NATO ASI Series
Advanced Science Institutes Series

A series presenting the results of activities sponsored by the NATO Science Committee, which aims at the dissemination of advanced scientific and technological knowledge, with a view to strengthening links between scientific communities.

The series is published by an international board of publishers in conjunction with the NATO Scientific Affairs Division.

A Life Sciences
B Physics
C Mathematical and Physical Sciences
D Behavioral and Social Sciences
E Engineering and Materials Sciences
F Computer and Systems Sciences
G Ecological Sciences

Recent Volumes in this Series

Volume 89—Sensory Perception and Transduction in Aneural Organisms edited by Giuliano Colombetti, Francesco Lenci, and Pill-Soon Song

Volume 90—Liver, Nutrition, and Bile Acids edited by G. Galli and E. Bosisio

Volume 91—Recent Advances in Biological Membrane Studies: Structure and Biogenesis, Oxidation and Energetics edited by Lester Packer

Volume 92—Evolutionary Relationships among Rodents: A Multidisciplinary Analysis edited by W. Patrick Luckett and Jean-Louis Hartenberger

Volume 93—Biology of Invertebrate and Lower Vertebrate Collagens edited by A. Bairati and R. Garrone

Volume 94—Cell Transformation edited by J. Celis and A. Graessmann

Volume 95—Drugs Affecting Leukotrienes and Other Eicosanoid Pathways edited by B. Samuelsson, F. Berti, G. C. Folco, and G. Velo

Volume 96—Epidemiology and Quantitation of Environmental Risk in Humans from Radiation and Other Agents edited by A. Castellani

Series A: Life Sciences
CONTENTS

Radiation Carcinogenesis ................................................. 1
E. E. Pochin

Strategy of Assessment of Health Risks in Environmental and Occupational Health. ................................. 17
R. L. Zielhuis

Choice of Comparison Groups in Environmental Studies and Dealing with Background Morbidity in Various Subpopulations .................................................. 33
O. Axelson

The Probability of Causation: An Approach to the Problem of Toxic Torts, Especially with Respect to Exposures to Ionizing Radiation. ................. 47
S. Jablon

The Carcinogenic Effects of Diagnostic and Therapeutic Irradiation. .................................................. 63
P. G. Smith

Dose-Response in Radiation Carcinogenesis: Animal Studies. .......................................................... 93
D. G. Hoel

Dose-Response in Radiation Carcinogenesis: Human Studies. .......................................................... 105
D. G. Hoel

Fundamentals of Dosimetry and Microdosimetry and the Relative Biological Effectiveness of Ionizing Radiations. .................................................. 123
A. M. Kellerer

Critical Review of Case-Control and Cohort Study Methodologies. .................................................. 141
P. G. Smith
In Vitro Malignant Transformation - a Multi-Stepped Process ........................................ 157  
J.J. McCormick and V.M. Maher

Problems in Dose Response and Risk Assessment:  The Example of Asbestos ....................... 175  
J. Peto

Role of DNA Damage and Repair in the Mutagenesis of Human Cells by Carcinogens .................. 187  
V.M. Maher and J.J. McCormick

Variations in DNA Repair Among People .............. 205  
R.B. Setlow

Cancer-Prone Families: A Resource for Etiologic Studies .................................................... 213  
M.H. Greene

The Role of Human RAS Proto-Oncogenes in Cancer .............................................................. 225  
S.R. Tronick, A. Eva, S. Srivastava, M. Kraus, Y. Yuasa, and S. Aaronson

Hereditary and Familial Disorders Linking Cancer Proneness with Abnormal Carcinogen Response and Faulty DNA Metabolism ...................................................... 235  
M.C. Paterson, N.E. Gentner, M V. Middlestadt, R. Mirzayans and M. Weinfeld

Application of Statistical Methods to Experimental Radiation Studies and to Radiation Epidemiology .......................................................... 269  
A.M. Kellerer

Biological Monitoring Studies in Occupational and Environmental Health ............................. 291  
R.L. Zielhuis

The Recognition of New Kinds of Occupational Toxicity ....................................................... 307  
J.A.H. Lee, T.L. Vaughan, P.H. Diehr, and R.A. Haertle

Occupational Exposure to Ionizing Radiation .......... 339  
J.O. Snihs

Non-Occupational Exposure to Ionizing Radiation .................. 363  
J.O. Snihs

Risk Assessment of Low Doses of Radiation and Chemicals .... 375  
R.B. Setlow
INTRODUCTION

The effects of ionizing radiations have been explored in innumerable biological experiments, but they have also been inflicted - often with tragic negligence or irresponsibility - on human populations. The worldwide fascination with x-rays immediately after Röntgen’s discovery was motivated by optimistic expectations and permitted little attention to biological damage seen immediately, such as skin-lesions, or to the later occurrence of leukemias in radiologists. Several decades after their discovery x-rays were still widely assumed to have general positive effects and nearly universal medical applicability. A painful process of learning then led to the stepwise development of adequate radiation-protection procedures and to a more realistic assessment of the beneficial and detrimental potential of ionizing radiations. As a reaction to past industrial misuses of radio-isotopes and errors in their medical application one has, today, in many ways gone to the other extreme. Beyond this, it has become difficult, after Hiroshima and Nagasaki, to draw a rational balance between the uses and the misuses of nuclear energy.

The resulting attitude and public perception of ionizing radiations has made it difficult to discern similarities and dissimilarities between the actions of ionizing radiations and other agents, such as chemical carcinogens. In a discussion of fundamentals of dosimetry and microdosimetry one may, therefore, consider first presumed or real particularities of ionizing radiations and their
biological effects. The subsequent short survey will deal with some of the essentials of radiation physics, with the attendant problems in dosimetry, particularly in epidemiological studies, with parameters that characterize radiation quality, and with some general implications for the action of radiations.

Absorbed dose is - in a simplified formulation - the energy transmitted from a radiation field to a small element of matter divided by its mass (1). The macroscopic distribution of absorbed dose in an irradiated body and the microscopic random fluctuations of energy deposition are the two essential factors that determine the effectiveness of different types and energies of ionizing radiations. The former are the objective of conventional dosimetry, the latter the objective of the more recent branch of radiation physics, microdosimetry. Before these two areas are considered it is helpful to illustrate the order of magnitude of the energy densities that cause observable biological effects.

It is sometimes thought that ionizing radiations produce specific deleterious effects, and that they produce them by extraordinarily small amounts of energy. Both assumptions are erroneous. There is no effect of ionizing radiations that cannot also be produced by chemical compounds. The remarkable feature of ionizing radiations is merely the extremely broad spectrum of biological endpoints. The energies required to produce biological effects would seem to be minimal if compared to thermal energy. A lethal dose to man transfers an energy to the body that increases its temperature by less than 0.001 degree centigrade. However, the comparison to temperature - the most degraded form of energy - is misleading. It is somewhat more informative to consider the total energy corresponding to a lethal dose of 5 gray, which is 350 joule or 350 watt*seconds. An even better illustration is the comparison to mechanical energy. One gray corresponds to the energy required to lift the exposed object by 0.1 metre in the earth's gravitation; the lethal dose corresponds to an elevation by 0.5 metre, evidently sufficient energy to produce damage. Visualizations of the effects of ionizing radiations on the microscopic or the atomic level can be similarly disparate. At a dose of 1 gray, only one out of ten to hundred billion electrons in the exposed material is disturbed. On the other hand, there are, at this dose, roughly 100 000 electronic displacements in the nucleus of a mammalian cell.
All ionizing radiations work ultimately through the action of electrons. Electrons can be the primary radiation, or they can be produced as secondary radiation by x-rays or gamma-rays. The electrons can also be the secondary radiation produced along the tracks of heavy charged particles. Finally they can be the tertiary radiation occurring with high energy neutrons; they are then released by the heavy charged recoils of the neutrons. In radiation protection one deals mostly with uncharged primaries, i.e. with x-rays, gamma-rays, or neutrons, when the body is exposed to external sources. Charged primaries are of concern mostly in connection with internal emitters.

Fig. 1
Comparison of the mean free path of photons and neutrons in tissue, and of the ranges of their charged secondaries, electrons and protons.
The dosimetry of ionizing radiations is never trivial when one is concerned with large exposed objects, such as the human body. With energetic photons or neutrons beyond 20 MeV the total body irradiation may be nearly uniform. However, for these very energetic radiations cross-sections, and specifically the nuclear cross-sections, are still inadequately known. At the more common intermediate energies, in the range of 0.1 to 20 MeV, the cross-sections are adequately known, but the penetration of the radiation is then limited, and dose distributions in an exposed body are complex and depend on numerous parameters.

Fig.1 gives for uncharged and for charged particles their mean free path and their range for energies between 10 keV and 10 MeV. The essential observation is, that the mean free path of the uncharged particles is always considerably larger than the ranges of the charged secondaries. For many purposes one can, therefore, simplify dosimetric computations by neglecting energy transport by the charged secondaries. With this simplification one obtains the quantity kerma (Kinetic Energy Released in Matter) instead of absorbed dose. It is evident that kerma and absorbed dose can be used interchangeably if, in a specified geometry, all dimensions of interest exceed the maximum ranges of charged particles. If this condition is not fulfilled, one must account for the different spatial distributions of the two quantities. Absorbed dose includes a further degradation process; the gradients of absorbed dose are therefore always less than those of kerma.

Beyond the facilitation of computations, the concept of kerma permits a further simplification. Kerma for any specified material is defined even in a receptor free geometry, e.g. in free space. A similar possibility does not exist for absorbed dose, which is always a complex result of attenuation and backscatter, and of the build-up of charged particle equilibrium in a specified geometry. These complexities of absorbed dose are sometimes disregarded with the silent assumption of a reference volume large enough to attain charged particle equilibrium but small enough that attenuation and backscatter can be disregarded. For crude estimates this may be an admissible procedure. In rigorous statements the reference to absorbed dose without specified geometry must be avoided. Fig.1 illustrates the difficulty by showing that the ranges of the released electrons can, at high energies, be equal to several percent of the mean free path of photons.

Although the use of exposure and its units röntgen or C/kg is now discouraged one may note that this quantity,
too, is defined regardless of energy transport by charged particles, and that it is, therefore, defined even in receptor free conditions.

For dose planning and dose assessment in radiotherapy inaccuracies must not exceed a few percent. Precise measurements and accurate computations are thus required. Similar requirements for dose specification can be met in many radiobiological studies, either with cell cultures or with small laboratory animals. In epidemiological studies the inaccuracies are far greater and far more complex.

The difficulties and complexities of the dosimetric problems are exemplified by the studies on the atomic bomb survivors. The current reevaluation of the dosimetry has been necessitated by inaccuracies of the input data for the tentative Oak Ridge dosimetry of 1965 (TD 65). There were uncertainties concerning the yields and the energy spectra of the neutrons and the gamma-rays as well as the geometry of the bomb assemblies and the humidity of the atmosphere at the time of the bombings. Improvements in the transport codes, particularly for neutrons, are equally important. As a result the tissue-kerma values in air have been substantially changed. However, as a new consensus on the dosimetry appears to emerge there remain large areas of uncertainty. Perhaps most importantly, new individual shielding factors remain to be established. The free air kerma values have to be reduced to kerma in the buildings where individuals were at the time of the bombing; the reduction can be appreciable and it depends strongly on energy. The further reduction from kerma within the building to organ doses is also substantial. For the deeper organs the reduction factors are 0.7 to 0.85 for gamma-rays, and 0.1 to 0.2 for neutrons (2,3). For the superficial organs, such as the breasts, there is the additional complexity of a dependence on the orientation of the person at the time of the explosion and during the subsequent seconds of delayed irradiation.

The relative contribution of the delayed radiation is still inadequately known. So are possible contributions from fall-out, including the possible role of the so-called black rain.

It is characteristic for radiation epidemiology that the dosimetric problems are further complicated by far less tangible uncertainties. Rules of compensation and medical care for the atomic bomb survivors were partly dependent on dose received; they may therefore have influenced the statements of individuals concerning their localization at
the time of the blasts. There could also have been an opposite effect due to the desire to avoid any social stigma linked to heavy exposure. To name still another possible difficulty, there had been severe shortages of x-ray films in the period after the bombing, and this may have led to extensive use of fluoroscopy and thus to radiation doses in addition to those from the bomb.

The dosimetric studies for Hiroshima and Nagasaki have been referred to as examples of difficult and partly unresolved problems in radiation epidemiology. The same studies are, however, also exemplary and impressive efforts. Such efforts must continue, because the various collectives of substantially exposed persons are unique and will, hopefully, remain so.

The numerous investigations of the effects of internal emitters pose problems of comparable or even higher complexity (see for example (4)). Internal emitters produce - with few exceptions such as tritium - highly non-uniform exposures. For example in patients that have been exposed to the short lived radium-224 by far the largest doses were produced in narrow regions on the bone surfaces (5). Still further complexities occur with inhaled activity such as radon daughters. The study of the distribution of the radon daughters in different areas of the lung is, by itself, a specialized field of inquiry, as is the investigation of the dose dependence and the geometric and temporal distribution of lung tumors induced by the inhaled activity.

The microdistribution of absorbed dose in the vicinity of particulate alpha-emitters in the lung is an additional complexity of inhalation studies. This hot spot problem exemplifies further the wide range of dosimetric problems, and poses problems intermediate between conventional dosimetry and microdosimetry (6); it reaches beyond the scope of this survey.
MICRODOSIMETRY

The Microscopic Distribution of Energy

Absorbed dose is defined in terms of the expected value of the energy transferred by ionizing radiation to a mass element. It is, accordingly, a statistical concept that loses applicability when one deals with small doses, with small structures, and, especially, with densely ionizing radiations. The microscopic fluctuations of energy deposition can then be considerable. Fig. 2 indicates, for sparsely and for densely ionizing radiations, the sizes of spherical regions in tissue and the doses where the standard deviations of energy deposition exceed 20%.

![Fig.2](image)

Fig. 2. The shaded areas indicate those combinations of site sizes and absorbed doses where the standard deviations of energy imparted exceed 20%. Absorbed dose can then not be applied naively, and a treatment in terms of microdosimetry is required.

The figure is based on microdosimetric computations and measurements, but its meaning can be understood even before the principles of microdosimetry are formally introduced. At doses of several mGy, i.e. at the level of radiation protection, the absorbed dose is never meaningful, even if the entire nucleus of the cell or the cell itself is con-
sidered. Most cells receive, in this dose range, no energy deposition at all; those cells that are traversed by a charged particle receive energies that can be far in excess of the expectation value corresponding to absorbed dose. Although the affected cells are only a minor fraction of all cells, their total number is, of course, very large. The important consequence of this basic feature of ionizing radiations is that no threshold in absorbed dose can hold for cellular effects. For smaller cell structures, such as individual chromosomes, the dose concept remains inapplicable even at the highest doses of biological interest.

The discontinuous energy transfer by ionizing radiations has attracted attention early in the development of radiation biology. It has led to the hit and target theories (for surveys see (7-9)). Such theories, although they were valid as heuristic principles, have had only limited pragmatic success. They were based on the postulate of equal and statistically independent hit processes and of hypothetical cellular targets which have never been identified. A more successful approach requires realistic physical parameters of radiation quality. The most simplified, but still the most common, parameter is linear energy transfer (LET), also called collision stopping power, of charged particles. It characterizes the average local concentration of energy along the track of a charged particle, and it is still the parameter that determines the quality factor employed in radiation protection (10). However, LET itself is merely a statistical expectation value. Energy-loss straggling, the radial transport of energy away from the particle track by delta-rays, and the change of LET along the particle trajectory are factors that co-determine actual microscopic concentrations of energy. For heavy ions there are conditions where LET and its probability distributions permit adequate estimates of energy transfer by individual charged particles to the nucleus of the cell or comparable sites. For electrons the LET concept is never adequate (11).

The shortcomings of the LET concept have been responsible for the development of a new branch of radiation physics. When H.H.Rossi attempted to determine the LET distribution of the recoils produced by high energy neutrons he found that these distributions were not directly measurable. He then recognized that the seemingly inadequate response of the proportional counters was, in fact, more meaningful than the theoretical LET values. The spherical proportional counters - now known as Rossi counters - respond to energy actually imparted to their gas volume which simulates a microscopic tissue region. The basic
principle of microdosimetry is that cellular effects are determined by actual energy concentrations, not by their expectation values. When this simple but fundamental principle was understood (12), the subsequent steps followed of necessity. A conceptional framework of microdosimetry was established and suitable experimental techniques were developed that could be applied to any radiation field to determine the probability distributions of energy concentrations on the microscopic scale (13-15).

There are a number of closely interrelated microdosimetric quantities:

- The energy imparted, \( e \), is the radiation energy transferred to a given reference volume of matter.
- The specific energy, \( z \), is the energy imparted, as defined above, divided by the mass, \( m \), of the reference volume of matter:
  \[
  z = \frac{e}{m}
  \]
- The lineal energy, \( y \), is the energy imparted, as defined above, divided by the mean chord length, \( l \), resulting in straight random traversals of the reference volume *):
  \[
  y = \frac{e}{l}
  \]

The specific energy, \( z \), is the random variable corresponding to the non-stochastic quantity absorbed dose, \( D \). The linear energy, \( y \), relates only to individual energy deposition events (i.e. individual charged particles), it is the stochastic counterpart of the non-stochastic quantity LET. In view of the simple relation between \( z \) and \( y \), it is usually sufficient to use the specific energy, \( z \), as will be done below.

*)
If the reference volume is a sphere of the diameter \( d \), the mean chord length is \( l = \frac{2d}{3} \). For any convex volume the mean chord length is equal to four times the volume divided by the surface (16).
4000 simulations are performed per decade of dose for each graph. The decreasing number of points at low dose is due to the increasing number of events with zero specific energy.

Fig. 3. Scatter diagrams of the distribution of specific energy in small and large sites and for sparsely and densely ionizing radiation.
A definite value of the specific energy can not be predicted for a microscopic volume, even under fully defined irradiation conditions. Instead the possible values of the specific energy are described by a probability density, \( f(z;D) \). The objective of microdosimetry is the calculation or the experimental determination of the probability densities of the specific energy for various types of radiation and specified reference volumes. The experimental determinations are carried out not directly in solid material, but in tissue equivalent gas volumes simulating microscopic regions in tissue. Without going into the technical details of the construction of the Rossi counters it is sufficient to note that the instruments can be used for measurements in a wide variety of radiation fields. It is possible to simulate tissue regions down to a diameter of about 0.3 micrometer. Microdosimetric data for much smaller regions are also of considerable interest, but they have to be obtained by computations. Experimental techniques to determine such data have not, as yet, been developed.

It is not necessary to measure the spectra of \( z \) for different values of the absorbed dose. Instead it is sufficient to determine the single-event spectra, \( f(z) \), i.e. the densities of the increments of the specific energy due to single charged particles including their secondaries. If the single-event spectrum is known, it is possible to calculate the dose dependent spectra as solutions of a compound Poisson process (17). Fig.3 illustrates, in the form of scatter diagrams, the distributions of specific energy for a densely ionizing and a sparsely ionizing radiation and for sites of 0.5 and of 6 micrometer diameter. These diagrams illustrate the large fluctuations of specific energy; they also show, by the absence of points at small doses, the increasing probabilities for no energy deposition.

In most applications of microdosimetry to radiobiology and to radiation protection it is not actually required to utilize the dose dependent distributions of specific energy. Important conclusions can, instead, be based directly on the single-event spectra and their moments.

Typical examples of single-event distributions are shown in Fig.4. These spectra relate to spherical tissue regions of 1 micrometer diameter. The pronounced differences between sparsely ionizing and densely ionizing radiations are evident, but the very wide range of values of \( z \) for the different radiation types are equally notable. They extend over several orders of magnitude, i.e. a
densely ionizing radiation can always produce events with relatively small energy deposition, and, vice versa, moderate to high values of z occur even with sparsely ionizing radiations. There is, accordingly, no sharp dividing line between densely ionizing and sparsely ionizing radiations.

![Graph](image)

**Fig. 4.** Single event distributions of specific energy and lineal energy for a spherical tissue region of 1 micrometer diameter. Distributions of dose, rather than event numbers, are given relative to the logarithmic scale (18).

The larger the increments of specific energy per event, the smaller is the mean number of events per unit of absorbed dose. Table 1 shows event frequencies for various types of radiation. Fig. 5 indicates, largely in analogy to Fig. 2, those site sizes and doses where the mean event frequency is less than 1. These data permit important conclusions. In particular, dose-effect relations must always be linear when the mean event number in the cell or in the sensitive cell organelles is much smaller than 1. With densely ionizing radiation this condition is met even at doses of the order of several gray. However, the argument applies only to dose-effect relations for autonomous cells, i.e. to cells that are not influenced by energy deposition in adjacent cells or by radiation induced reactions of the tissue (22).
The postulate of radiation action on autonomous cells appears to apply to hereditary effects which are due to

Table 1: Event frequencies in spherical tissue regions of specified diameter.

<table>
<thead>
<tr>
<th>SITE DIAMETER (µm)</th>
<th>TYPE OF RADIATION</th>
<th>NEUTRONS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>60Co-γ-Radiation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>^°Co-Y-Radiation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>γ (Gy⁻¹)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>.43 MeV</td>
<td>5.7 MeV</td>
</tr>
<tr>
<td></td>
<td>15 MeV</td>
<td>15 MeV</td>
</tr>
<tr>
<td>12</td>
<td>2000</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>360</td>
<td>4.2</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>.39</td>
</tr>
<tr>
<td>1</td>
<td>12</td>
<td>.08</td>
</tr>
<tr>
<td>.5</td>
<td>1.7</td>
<td>.02</td>
</tr>
</tbody>
</table>

Fig. 5. The shaded areas indicate combinations of site sizes and absorbed doses where the expected number of energy deposition events is less than 1, and dose dependences — for autonomous response — must accordingly by linear.
mutations or chromosome aberrations in individual cells. It is far less certain when applied to radiation carcino-
genesis. In fact, non-linear dose-effect relations have been found at neutron doses far too small for an appreciable probability of multiple events in the cell (19-21). One must conclude that radiation tumorigenesis is co-
determined by dose dependent tissue factors that are, as yet, unresolved. Linearity at low doses remains, therefore, a mere hypothesis for radiation carcinogenesis.

**IMPLICATIONS FOR RADIATION PROTECTION**

**Dosimetry**

Absorbed dose and the related quantity dose equivalent are utilized in the limitation principle of radiation protection. This principle is based on annual dose-
equivalent limits which obviate the need to retain information on exposures of individuals in earlier calendar years. Another convenience has been - up to a recent change - that the maximum dose equivalent in any organ rather than a more complex quantity has been limited. A further feature of the limit system is the absence of any hypothesis concerning the form of the dose-effect relations.

However, there has been in past years a gradual change away from the limit to the assessment system. H.H.Rossi has recently analysed the change and its consequences in depth (22), and only some of the essentials will be considered here. For what has been called non-stochastic effects (10) - perhaps a somewhat artificial notion - the limit system has been retained. For the stochastic effects, i.e. hereditary effects and radiation carcinogenesis, which are of predominant concern in radiation protection, ICRP has shifted towards an assessment system that aims at an optimization of detriment and benefit. To be practicable such a system requires the assumption of linearity of the dose-effect relation at small doses, a postulate that is, at least for radiation carcinogenesis, entirely hypo-
thetical.

The assessment system has also made it necessary to define and introduce into the practise of radiation protection a new quantity to replace the former dose equivalent. The new quantity, effective dose equivalent, is
a dose equivalent averaged with specified weight factors over all organs of concern. The rules of radiation protection for individuals retain numerically the earlier annual limits. One may note that - except for uniform exposures of the body - the limitation in terms of the new quantity is less restrictive than the earlier limitation in terms of the maximum dose equivalent in an organ. In fact, it has been necessary to introduce additional limitations on certain organ doses to ensure that non-stochastic effects be avoided.

The new system and its implied assumption of linearity have also been responsible for the increased use of concepts such as collective dose (equivalent) or committed collective dose (equivalent). It is not surprising that these new, and somewhat contrived, notions lead to novel conceptual difficulties when applied to specific situations. There have also been new problems in radiation-protection monitoring. It had been the practise to employ for purposes of area monitoring, or for personal monitoring, quantities that provide conservative rather than best estimates. Within the new philosophy this is inadequate. Accordingly the ICRU is about to present the definition of operational quantities for radiation protection that can be determined in area monitoring and personal monitoring. These quantities, ambient dose equivalent and individual dose equivalent, will serve as fair, if still somewhat conservative estimates of effective dose equivalent. When these quantities are introduced into the practise of radiation protection a reasonable compromise between the limit and the assessment system might be achieved. However, it must be noted that any epidemiological investigation will require information beyond the summary doses determined for radiation protection monitoring. The rules of radiation protection are aimed at keeping the risk sufficiently low to be unobservable statistically. If exposures beyond such safe levels occur, dosimetric information is needed beyond routine requirements. Effective dose equivalent, or its operational substitutes, can not be suitable reference parameters for radiation epidemiology.

**Microdosimetry**

The change from dose equivalent to effective dose equivalent is to account for the macroscopic distribution
of absorbed dose. Another current development in radiation protection relates to the microscopic distribution of radiation energy. This is the possible revision of the quality factors.

Microdosimetric considerations (23) had first led to the recognition that the linear component of the dose-effect relation is related to the average energy concentration produced in subcellular regions by single events, while the quadratic component reflects a cumulative damage due to the interplay of several events. There is no certainty, as yet, on the critical distances for which the energy concentrations are relevant. However — largely independent of the distances — one has a ratio of average single event sizes for fast neutrons and for sparsely ionizing radiations of 30 to 60. At low doses where the linear component of the radiation action predominates one expects, therefore, RBE values of neutrons versus sparsely ionizing radiations of this magnitude. For neutrons of about 400keV the RBE was indeed found, in various experiments, to reach such values or still larger ones (23). Perhaps even more importantly, an inverse dependence of the neutron RBE on the squareroot of the neutron dose has been consistently found in these experiments, which corresponds to a linear-quadratic dose dependence of the underlying damage for both radiations. This has been so, even when the dose-effect relations were substantially different from the linear-quadratic relation. One concludes that the RBE-dose dependence is more fundamental and more closely indicative of the initial steps of radiation action than the dose-effect relation which may be co-determined by complex tissue factors.

On the basis of the T65 Oak Ridge dosimetry it appeared that the dose-effect relation for leukemia in Hiroshima compared to the one for Nagasaki was in agreement with the high neutron RBE (24,25). The resultant high risk values for neutrons may have been an added motivation for the revision of the T65 dosimetry. As of now, the estimates of the neutron doses are so small, even for Hiroshima, that no conclusions on neutron RBEs can be expected from the Japanese data. This gives added importance to experimental data and to new evidence on high neutron RBE, such as the life shortening data from the Argonne experiments (26) and the transformation data obtained by Han et al. (27) with fractioned neutron exposures.

In view of these developments certain changes are envisaged. If, as it appears now, the RBE of densely ionizing radiations continues to rise at small doses below
a few mGy, higher quality factors will have to be adopted for stochastic effects. The change will be unavoidable, because it is a basic tenet of the assessment system that risk estimates be realistic and that optimization be applicable even to doses substantially below annual limits. A substantial change of the quality factors will, on the other hand, make the new values inapplicable to non-stochastic effects. For these effects the limiting principle is still retained, with dose-equivalent limits in excess of 0.1 sievert. It is difficult to ignore the dualistic nature of the present system of radiation protection.

Acknowledgement

This work has been partly supported by EURATOM research contract BIO 286 D.

REFERENCES

INDEX

Aberdeen, 65
absolute risk model, 55
additive interaction, 62
absorbed fatal dose, 520
Adult Health Study, 416
aflatoxin, 190
age at exposure, 81, 118
ageing, effect of radiation, 69
AIDS, 249
air borne particles, 405
air dose curves, 423
alkilating agents, 377
aliphatic hydrocarbons, 295
ambient, 291
ambient dose equivalent, 137
American Embassy personnel in Moscow, 487
analytical epidermiology, 499
anchorage independence, 158, 165
and DNA repair, 195
ankylosing spondylitis, 71, 106, 141, 142, 149, 273
aniridia, 390
annual limit of intake (ALI), 390
Biological Quality Guide, 296
ara, C, 247
arsenic, 8, 301, 400
arsenic compound, 18
arsenic trioxide, 320
artificial menopause, 144
asbestos, 176, 182, 309, 314
asbestosis, 308
ataxia telangiectasia, 205, 236, 246
Autopsy Pathology Program, 415
aviation (commercial), 371
8-azaguamine, 188
azathioprine, 510
background radiation, 40, 65
bactenophage T4, 239
BALB-MSV, 226
BEIR committee, 52, 64, 110, 426
BHK-21 cells, 162
B-K mole syndrome, 216
B-lym, 227
benign breast disease, 481
benzene, 48, 30
benzo-(a)pyrene, 159, 161, 199, 239
benzoyltrichloride, 316
beta-naphthylamine, 511
Biological Exposure indices, 292
Biological Monitoring programs, 291, 296
bioreductive enzime deficiency, 260
bischloromethylether, 18
black lung disease, 307
bladder cancer/carcinoma, 168, 230, 313, 316, 320, 511
bleomycin, 513
bone cancer, 55, 111
bone cells, 9
bone marrow cancer, 566
Atomic bomb Casualty Commission
brain cancer, 320
383, 414, 516
breast cancer
age incidence curves, 480
and leukemia, 506
cancer gene, 490
estrogen receptor, 481
etiology, 479
exposure-age, 82
familial syndrome, 255
genetic factors, 480
initiation and promotion, 489
in AHS, 416
incidence, 51
post/pre menopausal, 481
radiation, 313, 566
risk factors, 482
Tuberculosis patients, 7
bronchitis, 405
cadmium, 20, 293
cancer/carcinoma
bladder, 230, 313, 511
brain, 322
breast, 7, 51, 82, 255, 313, 416, 506, 479
cervix, 150
choroidal melanoma, 323
colon, 59, 230
colorectal, 507
digestive system, 444
epidermoid, 401
epitelial, 112, 119
esophageal, 316
eye melanoma, 323, 476
gastrointestinal, 507
glioblastoma, 258
hematopoietic, 227
Hodgkin's, 249, 324, 503
Hutchinson's malignant
freckle, 474
Kaposi sarcoma, 249
lentigo maligna, 474
leukemia (see leukemia)
liver, 7
liver angiosarcoma, 294, 315
lung (see lung carcinoma)
mammary, 230
melanoma, 9, 253, 322, 474
mesothelioma, 176, 308
multiple myeloma, 505
multiple poliposis, 259
nasal cancer, 313, 322
nevoid basal, 215
neuroblastoma, 230
osteosarcoma, 273
ovarian, 506
retinoblastoma, 215, 390
skin cancer, 12, 565
stomach, 9, 59, 322
testicular, 322, 509
thyroid, 12, 51, 416, 561
vaginal, 315
Wilms', 390
cancer risk
assessment, 2
baseline incidence, 50
cervix cancer treatment, 79
compensation, 49, 61
dose-rate effects, 97
genetic risk, 394
familial disorders, 235
models/modelling, 96, 100
natural radiation, 10
occupational exposures, 8
occupationally related, 49
prone-families, 213, 254
prone races, 52
radiotherapy, 5
spontaneous patients, 86
cancer proneness (see susceptibility)
cancer prone families, 213
cancer susceptibility
DNA repair, 206
genetic, 235
individual, 20
population, 105
cancer total incidence, 323
carbon disulfide, 308, 311
carbon monoxide, 21
biological monitoring, 40
cardiovascular disease, 40
carcinogens
early and late acting, 181
hyperresistance, 254
cardiovascular diseases, 416
cardiovascular mortality, 40
cardiovascular toxicity, 311
cataracts, 447
CBA mice, 95
CB radios, 434

cell killing effect, 68, 79, 85, 94, 101, 109, 111, 118, 153
cell transformation (see transformation)
cellular chemiosensitivity, 249
censoring of data, 270
cervix cancer, 150
chemical hazards, 537
chlorinated benzenes, 26
chlorinated phenols, 26
chloracne, 540
chlorornaphazine, 511
chloro-methyl-ether, 316
cholinesterase, 293
chondrodystrophy, 396
choroidal melanoma, 323
chromium, 18, 302
chromosome aberration/abnormalities, 283, 384, 391, 429
chromosome breakage disorders, 214
chronic lymphatic leukemia, 4
chrysotile miners, 176
chrysotile textile workers, 176
C 3H/10T\textsuperscript{4} cells, 162
citotoxicity of base damage, 376
clinical studies versus epidemiological, 19
coal power plants, 371
collective dose, 137
collision stopping power, 342
colon carcinoma, 59, 230
combined parental exposure, 386
comparability, 40
comparison group choice, 40, 144
compensation, 52, 60
competing risk, 270, 286
confounding effects/factors, 36, 39, 150, 530
congenital abnormalities, 365, 544
Connecticut Tumor Registry, 508
consumer products, 370
continuous cell lines, 162
cost-benefit analysis, 348
Cox algorithm, 276, 289
crocidolite, 176
C-retroviruses, 459
cross-links, 260
cumulative tumor incidence, 272
cumulative tumor rate, 271
curable cancers, 569
cyclamates, 318
cyclophosphamide, 504
delayed gammas, 422
delayed radiation, 127
N-7 deoxyguanosine, 375
detection limits, 299
determinants of diseases, 33, 37
N6-d guo, 377
(cis)-diaminedichloroplatinum, 257
diesel truck drivers, 316
diethylstilbestrol, 315, 161
diencephalic syndrome, 444
digestive system cancer, 322
dimethylnitrosamine, 375, 377
dioxins, 537
direct standardisation, 42
Displastic Nevus Syndrome, 215, 253
sporadic variant, 220
DNA apurinic site, 240
base damage citotoxic, 376
blocking damage, 195
damage accumulation, 378
damage mutagenic and cancerogenic, 375
damage repair, 187
faulty metabolism, 235
glicosylase, 240
lesions from carcinogens, 191, 236
ligase, 245
methyltransferase, 198
polimorphism, 395
recombinant methods, 430
repair and skin cancer, 205
sequencing, 395
synthesis on damaged template, ethylating agents, 375
damaged template, 236
transmethylase, 249
unrepaired lesions, 187, 197, 242
UV endonuclease sites, 243
DNA repair (see repair)
DNA tumor viruses, 168
dose
assessment, 369
distribution, 358
equivalent, 342
equivalent for infants, 368
estimate for AT survivors, 415
limits, 349
limitation ICRP system, 346, 364, 369
monitoring, 369
optimization, 347, 364
rate effects, 97
rate effectiveness factor (DREF), 97
response, 42, 65, 77
to organs (see organ dose)
dosimetry T65 (see T65)
Down's syndrome, 390, 459
drugs carcinogenic potential, 499
drosophila, 15
double strand break, 376

ecogenetic, 236
E.coli, 239
effective dose equivalent, 4, 136, 343, 365
EJ human bladder carcinoma, 168
Ela gene, 169
electrophoretic variants, 392
endometrial carcinoma, 317
env oncogene, 460
environmental monitoring, 291
enzyme deficiency, 392
epidemiological studies, 19
epidermoid cancer, 401
epitelial cancers, 112
epiloia, 390
erb-B oncogene, 466
esophageal cancer, 316
estrogen, 317
ethylate dibromide, 312
ethynitrosurea, 157, 378
etiologic fraction, 38
excision repair, 188
anchorage independence, 197
cell cycle dependence, 193
deficient XP cells, 193
in G1 cells, 193
rate, 190
exposure
age at, 270
ascertaining, 147
assessment, 19, 293, 296
biological indices, 292
combined parental, 386, 389
dioxins, 542
duration, 185
Edinburgh, 65
environmental, 24
epitelial cancers, 112, 114, 119
indoor, 24
lifetime risk, 120
limits, 302
medical, 363, 368, 371
non occupational, 363
occupational, 24, 339, 359
paraoccupational, 24
quantitative, 24
to microwave, 433
to the public, 371
extrapolation, 152, 378
eye color, 476
eye melanoma, 323, 476
fallout, 370
familial cutaneous malignant melanoma, 214
fatal accident rates in industry, 553
fatality annual rate occupational, 308
Fat Man, 420
Federal Tort Claim Act, 49
Fl Mortality Study, 365, 388
focus formation, 158
follow-up of cohorts, 499
of patients, 500
fractional uptake, 19
fractionation of dose, 81
Fuchsin dye, 315

Gametic doubling dose, 389
Gardner syndrome, 249
Genetic and cancer risks, 394
Genetic effects, 430, 567
Genetic lesions in human tumors, 229
Genodermatoses, 214
glioblastoma, 258
G0 release, 190
growth factors, 462
guanil adducts, 246

Hair, 471
Ha-ras oncogene, 168
Hamartomatous disorders, 214
Harm (industrial), 557
Harvey murine sarcoma virus, 225
Health, 64
hazards quantification, 42
physics research reactor, 424
risk assessment, 17, 26, 293
surveillance, 292, 321
Healthy worker effect, 34, 40
Hematopoietic neoplasms, 122
Hemoglobin alkilation, 377
Hereditary cancers, 215
Heterozygotes frequency, 529
Hexachlorocyclohexane, 26
High-fat diet, 488
Hit and target theories, 130
HLA phenotypes, 392
Hodgkin's disease, 346, 503
Hormones synergism with radiations, 282
HPRT, 188
HS, 250, 228, 241
HSO, 230
Human epidermal growth factor receptor, 466
Human fibroblast, 165
Human oocyte, 387
Human platelet derived growth factor, 462
HUT 14 cells, 165
Hutchinson'd maglignant freckle, 473

Hypermutable fibroblast in DNS, 221
Hypothesis validation, 317

IARC animal carcinogens, 312, 511
ICRP, 340, 346
Immune deficiency states, 214
Increased radioresistance, 256
Indefinite lifespan (cellular), 166, 160
Individual dose equivalent, 137
Infant Autopsy Program, 181
Inhalation studies, 284
In-houses radon, 368, 370
Initiation and promotion, 181
Inorganic lead, 296, 302
Insulation workers, 177
Intelligence tests, 521
Interaction models, 56
Internal emitters, 128
In-utero exposure, 66, 568
Age at, 81
carcinogenic effect, 143, 148
Childhood cancer, 146
Nervous system, 515
Radiation risk, 81
twin, 67
Ischemic heart disease, 322
Isotonic regression, 282
Justification, 347, 364

Kaplan-Meier formual, 273, 282
Kaposi sarcoma, 249
Kerala, 11
Keratoses, 476
Kerma, 125, 341, 414, 422
Kirsten leukemia viruses, 225
Kirsten murine sarcoma virus, 225
Klinefelter's syndromes, 390
Korean war veterans, 437
Large bowel cancer, 322
Lead, 20, 298
Lentigo maligna, 474
Lethal lesions and critical cell proteins, 195
leukemia, 14, 65
actinomycin D, 509
acute myeloid, 38
adjuvant chemotherapy, 500
adriamycin, 510
age at exposure, 83, 84, 106
alkilating agents, 505
and aplastic anemia, 72
and thorotrast, 7
ankylosis spondilitus, 80, 106, 111
antimetabolite therapy, 509
atomic bomb survivors, 107
benzene and xilene, 313
bone marrow dose, 60
breast carcinoma, 508
busulphan, 509
chemotherapy related, 499
children of AT survivors, 390
chlorambucil, 506
chronic granulactis, 58
colloidal gold, 502
colorectal cancer, 507
cumulative bone marrow dose, 504
cumulative rate, 271
cyclophosphamide, 504
cytoxan, 509
duration of chemotherapy, 504
excess deaths, 427
gastrointestinal cancer, 507
high-low rate, 51
hydroxyurea, 510
in CBA mice, 79
in Hodgkin's disease, 503
latency period, 106
lifetime risk, 113, 351
lung carcinoma, 509
lymphocytic, 313
melphalan, 506
methotrexate, 510
MOPP, 502
multiple myeloma, 505
myelogenous, 500
myeloid in mouse, 94
natural rate, 151
non-lymphocytic, 500
ovarian cancer, 506
Pierce-model, 111
platinum, 510
polythemia vera, 506
probability of causation, 59
radiation induced, 75, 313
registry, 406
risk in time, 74, 425
rubber workers, 322
streptozotocin, 508
temporal pattern of risk, 106
testicular cancer, 509
treosulfan, 507
vincristine, 510
VP 16, 510
life long risk, 178
life shortening effect, 68
life span study, 415, 420
life time risk, 110
Li-Fraumeni familial syndrome, 255
linear dose response model, 52
linear quadratic,
   risk estimates, 52
dose-response function, 100
dose-effects, 109
Little Boy, 420
Livemore, 315
liver angiosarcoma, 294, 315
liver cancer, 7
location of AB survivors, 414
long term problems, 367
Love Canal, 21, 48
low doses risk, 12
lung cancer
arsenic, 313
asbestos workers, 179
by shipyards, 313
fission neutron, 284
fluospar miners, 400
goldminers, 400
hematite miners, 400
high and low rate, 51
histology, 400
in butchers, 313
indoor radon, 41, 402
insulation workers, 177
K-ras oncogene, 226
Livemore, 325
Lung cancer (continued)
maximum of risk, 401
model, 178
motor vehicles drivers, 321
mustard gas, 315
Navajo Indians, 404
nickel workers, 180
probability of causation, 59
radiation, 566
risk, 8, 176
small cell, 401
smelters, 313
smoking, 57, 177
sugar cane farmers, 322
tin miners, 322
uranium miners, 8, 87, 399, 556

malignancies natural radiation
induced, 4
mammary carcinogenesis, 487
mammary carcinoma, 230
mammary gland differentiation, 487
mammary tumor rate, 278
marrow dose, 79, 81
melanoma, 4, 253, 322, 324, 474
melanoma prone families, 215
menopause radiation induced, 70, 144
mental health, 21
mental retardation in AB survivors, 515, 518
Mer, 376
Moloney leukemia virus, 225, 460
Monazide sands, 11
monitoring, 291
mortality from causes other than cancer, 425
rate in infant and childhood, 385
mouse oocyte, 387
mouse radiation studies, 94
multistage, 181
multi-Stage, 181
mutational, 101
Weibull, 280
Mumps, 51
morphological transformation, 161
multiple exposure, 36
multiple poliposis/sarcoma family, 259
multiplicative interaction, 56, 82

microdosimetry, 124, 129
radioprotection, 138
specific energy, 133
microwave radiation
as co-carcinogen, 451
exposure dose, 436
malignant neoplasms, 437
morbidity studies, 442
mortality studies, 435
reproductive efficiency, 450
mitomycin C, 258
MMC hyperresistance and cancer predisposition, 258
MNNG, 198
MNNG treated adenoviruses, 248
models
age linear, 115
carcinogenesis, 175
derror, 184
incidence rate of tumors, 113
lung cancer, 178
mesothelioma, 179
multi-stage, 181
Pierce, 111
proportional hazards, 275
relative risk, 109
time incorporated, 101
time linear, 115
time shift, 279
tumor incidence and dose, 100
two-stage mutational, 101

Moloney leukemia virus, 225, 460
Monazide sands, 11
monitoring, 291
Mormons, 51
morphological transformation, 161
mortality from causes other than cancer, 425
rate in infant and childhood, 385
mouse oocyte, 387
mouse radiation studies, 94
multiple exposure, 36
multiple poliposis/sarcoma family, 259
multiplicative interaction, 56, 82

579
mutation induction, 188
myc oncogene, 169, 467
myelodisplastic syndromes, 501
N-acetoxy-2-acetylaminofluorene, 239
nasal cancer, 313, 322
natural radiation, 10, 339, 363, 368
neoplastic transformation, 163
nerous system microwave effects, 445
Nevada test, 419
Nevi natural history, 216
nevoid basal cell carcinoma syndrome, 215
neurasthenic syndrome, 444
neurablastoma, 230
neurofibromatosis, 390
neuronal migration, 529
neutron exposure, 385
erma, 422
RES, 167
residual radiation, 413
NIH/3T3 cells, 460
nickel, 18, 302
nickel refinery workers, 180
nine parameters formula, 424
nigrogen mustard, 503
4-Nitroquinolin d-oxide, 221, 239, 246, 260
N-methyl-N1-nitro-N-nitrosoguanidine, 246
N-methyl-N-nitrosourea, 247
age increasing toxicity, 251
non-stochastic processes, 206
N-ras oncogene, 226
nuclear reactors releases, 370
Occupational injuries, 552
surveillance, 334
toxicity, 310
ocular effects of microwave, 447
odds ratio, 39
oncogenes, 168
onc-proteins, 462
optimization of dose, 347
organ dose, 53, 58, 127, 136, 344, 350, 366, 374, 420
organochlorine contaminants, 302
ORNL studies, 97
osteosarcoma, 273, 280
over-exposed workers management, 354
ovarian cancer, 506
ovaries x-irradiated, 70
Pace-Marcum dosimetry, 425
particulate-x-emitters, 128
p21 coding sequences, 228
personal dosimetry, 47
phosphoglucomutase, 393
photoreactivation, 206, 241
Pierce model, 111
pneumoconiosis, 307
point mutation, 229
polycythemia vera, 511
polyoma virus, 159, 169
middle T gene, 169
large T gene, 169
power density of microwave, 434
pregnancy loss, 20
outward rate, 387
premature death, 384
probability of causation tables, 49
cancers, 59
procarbazine, 503
prompt radiation, 421
protein kinase, 462
protein molecules abnormalities, 392
prato oncogenes, 225, 459
p 28 sis processing, 463
pyrimidine dimers, 190, 206, 237, 376
radiation DNA synthesis depression, 258
hormones synergism, 282
induced menopause, 70
interactions, 82
radiation (continued)

occupational exposure, 339
smoking interaction, 57
total population exposure, 64
radiation carcinogenesis
animal studies, 94
epidemiological studies, 3
tissue factors, 136
Radiation Effects Research Foundation, 383, 414, 516
radiactive nuclides repositories, 364
radiologists, 68, 145
radionuclides, 4
radiofrequency bands, 435
radioresistance increased in cancer prone families, 257
radiotherapy
ankilosing spondylitis, 71
 cervix cancer, 71
non-malignant diseases, 6
radiowave sickness, 444
radium, 224, 128, 273
radium dial painters, 9
radon, 8, 551
daughter products, 9, 128, 400
indoor exposure, 41, 368, 370, 402
miners' exposure, 41
quantitative risk, 406
ras oncogene, 169, 225, 472
in human cells/tumors, 131, 230
rat brain tumor, 157
rat mammary tumor, 157
Rous sarcoma virus, 167, 459
RBE, 342, 419
reference levels, 350
refractory anemia, 501
repair (DNA-repair)
aberrant, 242
alkyl repair in smokers, 211
alkyl transfer, 206
and cancer susceptibility, 207
bulky lesion-repair complex, 244
cell cycle dependence, 197
daughter strand, 237
repair (continued)
deficiency and breast cancer, 485
deficient cells, 187
in AT cells, 246
incision step, 239
in microbial systems, 240
in XP cells, 242
levels in tissues, 378
mechanisms, 98, 206
O'-methylguanine, 198, 247, 375
4 NQO lesions, 246
nucleotide excision, 206, 239, 245
rate in human cells, 380
time available, 195
transformation, 187
variation, 207
respiratory volume, 25
retinol binding protein, 20
retinoblastoma, 215, 389
retroviruses, 225
Rh locus, 219
risk
absolute, 53
acceptance/acceptability, 182, 367
by age, 427
bone marrow irradiation, 7
coefficients, 53
comparison, 352, 551
evaluation and duration, 73
estimation, 393
extrapolation, 428
geneetic, 383
linear quadratic, 52
liver irradiation, 7
of CMM, 218
of death in sport, 308
perception, 182
quantification, 4, 218
relative risk model, 55
RNA tumor viruses, 162
Rossi-counters, 130
Rothmund Thomson syndrome, 253
safety levels, 2
safety of chemicals, 311
sampling, 151, 298
sensitivity individual organ, 4
sentinel phenotypes, 384, 390
sequential cloning assay, 163
Seveso accident, 538
Seveso birth defect registry, 540
sex dependent differences in kinetics, 294
sickle cell anemia, 530
Simian sarcoma virus, 459
single gene disorders, 213
sis oncogene, 459
sister chromatid exchange, 391
skeletal dose, 275
skin cancer, 12, 569
SK-H-SH cells, 230
smoking
alkyl acceptor levels, 211
and arsenic trioxide, 320
and radon, 403
as behavioural factor, 33
by miners, 8, 87
influence on lung cancer, 400
in probability of causation, 57
insulation workers, 177
mesothelioma, 177
mucous stimulation, 409
radiation interaction, 57
smoke detectors, 371, 373
soft x-rays, 356
solid tumors following chemotherapy, 510
somatic cell mutation, 160
specific absorption rate, 435
src oncogene, 167
(non) stochastic effects, 341, 366
stomach cancer, 9, 59, 322
streptomyces griseus, 241
streptozotocin, 508
study/ies
base, 34
case-control, 142, 500
cause direct, 22, 296
cohort, 142, 499
design choice, 144
study/ies (continued)
disease oriented, 143
exposure oriented, 142
individual direct, 22
observational, 142
situation direct, 22, 296
susceptibility (see cancer susceptibility)
SW 1271 cells, 230
SW 480 cells, 230
T4 bacteriophage, 239
T24 bladder carcinoma cells, 226, 241
T24/EJ bladder tumor oncogene, 228
TCDD, 26
TCDD teratogenicity, 538
T65 (Oak Ridge) dosimetry, 138, 385, 414, 424, 517
testicular cancer, 323, 509
thalidomide, 532
6-thioguamine, 188
thorium, 7
thorotrast, 7,
Three Mile Island, 47
threshold dose, 3, 130, 181
thyroid cancer, 4, 12, 51, 416, 566
thyroid gland, 47
time loss industrial injuries, 556
timepiece luminous, 372
tinea capitis, 515
tissue dose, 343, 523
toluene, 26
Tort law, 45
toxic effects recognizing, 310
toxicokinetics, 293
trace metals, 40
training, 353
transformation (in vitro)
anchorage independence, 157, 165, 185
assay, 159, 162
DNA repair, 187
efficiency, 460
frequency, 160
morphological, 161
partial, 168
proteins, 459
transformation (continued)
SV40 viruses, 198
transforming viruses, 167, 459
trichloroacetic acid, 297
TRIS, 312
tritium, 127, 372
tuberculosis, 273
tuberosus scherosis, 253
tumor registry, 416
tumors regression, 166
Turner's syndrome, 390
tylosis, 215

UNSCEAR, 52, 64, 68, 71, 151, 373, 554, 567
Unified Population Studies at RERF, 418
unscheduled DNA synthesis, 208
unusual disease recognition, 314
upper bounds, 366
uranium fuel cycle, 340
uranium miners, 8, 87
U.S. Foreign Service Study, 440
U.V. radiation
aberrant repair, 242
cell killing effect, 221
citotoxic effect, 189, 194, 97
endonuclease sensitive sites, 243
excision repair, 188
flux and skin cancer, 205
human fibroblast irradiation, 166
immune system, 379
mutagenic effect, 189, 194, 202
pyrimidine dimers, 245

vaginal adenocarcinoma, 315
vinca alkaloids, 513
vinylchloride metabolites, 294
vinylchloride monomer, 310
vital status, 149
volatile organic solvents, 292, 300

Waste (radioactive high level), 370
weighting factor, 344
Weibull model, 280
WHO study lead and cadmium exposure, 20
Wilms' tumor, 390
workers
aircraft crew, 339
asbestos, 179, 561
aviation electronics technicians, 436
Beta naphtalene manufacture, 561
broadcasting transmitters, 433
butchers, 313
by shipyards, 313
carpenters, 334
cutting oil, 561
construction industries, 308
diesel truck drivers, 316, 322
dye fucsin preparing, 315
electronics technicians, 436
fire control technicians, 436
flight-deck crew, 446
fluorspar miners, 400
goldminers, 400
hangar-deck crew, 446
hematite miners, 400
industrial radiography, 360, 565
iron ore miners, 400
insulation, 177
miners, 334, 355
motor vehicle drivers, 321
mustard gas, 315, 561
nickle, 180, 561
nuclear milling, 360
nuclear fuel manufacture, 360
nuclear reactors, 360, 555
nuclear reprocessing, 360, 555
nuclear research, 360, 555
offshore oil, 308
overexposed, 354
painters, 322
petrochemical, 322
workers (continued)
pesticide applicators, 322
phosphate fertilisers, 339
physiotherapists, 447
pitchblende miners, 561
printing trade, 561
radar operators, 436, 443
railway staff, 308
rubber, 322, 561
rubber vulcanising, 316
shoe making, 561
smelters, 313
spectacle lens makers, 322
sugar cane farmers, 322
tin miners, 322
uranium fuel cycle, 340
uranium mining, 399, 556
wood dust, 313, 314
working levels, 399
xeroderma pigmentosum, 188, 205, 237, 242, 238
xylene, 26? 313
zinc protoporphyrin, 296