CHAPTER 18

Radiation Biology and Radiation Protection

Contents

The biological effects of ionizing radiation were discovered soon after the production of intense radiation sources in the form of X-ray machines and radioactive elements about a

century ago. Radiation was found to stop cell division and could therefore be used therapeutically to stop cancer growth. On the other hand, radiation applied locally was found to cause wounds, which were difficult to heal, and to induce cancer. Many serious accidents occurred as a result of the use of radiation before an adequate understanding of its biological effects led to formulation of rules for protection of workers. By 1922 approximately 100 radiologists (not patients) had died as a result of biological radiation damage.

The biological effect of *very large whole-body doses* is radiation sickness and early death, while *large organ doses* lead to local cell destruction and, possibly, organ death. The effects at *lower doses* are cell changes (decreased surviving fraction, decreased rate of division, chromosomal abberations, etc), which usually can be observed by microscope soon after irradiation. The induction of cancer may take years to observe and genetic changes may not be discovered until after several generations.

The creation of our world occurred in intense radiation fields and, consequently, we have inherited an Earth drenched in radiation from cosmic sources and the minerals in the ground (Ch. 5, 10 and 17). Though the intensity of these radiation sources is much smaller than produced by human techniques, no human can avoid these natural sources. Therefore, the effects of the natural radiation background has become an important health issue, particularly radon levels in houses. Closely related to this problem is the effects of man-made sources of similarly low levels, such as the storage of nuclear waste. Much research is presently devoted to the effects of low-level radiation.

Through extensive research in this field, our knowledge has grown enormously. Initially, the effects of radiation on local organs were studied; then the effects on various specific tissues and cell types were of concern; today, the focus is on the effects at the molecular level. This development is understandable as cancer induction and genetic changes are

TABLE 18.1. *Parameters in biological effects of radiation*

- *Physical parameters*
  - Kind of radiation: α, β, or γ
  - Internal or external source
  - Size of total dose
  - Dose rate
  - Exposure time: instantaneous, temporary, recurrent, chronic
- *Microscopic effects*
  - molecular: DNA changes
  - chromosome: abberations
  - cellular (single or a few cells, *in vitro* or *in vivo*):
    - kind of cells (nervous system, bone marrow, liver, etc)
    - cell cycle (stage, rate of cell division, inactivation, etc)
    - temperature
    - oxygen content
    - cell poisons present (increasing radiation sensitivity)
    - protective agents present (anti-oxidants)
  - tissue and organ: cancer growth or death
- *Macroscopic effects* (inactivation, lethal dose (LD), cancer, etc.)
  - Somatic: rapid (within a month), delayed (up to 20 years)
  - Genetic: observed in offspring (one or several generations later)

believed to have their roots in alterations in the DNA molecules in the cells. In Table 18.1 we list a number of factors which affect the actual extent of the biological damage caused by radiation; most of these factors are discussed in this chapter.

Many groups are actively engaged in research on the biological effects of ionizing radiation: *radiologists* use radiation for diagnosis and treatment of tumors; *health physicists* have the responsibility of controlling the use of irradiation equipment and protecting people from unnecessary exposure to radiation; in collaboration with *oncologists* (tumor researchers) and *geneticists*, *radiobiologists* conduct research to explain the effects of radiation on the cellular and molecular level, *radiation chemists* are interested in the interaction between radiation and the DNA molecule.

18.1. The biological target

The discussion of the effects of radiation on biological systems requires some familiarity with the target composition and common terminology.

The human body contains some 10^{14} cells. Figure 18.1.A shows schematically the cell and its nucleus, which contains thin thread-like *DNA-molecules* (*deoxyribonucleic acid*). The DNA carries the "genetic code" and are the most important molecules of an organism. It consists of two strands of sugar-phosphate chains, attached together by *base pairs* (forming so-called *nucleotides*), in a double helix form (Fig. 18.1.H–J). The human DNA contains 2.9×10^9 nucleotides; the DNA of simpler organism have fewer nucleotides (down to about 5000). The nucleotides are combined in triplets (called *codons*), each one with the ability to produce (through some intermediate steps) a certain protein. The codons are ordered in long groups; the ordering is referred to as the *genetic code*. Because these long groups carry the information necessary to produce proteins for the different tissues, they are called *genes* ("makers"). In humans, the DNA is distributed over 23 pairs (altogether 46) *chromosomes*. In the chromosome, the DNA is wound around *histone* protein cores (Fig. 18.1.G) and highly twined ("condensed") to facilitate cell division; the DNA + histone unit (containing some 200 base-pairs) is referred to as the *chromatin*; these repeating units are known as *nucleosomes*. Figure 18.1.D shows some of the 23 chromosome pairs, and Figure 18.1.E a single one. The total amount of genetic information in the cell is called the *genom*. Stretched out the total genetic material is about 1.5 m long, but its diameter is only 2 nm; the molecular weight is about 10^{11} per chromosome. While the cells comprise most of the body, the volume of the chromosomes only occupy $\sim 1\%$ of the cell volume and only about 1/10 of the chromosome volume carries a genetic message; thus the genetically significant target is rather small.

The nucleotides are held together by hydrogen bonds between the nitrogen bases, which have their nitrogen rings perpendicular to the plane of Figure 18.1.I (i.e. turned 90° compared to the paper surface). The nitrogen rings contain some π-electrons, which interact between the planes and stabilize the chain structure. The unsaturated bonds in the nitrogen bases are sensitive to oxidation. Further, the phosphate oxygens are ionic. Thus, the DNA presents all types of chemical bonding and is sensitive to many types of reactants.

The *cell cycle* plays an important role in radiation damage (Figures 18.1.B and C) (i) during the S-stage proteins are synthesized, (ii) in the "gap 2", G_2, stage, the cell is being prepared for division (the DNA-chains are split up and copied), (iii) in the *cell division*

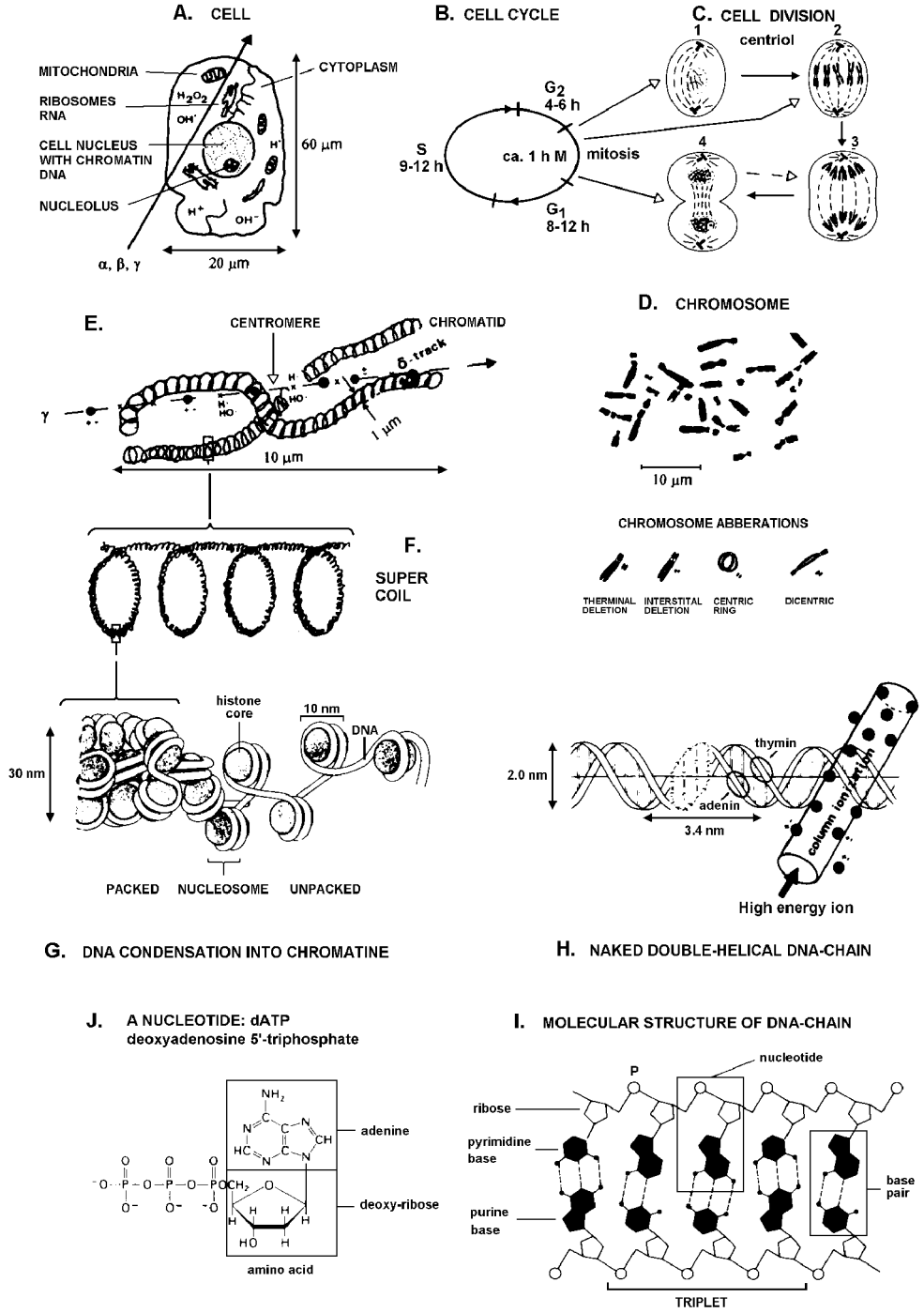

FIG. 18.1. The cell and DNA biochemical system.

(*mitosis*) the chromatin condenses into chromosomes, which are split and move in opposite directions, while the original cell is divided at mid-level (Figs. 18.1.C.3 and C.4), after which (iv) the cell "rests" or matures in the G_1-state.

18.2. Radiation effects on the molecular level

When a high energy particle (whether α, β or γ) strikes a human cell it produces a narrow track, less than 1μm thick (cf. Figs. 6.5 and 7.1). The interaction with water, which is the main constituent of the cell, leads to radiolysis products, as described in Chapter 7. To a lesser extent, the radiation may interact directly with the molecules of the cell ("direct hit"). Only the effects (direct or indirect) on the cell nucleus DNA are thought to cause severe biological damage.

18.2.1. *Radiation physics*

High energy γ-rays lose most of their energy in a few compton scattering events. A "typical" natural radiation background gamma quantum of 1 MeV loses about 75% of its energy in 20 cm of water (a "typical" human thickness). This loss occurs to 50 – 80% in a single compton scattering event, producing an electron with up to 0.8 MeV kinetic energy, depending on the scattering angle. In the next compton interaction, the ≥ 0.2 MeV γ loses ≥ 50% of its energy; the distance between these initial two interactions exceeds cellular dimensions. Thus, the 1 MeV γ-absorption on the cellular level can be considered as the production of a single high energy electron. However, at very low energies (compton γ's and X-rays), low energy electrons are produced at densities of several electron pairs per μm (cf. Fig. 6.5.D and Table 6.2; 1 mm air is considered equivalent to about 1 μm of water or tissue).

High energy electrons lose most of their energy in low energy collisions (cf. Figures 6.5 and 6.7). A typical LET-value is 200 eV/μm (Table 6.2), corresponding to 5 – 10 ion pairs/μm; a 10 keV electron produces about 10 ion pairs/μm according to Figure 6.7.

Alpha particles cause dense ionization (Figs. 6.5 and 6.7) with typical LET-values of 200 keV/μm (Table 6.2) and production of several thousand ion pairs per μm (i.e. several ion pairs/nm).

High energy neutrons are absorbed in water mainly by collisions with H-atoms, forming energetic protons which ionize similar to alpha particles (Table 6.2 and Fig. 6.7). In the collision process the H-atoms are knocked from their positions in the molecule; also other atoms may be knocked out. The neutron ends its life by being absorbed in an (n,γ) process or leaves the system.

18.2.2. *Radiation chemistry*

The absorbtion of low-LET radiation and high-LET radiation is illustrated in Figure 18.1.E and 18.1.H, respectively. Table 18.2 gives the number of ion pairs formed in the DNA, nucleosome and chromatin by α's and γ's (^{60}Co). Table 18.3 shows the damage caused to the DNA and cell nucleus. The wide range of values in parentheses indicate the

TABLE 18.2. *Ionization clusters produced directly in a DNA-related target by a single radiation track. (From Goodhead, UNSCEAR)*[†]

Radiation	Average number of ionizations in		
	DNA segment (2 nm long)	Nucleosome ($\varnothing \sim 10$ nm)	Chromatin segment (25 nm long)
γ-rays	1 (0 to < 8)	2 (0 to < 20)	2 (0 to < 45)
α-particles	2 (0 to < 15)	10 (0 to < 90)	50 (0 to < 200)

[†] UNSCEAR = United Nations Scientific Committee on the Effects of Atomic Radiation.

uncertainty as well as the dependence on the particle energy (in general, higher ionization at lower energy).

The radiation is largely absorbed in water, as the cell contains some 70% H_2O, and produces ions, free radicals and excited atoms. A momentaneous lethal dose of 20 Sv produces a concentration of 14 μM of reactive products (·OH, e^-_{aq}, H_2O_2, etc). Trace metals in the body (e.g. Cu, Cr, Se) are also poisonous at this concentration level, but essential at lower levels (e.g. a daily intake of 40 μg Se is recommended). The ions produced will probably have little effect as the DNA contains numerous ionizable positions at the phosphate group. Free radicals like HO· and oxidizing products like H_2O_2 are highly reactive and can add to unsaturated bonds, which upsets the sensitive hydrogen-π-bonding and may break the bonding between the two helices. Excited hydrolysis products may transfer the excitation energy to the DNA, leading to a localized break in the sugar-phosphate chain. The damage to the DNA may also lead to a substitution reaction in the nucleotide or a loss of a segment. Actually, hundreds of different DNA-damage products have been identified. If the damage is limited to one of the strands of the helix, it is referred to as a *single strand break*.

The cell is protected by different *DNA repair mechanisms*, which try to restore the damage. We don't know the details, except when the repair goes wrong (e.g. a replacement of a lost nucleotide by a "wrong" base-pair, etc.). It is believed that most single strand breaks are correctly repaired. If not, this may lead to somatic effects for the organism (e.g. cancer) or to an inheritable DNA-defect. The repair system is believed to be more effective in a living organism, where the cells are in continuous exchange with surrounding cells and body fluids, than in the tissue samples often studied in the laboratory. This should be kept in mind below, where effects on whole organisms as well as on cell cultures in "test tubes" (*in vitro* studies) are described.

TABLE 18.3. *Damage products in a single-cell nucleus traversed by a single radiation track (From Goodhead, UNSCEAR)*

Radiation	Average number of ionizations	Average number of induced breaks	
		DNA single strand	DNA double strand
γ-rays	70 (1-1500)	1 (0-20)	0.04 (0-few)
α-particles	23 000 (1-100 000)	200 (0-400)	35 (0-100)

The cell contains natural *radical scavengers*. As long as they are in excess of the radiolysis products, the DNA may be protected. When the products exceed the amount of scavengers, radiation damage and cancer induction may occur. In principle, there could thus be a *threshold* dose for radiation damage, at which the free radicals formed exceed the capacity of scavenging. The scavenging capacity may differ from individual to individual, depending on his/her physical condition.

A low-LET gamma ray "hit" may cause 1 ionization (or < 8) in a 2 nm DNA-segment. This corresponds to a deposition of some 30 eV (or < 250 eV) in about 6 base-pairs + sugar-phosphates. The radiation energy may distribute over a large number of bonds, so that no bond gets enough energy to dissociate. Thus, the radiation interaction may leave the DNA-segment mainly unchanged.

Low-LET radiation sometimes form clusters of ions along the particle track, i.e. produces high-LET "spots". Such spots mean increased risk of damage because a larger amount of energy is then deposited in the small volume occupied by the DNA-helix. High-LET spots therefore increase the possibility of damage to both strands of the helix, causing a *double strand break*.

It has been found that for each 100 single strand breaks produced by low-LET radiation about 3 double strand breaks occur. Because the DNA-chain is rather rigid, a double strand break does not lead to the two halves snapping away from each other. Instead, they are resting, waiting for the repair mechanism to start. Nevertheless, the repair is more difficult and the chances of "repair errors" (mutations) are much larger than for the single strand break. This is demonstrated by two facts: (i) the repair time for a single break is on average 10 minutes, while that for the double break some hours; (ii) *chromosome abberations* (Fig. 18.1.D) only occur after double strand breaks. The chromosome abberations may be due to that the cell undergoes mitosis before the double strand break has been repaired. Cells with severe chromosome abberations are not viable. Minor repair errors may be carried on to next generation of cells as a change in the genetic code or may stop the cell division process.

In addition to double strand breaks being more difficult to repair than single strand breaks, double strand breaks caused by high-LET radiation are more difficult to repair than those caused by low-LET radiation. The high energy deposited at the hit area causes "havoc" on the DNA (cf. Table 18.3). A few percent of low-LET radiation causes double-strand breaks in contrast to 10-20% for high-LET radiation.

After a low-LET dose of 3 Gy, every cell in the human body contains 3000 single strand and some 100 double strand breaks; if given in a short time the cell (and organism) has great difficulties in repairing this damage (resulting in death in the case of no medical treatment). However, spread out over a week only chromosomal abberations will be noted. In the subsequent sections, we shall discuss macroscopic effects of various kinds and doses of radiation.

18.2.3. *Radiation weighing factors*

In order to take into account the biological effects of different kinds of radiation, *radiation weighing factors*, w_R, have been introduced and are given in Table 18.4. Earlier, two similar concepts were used with about the same meaning: the "quality factor", Q, and "rela-

TABLE 18.4. *Radiation weighting factors, w_R (ICRP 1990)*

LET in water (eV/nm)	Weighting factor w_R	Type and energy of radiation
0.2 - 35	1	photons (X-rays and γ's)
0.2 – 1.1	1	all electrons > 5 keV
20	5	slow neutrons < 10 keV
50	20	intermediate n's 0.1 - 2 MeV
	10	fast n's 2 - 20 MeV
	5	protons > 2 MeV
130	20	α-particles ~ 5 MeV, high energy ions

tive biological effectiveness", RBE. The ICRP 1990 dose concept, the biologically effective dose, is termed *equivalent dose* and abbreviated H_T, and defined as:

$$H_T \text{ (Sv)} = \Sigma\, w_R\, D_{T,R} \tag{18.1}$$

$D_{T,R}$ is the absorbed dose averaged over the tissue organ T, due to radiation R. H_T is measured in sieverts (Sv); 1 Sv = 1 J kg^{-1}. The earlier, but similar concept was the *rem* (radiation equivalent man), where 1 Sv equaled 100 rem. Until 1990, H_T was called dose equivalent. $D_{T,R}$ is measured in the units of gray (Gy). The summation is taken over all sources irradiating the target.

TABLE 18.5. *Effects of γ-radiation doses on micro organisms, plants and animals*

Doses for inactivation (Gy):	enzymes		> 20 000
	virus (dry)		300-5000
	bacteria		20-1000
	human cells		≥ 1
Flowers (Senecio) survive at	10	Gy/d	during the
Trees do not survive at	> 1	Gy/d	growing season
Trees normally survive at	≤ 0.02	Gy/d	(normally spring)
$LD_{50/30}$ (Gy) for	amoeba		1000
	fruit fly (Drosophila)		≥600
	shellfish		200
	goldfish		20
	tortoise		15
	song sparrow		8
	rabbit		8
	monkey		6
	man		~ 4
	dog		3.5

18.3. Radiation effects on different types of cells

We can distinguish between two types of cells: those which are directly involved in the functioning of the organ (e.g. the cells of bone marrow, liver, or the nervous system) and those which are associated with reproduction. Radiation damage gives rise in the former to *somatic effects* (i.e. limited to the organism irradiated) such as cancer induction or cell death, and in the latter to *genetic effects* (i.e.limited to future generations).

Cells which are undergoing frequent division, and organs and tissues in which the cells are replaced slowly, exhibit high radiation sensitivity. Of the some 200 different kinds of cells in our body, some never divide (e.g. in the ovary, some sense organs and part of the central nervous system, except in the embryo state), while others divide frequently (bone marrow, intestinal epithelium, male gonads). The cell cycle time varies from hours to days. Usually, tumor cells divide much faster (3-5 times) than surrounding healthy tissue.

In general, the more differentiated the cells of an organ (i.e. the higher the organ is on the biological evolutionary scale), the greater the sensitivity to radiation. This also holds for different organisms, as reflected in Figure 18.2 and Table 18.5. Figure 18.2 shows the *inactivation dose* (i.e. leading to no further cell division) for organisms with different cell sizes. Table 18.5 gives doses which are inactivating or lethal to organisms within 30 days ($LD_{50/30}$) after short-time irradiation. A 10-fold dose is required to kill rather than to inactivate micro-organism cells.

Because of the varying radiation sensitivities of the different cell types, a *tissue weighing factor*, w_T, is introduced. It represents the relative contribution of that tissue to the total detriment from uniform irradiation of the body; Table 18.6 gives tissue weighing factors. This leads to another dose concept (cf. eqn. 18.1), the *effective equivalent dose*, H_E, which is the sum of the weighted equivalent doses in all tissues, as given by

$$H_E \text{ (Sv)} = \Sigma\, w_T\, H_T \tag{18.2}$$

The weighing factors are important in medical radiation therapy and e.g. for evaluating the effects of internal radionuclides, §18.13.5. For low-LET whole-body irradiation w_R and $\Sigma w_T = 1$, i.e. the indici in (18.1) and (18.2) may be dropped.

18.4. Some concepts of radiation biology

In radiology, the biological effects of radiation are usually discussed along two lines: the matrix effect and target theory. The *matrix effect* considers the particle-water interaction in which ions, radicals, and excited atoms are produced. This is the dominating effect at large

TABLE 18.6. *Tissue weighing factors, w_T (ICRP 1990)*

0.20	gonads
0.12	lung, bone marrow, stomach, colon
0.05	thyroid, liver, oesophagus, bladder; "remainder"
0.01	skin, bone surface

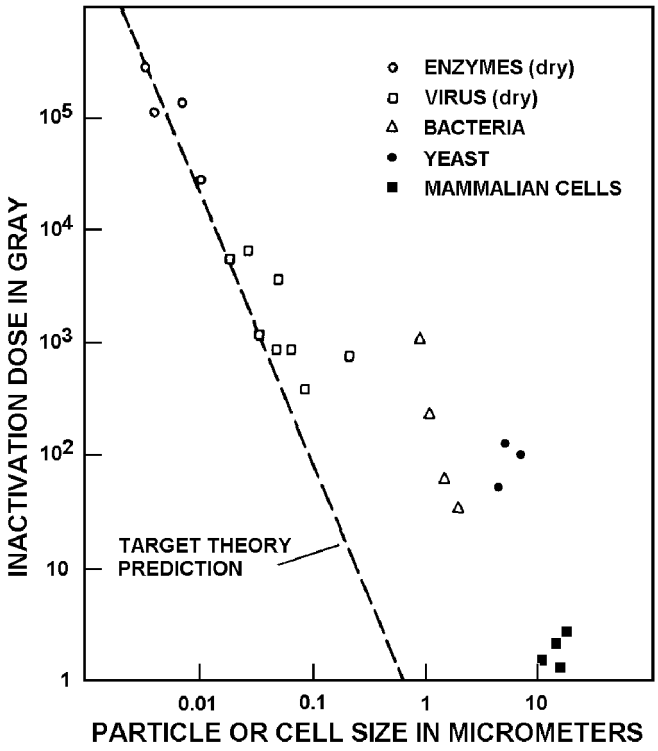

FIG. 18.2. Inactivation doses for cells and particles of different sizes.

radiation doses and dose rates; the lethal dose of 10 Gy generates about 10 000 electron tracks in each human cell. Free radicals and oxidizing products interact directly with cell DNA, causing the DNA-strands to break as described in §18.2.2. One can state that at such high doses the cell is simply poisoned by decomposition products, and the whole organ may be destroyed. It should be noted that in cancer therapy even much higher doses are given.

Inactivation of cell populations (Figure 18.2) and organisms (Table 18.5) requires comparatively large doses and the matrix effect should dominate. However, a 10 Gy dose to cells 1/1000 the size of human cells produces only 10 electron tracks per cell. The cell repair mechanisms are able to overcome the poisonous products. Consequently, doses required for inactivation of enzymes and viruses must be 10^5 – 10^6 times larger than the ones that are lethal to man.

Target theory depicts the DNA molecule as the site of reaction. Even if matrix effects can never be excluded, target theory is the essential model at low levels of irradiation because a single change in a DNA molecule may convert it into an *oncogene* (tumor producing gene) with fatal consequence to the organism. Natural background radiation is mainly low-LET. At a common level of 1 mGy/y, each human cell receives on average one track intersection per year. Nevertheless, it is claimed (e.g. UNSCEAR 1993) that this low-level low-LET radiation may be responsible for many of the malignant cancers in the population, though no laboratory experiments have confirmed this, as larger doses are required to produce observable laboratory results.

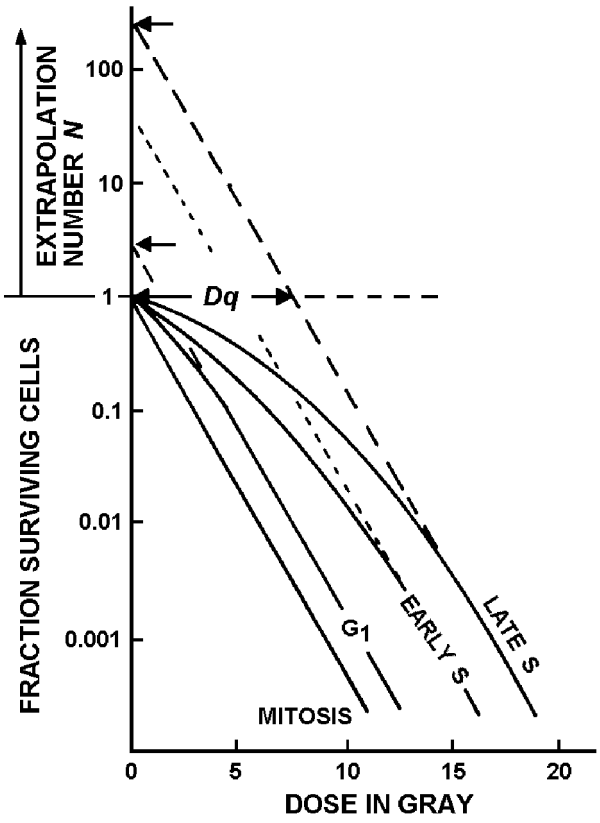

FIG. 18.3. Survival curves for Chinese hamster cells at different stages of the cell cycle. (Sinclair and Morton 1966, from Nias.)

Figure 18.3 shows typical *dose-response curves*: the effects of X-ray irradiation of hamster cells (*in vitro*) at different stages of the cell cycle. The surviving fraction of cells decreases with increasing dose. Cells in the late G_2 stage and in mitosis are more sensitive than cells at G_1 and the S stage. This is a general observation, which can be explained by assuming that the likelihood for double strand breaks of the DNA is greater and the cell repair mechanism less efficient when the DNA is in the condensed chromosome state as compared to when it is in the chromatin state (S-state). In Figure 18.3, the response function for mitosis seems to be linear while the "late S" function is curved. Extrapolation of the straight part of the S-curve extends it to the zero dose line at ~ 100; this number is referred to as the *extrapolation number*, *N*. Its significance is not quite clear. The typical values for human cells and X- and γ-radiation are 2 – 10. The value of the extrapolated line at 100% cell survival (or $N = 1$) is referred to as the "*quasi-threshold dose*", D_q. The "shoulder" in the dose-response curve is typical for X- and γ-irradiation of human cells while neutrons and alpha particles hardly produce any shoulder. Also, a shoulder does not form when very simple organisms, such as viruses, are irradiated by X- and γ-rays. A simple straight dose-response relation (the mitosis line) is taken as support of a *single-cell hit killing*, which is purely random. We have already concluded that n and α radiations are likely to severely damage DNA, particulary during the G_2 and mitosis stages.

The existence of a shoulder is taken as support of a *multi-target model*: the DNA must be damaged at several points by X- or γ-rays in order to cause the cell to die because of the efficient repair mechanism for single-strand breaks.

The slope of the straight part of the line allows calculation of the *mean lethal dose*, D_o, which is the dose required to inactivate the fraction $1 - e^{-1}$ (i.e. 63%) of the cells. Designating the surviving fraction as f_S gives

$$f_S = e^{-D/Do} \tag{18.3.a}$$

for the straight line (mitosis). The curve can be described by

$$f_S = 1 - (1 - e^{D/Do})^N \tag{18.3.b}$$

18.5. Further regularities at large doses

Figure 18.4 shows the number of dicentric chromosome abberations observed in a cell population as a function of neutron or gamma/X-ray energy. *Dicentric abberations* (Fig. 18.1.D) seem to be the most consistent index of radiation damage and represents about 60% of all observable unstable abberations following acute irradiation. Their background

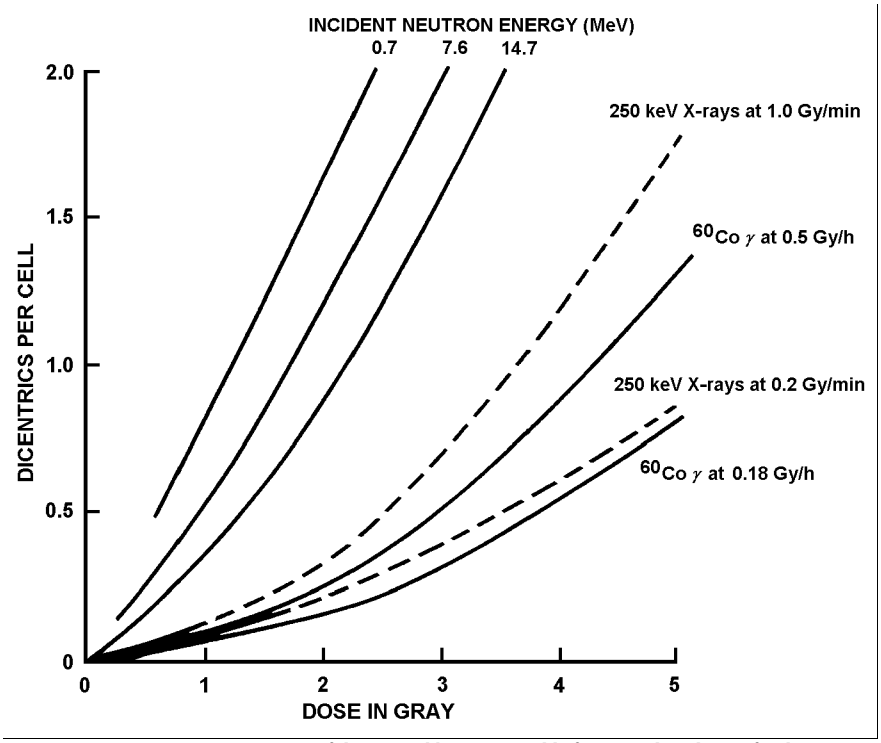

FIG. 18.4. Dose response curves of dicentric abberations yields for several qualities of radiation (Lloyd and Purrot 1981, from Nias.)

frequency is very low (about 1 in 1000 lymphocyte cells). From Figure 18.4, it is seen that the lower the radiation particle energy is, the larger the damage (of course, until the energy has decreased to such low levels that its ionization effects begin to drop abruptly, see Figure 6.7). This is attributed to the increasing ionization density with decreasing particle energy, as described in Ch. 6; see also Tables 18.2 and 4.

Figure 18.4 also shows that the damage increases with increasing *dose rate*. This is a general and significant phenomenon which is probably related to the cell (DNA) repair mechanism. At high dose rates, the repair mechanism may become saturated. If a large number of cells are damaged almost simultaneously, the tissue may cease to function. This is seen in the nerve cells at large doses and dose rates.

In animal experiments, it has been found that a higher dose rate also produces earlier cancerogenesis (i.e. shorter latency) and more severe forms of the tumor (higher malignancy).

Figure 18.5.A illustrates the effect of *dose fractionation* on cell survival at high doses and dose rates. After each succeeding dose fraction, the curve exhibits the same shoulder and slope, indicating that within a given period part or all of the damage is repaired.

Figure 18.5.B illustrates a matrix effect during irradiation in air and in an oxygen deficient (*hypoxic*) system. OER, the oxygen enhancement ratio, is the relative dose increase needed to produce the same biological effect in the hypoxic as the oxic case. For X-rays and γ, cell survival increases when oxygen is reduced; the addition of oxidants has the opposite effect. This indicates that it is the oxidative radiolysis products of water which are most damaging to the cell. However, no oxygen effect is seen for α radiation, thereby supporting the model of double strand breaks by direct hits of the α's.

This result suggests that the addition of a reductant would reduce the radiation effect which is also observed. For example, 20 Gy is required to kill 80% of a cell population in the presence of cysteine (or cysteamine), while in the reference system without cysteine the same effect is caused by only 5 Gy. Cysteine is oxidized to cystine.

Several other *radiation protection agents* are known. These compounds are typically amino thiols, similar to the natural amino acid cysteamine. They probably function as scavengers for the products of water radiolysis. Their effectiveness is evaluated by determination of the *dose reduction factor* (DRF), which is the ratio of $LD_{50/30}$ for protected and unprotected animals. Because of their chemical toxicity, many can only be administered in small doses.

No evidence has been found for cells or of higher organisms supporting the development of long-lasting *radiation resistance*. Certain bacteria have been shown to develop a seeming resistance to radiation after receiving small radiation doses over a long period of time. However, this is possibly due to the formation of mutated organisms with a different sensitivity to radiation than the original ones.

18.6. Epidemiological observations of effects at large radiation doses

We may distinguish between accidental (e.g. Japan and Chernobyl) and deliberate (as given in radiotherapy) exposure to large radiation doses. The former are said to be *stochastic* because the harm caused is statistically distributed over the exposed population; the frequency of tumor induction is assumed to increase linearly with the dose. Deliberate

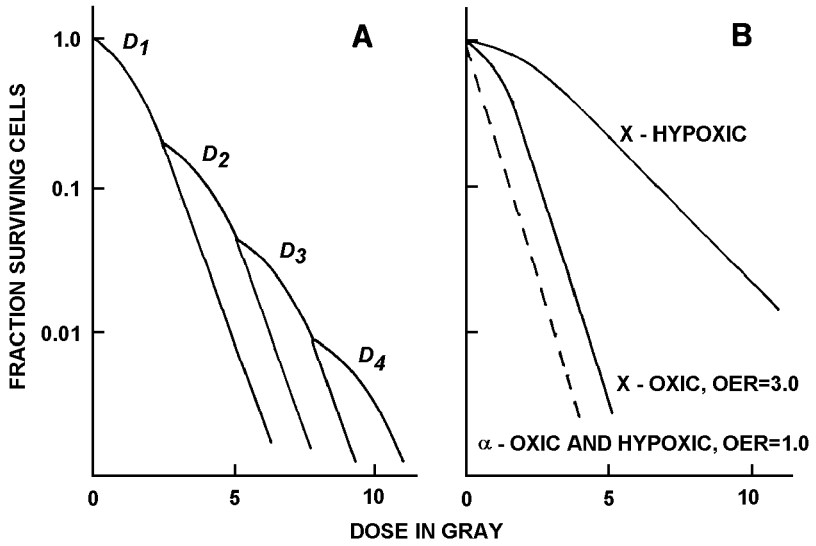

FIG. 18.5. Fraction of surviving mammalian cells as a function of dose. A) Effect of dose fractionation. B) Irradiation by X-rays and by α-particles under aerated and hypoxic conditions.

large irradiations are *deterministic* because the damage is caused intentionally to a certain organ or population; such irradiations are considered to have a *threshold value*, below which no effects are observed. We begin by discussing the deterministic cases.

18.6.1. *Radiation sickness after accidental exposure*

Very large instantaneous doses (> 10 Gy) occur in explosions of nuclear weapons, in accidents involving nuclear reactors, or from carelessness in working with accelerators, X-ray equipment or radioactive installations (e.g. ^{60}Co sources used for technical and therapeutic purposes), criticality accidents, and in handling unshielded strong radiation sources or unshielded radioactive waste. Such doses are very unlikely to be received in work involving amounts of $\leq$ 1 GBq of radioactivity.

Instantaneous whole body doses (i.e. those received within a few hours) of $\gg$ 10 Sv lead to death within 24 h through destruction of the neurological system. At 7 – 8 Sv, the main damage is to the gastrointestinal tract, causing severe bleeding which may lead to death within several days to a month. Doses < 0.5 Sv are rarely lethal. For doses between these two levels, intensive hospitalization is required for survival. At the higher end of this range, death usually occurs from 4 to 8 weeks after the accident through infection as because of the destruction of the leukocyte ("white blood cells") forming organs. Those surviving this period usually recover completely. For doses < 0.5 Sv, the only proven effect is a decrease in the white blood count (leukopenia). The threshold value for early somatic damage for short irradiation times appears to be about 0.25 Sv.

The most common type of overexposure in radioactive work involves high instantaneous doses to the hands. Fortunately, the hands, of which the skin is the most sensitive tissue,

TABLE 18.7. *Observed effects of instantaneous radiation doses to the hands*

< 2 Gy	No proven effect
~ 4 Gy	Erythema, skin scaling, follicle deaths
6 – 7 Gy	Skin reddening after a few hours, which then decreases, later strongly increases after 12 – 14 d, then finally disappears within a month; pigmentation
> 8.5 Gy	As above, but irreversible degeneration of the skin is visible to the naked eye (the skin becomes hard and cracked);degeneration of the binding tissue with increasing dose
50 – 80 Gy	Development of non-healing skin cancer; amputation necessary

can stand fairly large doses (Table 18.7). If they do receive extremely high doses (≫ 10 Sv β or γ), amputation is usually required. Although in some cases, skin transplants have provided temporary relief.

18.6.2. *Radiation therapy and deterministic studies*

Radiation therapy usually consists of the delivery of large instantaneous or fractionated doses to tissues for which surgical operation is impossible or undesirable. The effects of large organ doses is well described in the literature and is one of the main forms of tumor treatment. Radioactive ^{60}Co (up to 200 TBq) or ^{137}Cs (up to 20 TBq) γ-sources are used for treatment of deeply located organs; otherwise, X-rays are used more commonly. The organ doses for malignant tumors are usually < 100 Sv for mature breast, prostate and blood; typically ≤ 50 Sv for other internal organs and skin (often given in a series of smaller doses) and 10 – 20 Sv for the gonads, breast and bone marrow. In comparison, diagnostic radiation doses are ≤ 0.1 Sv. The use of internal radiation sources for therapy is described in §9.5.4.

A special form of radiation therapy uses heavy high energy ions from accelerators. The decreasing velocity of charged particles in matter results in a very high specific ionization near the end of the path (the Bragg peak, Fig. 6.7.b). The energy of the particles is selected according to the depth and type of tissue to be penetrated so that the particles have the proper range to provide a very high local dose in the proper volume of the sick tissue. This technique (the "proton knife") has been particularly important in treating diseases of the pituitary gland, which is located deep inside the brain.

In some cases, local irradiation of some tissues is produced by the use of radioactive nuclides implanted in the tissue by means of needles or small capsules. For example, needles of ^{90}Sr–^{90}Y, pellets of ^{198}Au, etc., have been implanted in the pituitary gland (for acromegalia, Cushing's disease, and cancer), in the breast (for breast cancer), in the prostate, and in the nerves (to reduce pain). The local dose may be 100's of Sv. Also, radioactively labeled tumor seeking compounds are used.

It should be noted that a patient's response to a certain radiation dose is highly individual; thus, all patients cannot be treated alike for the same tumor. Statistically up to 20% of the patients may be "lost" if this individuality is neglected! It is explained by the different "normal levels" of the patient's immune defense, which may have a hereditary cause. Small radiation doses seem to activate the immune response system by stimulating antigen

production. This is used in radiation therapy by exposing the patient to a comparably small "pre-treatment" dose (~ 0.5 Gy) before the large organ doses are delivered in order to hasten the recovery of the patient after the treatment. The immune system then rapidly takes care of the radiation products.

18.6.3. *Stochastic cancer induction*

The first *radiation induced cancer* in a human was reported in 1902 when skin cancer was observed on the hand of a radiologist working with X-rays. During the following decades, quite a number of such cases were reported and occurred in either persons employed in medical radiology or in patients treated with radiation for benign lesions (e.g. eczema, birth marks or tuberculous lymph nodes). Other types of radiation induced cancers were reported as thyroid cancer and sarcoma in bone or soft tissues. The cumulative doses were usually quite high (several 10ths of Gy). Today this type of radiation induced cancer is rather uncommon due to increased knowledge in radio-physics and clinical radiobiology.

The A-bomb survivors in Japan are the most important source of information on human whole-body irradiation. The population was large and varied as regards age and sex, the time of exposure was short and well defined, and it has been possible to make reliable estimates of the dose to each individual. The most recent evaluation (BEIR V, the so-called DS86 dosimetry) comprises 76 000 persons, who had been exposed to $\leq 7 - 8$ Gy of instantaneous gamma and neutron irradiation. Their health and their children's health has now been followed in detail for 50 years. Figure 18.6 shows in (A) the chromosomal aberration frequency, and in (B) the number of leukemias observed as a function of dose. The excess leukemia frequency is 3.16 by the original 1965 estimation (T65) and 3.10 by the new 1986 dosimetry (DS86). The excess malignancies are rather low for other types of cancer.

The raw data in Figure 18.6.A show "best" lines for the Hiroshima and the Nagasaki victims; the central line is a common fit. The difference between Hiroshima and Nagasaki is believed to be due to a much higher contribution of neutrons in Hiroshima due to the construction of the bomb; Nagasaki was probably only gamma radiation effects. This is in agreement with the higher damage produced by high-LET radiation in Figures 18.4 and 18.5.B.

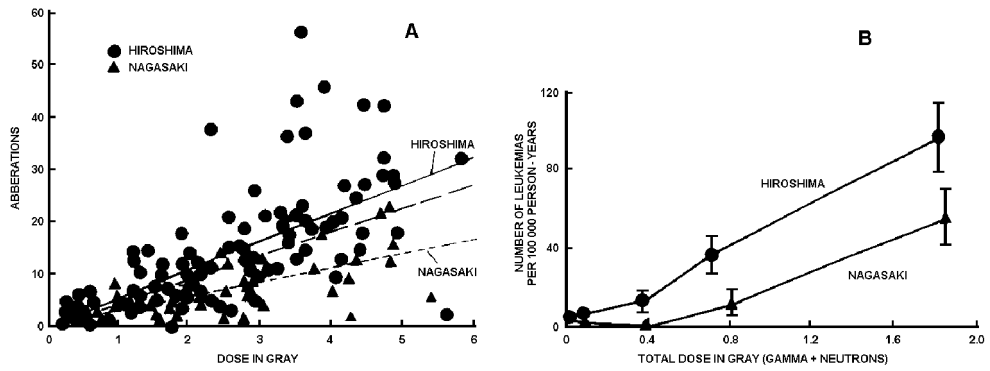

FIG. 18.6. Radiation effects on population in Hiroshima and Nagasaki as a function of dose. A. Chromosome abberations. B. Leukemia frequency.

The total leukemia frequency is five times lower for the Japanese bomb victims who received only a slightly larger radiation dose than the average of the whole Japanese population. This may be caused by an early removal of "leukemia sensitive" individuals (i.e. pre-destined victims of leukemia because of inherited leukemia oncogenes) from the group or "protection by radiation" related to the stimulation of the DNA repair mechanism as discussed above, which reduces the susceptibility to the normal incidence of leukemia.

It is important to bear in mind that the number of radiation induced cancers in this cohort (a group of persons with a common statistical characteristic) is relatively small and thus the statistical uncertainty is large: in 1950-1985 a total of 5,936 cases of cancer were reported compared to the statistically expected 5,596 in an unirradiated reference group of similar sex-age composition, i.e. an excess of only 6% (350 cases).

Following large dose exposure, *leukemia* appears first after an approximately short latent period of about 2 – 3 years. The incidence of leukemia reaches peak frequency around 6 – 8 years and then declines and almost disappears about 25 years after exposure. Cancers others than leukemia, however, tend to exhibit a different behavior. They appear after a latent period of 10 years following the exposure and then show progressive increase with time. The *breast* seems to be one of the most susceptible organs for radiation induced cancer, but the A-bomb cohorts indicate a risk only in the younger age group (< 40 y at exposure). Except for the breast, the *thyroid* is the most susceptible organ in humans for radiation induced solid tumors. This is the only cancer induction (an 80-fold increase among children) observed so far among the Chernobyl victims. The mortality risk, however, is very low because most of these tumors are benign. *Lung cancer* can be induced by γ-rays, but interest is presently focused on the risk from radon daughters in air. *Bone sarcoma* may develop after local exposure to X-rays or γ-rays. The latency period is 5 – 10 years for large doses (20 – 70 Gy).

For the Japanese survivors, increased detection of leukemia (13 times higher than naturally expected), multiple myeloma (6 times), cancer in the colon, urinary tract and breast (about twice) have been reported. In comparing an observed frequency of cancer with an expected one, it is important to correct for differences in sex and age groups.

Information on radiation effects from ingestion or inhalation of large amounts of radioactive substances is mainly limited to four cases: (i) uranium mine workers who inhaled and ingested Rn and Rn-daughters; (ii) the painters of luminous dials in Europe (before 1930, they ingested radium while sharpening their brushes by licking them); (iii) people living where the air has a high Rn concentration; (iv) patients treated by high amounts of ^{131}I for thyroid disorders (a non-stochastic investigation). The first two groups have been followed for more than five decades with the lifetime risks for fatal cancers estimated as 0.05% per Sv for bone sarcoma and 0.2% per Sv for cancer of the bone marrow. Radon is discussed in §§18.10, 18.11.1 and 18.13.5.

Saenger et al. (1968) studied 36 000 patients with hyperthyroidism (a cancer causing the thyroid to grow), of which 22 000 were treated with ^{131}I (only β, no γ; local doses of several hundred Sv) while the rest underwent surgery or chemical therapy. Although the ^{131}I patients received bone marrow doses of about 100 mSv, no difference was observed in relation to the non-irradiated group with respect to incidence of leukemia.

In 1988 Holm et al. reported a similar comprehensive study of 35 000 patients who had been administered 2×10^6 Bq ^{131}I each, which caused a thyroid dose of about 0.5 Sv per person. The mean time of examination was 44 years for patients of all ages. In this group 50 thyroid cancers were discovered (compared to the expected 40 cases for untreated),

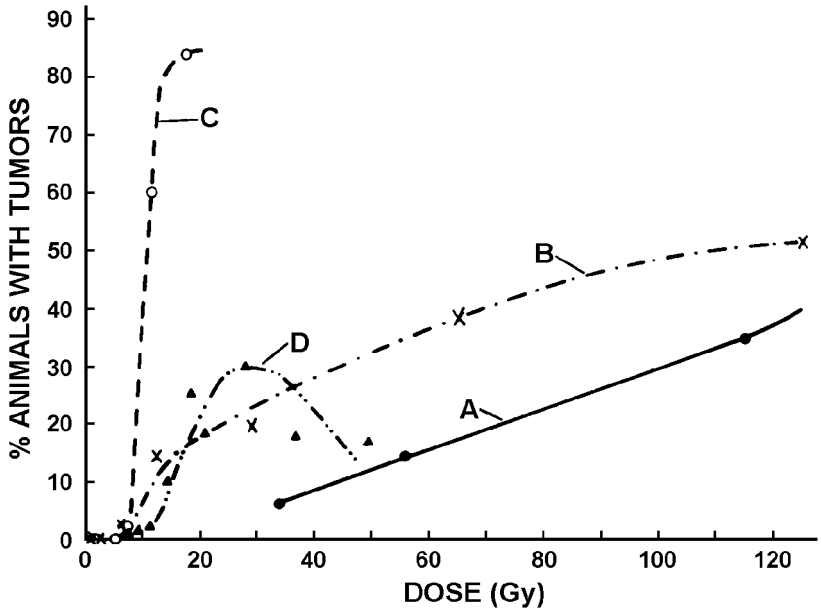

FIG. 18.7. Tumor frequency as a function of absorbed dose; see text.

indicating a relative risk of 1.27 ± 0.33 (95% confidence interval). The excess of 10 thyroid cancers is so small that it falls within statistical uncertainty. Thus, Holm et al. conclude that "these data provide little proof that ^{131}I is carcinogenic in humans" at these doses and dose rates. The examples illustrate the difficulty in proving carcinogenesis even at relatively high doses.

Information on the effects of large "whole-body internal" radiation doses comes mainly from laboratory experiments on animals. Figure 18.7 shows the excess tumor frequency for mice irradiated with doses up to 120 Gy in a comparison of the effects of different radiation sources: A, ^{90}Sr-induced osteosarcomas in female CBA mice (Nilsson 1975); B, bone tumors in humans from incorporated ^{226}Ra (Rowland 1971); C, kidney tumors in rats by X-radiation (Maldague 1969); D, skin tumors in rats by electrons (Burns 1968). Figure 18.7 seems to indicate a threshold dose at ≤ 5 Gy below which no effect is observed.

18.6.4. *Mental retardation*

In Hiroshima and Nagasaki, both severe mental retardation and lower intelligence levels (obtained from intelligence tests) occurred following prenatal exposure during the 8-15 weeks after pregnancy. In the following 16 – 25 weeks after ovulation, lesser vulnerability was observed. The exposure to 1 Gy during the early period increased the frequency of mental retardation 40% (normal frequency about 0.8%), and lowered IQ by 25 – 30 points. No cases of severe mental retardation has been observed at exposures < 0.5 Gy. No radiation effects on the brain have been observed at low dose rates.

18.7. Radiation sterilization

Figure 18.2 and Table 18.5 illustrate that at appropriate dosages radiation is an effective means of destroying higher organisms with less harm to simpler ones. This has a practical consequence because radiation can be used for the conservation of food in a quite different manner than the conventional methods of heat, canning, and freezing. Conservation by radiation attempts to achieve the complete destruction of all bacteria with minimum change in the taste of the food (due to the formation of small amounts of decomposition products). Radiation pasteurization (i.e. partial sterilization with lower doses) and irradiation at low temperatures cause correspondingly smaller taste changes.

The safety of food irradiation has been accepted by IAEA, FAO (Food and Agricultural Organization) and WHO. It has been used for several decades without any negative health effects. More than 35 countries have approved some 50 different irradiated food products for unrestricted human consumption. Examples of the foods are (country, maximum dose): potatoes (Canada, 100 Gy), onions (Israel, 100 Gy), shrimp (Netherlands, 1000 Gy), fried meat in plastic bags (Soviet Union, 8000 Gy), and wheat and wheat products (USA, 500 Gy).

Medical supplies, which must be sterile, can be manufactured and packed by conventional techniques, after which the packages may be exposed to high energy penetrating radiation (e.g. ^{60}Co, ^{137}Cs or electrons from small accelerators). The radiation kills all bacteria with little damage to low molecular weight compounds. In this common technique, the irradiation source is quite large (0.1–1 MCi; around 10^{11}Bq). The packages slowly pass through the source, such that the doses are on the order of 10 – 30 kGy. The same facilities can be used also for other purposes such as food sterilization.

Radiation doses of ~2 Gy produce sterility in the human male for about 12 months while higher doses lead to permanent sterility; libido and potency are unchanged. Permanent sterility occurs in 60% of young women given 8 Gy of fractionated irradiation to the ovary, but occasional pregnancies can occur after doses of up to 5 – 8 Gy; the children are apparently normal at birth (BEIR V).

Radiation has been used to sterilize (80 Sv) the males of certain insect species which when released (the ratio between the sterilized and untreated males was approximately 4:1), mate with females and prevent further reproduction of the species. This technique has been used in the US, Mexico, Egypt, Libya, etc to eradicate screw worm flies which can cause huge damage to the cattle industry. The technique is now also used against other insect species which are threats to agriculture.

18.8. Genetic effects

In 1927, Muller showed how irradiation of fruit flies (Drosophila M.) could produce new species that were defective with regard to the parents (e.g. lacked wings). This defect was carried in the genes to later generations. This dramatic demonstration of the mutagenic effect of radiation has been extended to other primitive species. The vast majority of such changes are recessive, i.e. in order to become dominant both parents must carry the same DNA-damage. From all experience as well as the theoretical considerations described

TABLE 18.8. *Effective dose (normal → elevated value) in mSv/y (UNSCEAR 1993) or average annual dose values (Nias 1990)*

Source		Value
Cosmic rays		0.3 → 2.0 (LaPaz) mSv/y
Terrestrial, external		0.3 → 4.3 (Kerala) mSv/y
Intake		0.052 (ingestion), 0.01 (inhalation) mSv/y
Radionuclides in body†		0.23 → 0.6 mSv/y
Rn in water supplies and air:		see §5.6
Rn in body		1.3 → 10 mSv/y
Buildings‡: wood/gypsum		0.18 mSv/y (K 150, Ra 20, Th 5 Bq/kg)
" : typical masonry		0.7 " (K 500, Ra 50, Th 50 Bq/kg)
" : alum shale concrete		5.9 " (K 770, Ra 1300, Th 67 Bq/kg)
Nuclear power plant: to critical group (Sweden)		< 0.1 mSv/y
X-ray investigation:	barium meal (intestine)	5-8 mGy
	intravenous urography	4-5 "
	abdomen and lung	~ 1 "
	mean gonadal dose (abdomen),	< 0.2 "
	genetically significant dose	0.1-0.5 "
	dental	0.02 "
Total average		2 - 4 mSv/y

† Except Rn. ‡ Staying indoors at 8760 h/y; masonry building in temperate climate.

above, the likelihood for two identical DNA impairments to come together in the fertilized cell is extremely small. No radiation induced hereditary effects have been observed in mammals. Irradiation of the sexual organs of 2000 carefully selected mice (~ 2 Sv each) for 19 generations (in total 38 000 mice, all inbred) showed no genetic changes (Lüning 1970). A thorough investigation of the 75 000 children born to parents who were exposed to the A-bomb irradiation in 1945 have not shown any increase in the frequency of hereditary diseases (or cancer). The 35 000 children born to parents of which at least one had been exposed to ≤3 Sv (average exposure 0.2 Sv) showed no genetic differences (analyzing still births, birth weight, congenital abnormalities, infant mortality, childhood mortality, leukemia or sex ratio) from children born to non-irradiated parents within statistical uncertainty.

Large doses to plants have caused mutations which have either improved the quality of the species or produced effects which are disadvantageous to the species, but desirable to society. Although irradiation of plant seeds results in a ratio of about 1000 to 1 of the harmful to the advantageous mutations, by cultivating those few plants showing improvement in properties, new plant variations have been obtained. This has resulted in species of grains and legumes which have stronger stocks, higher yields, and improved resistance to mold and to fungi. In northern countries such as Sweden, most of the grain that is grown today is radiation-produced species possessing much greater cold resistance.

TABLE 18.9. *Relative contribution of sources of radiation to the population (UK National Radiation Protection Board, 1989); annual average dose is 2.2 mSv*

Natural sources	87%
radon	47%
food and drink	12%
γ's from ground and buildings	14%
γ's from cosmic rays	10%
Artificial sources	13%
medical	12%
fall-out	0.4%
work	0.2%
occupational†	< 0.1%
others	0.4%

† Sellafield reprocessing plant, average 5 mSv/y

18.9. Radiomimetic substances

Many chemical substances when administrated to the body show the same effects as irradiation. Because cancer caused by radiation has been investigated more than cancer induced by chemicals, such substances are called *radiomimetic* (mimetic = imitative). In order to qualify as a radiomimetic agent, the substance must do the following: stop cell division, stop tumor formation, produce chromosome aberrations, cause mutations, kill lymphocytes, and be carcinogenic. Chemical substances which meet a few, but not all of these requirements are not considered radiomimetic. The effects depend on the concentration of the substance; e.g. cell division is interrupted by many radiomimetic substances at concentrations $\leq 10^{-5}$ mole l^{-1}.

Typical radiomimetic substances are organic peroxides (e.g. ethylene oxide), ethylene di-imine, mustard gas and derivatives, aliphatic dichloro-amines, etc. These compounds or chemical groups occur in many familiar materials such as tobacco smoke. The effect of a certain amount of a radiomimetic substance can be calculated to correspond to a radiation dose. Thus, smoking a pipe of tobacco corresponds to an average radiation dose of about 0.04 mSv.

18.10. Radiation background

Through life, everyone is constantly exposed to ionizing radiation from a variety of sources. Table 18.8 gives radiation doses which are representative for a large number of countries with the exception of extreme conditions like cosmic radiation at high altitude (e.g La Paz at altitude 3900 m) and locations on monazite sand (e.g. Kerala, India, and Esperito Santo, Brazil). Table 18.9 gives the relative contribution of sources of radiation to the UK population. The values are representative for most countries in the northern hemisphere. Within the same country, the total background dose commonly varies within a factor of 3 – 5 between lowest and highest areas. Brick and concrete houses contain varying amounts of uranium and/or radium, depending on the source of the building material. Because of radioactive soil, all foods contain some natural radioactivity. An approximate average value

in northern Europe is < 0.3 Bq/kg from U-decay products in food or beverage, while vegetables in the monazite areas in India (e.g. roots) have been found to have > 10 Bq/kg.

Presently great concern is directed towards people living in dwellings with high radon concentration (≥ 400 Bq/m^3) because the radon and daughters are assumed to make the largest contribution to the present radiation background. Typical indoor values are 50 – 400 Bq/m^3 air; we discuss this further in §18.13.5.

18.11. Somatic effects of low radiation doses

The effect of low radiation doses such as the natural radiation background or from the nuclear power fuel cycle (and possible accidents) is controversial because the evidence is inconclusive.

18.11.1. *Epidemiological results*

Of the large number of epidemiological investigations on the effects of low-LET low-level radiations, we will only mention a few representative ones.

Figure 18.8 shows the malignant mortality rate of the US white population accumulated over 18 years (1950 – 1967) in 46 states as a function of the natural radiation background. Each point represents an average of about 100 000 deaths and is thus significant. The average background value for the whole US population is 1.3 mSv/y and the average annual mortality rate in cancer (horizontal line) corresponds to 0.15%. The only significant trend seems to be a decrease in cancer deaths with increasing background up to about 2.5 mSv/y. Although the background radiation in the 7 highest states is 2.1 mSv/y as compared to 1.3 mSv/y for the US average, the frequency of all malignancies is lower (126 per 100 000) in the former than in the latter (150 per 100 000) case. The frequency of leukemia, breast cancer, thyroid cancer, and all child malignancies (age 0 – 9 y) is slightly lower or the same. Although attempts have been made to correlate the cancer decrease rate with other

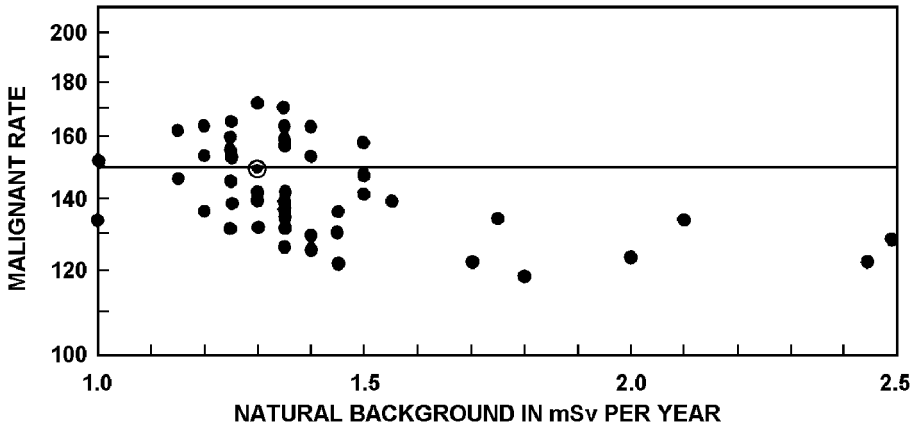

FIG. 18.8. Malignant mortality rates per 100 000 by state and natural average radiation background. (From Frigerio, Eckerman and Stowe, 1973.)

factors, such as living habits (including sexual frequency and divorce!), no convincing explanation has been given.

In the Han province of China, 150 000 peasants with the same genetic background and lifestyle were examined. Half of the group lived in a region where they received almost a threefold higher radiation exposure because of radioactive soil. The investigation of radiation effects such as chromosomal abberations, frequencies of hereditary diseases and deformities, frequency of malignancies, growth and development of children, and status of spontaneous abortions failed to disclose any difference between the two groups.

There are many similar studies from the US, UK, Canada, France, Sweden, Finland, etc, covering millions of people which fail to show a correlation of cancer incidence with small excesses in low-LET radiation. For example, the county in Sweden (Västergötland) with the highest average background radiation has the lowest total cancer frequency.

However, opposite results have also been reported. Kendall et al. (1992; in all 13 authors) have studied the cancer mortality and occupational exposure of 95 000 radiation workers at 24 different sites in England; the mean life-time dose was 34 mSv. They concluded that the frequency of cancers correlated slightly with dose. For multiple myeloma the correlation was "strong" and "for leukemia the trend was significant". 52 leukemia cases were observed while the expected range was 45 ± 13, excluding chronic lymphatic cancer which is assumed not to be related to radiation. Nevertheless, the observed leukemia frequency was lower than the UK average. The number of all cancers observed was 1363, as compared to an expected 1569 ± 20 in the general population. These "low results" are explained by "the healthy worker syndrome"; i.e. they belonged to a selected group of people with healthy living conditions and good health care and, consequently, the group was assumed not to be representative of the population in general.

A somewhat similar study of Hanford, USA, (see Ch. 19 & 20) workers during 1945 – 1981 (Gilbert et al. 1989) failed to discover any increase in leukemia, but instead found an increase in multiple myeloma, which also was explained by "the healthy worker syndrome". Multiple myeloma is a skin disease which is common among people who spend much time outdoors and expose themselves excessively to sunshine.

Many studies have tried to relate lung cancer frequency with the Rn-concentrations in ordinary air (≤ 200 Bq/m^3). Except for the study of uranium miners (§§18.11 and 18.13.5), all these investigations, though carried out with utmost care, have failed to statistically prove such a relation. However, such a relation is still assumed to exist.

18.11.2. *Problems in studies of low-level low-LET radiation*

In searching for effects of low-level low-LET radiation, the research has focused on the formation of cancer, particulary leukemia, which is a proven effect of large radiation doses, but is a rare form of cancer in the normal population. The normal frequency of leukemia in the US population is 0.012%/year (i.e. 12 cases per 100 000 deaths). The few cases in a large population leads to statistical problems and large uncertainty in the results, as well as difficulties in obtaining a homogenous cohort. Corrections have to be made for sex, aging, changes in the environment (which contain a large number of genotoxic agents), etc. For example, in order to be certain of an increased incidence of breast cancer, which is > 10 times more common than leukemia, following an acute exposure of 10 mSv to both

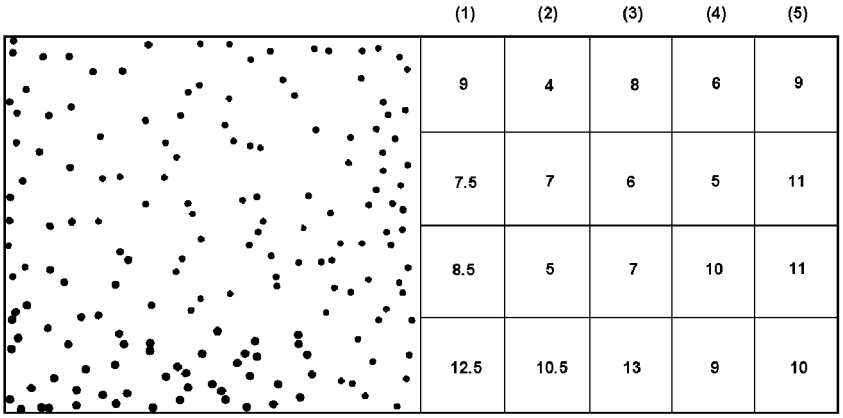

FIG. 18.9. Left, distribution of raindrops on a window. Right, matrix, to be put on top of the left Figure. Counting drops in the squares yields the figures noted; error (1σ) is ± 6.

breasts at age 35, would require a cohort of 100 million women (Land, Walinder).

To illustrate the difficulty with low numbers of incidents, we use Figure 18.9 which shows a purely accidental distribution of 165 raindrops on a window. Subdividing the window into 20 squares, A1 to D5 (right figure), one finds a range of 4 (A2) to 13 (D3) drops per square. The difference between the lowest and highest value is over a factor 3! Small excess numbers of cancers, presumably assigned to radiation, carry little weight. Walinder has pointed out that from an epistemological (science theoretical) standpoint, it is impossible to prove that low radiation doses (in the 1 mSv range) are harmful or harmless.

It has been convincingly proven that several damages to the DNA must occur almost simultaneously before a cancerogenic process starts. In §18.2, it was described that low-LET radiation mainly causes single-strand breaks, which are likely to be repaired by the biological system. It was also mentioned that at low dose rates, the radical scavenging system (more generally, the DNA repair system) is more effective than at high dose rates. Further, it was pointed out that at high doses, each cell in a tissue may be hit several times, while at low doses a "hit" cell usually is surrounded by undamaged cells. Low-level low-LET dose effect studies are further complicated by the fact that damage to the *stem cells* in the M phase is the dominating risk. About 0.01 – 0.1% of all cells are stem cells, which act as breeding sources (especially in the bone marrow) for other cells (which then mature in the thymus or elsewhere for specialized purposes). Thus, research may have to be concentrated on a very small fraction of cells.

Many researchers claim that there are several arguments for the assumption that responses from high-level and high-LET radiation may not be directly extrapolated to low-dose low-LET radiation. Many are of the opinion that the natural radiation background is harmless, and some even claim that it is beneficial (radiation *hormesis*). Thus, looking for effects at low doses can be a vain study. Walinder has pointed out that it is impossible to arrive to a reliable dose-effect relation at doses < 50 mSv by epidemiological studies.

A complicating factor in judging the risk of low-LET low-dose radiation is the different sensitivity of the exposed individuals. Though rats etc. can be inbred to produce a single

genetic strand, that is not possible with humans. At the beginning of the 20:th century, dozens of young people, mainly female, were employed in the laboratory of Marie Curie making calibrated radium sources, during this work they exposed themselves to radiation doses of many Sv a year. It is reported – though supressed at that time – that the health of many of these young people rapidly deteriorated so much that they had to leave, some having accured anemia and other radiation related deceases, while others worked for decades without any obvious detrimental health effects. The explanation for this difference is assumed to be due to differences in the individuals immune defence system.

A similar conclusion can be drawn from Figure 18.6.A, where the number of cell abberations – measured a long time after exposure – varies with at least a factor of 5 (i.e. 500% !) for the same dose.

18.12. The dose-effect curve

Figure 18.10 shows a number of hypothetical dose-effect relations: The "unmeasurable range" is indicated within the circle. The dashed-dotted line outside the circle indicates the uncertainty in the "measurable range". Line a is based on the ICRP recommendations and the message is clear: the risk is zero only at zero radiation dose. Curve b indicates a threshold around 50 mSv, below which their is no increase in cancer (or other radiation induced diseases); many radiologists support this hypothesis. Curve d assumes that there is a constant risk at the lowest doses. Curve c illustrates the "quadratic-linear" model, which presently seems to be favored by several radiation protection agencies (incl. ICRP), who assume that the slope near zero is one half of the slope at higher doses and dose rates. As this slope is unknown, it could as well be less.

Many studies suggest the existence of a dose threshold level around 100 mSv, below which no health effects from radiation are observed. Other studies claim that health effects are observed even in the range 10 - 50 mSv. This has lead to "schools" of radiation health experts, those who clain that the NTLE (No Threshold Linear Effect) hypothesis is scientifically validated, and those who claim that it is not.

Figures 18.6, 18.7, and 18.8 show that it is impossible to assess the risk at the 1 – 5 mSv level, which is the range of natural radiation background. As epidemiological investigations seem to fall short, it has been suggested (Sondhaus, Yalow, Sagan, Cohen etc) that the only way to resolve this question is through *in vivo* radiation studies at the molecular level.

18.13. Regulatory recommendations and protection standards

18.13.1. *Risk of cancer induction by radiation*

The International Commission on Radiation Protection (ICRP) was formed in 1928 and has been the main international organization solely devoted to recommendations to prevent humans from being harmed by ionizing radiation. Their recommendations form the basis for national regulatory decisions.

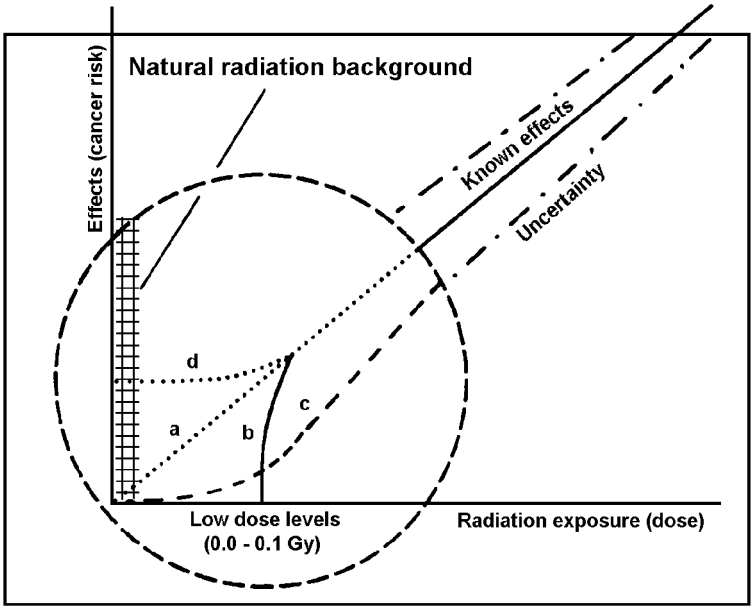

FIG. 18.10. Dose–effect relations in the known (with spread) and in the unknown (within circle) range, and some hypotheses.

In 1990, the ICRP concluded (Publ. # 60) that *the risk of cancer induction, L_c, is 5% per Sv* or

$$L_c = 0.05\, H_E \tag{18.4}$$

for low-levels of low-LET radiation (i.e. NTLE is assumed). Thus, for a dose of 20 Sv, the probability of acquiring cancer is set at 100%. Here L_c is the probability for an individual to acquire (and die) of cancer if exposed to the effective equivalent dose H_E (§18.4). This rule is based on the probabilities in Table 18.10.

In §18.6.1, it was stated that the lethal dose for instantaneous low-LET radiation is 10 Sv. The value 5%/Sv is half as large, which is a concession to the fact that biological harm depends on dose-rates as described in §18.5. In ICRP terminology, the *dose reduction factor* is chosen to be 2, although UNSCEAR 1993 (p.688) notes that it is more likely 2 – 10.

TABLE 18.10. *Nominal probability coefficients for stochastic effects in detriment percent per Sv (10^{-2} Sv^{-1}) (ICRP #60, 1990)*

Exposed population	Fatal cancer	Non-fatal cancer	Severe hereditary effects	Total
Adult workers	4.0	0.8	0.8	5.6
Whole population	5.0	1.0	1.3	7.3

UNSCEAR collaborates closely with the United Nations Environment Program (UNEP), the World Health Organization (WHO), the International Atomic Energy Agency (IAEA), the International Commission on Radiation Units and Measurements (ICRU) and the ICRP.

In the light of previous discussion, one may state that the ICRP rules are "extra-safe". However, it is unlikely that the risk is underestimated, which is an important safety aspect. The ICRP does not recognize a threshold value, below which there is no harm at all. The ICRP notes (see e.g. BEIR V or UNSCEAR 1993) that the straight line a in Figure 18.10 may overestimate the true risks at low radiation doses and low dose rates, but should nevertheless be adhered to for safety reasons. However, it should not be used for prediction of cancer induction in large populations.

18.13.2. *Recommended dose limits*

The ICRP and the IAEA regularly issue recommendations for proper handling of radiation sources. The purposes of the recommended system of *dose limitations* are to ensure that no exposure is unjustified in relation to its benefits, that all necessary exposure is kept as low as is reasonably achievable (the *ALARA principle*), and that the doses received do not exceed the specified limits. The ICRP stresses the values given in Table 18.11; they apply to the sum of the relevant doses from external exposure in the specified period and the 50-year committed dose (for children 70 years; see also next §) in the same period. These values must be respected. They are intended to limit somatic effects in individuals, hereditary effects in the immediate offspring of irradiated individuals, and hereditary and somatic effects in the population as a whole.

The effective equivalent dose limit refers to the sum of the equivalent doses to all tissues from external sources and from radioactivity taken into the body. The limits do not include contributions from any medical procedure or from normal natural radiation.

The dose limits should not be regarded as a dividing line between safety and danger. When limits have been exceeded by a small amount, it is generally more significant that there has been a failure of control than that one or more individuals have exposed themselves to dangerous radiation levels.

18.13.3. *The collective dose*

The linear relationship between dose and effect, as illustrated by eqn. (18.4) and the line a in Figure 18.10, are based on the assumption that cancer induction is a stochastic single hit process independent of dose rate or dose fractionation. Thus the detriment to the population is the same whether one person receives 20 Sv, or 20 000 receive 1 mSv each. Using the dose-effect relation of (18.4) there will be a 100% chance of cancer in both cases. We can express this by saying that the *collective effective dose* is 20 man sieverts (manSv). The collective effective dose, S_{coll}, is the sum of the effective doses to all n individuals:

$$S_{coll}\ (\text{manSv}) = \sum^{n} H_{E,i} n_i \qquad (18.5)$$

TABLE 18.11. *Recommended dose limits (ICRP #60, 1990)*

Applications	Occupational	Public
Effective dose	20 mSv per year†	1 mSv in a year††
Annual equivalent dose		
in the lens of the eye	150 mSv	15 mSv
in the skin	500 mSv	50 mSv
in the hands and feet	500 mSv	–

† Averaged over defined periods of 5 years, but the effective dose should not exceed 50 mSv in one year.
†† The value may be exceeded as long as the 5-year average dose does not exceed 5 mSv.

For simplicity, we consider only whole body doses although the collective dose concept is equally useful for organ or tissue risk evaluations (mine workers, thyroid patients, etc). In the equation, *i* refers to a situation where each of the *n* persons has received different *personal doses*, $H_{E,i}$.

For example, in the Chernobyl accident (1986), it is estimated that the 24 000 people that were evacuated from the Pripyat area received a collective dose of 11 000 manSv. According to (18.4), this would mean an expected increase in cancer incidents of 550 cases spread over the lifetime of these people.

The collective (effective) dose concept is commonly applied to natural radiation background. At an average level of 3 mSv/y; 0.015% (18.4) of the population should die of cancer each year from natural radiation. For a population of 50 M people, the collective dose becomes 150 000 manSv/y and corresponds annually to 7 500 additional cancers (out of an expected 100 000 cancer deaths/y). Consequently, the background radiation may be responsible for about 5 – 10% of all cancers; a more prudent statement is "$\leq$10% of all cancers". This claim is not possible to confirm by epidemiological investigations.

Suggestions have been made to also apply the collective dose concept to chemical poisons. We illustrate the consequence of this with an example: copper is a natural and needed constituent of our body (0.00010%) that takes part in enzyme reactions. However, an amount of $\sim$6 g of copper as a salt is lethal (*minimum lethal dose*). Using the collective dose concept, one finds that one of every 6×10^6 persons should die of copper poisoning. This is a condition for which there is no scientific support.

18.13.4. *Committed doses*

In order to relate the emissions of radioactivity from nuclear power installations or the accumulation of radioactivity in the body from fall-out to a resulting dose to the population, the ICRP has introduced the *committed dose* concept (equivalent or effective), S_{comm}. S_{comm} is the total dose contribution to the population over all future years of a specific release or exposure. It is defined as the infinite time integral of (i) the *per caput dose rate* ($\dot{H} = dH/dt$), or (ii) the *man-Sievert dose rate* ($\dot{S} = dS/dt$) due to a specific event for a population (such as a critical group or the world population):

$$H_{comm}(t)\ (\mathrm{Sv}) = \int \dot{H}(t)\, dt \qquad (18.6a)$$

$$S_{comm}(t)\ (\text{manSv}) = \int \dot{S}(t)\ \mathrm{d}t \qquad (18.6b)$$

The concept is best described by Figure 18.11, where each rectangle represents the dose delivered in one year from an annual release. A is the dose from the first year's release; the next year contains a smaller dose B because of radioactive decay (or other removal processes); the third year yields an even smaller dose C. We assume that the fourth year is the last year that the dose contribution (D) is significant. In this same fourth year, we have a "first year release", A', equal in amount to A, plus what is left from the previous years, B' and C'. Thus, the annual dose at release equilibrium is equal to the dose commitment for one year.

Eqns. (18.6) are integrated between the time of release and infinite time. If infinity is considered unreasonable, one uses "truncated time": e.g. for a person it may be 70 years, while for the human population a common figure of 500 years is often used. It is sometimes claimed in such calculations that improvements in medical science are incorporated (e.g. improved leukemia treatments reduce mortality probabilities).

The collective dose concept allows for extrapolation of the consequences from large scale introduction of nuclear power, which, in turn, establishes the need to ensure that the total annual dose stays within agreed safe limits. If it is assumed that fission power will be used for only about 100 y, the dose commitment integral may be limited to 100 y (sometimes called "incomplete collective dose").

18.13.5. *Internal radiation and ALI values*

When a radioactive substance is taken into the body by ingestion or inhalation in sufficient amounts to be a hazard, the procedure is to attempt to remove it as fast as possible so that it does not have time to become incorporated into tissues that have relatively long *biological lifetimes*, such as the bones. Administration of chemical complexing agents, which form stable complexes with the radioactive substances, provides a mechanism for the removal of radioactivity from the body.

A substance which represents a hazard within the body due to its radioactivity is referred to as *radiotoxic*. The radiotoxicity depends on the properties of the radiation and on a number of physical, chemical, and biological conditions such as mode of intake (via air, in water or food, through wounds, etc.), the size of the ingested or inhaled particles, their chemical properties (e.g. solubility), metabolic affinity, and ecological conditions. Most of these conditions are considered in the ALI concept. ALI (*Annual Limits of Intake*) and DAC (*Derived Air Concentrations*, from the ALI value) and other relevant data are presented in Table 18.12. An annual intake of 1 ALI corresponds to an annual committed dose equivalent of 50 mSv.

In Table 18.12, t_{eff} is the *effective half-life* of the radionuclide in the body, defined by

$$t_{eff}^{-1} = t_{½}(\text{biol})^{-1} + t_{½}^{-1} \qquad (18.7)$$

where $t_{½}$(biol) is the biological half-life. For example, taking the whole body into account $t_{½}$(biol) is 230 d for C, 19 d for Na, 38 d for K, 130 d for I, 190 d for Sr, and 20 000 d

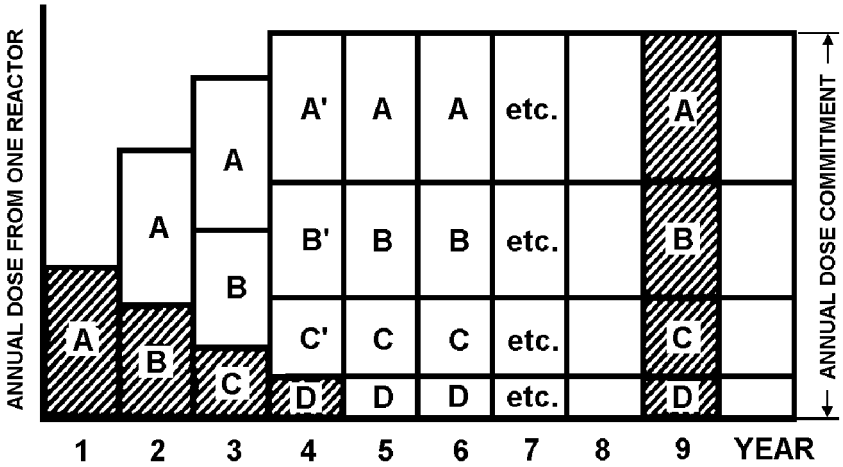

FIG. 18.11. Dose commitment for continuous radioactive decay.

for Ra. For strontium incorporated in bone, $t_{½}$(biol) is 4000 d. Radium is assumed to enter into the bone structure. In Table 18.12, a *critical organ* is selected by weighing of two factors. It is the organ for which the nuclide has the greatest metabolic affinity and for which the damage by radiation is greatest. Some of the commonly used nuclides are listed in Table 18.13 according to their relative radiotoxicities.

Eqn. (18.7) is quite general and may also include terms for other removal processes, such as washing of deposits of ^{90}Sr or ^{137}Cs from the soil, etc.

Beta-ray emitters dissipate their energy over a somewhat larger volume than that of alpha-emitters, but the energy absorbed per unit length is still sufficient to be very damaging to the tissue. Elements such as sodium and potassium represent slight hazards as their body chemistry does not tend to localize them in any particular organ and their exchange rate is high, leading to rapid elimination. Strontium and iodine, on the other hand, are localized and retained, and therefore are more hazardous.

Heavy elements such as radium and plutonium are often concentrated in the most sensitive areas of the bone where their α-emissions provide essentially lifetime irradiation since the rate of exchange is quite small. The energy is dissipated in the small volume where the element is concentrated and considerably increases the local biological damage.

It is now believed that the largest contributor to population radiation dose comes from *low radon and radon daughter* concentrations in air (see §18.10 and Tables 18.8 and 18.9). These sources were discussed in §5.6. In the UK, the average radon dose is 1.2 mSv/y, with a variation between 0.3 and 100 mSv/y. Though these are large differences, the epidemiological investigations have failed to show any statistically significant correlation between the radon doses and lung cancer. However, at larger doses there is clear evidence of correlation. Of the uranium miners in Erzgebirge from 1875 through 1912, 25 – 50% (the statistics is somewhat uncertain) died by lung cancers due to inhaled radon. Note that the "Rn-dose" is not delivered by isotopes of radon (when inhaled they are rapidly expelled), but by the Rn-daughters (see Fig. 1.2) which are associated with particles in the air (aerosols) containing the Rn. It has also been found that smokers among uranium miners in the United States have an incidence of lung cancer 10 times higher than nonsmoker

TABLE 18.12. *ICRP values (1993) for effective half-lives, dose equivalent conversion factors for ingestion, ALI and DAC values. DAC is Class D (except when W or Y), particle size 1μm*

Nuclide (a)	$t_{½}$	t_{eff} (days)	Conversion factors (Sv/Bq) (g, h)	Ingestion ALI (Bq) (b)	Inhalation DAC (Bq/m^3) (f)
^{3}H body tissue	12.35 y	12	2×10^{-11} h	10^{9}	8×10^{5}
^{14}C fat	5730 y	12	2×10^{-9} g	4×10^{7}	2×10^{4} c
^{24}Na GI(SI)	15.0 h	0.17		5×10^{7}	2×10^{4} c
^{32}P bone	14.3 d	14	2×10^{-9} h	8×10^{6}	1×10^{4}
^{35}S testis	87.4 d	76		7×10^{7}	3×10^{4} c
^{42}K GI(S)	12.4 h	0.04		5×10^{7}	2×10^{4} c
^{51}Cr GI(LLI)	27.7 d	0.75	3×10^{-11} h	5×10^{8}	7×10^{5}
^{55}Fe spleen	2.7 y	390		1×10^{8}	4×10^{4} c
^{59}Fe GI(LLI)	44.5 d	0.75	4×10^{-9} h	1×10^{7}	5×10^{3}
^{60}Co GI(LLI)	5.27 y	0.75	8×10^{-9} g	7×10^{6} W	3×10^{3} W
^{64}Cu GI(LLI)	12.7 h	0.75		2×10^{8}	8×10^{4} c
^{65}Zn total	243.9 d	190		5×10^{6} Y	2×10^{3} c
^{89}Sr total	50.5 d		2×10^{-9} h	6×10^{6}	1×10^{4}
^{90}Sr bone	29.1 y	6000	4×10^{-8} g	6×10^{5}	3×10^{2}
^{95}Zr bone surface	64.0 d	0.75	5×10^{-9} h	2×10^{7}	3×10^{2}
^{99}Tc GI(LLI)	2.1×10^{5} y	0.75	3×10^{-10} g	3×10^{7}	1×10^{4} c
^{106}Ru GI(LLI)	370 d	0.75	2×10^{-8} h	2×10^{6}	1×10^{3}
^{129}I thyroid	1.57×10^{7} y	140	6×10^{-8} g	2×10^{5}	
			5×10^{-8} h		1×10^{2}
^{131}I thyroid	8.04 d	7.6	9×10^{-9} h	8×10^{5}	7×10^{2}
^{137}Cs total	30.0 y	70	1×10^{-8} g	1×10^{6}	
			9×10^{-9} h		2×10^{3}
^{140}Ba GI(LLI)	12.7 d	0.75		6×10^{6}	3×10^{3} c
^{144}Ce GI(LLI)	284 d	0.75	5×10^{-8} h	2×10^{6}	4×10^{2}
^{198}Au GI(LLI)	2.7 d	0.75		1×10^{7}	4×10^{3} c
^{210}Po spleen	138 d	42	5×10^{-7} g	9×10^{4}	4×10^{1} c
^{222}Rn k lung	3.8	(3.8)	(k)	~ 70 (k)	
^{226}Ra k bone	1600 y	16000	3×10^{-7} g	9×10^{4} W	
			2×10^{-6} h		1×10^{1} W
^{232}Th bone	1.4×10^{10} y	73000	4×10^{-4} h	5×10^{4} W	2×10^{-1} W
^{233}U bone,lung	1.58×10^{5} y	300	3×10^{-7} g	7×10^{5}	3×10^{2} c
^{238}U lung,kidney	4.5×10^{9} y	15	3×10^{-7} g	8×10^{5}	2×10^{1}
				3×10^{6} W	1×10^{1} W
^{238}Pu bone	87.7 y	23000	1×10^{-4} g	4×10^{4} W	1×10^{-1} W
^{239}Pu bone	24065 y	72000	1×10^{-6} g	4×10^{4} W	
			1×10^{-4} h		1×10^{-1} W
^{241}Am kidney	432 y	23000	9×10^{-7} g	3×10^{4} W	1×10^{-1} W

(a) GI gastrointestinal, LLI lower large intestine, S stomach, SI small intestine. (b) From ICRP#61. (f) From ICRP #54, or calculated "c" by the relation DAC = ALI/2400 Bq/m^3. (g) For ingestion; ICRP #30 or #56. (h) For inhalation; ICRP #54. (k) Including daughter products;conversion factor for a 1 year exposure is 0.08 mSv/Bq m^3; see text.

miners. Such synergistic effects seem common to cancer. In this particular case, there are several synergistic factors such as the "mine dust" (sharp mineral fragments in the air), but

TABLE 18.13. *Classification of radionuclides according to their radiotoxicity*

I.	*Very high*:	^{90}Sr, Ra, Pa, Pu
II.	*High*:	^{45}Ca, ^{55}Fe, ^{91}Y, ^{144}Ce, ^{147}Pm, ^{210}Bi, Po
III.	*Medium*:	^{3}H, ^{14}C, ^{22}Na, ^{32}P, ^{35}S, ^{36}Cl, ^{54}Mn, ^{59}Fe, ^{60}Co, ^{89}Sr, ^{95}Nb, ^{103}Ru, ^{106}Ru, ^{127}Te, ^{129}Te, ^{137}Cs, ^{140}Ba, ^{140}La, ^{141}Ce, ^{143}Pr, ^{147}Nd, ^{198}Au, ^{199}Au, ^{203}Hg, ^{205}Hg
IV.	*Low*:	^{24}Na, ^{42}K, ^{64}Cu, ^{52}Mn, ^{76}As, ^{77}As, ^{85}Kr, ^{197}Hg

it is not considered in the investigation.

The lifetime risk of lung cancer from radon daughters have been estimated to be 0.2 – 3 lung cancers per year in a population of one million people continually exposed to 1 Bq/m^3. The probability of obtaining lung cancer from inhaling Rn-daughters is given by ICRP as $1 - 4 \times 10^{-4}$ WLM^{-1}; 1 Working Level Month is reached after 170 hours of exposure to 3700 Bq (0.1 μCi) Rn-daughters/m^3, corresponding to 72 Bq/m^3 y; in SI-units 1 WLM = 3.5×10^{-3} J h m^{-3}. Authorities apply an expected death rate value for lung cancer of 1.2% for a person living in a space of 100 Bq/m^3 in 80% of the time for 60 years. In several countries, radon "action levels" have been set: e.g. at ≤70 Bq/m^3 no action is taken, but at ≥400 Bq/m^3 action must be taken to reduce the level. An international "action limit" is proposed for dwellings exceeding 200 – 600 Bq/m^3.

It may be noted that the carcinogenic effect of low levels of Rn (i.e. < 400 Bq/m^3) is not statistically proven, and therefore contested by some scientists.

18.13.6. *Radiotoxicity and risk*

A common question in practical work with a particular amount of radioactivity is how "hazardous" it is. Considering both the *intrinsic properties*, *In*, and the *extensive* (*external*) *conditions*, *Ex*, we may designate the hazard (or risk) as a product

$$Ha = In \times Ex \tag{18.8}$$

It is often assumed that a risk *Ha* is high if the probability for its occurrence is ≥ 1%. Authorities usually state that the risk to an individual's health shall be < 0.1% to permit an undertaking, such as work with radioactive material. Thus, the probability to induce cancer shall not increase by more than 1/1000.

The intrinsic properties are the amount of radioactivity and factors which give a measure of the risk for the worker (e.g. the radiotoxic properties of the particular nuclide as given by the ALI or DAC values). It is not possible to draw any definite conclusions about the hazard from a certain amount of a radiotoxic substance. The hazard risk may only be evaluated from its radiotoxicity value. For that purpose, it is also necessary to consider its chemical form and pathways to man, which are considered to be extensive properties. ALI values do take into account if the chemical form is "soluble" or "insoluble", but this is, of course, a rather crude subdivision. The DAC values consider the particle size and time of exposure to that particular air condition (e.g. in a factory). However, it does not consider the particular ways by which the substance is released to the environment (cf. §21.11.1).

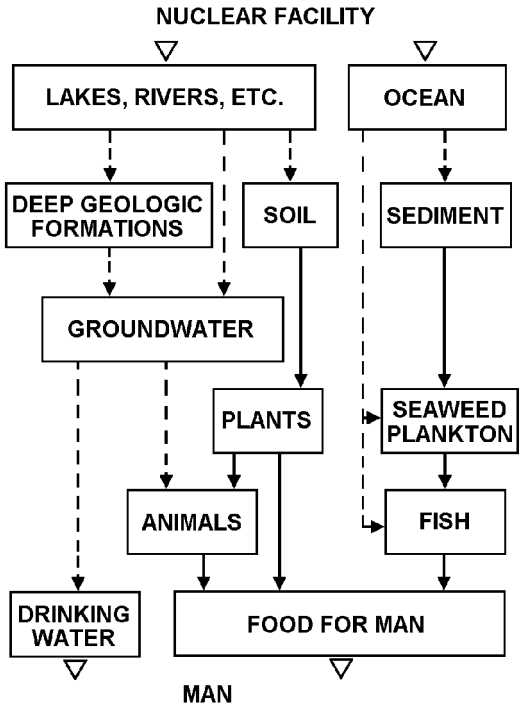

FIG. 18.12. Pathways of dissolved plutonium from a nuclear facility to man.

The pathway of a radioactive substance from its point of release until it reaches a person is the domain of *radio ecology*. Extensive knowledge in this field is essential to the evaluation of the hazards caused by nuclear power. Figure 18.12 pictures the more important pathways for plutonium; dashed lines refer to predominantly liquid flows.

Ex may be > 1 if concentration of the radioactive substance occurs (e.g. from grass to cow, or from cow to milk, etc) or < 1 if the substance is highly insoluble (precipitates out from the water). This is usually expressed through *transfer* (or "*enrichment*") *factors*, commonly abbreviated k_d. The k_d value is the radionuclide amount per kg product (e.g. milk) divided by the radionuclide amount per kg source (e.g. grass). Typical k_d values for ^{90}Sr and ^{239}Pu from soil to vegetables are 0.2 and 0.0002, respectively, while values for the same nuclides in the water → fish system are typically 1 and 40, respectively. Thus, plutonium is enriched in fish but not in vegetables. Note that there is an alternative pathway: water → sediment → seaweed → fish. The values are "site specific", i.e. measured at two different locations (e.g. Lake Michigan and the Baltic Sea), values are obtained which often differ by more than a factor of ten. See also Ch. 22.

By considering all possible transfer routes, one can estimate what amount of a radionuclide released to the environment may end up in plants, animals, or man. When these figures are combined with the *dose conversion factors* ("committed effective dose equivalent per unit intake", according to ICRP) in Table 18.12, it is possible to calculate the dose received by man from intake of a radionuclide in the environment. The dose conversion factors depend on the mode of intake (usually only inhalation or ingestion). Thus

FIG. 18.13. Label for shipment of radioactive material of class II. "II" in red with a yellow background.

the dose factor of ^{239}Pu is 10^2 larger for inhalation then for ingestion. Both kinds of data are given in Table 18.12, depending on available data (see ICRP publications).

Such calculations are applied in the risk analyses of contemplated nuclear waste repositories and in the risk evaluation of radium or plutonium content in drinking water. They are also used to establish limitations for intake of food from a contaminated area; e.g. in Sweden reindeer meat with > 1500 Bq/kg is considered unfit as food (reindeer meat is the main protein intake for the Laps living in Northern Sweden).

18.13.7. *Classifications, working rules, etc*

Radioactive substances of various activities, concentrations (or specific activities), decay modes, etc., constitute quite different hazards, and must be handled accordingly. Various countries classify radioactive material differently and issue different working rules. We give a few classifications and rules, adhering primarily to the recommendations of the IAEA.

Figure 18.13 shows the international transportation label with the symbol for ionizing radiation (with a white or yellow background, wbkg or ybkg). The radiation source and its activity should be given. The category number is shown in red, according to:

I-wbkg, radiation level	$\leq$ 5 µSv/h	at surface of package; for III-ybkg $\leq$1 mSv/h at 1 m
II-ybkg, "	$\leq$ 0.5 mSv/h	
III-ybkg "	$\leq$ 2 mSv/h	

For high levels, the source must be transported as a special cargo. The transportation carriage must fulfill a number of requirements with regard to resistance against fire, mechanical damage (drop tests), leakage (immersion tests), etc. Special regulations apply for spent reactor fuels and high-level waste (usually > 4 000 TBq; see Chapter 20). IAEA has issued rules for transportation of radioactive materials, which are of special importance to large nuclear facilities.

For radio-tracer work in common non-nuclear research laboratories, some general rules can be recommended (see also next section). Spills may result in increase in the radiation background. They may not constitute a hazard to the workers, but may ruin the scientific experiments if not cleaned up immediately. In all work with radionuclides, radioactive waste is produced. It is common practice to collect all such waste in special containers, and to dispose of it according to national rules. For short lived radionuclides of low hazard and low levels of radioactivity (e.g. as in ^{14}C-work), it is common practice to dispose of such waste by normal flushing to the sewer with several liters of tap water if such procedures are permitted by the national radiation protection organizations.

18.14. Protective measures for radiochemical laboratory work

Three basic principles are recommended for keeping radiation exposure to a minimum: shielding, control, and distance. If a radiochemical laboratory is designed properly and the work performed in such a manner that the general background contamination is sufficiently low to do valid low level tracer experiments, then the health aspects of radiation control are satisfied. We indicate the main principles for work with radioactive substances, but in each notion, special rules may apply.

18.14.1. *Tracer work with moderate β-γ-levels*

Ordinary chemical laboratories may be used for radiochemical work at low levels of short lived β-γ radionuclides (e.g. half-lives < 14 d and activity levels < 10 kBq). However, it is recommended that a special room be used for radioactive work. In the design of such a laboratory it is important that airborne contamination be prevented from spreading to counting rooms and to offices. Therefore, a pressure difference between the laboratories and the other areas is desirable. The air velocity in the fume hoods should never be below 0.25 m s^{-1}, and 0.5 m s^{-1} is recommended. With such a flow velocity, radioactive dust and fumes are retained in the hood and removed through the vents. The fume hoods should have filters for collecting radioactive particulates.

To minimize the possibility of ingestion as well as the chances of ruining experiments through accidental contamination, limiting the radioactive work to a minimum area is essential. There should be no radioactivity except in the immediate working area, and upon completion of the particular experiment, all activity should be removed and the area cleaned (*decontaminated*) if necessary. For low levels, this means working in a good hood with easily cleaned nonporous surfaces.

One operation which commonly results in contamination involves evaporation of a solution to dryness either on a hot plate or under a heat lamp. Although the percentage of the

sample carried away by spray may be very small, it may result in appreciable amounts of activity being spread around the area of the evaporation. Consequently, all evaporation should be performed in a hood and the vicinity should be protected from the active spray by a covering of absorbent paper.

For nuclides which emit only β-particles, the glass walls of the container may provide sufficient shielding. Sheets of glass or plastic (such as lucite) are commonly used to shield exposed solid samples.

For work with higher levels of β-γ-emitters of longer half-lives, special radiochemical laboratories should be used. The working surfaces and floors should be even, nonporous, and with a minimum of seams. Surfaces of plastic material, stainless steel, and artificial stone are acceptable bench materials. It is recommended that fume hood and benches be covered with an absorbing material such as absorbing paper, and that experiments be conducted when possible in trays of stainless steel or plastic. Such arrangements ensure that the radioactive material does not contaminate a larger area if a spill occurs. Radionuclide workers should wear surgical gloves and laboratory coats in the laboratory. If there is any danger of splashing, plastic face-hoods are recommended. It is extremely important that oral contamination be avoided. Beta-radiation from radioactive sources has ranges which rarely exceed 1 g cm^{-2}. Consequently, in a laboratory in which the level of β-emission is less than 1000 MBq, protection from the radiation can be achieved with a 1 cm plexiglass shield.

18.14.2. α-*laboratories*

For α-emitters the main hazard is internal, not external, to the body. For moderate activity levels a *glove box* under slightly reduced pressure provides a simple and convenient closed chemical laboratory. Samples of the actinide elements usually have high specific radioactivities. Therefore, special care must be exercised in working with them. Because these α- emitters usually are associated with weak γ-radiation or X- rays, chemical work with these elements must be conducted in more advanced gloveboxes (Fig. 18.14), which are kept at a pressure slightly below the surrounding atmosphere by circulation of pure air or inert gas through the box. The boxes should have alarm systems for monitoring hazards such as interrupted water circulation, electrical short circuits, oxygen in the inert gas, heat, etc. In Figure 18.14, the control panel for these protective arrangements is shown above the box.

In large alpha-box laboratories, one of the main hazards is radioactive dust. All room surfaces should, therefore, be made with as few seams and sharp corners as possible; particularly the floor must be of high quality. Electric power, water, waste, ventilation, etc., should be connected to piping in the ceiling. The air into the laboratory must pass through filters as must the air exiting the laboratory. The exit air should be monitored for α-activity. Entering and leaving the laboratory should be through airlocks, and the hands and feet must be monitored for activity on exit. All these protective measures make α-laboratories quite expensive, but smaller laboratories working with lower levels of α-activity can be constructed in simpler fashion for correspondingly less cost.

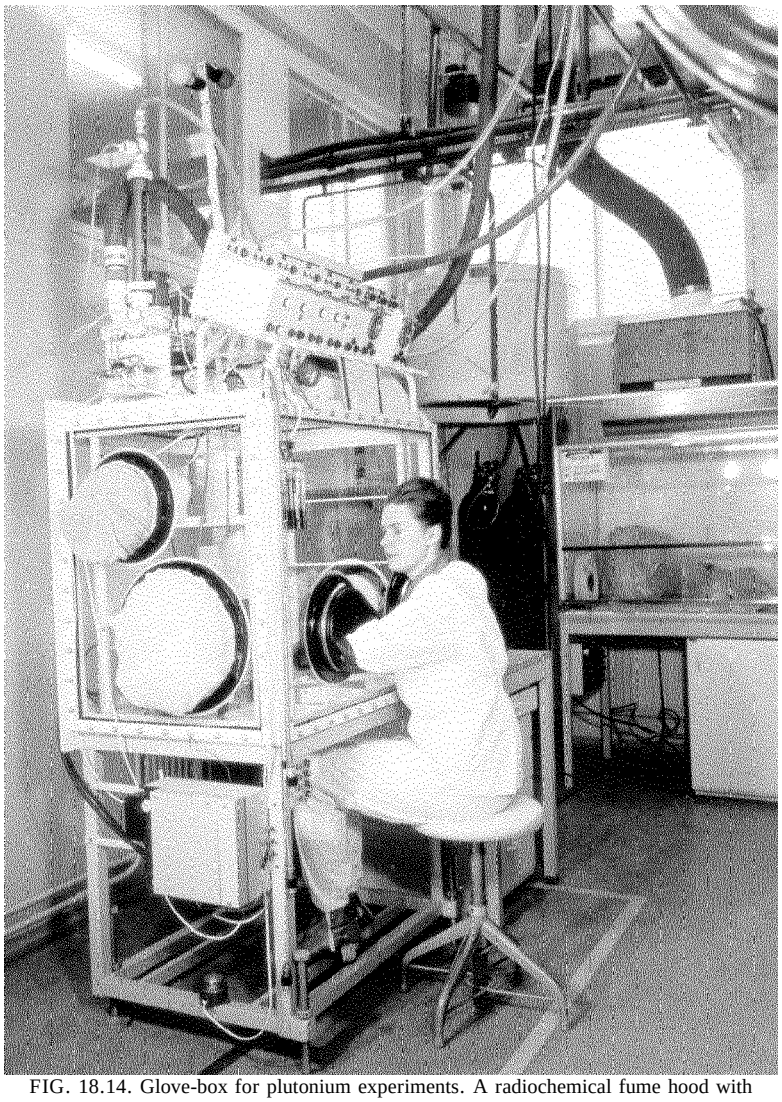

FIG. 18.14. Glove-box for plutonium experiments. A radiochemical fume hood with filter is seen in the background. Note that all connections are in the ceiling.

18.14.3. *High level* β-γ*-emitters*

Since the intensity decreases as the inverse square of the distance, maintaining maximum distance (by use, when necessary, of remote control apparatus such as tongs) when working with moderate or high levels of activity reduces the exposure appreciably.

High levels of γ, > 1000 MBq, require shielding with layers of concrete, water, steel, or lead, and the operations must be carried out by remote control. The eyes can be protected by the use of lead glass windows of high density, periscopes, mirrors, etc., see

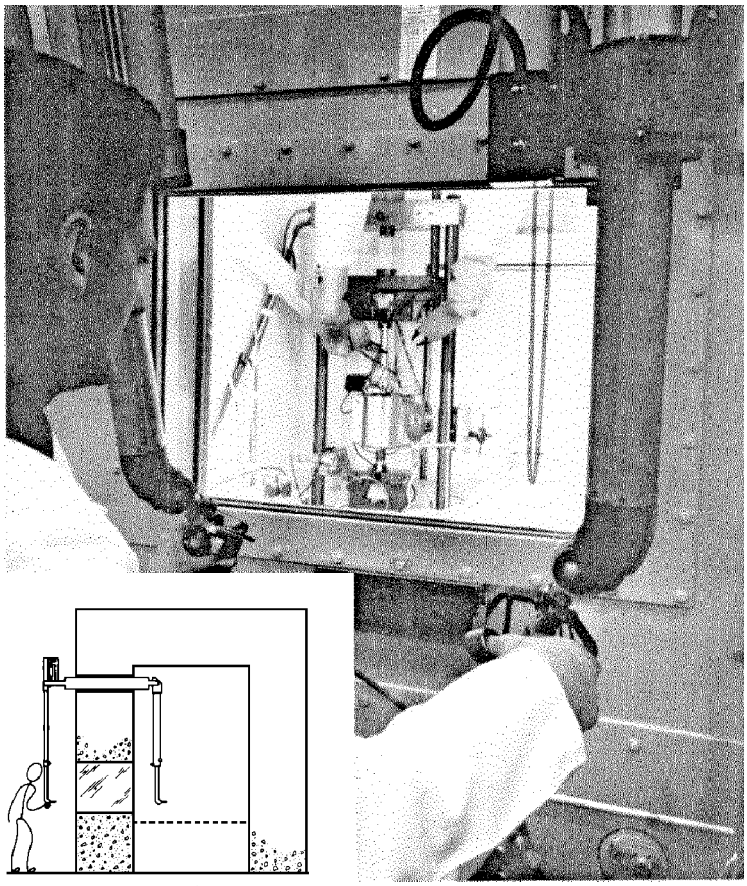

FIG. 18.15. High-active β-γ-work with master-slave manipulators. The window is filled with high density $ZnBr_2$ solution.

Figure 18.15.

Commonly, special shielded cells are used. These cells are sealed from the atmosphere and kept at a pressure lower than that for the working personnel. The smallest cells usually have lead walls which sometimes reach to the ceiling; by this arrangement, no scattered radiation reaches the working personnel. Experiments are carried out with the use of tongs passing through the lead walls or, for the thicker cells, with manipulators reaching above or through the walls. In cells for very high activities (≥ 10 TBq, or > 1 000 Ci), these manipulators are guided electrically or mechanically (*master-slave manipulators*). All movements of the operator are copied exactly by the slave hands inside the cell. For very complicated work and extremely high radioactivity, robots have been developed which can be guided to repair such items as unshielded nuclear reactors, radionuclide equipment, heavily contaminated radiochemical apparatus, etc.

18.15. Control of radiation protection measures

In larger organizations, the control of radiation hazards is the responsibility of specialists known as *health physicists* or, sometimes, *health chemists*. Their main duty is to ensure that work is carried out without hazard to the health of the people involved.

The protection follows three stages: prevention, supervision, and after-control. Preventive measures include use of fume hoods, α-boxes, radiation shielding, tongs, etc., as discussed above. The supervision stage involves the use of radiation instruments to monitor the radiation level (see Ch. 8). Small TLD, film or pocket pen dosimeters are used for individual monitoring (§7.9). For spills and contamination of hands, shoes, etc., special contamination instruments (counters) are used which are more sensitive than the monitoring dose instruments.

Contamination in the laboratory must be avoided. This is controlled by smear tests; i.e., a filter paper is wiped over the surface and the paper is checked with a suitable instrument. In a so-called "clean area", the fixed contamination should not exceed 2 Bq for α, and 4 Bq for β-γ on a surface of 100 cm^2. For an "active area" the rules are a maximum of 20 Bq for α per 100 cm^2, and 0.01 mGy h^{-1} from β-γ at a distance of 2 cm from the surface. Radioactive aerosols are monitored by air samplers in which a certain amount of air is drawn through a fine filter paper after which the paper activity is measured.

The after-control usually consists of checking personal dosimeters and a medical examination. Depending on the kind of work, the dosimeters are checked from twice a week to once a month. A medical examination is given once or several times a year, depending on the work conditions. In danger of inhalation or ingestion of α- or soft β-emitters, urine samples are analyzed. Such analyses are very sensitive and much less than a kBq in the body is easily detected. For workers who handle hazardous amounts of α-emitters (e.g. plutonium in more than milligram amounts), urine samples should be taken regularly.

If necessary whole-body counts are also taken. *Whole-body counting* is carried out with the subject being surrounded by numerous scintillation or solid state detectors in a heavily shielded room. The natural body content of ^{40}K is easily detected and is a control of the efficiency of this technique.

18.16. Exercises

18.1. "Reference man" consists of 18%C, 66% H_2O, 0.2% of K per body weight. He may also have accumulated 10 pCi ^{226}Ra in the body; assume 0.3 decay for each of the following 5 daughters. Calculate for a body weight of 70 kg the number of radioactive decays per unit time from ^{3}H, ^{14}C, ^{40}K and ^{226}Ra. Assume 30 TU in water.

18.2. Using the information above, how many grams of the body's molecules (assume average mole weight of 10^5) will be damaged in a year if the G(damage) value is 3.1×10^{-7} mol/J? Assume $E_{abs}(\beta) = E_{max}/3$.

18.3. Under the same assumption as above, what amount of damage will be caused by cosmic radiation? Assume that the cosmic particles produce 3×10^9 ion pairs s^{-1} m^{-3} of the body.

18.4. With the information in exercise 18.1, calculate annual doses received from (a) ^{40}K, and (b) ^{226}Ra and daughters. Assume $w_r(\alpha) = 20$.

18.5. Ten mg ^{238}U has been collected in the kidneys. Considering the biological half-life of uranium and assuming only one α-emission in ^{238}U decay, calculate the dose (in Sv) received by the organ if the uranium is evenly distributed. The weight of a kidney is 150 g.

18.6. A γ-dose rate of 1 Sv is assumed to inactivate (kill) human cells. The body contains $6x10^{13}$ cells in a cell weight of 42 kg for a 70 kg man. (a) What average energy (in eV) has to be deposited in a cell to kill it? (b)

Calculate the number or kidney cells destroyed for the dose received in exercise 18.5. For simplicity assume the cells to be cubic with a side length of about 11 μm.

18.7. A tumor has the weight of 80 g and we wish to destroy 20% of the cells by irradiating with 180 MeV protons with such penetration that half of the energy is deposited in the tumor. The particle beam is 5 μA. For what time must the irradiation be? A cell of weight 10^{-9} g is assumed to be killed on the absorption of 200 keV and no cell is assumed to be killed twice.

18.17. Literature

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