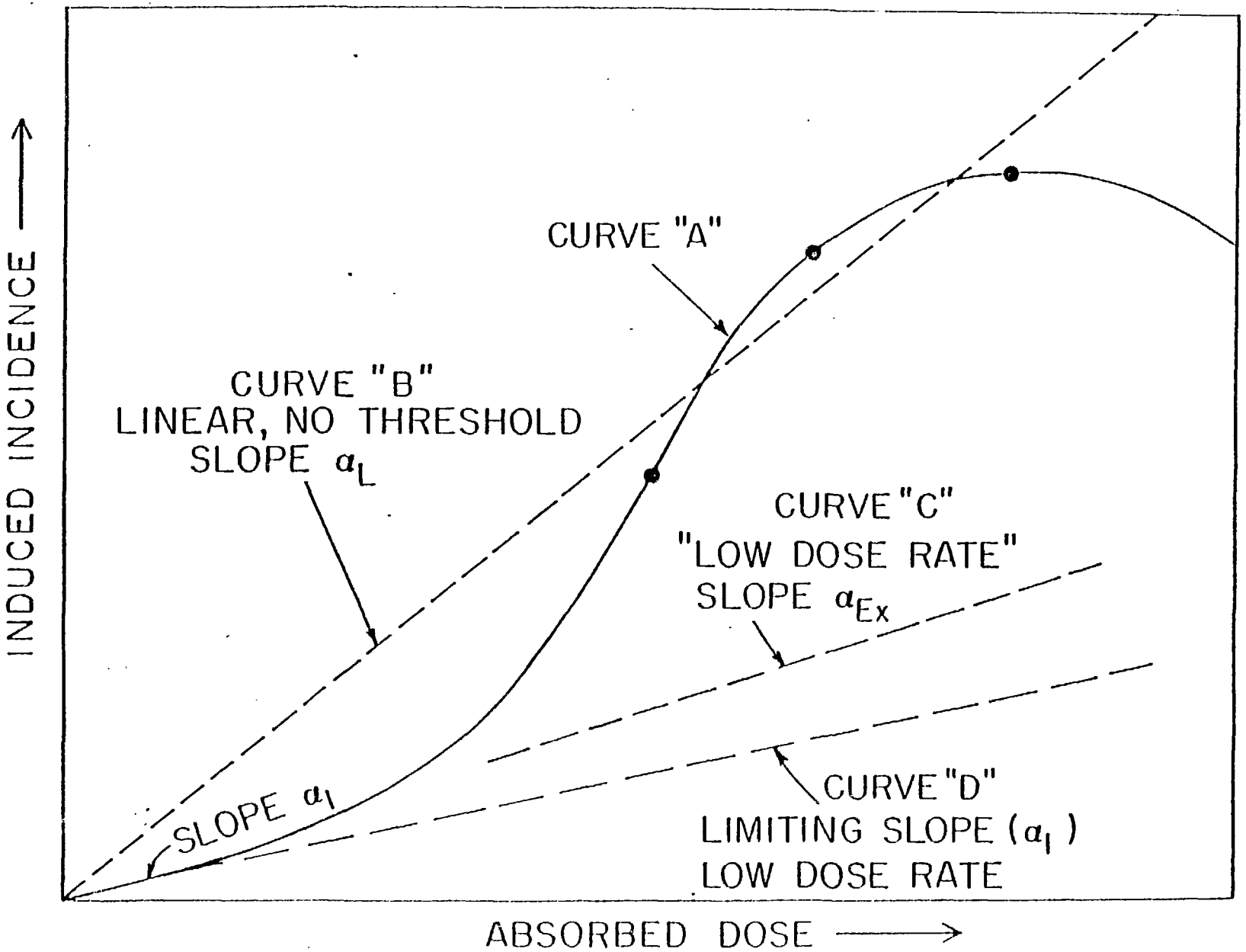
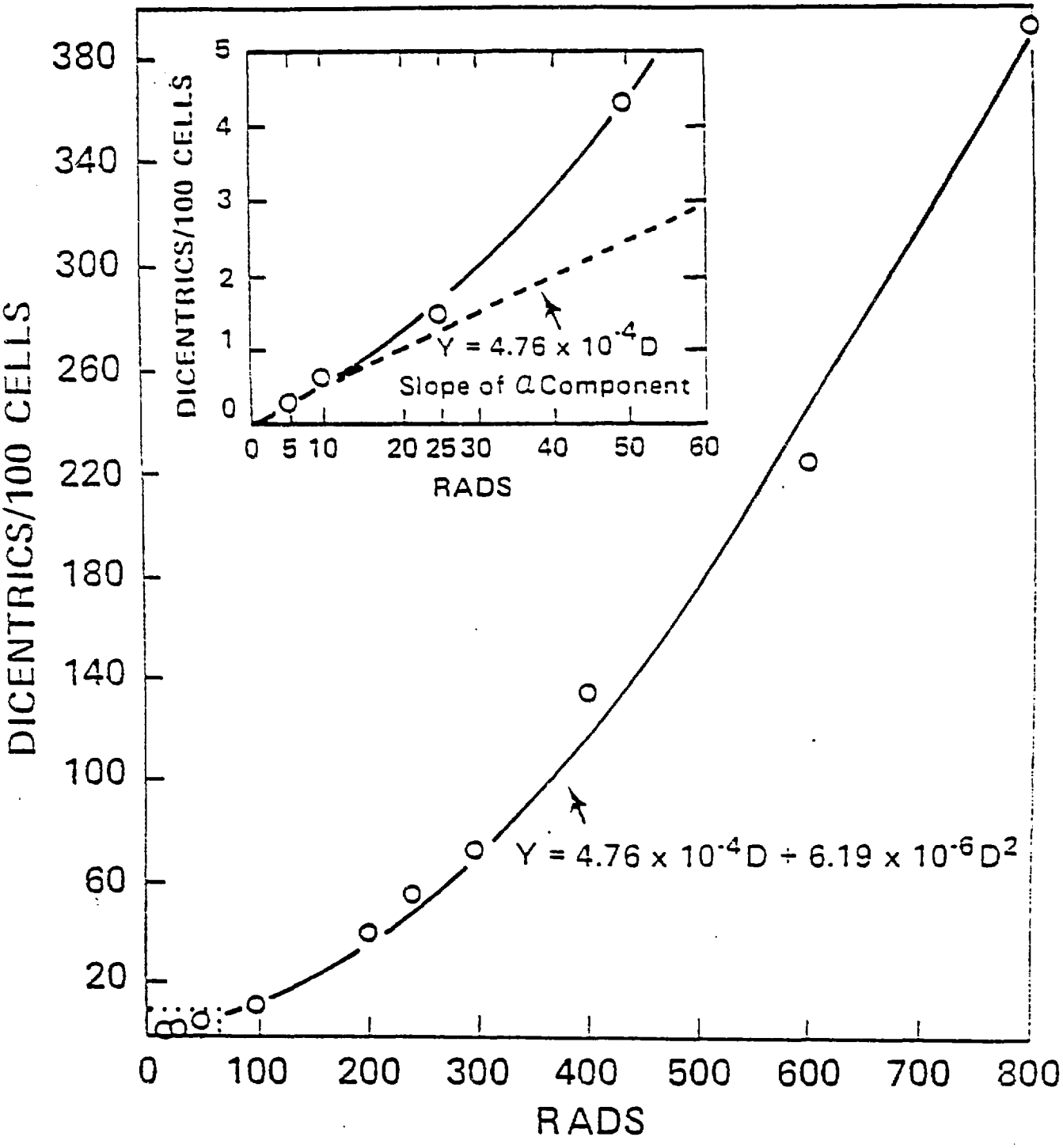

INDUCED INCIDENCE
CURVE "A"
CURVE "B"
LINEAR, NO THRESHOLD
SLOPE α_L
CURVE "C"
"LOW DOSE RATE"
SLOPE α_{Ex}
SLOPE α_1
CURVE "D"
LIMITING SLOPE (α_1)
LOW DOSE RATE
ABSORBED DOSE

Figure 1

Figure 2

Frequencies of dicentrics in human lymphocytes exposed to x-radiation doses ranging from 5-800 rads (250 KVP x-rays, 100 R/min). Over 14,000 metaphases were scored to obtain data for the 5, 10, 25, and 50 rad points. Insert is an expanded graph showing data at low dose points, and the slope of the α coefficient (Ref. 8).


DICENTRICS/100 CELLS
380
340
300
260
220
180
140
100
60
20
0
100
200
300
400
500
600
700
800
RADS
Y = 4.76 x 10^-4 D ÷ 6.19 x 10^-6 D^2
DICENTRICS/100 CELLS
5
4
3
2
1
0
0 5 10 20 25 30 40 50 60
RADS
Y = 4.76 x 10^-4 D
Slope of α Component

9-1106-78

Figure 3

X-ray dose-response curve, induced pink mutations in Tradescantia, on log-log plot to show detail in the low dose range. The solid circles indicate experimental points at high dose rate. Note that the low dose portion of the solid curve and its dashed-line extrapolation have a slope of unity, i.e., a linear, no threshold dose-effect relationship. The increased slope at higher intermediate doses indicates that the response in the ~~higher~~ dose range involves a higher exponent of dose (and a "cell killing" component at high doses). See text for explanation of the "$\alpha_1 D$" and "$\alpha_1 D + \beta D^2$" portions of the curve.

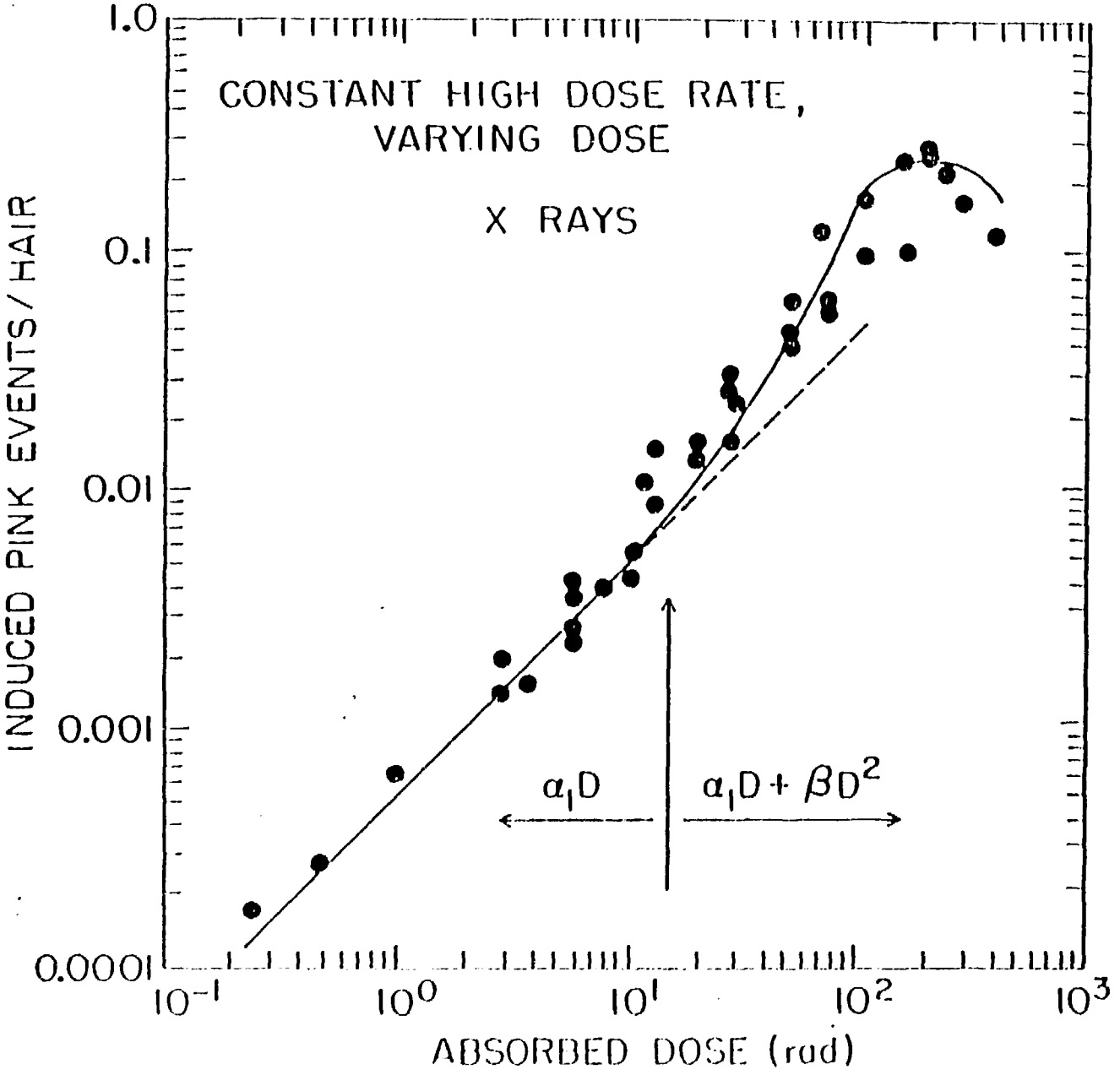

CONSTANT HIGH DOSE RATE,
VARYING DOSE
X RAYS
INDUCED PINK EVENTS / HAIR
1.0
0.1
0.01
0.001
0.0001
$\alpha_1 D$
$\alpha_1 D + \beta D^2$
10^{-1}
10^0
10^1
10^2
10^3
ABSORBED DOSE (rad)

Figure 1

Figure 4

Dose-response curves for pink mutant events/hair after x-irradiation at 0.05 and 0.5 rad/min (combined in one line), 5 and 30 rad/min. (Ref. 11). The dotted lines represent the alpha terms in Eqs. (2), for x-rays and gamma rays.

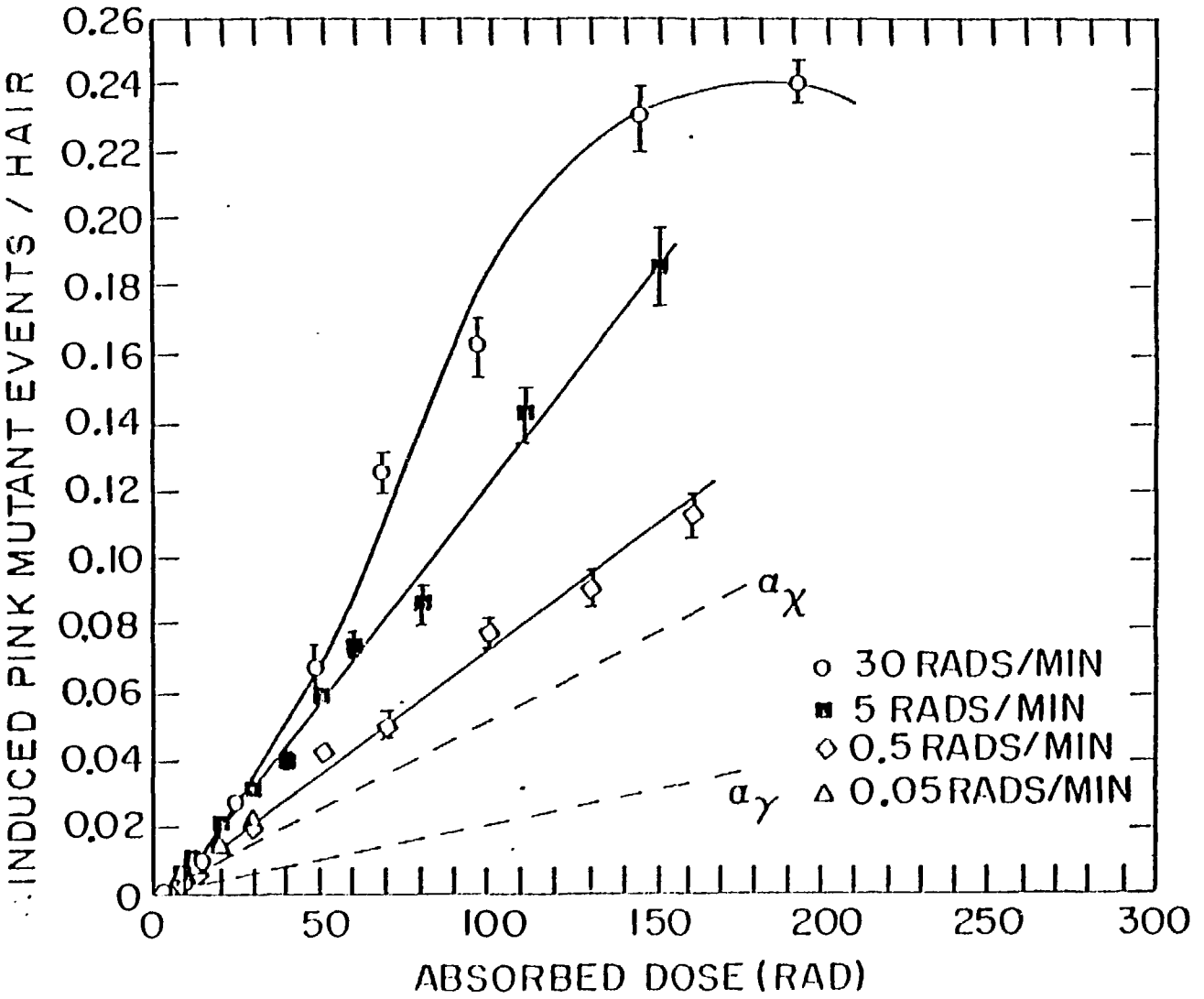
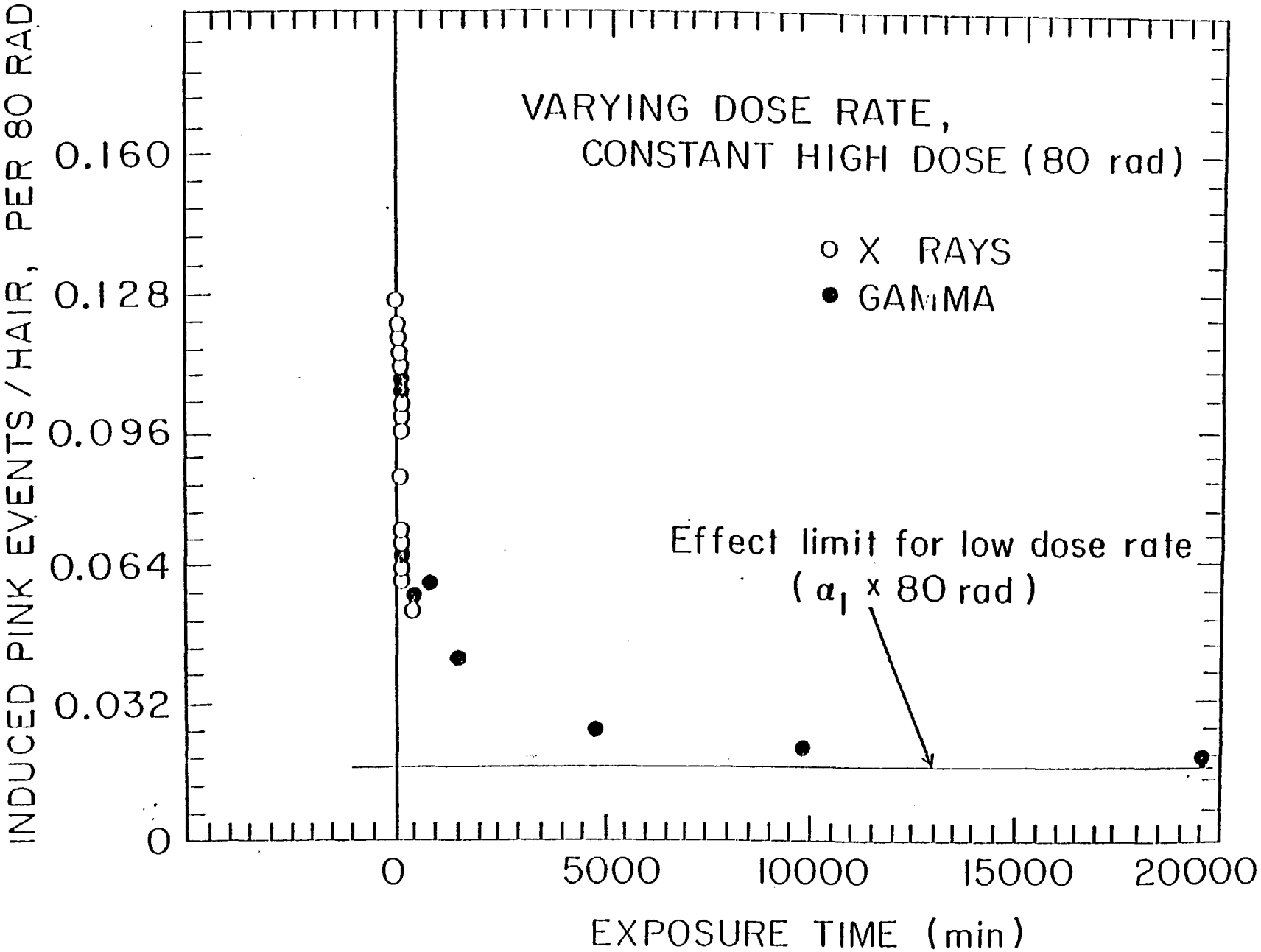

INDUCED PINK MUTANT EVENTS / HAIR
0.26
0.24
0.22
0.20
0.18
0.16
0.14
0.12
0.10
0.08
0.06
0.04
0.02
0
0
50
100
150
200
250
300
ABSORBED DOSE (RAD)
α_χ
α_γ
o 30 RADS/MIN
■ 5 RADS/MIN
◇ 0.5 RADS/MIN
△ 0.05 RADS/MIN

Figure 4

Figure 5

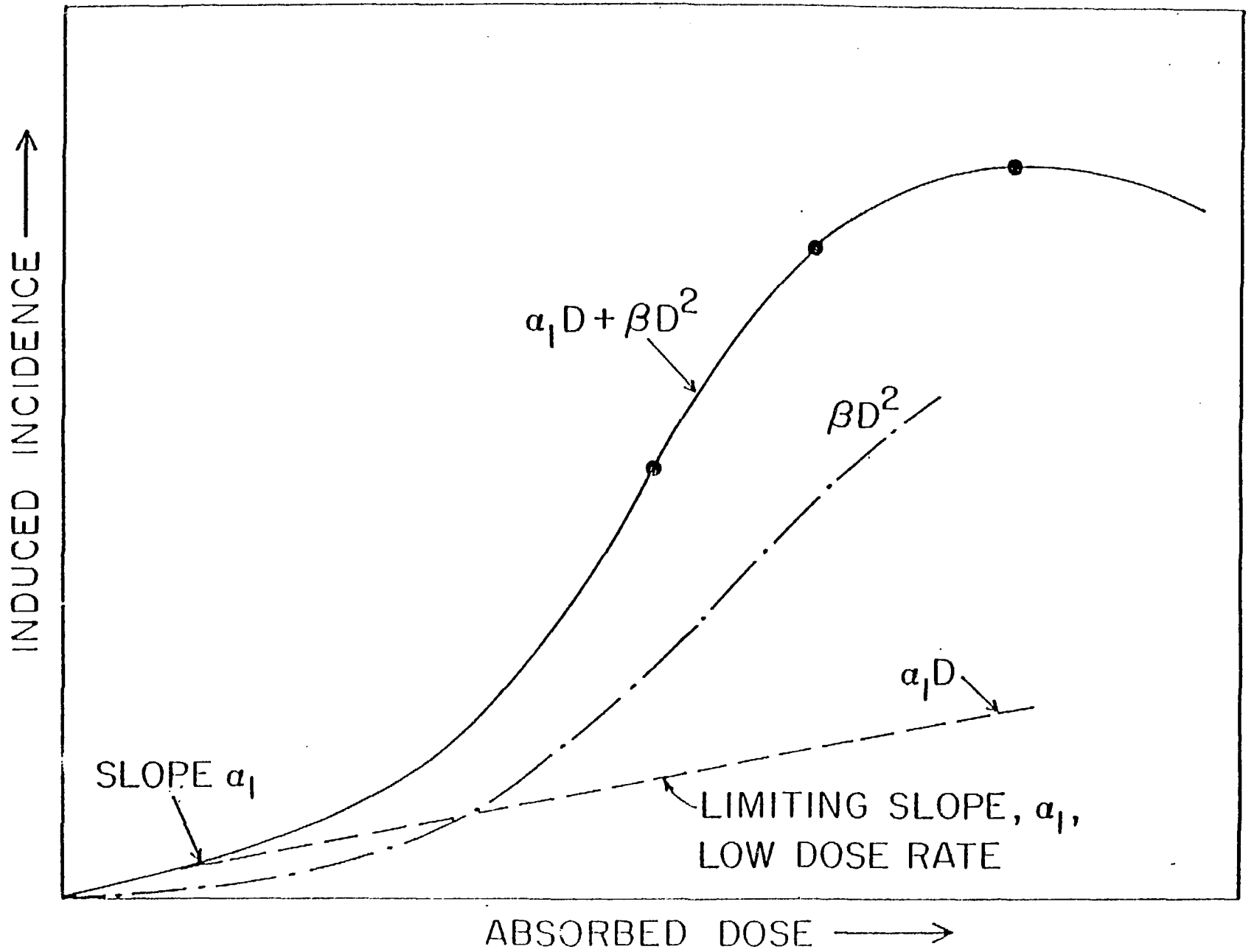
Effect of dose rate on the effectiveness of a single large dose of about 80 rad, for the induction of pink mutations in Tradescantia (11). The horizontal line represents the expected limiting low dose rate value for 80 rad (i.e., from the linear term of Equation 1, the value would be $2.1 \times 10^{-4} \times 80 = 0.017$). Note that the effect per 80 rad decreases appreciably as the exposure time is increased, and that the effect/80 rad at the lowest dose rates approaches asymtotically the limiting "QD" value for gamma radiation.


VARYING DOSE RATE,
CONSTANT HIGH DOSE (80 rad)
o X RAYS
• GAMMA
Effect limit for low dose rate
(α_1 x 80 rad)
INDUCED PINK EVENTS / HAIR, PER 80 RAD
0.160
0.128
0.096
0.064
0.032
0
0
5000
10000
15000
20000
EXPOSURE TIME (min)

10-34.78

Figure 6

The linear-quadratic dose response curve for Tradescantia, with the linear and squared components plotted separately. (a "cell killing" factor would be needed to describe the high dose region of the curve marked "$\alpha_1 D + \beta D^2$").


INDUCED INCIDENCE
$\alpha_1 D + \beta D^2$
βD^2
$\alpha_1 D$
SLOPE α_1
LIMITING SLOPE, α_1,
LOW DOSE RATE
ABSORBED DOSE

47 10-36-78

Figure 7

Incidence of myeloid leukemia in RF male mice. Shaded symbols denote results obtained with fast neutron irradiation; open symbols denote results obtained with X-rays. Solid lines denote results obtained with acute (single) exposures; dashed lines denote results obtained with chronic (23-hour, daily) exposures, (Ref. 5).

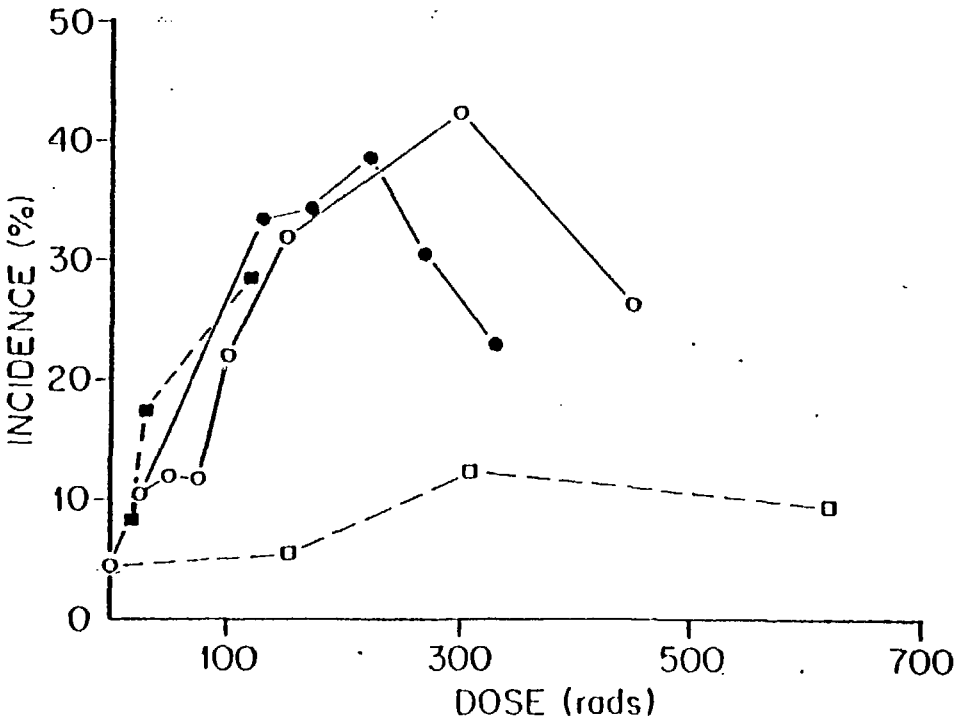


Figure 7

12-196-78

Figure 8

Incidence of Harderian gland tumors in RFM mice after ^{137}Cs gamma ray irradiation. 45 rad/min • ; 8.3 rad/day O (Ref. 30).

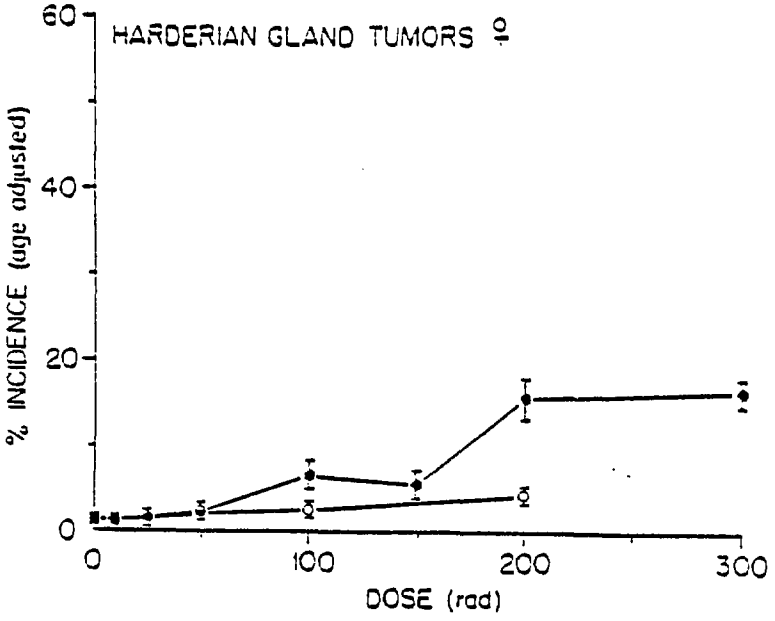


Figure 8

4-136-1-78

Figure 9

Incidence of ovarian tumors in RFM mice after ^{137}Cs gamma ray irradiation. 45 rad/min • ; 8.3 rad/day O (Ref. 30).

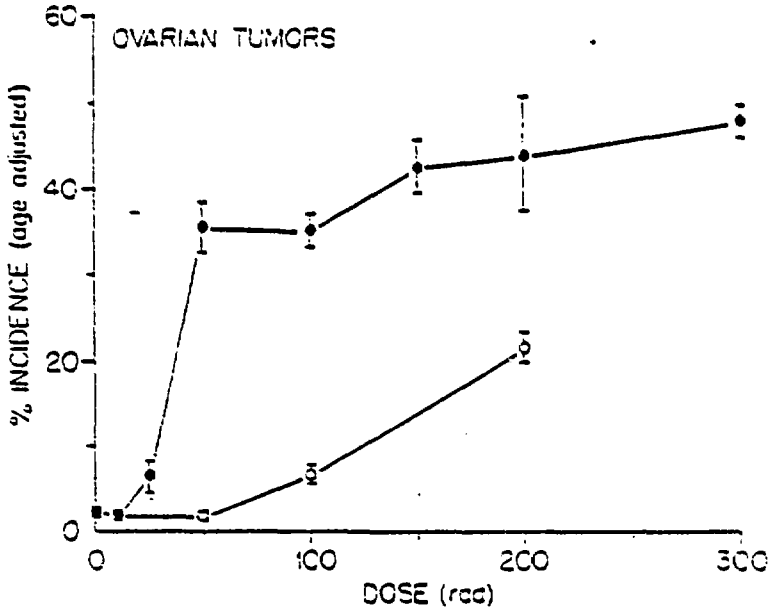

OVARIAN TUMORS
% INCIDENCE (age adjusted)
60
40
20
0
0
100
200
300
DOSE (rad)

Figure 9

Figure 10

Dose-effect curves for different tumors in mice that appear to have negative initial slopes (data taken from Ref. 27).

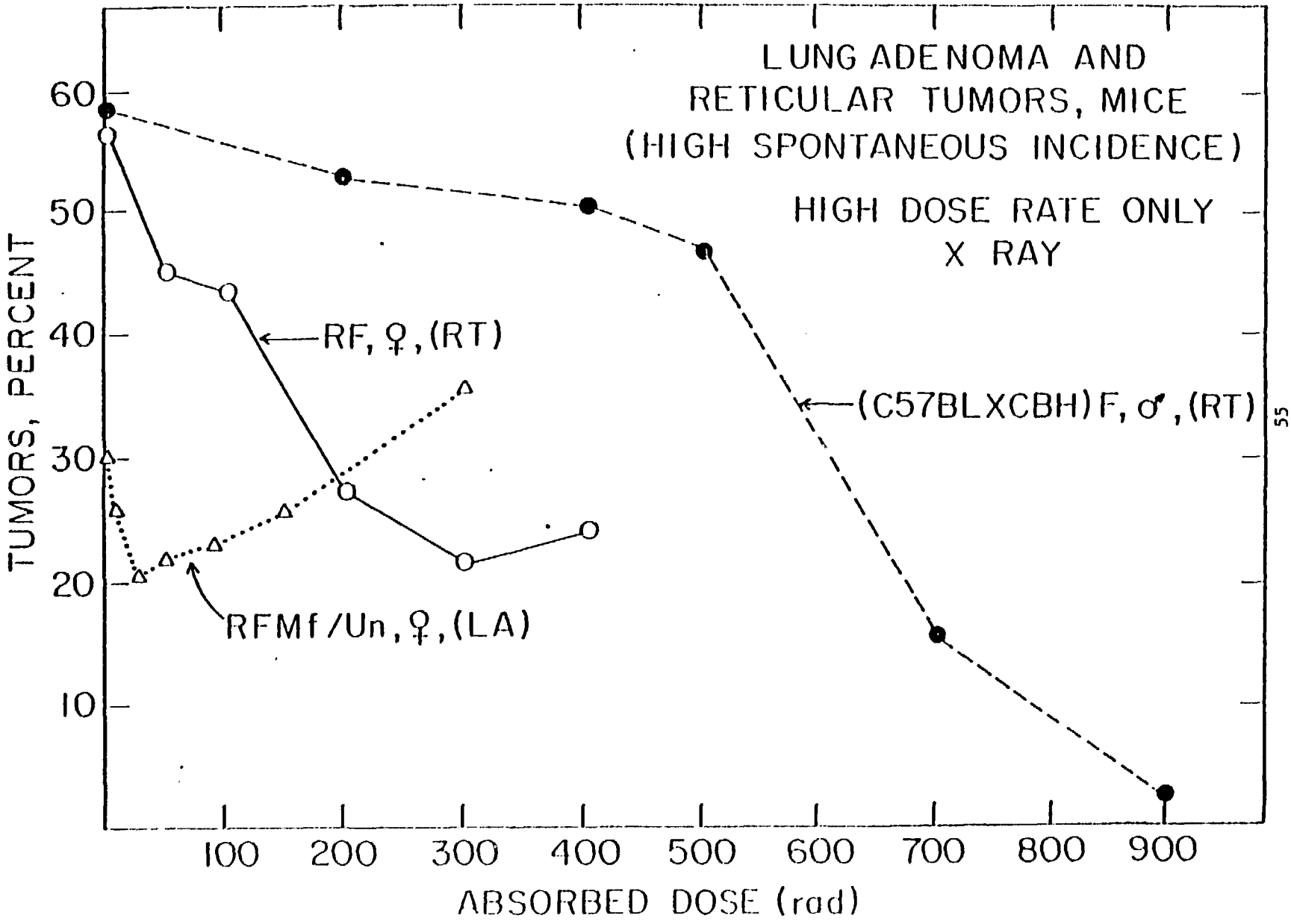

LUNG ADENOMA AND
RETICULAR TUMORS, MICE
(HIGH SPONTANEOUS INCIDENCE)
HIGH DOSE RATE ONLY
X RAY
RF, ♀, (RT)
(C57BLXCBH) F, ♂, (RT)
RFMf/Un, ♀, (LA)
TUMORS, PERCENT
60
50
40
30
20
10
100
200
300
400
500
600
700
800
900
ABSORBED DOSE (rad)

Figure 11

Schematic plot showing the essential elements of the system to limit and control exposure to hazardous agents. The limiting annual dose is determined by the intersection of the dose-effect curve and the level of "acceptable" effect, or risk of that effect.

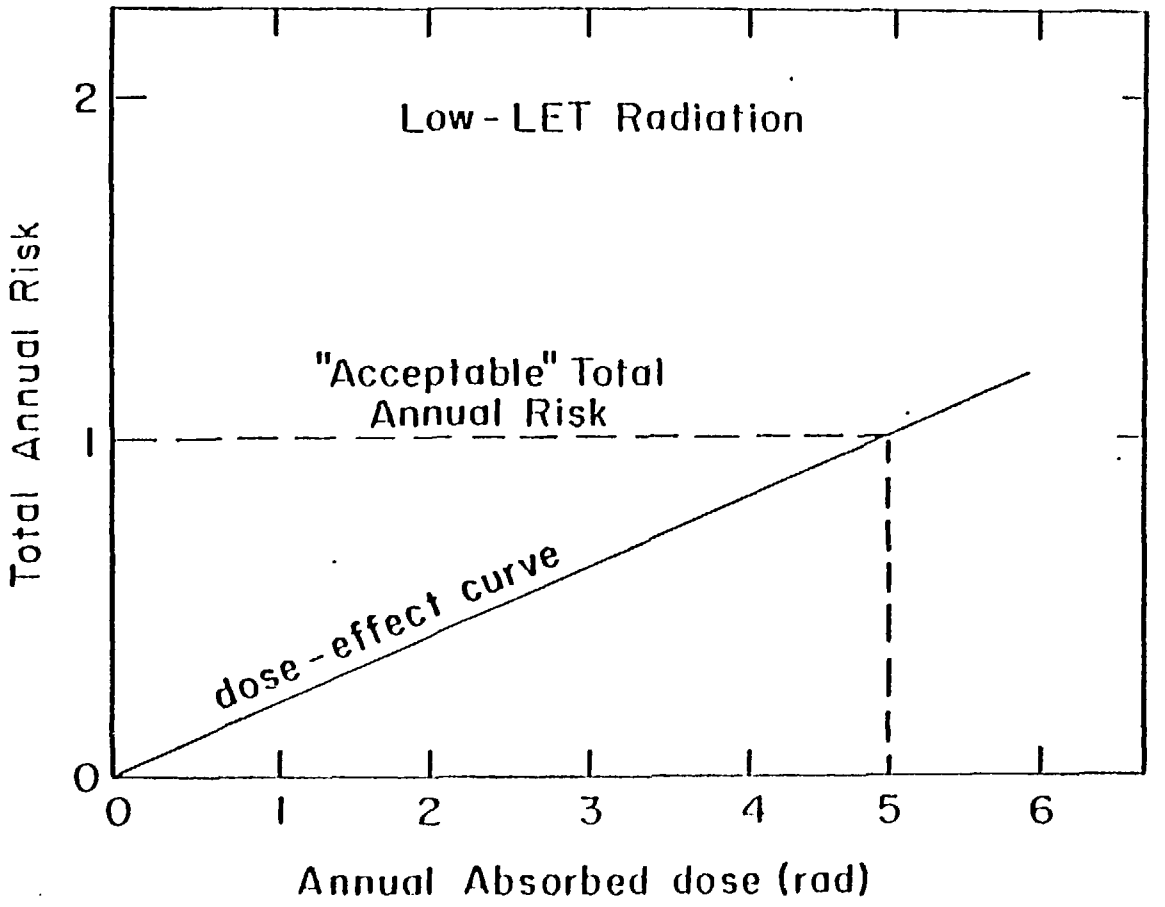

Low - LET Radiation
"Acceptable" Total
Annual Risk
dose - effect curve
Total Annual Risk
Annual Absorbed dose (rad)
0
1
2
0
1
2
3
4
5
6

Figure 11

Figure 12

Same schematic diagram as that shown in Figure 11, but including a dose-effect curve for a high-LET radiation, fast neutrons.

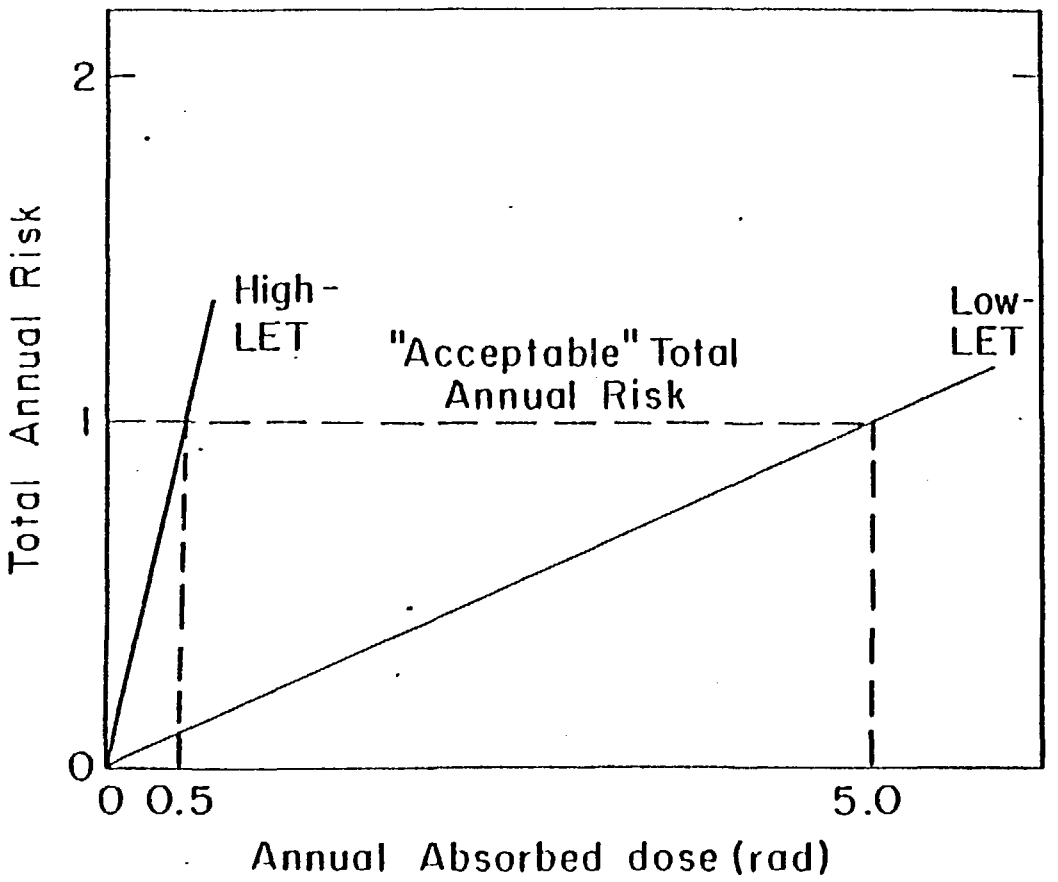

Total Annual Risk
2
1
0
High-
LET
"Acceptable" Total
Annual Risk
Low-
LET
0 0.5
5.0
Annual Absorbed dose (rad)

Figure 12

Figure 13

Neutron-induced leukemia vs. neutron dose, from human exposures in Hiroshima (Ref. 47).

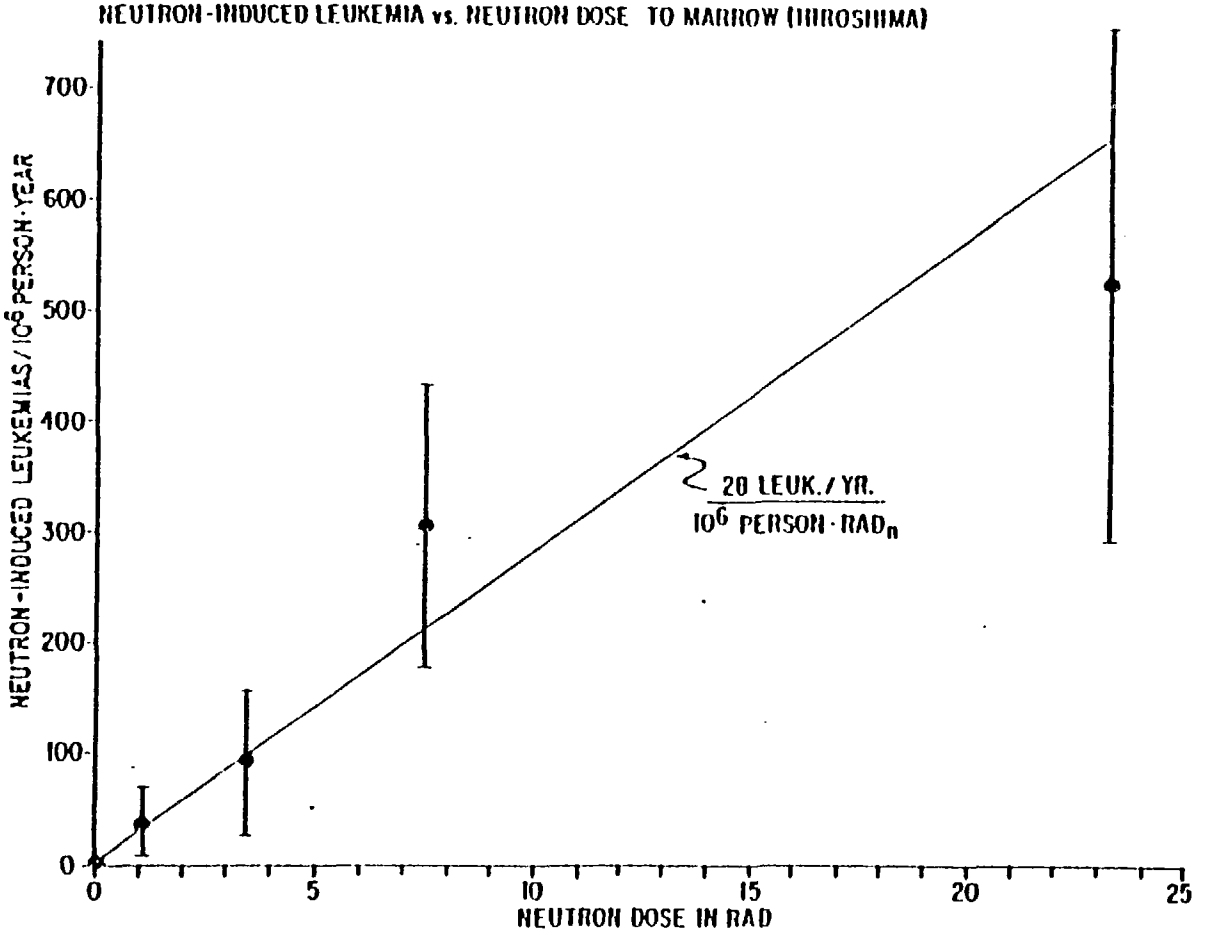

NEUTRON-INDUCED LEUKEMIA vs. NEUTRON DOSE TO MARROW (HIROSHIMA)
NEUTRON-INDUCED LEUKEMIAS / 10^6 PERSON-YEAR
700
600
500
400
300
200
100
0
0
5
10
15
20
25
NEUTRON DOSE IN RAD
≈ 20 LEUK. / YR.
10^6 PERSON · RAD_n

Figure 14

Log-log schematic plot showing the basic elements of an administrative protection system for radiation (or any other "no-threshold" toxic agent), i.e., the low-dose region of a radiobiologically-determined dose-effect (risk) curve and an independently-determined level of effect (risk) that is to be considered "acceptable." The annual upper limit exposure level is fixed in principle by the intersection of these two curves, e.g., the intersection of the "acceptable risk level" $2 \times 10^{-4}/P$ for leukemia, with the Y_ℓ leukemia dose-effect curve of slope 40×10^{-6}/person rad leads to $(2 \times 10^{-4}\ P^{-1})/40 \times 10^{-6}\ P^{-1}\ R^{-1}) = 5$ rads upper limit absorbed dose for gamma. "n", "Y_ℓ", and "Y_q" indicate neutron; linear, no-threshold gamma; and quadratic gamma dose-effect curves, respectively. Actual neutron risk values for 0.5 rad, Table I of Different placements of the 5 rads gamma comparison value.

Table I

Caption

Leukemia risk coefficients and RBE, neutron and gamma radiation, Hiroshima (Refs. 46-48).

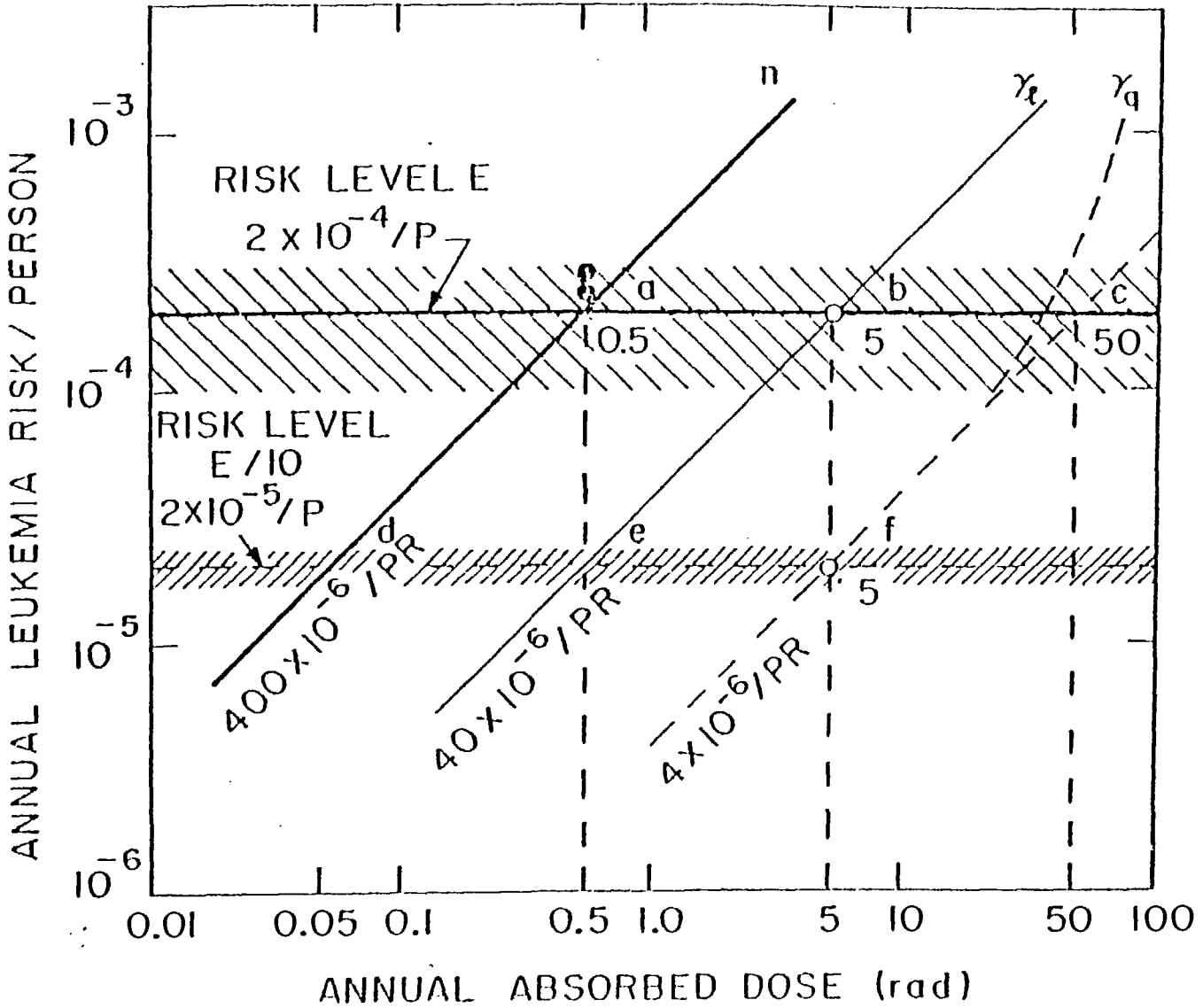

ANNUAL LEUKEMIA RISK / PERSON
10^{-3}
10^{-4}
10^{-5}
10^{-6}
RISK LEVEL E
2×10^{-4}/P
RISK LEVEL
E/10
2×10^{-5}/P
n
γ_t
γ_q
a
b
c
d
e
f
0.5
5
50
5
400×10^{-6}/PR
40×10^{-6}/PR
4×10^{-6}/PR
0.01
0.05
0.1
0.5
1.0
5
10
50
100
ANNUAL ABSORBED DOSE (rad)

Figure 14

TABLE I. LEUKEMIA RISK COEFFICIENTS AND RBE, NEUTRON AND GAMMA RADIATION, HIROSHIMA

AUTHOR(S)	RISK COEFFICIENTS		RBE
	NEUTRONS	GAMMA RAYS	
USING LINEAR MODEL FOR GAMMA RADIATION			
ISHIMARU, ET AL.	23×10^{-6}/PYR* (46×10^{-5}/PR)**	2×10^{-6}/PYR* (4×10^{-5}/PR)	~ 11.5
USING LINEAR-QUADRATIC MODEL FOR GAMMA RADIATION			
ISHIMARU, ET AL.	28×10^{-6}/PYR* (56×10^{-5}/PR)	0.2×10^{-6}/PYR (0.4×10^{-5}/PR)	~ 140 (LOW DOSE)
ROSSI-MAYS	28×10^{-6}/PYR* (56×10^{-5}/PR)	0.2×10^{-6}/PYR (0.4×10^{-5}/PR)	~ 140 (LOW DOSE)

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