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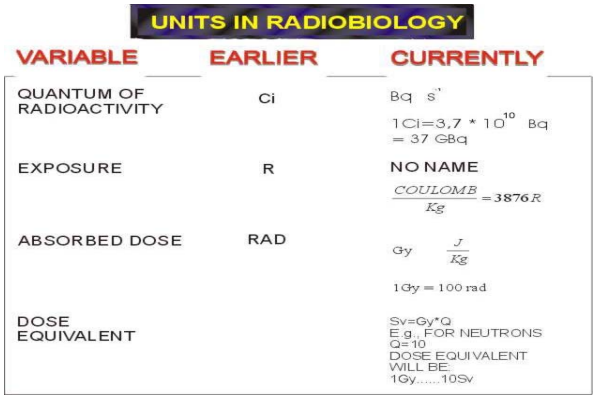
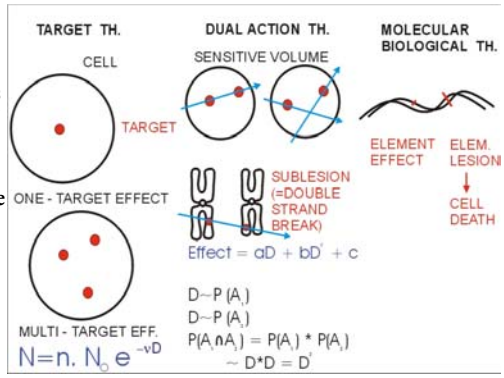
1. Units

Fig 1: Units in radiobiology



2. Theories of the effects of ionizing radiation

Fig. 2: Theories of the effects of ionizing radiation explain how the stabilized molecular damage is produced



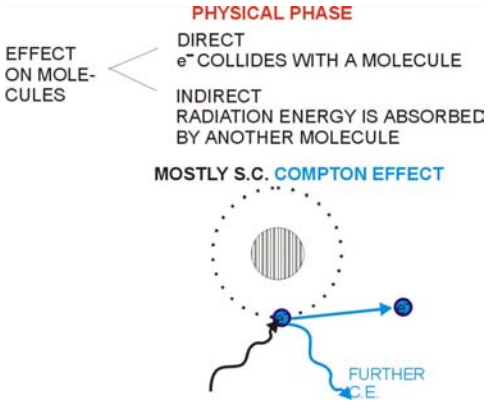
Target theory: Dose/effect curves are straight (with or without a shoulder) → there is a small sensitive target(s) in each cell with low probability to be hit, i.e., an amplifying process. Only formal theory

Dual action theory: Tried to explain reciprocal chromosomal translocations. 2 sublesions (double-strand breaks) in close vicinity → lesion = translocation.
Dense ionizing radiation → 1 particle 1 lesion → linear term aD
Sparse ionizing radiation → 2 particles 1 lesion → quadratic term aD^2
Theory not universally valid, but important accent: relative biological effectiveness (Sieverts!)

Molecular biological theory:
Again: one or two particles → a combination of two primary events → elementary lesion = double strand break → difficult repair → chromosomal break → chromosomal aberration → possibly cell death
Target = molecule, not nucleus
The close environment of a radiation event and the repair processes taken into account

Radical (ROS) theory: Amplification of the effects of corpuscular radiation by production of free radicals (ROS) in water environment. It is compatible with the theories mentioned above and could be combined with them

Fig. 3 Processes leading to the stabilized molecular damage



DURING 10^{-10}s A PAIR OF IONS IS FORMED:

$$A \rightarrow A^{+} + e^{-} \qquad e^{-} + B \rightarrow B^{-}$$

CHEMICAL PHASE:

FREE RADICALS ARE FORMED:

$$H_2O \rightarrow H_2O^{+} + e^{-} \qquad H_2O^{+} + H_2O \rightarrow H_3O^{+} + OH^{\cdot}$$

DURING 10^{-5} s FREE RADICALS RECOMBINE MUTALLY AND WITH "BIOLOGICAL" MOLECULES

DIRECT INTERACTION OF A BIOLOGICAL MOLECULE CD WITH A CHARGED PARTICLE:

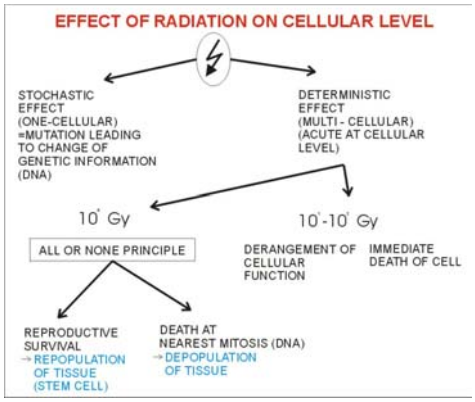
$$CD \rightarrow CD^{+} + e^{-} \qquad CD \rightarrow C^{+} + D^{\cdot}$$

OXYGEN SENSIBILIZING EFFECT: **(ORGANIC RADICAL)**

$$H^{\cdot} + O_2 \rightarrow HO_2^{\cdot} \qquad D^{\cdot} + O_2 \rightarrow DO_2^{\cdot}$$

3. Cellular level effects

Fig. 4 Effects of radiation on cellular level



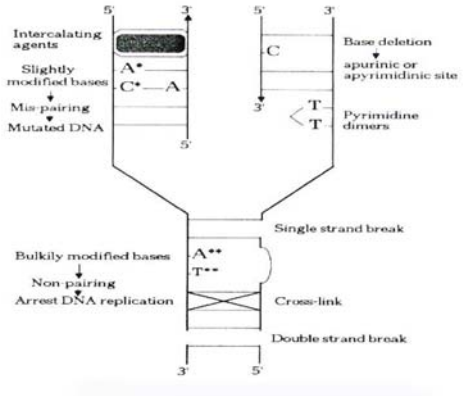
Reproductive survival (more exactly: an ability to cycle indefinitely) – the most sensitive test of radiation damage to cells (colonies in vitro). ($D_0 \rightarrow 1/e = 0{,}37$) ≈ 1 Gy
The main mechanism of radiation damage of cells:
DNA damage, membranes - ? Radiation → DNA damage → ↑p53 → apoptosis
Mitotic delay: 1 Gy → 10% of cycle duration
Hormesis: Positive effects of very low doses of radiation (and of toxic chemicals) reported

Criticisms:

- lack of a coherent dose-response theory
- necessity of a specific (adequate) study design – difficulties in replication
- only modest degree of stimulation – normal variation
- lack of appreciation of the practical/commercial applications

But if real → consequences for radiation hygiene

Fig. 5 Types of DNA lesions. Some of them represent a mutation, i.e. a gene which has undergone a structural change



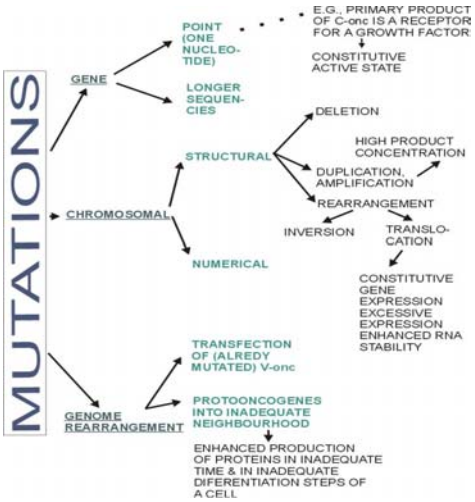
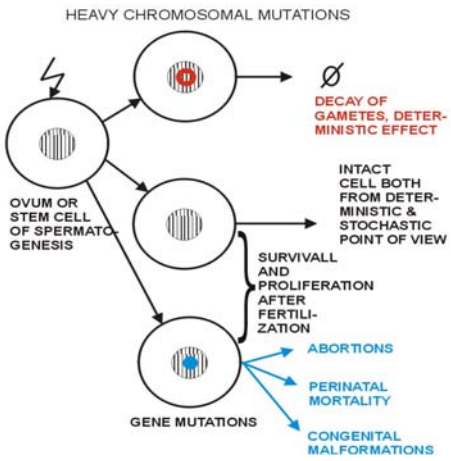


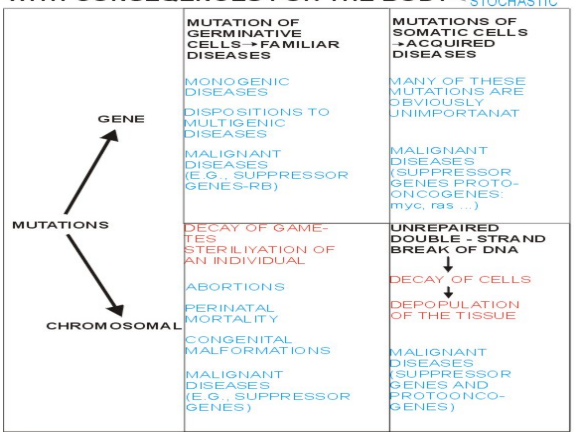
Fig. 6 Types of mutations. Consequences independent on the mechanism of origin or on the „age“ of the mutation

Fig. 7 Damage to the germ line cells by ionizing radiation
→ decay of gametes, sterility
→reproductive survival, but mutations→ abortions, perinatal mortality, congenital malformations (evolution: „hopeful monsters“).
One point mutation will be sufficient to do that

DAMAGE TO GERMINATIVE CELLS BY RADIATION



EFFECT OF RADIAT ON GENE LEVEL WITH CONSEQENCES FOR THE BODY — DETERMINISTIC / STOCHASTIC



Chromosomal mutations as a measure of the absorbed dose

Repair of radiation effects:
- DNA repair systems: physical continuity preferred information content → mutations
- reparative regeneration – on the level of tissues (see later)

Fractionation of dose or ↓dose rate → ↓biological effect, esp. in tissues with slow turnover (compared with tumors!)

Radiosensitivity of cells depends on:
- presence of oxygen
- effectivity of DNA repair systems
- phase of the cell cycle

The specific function of cells is relatively radioresistant

4. Tissue level effects

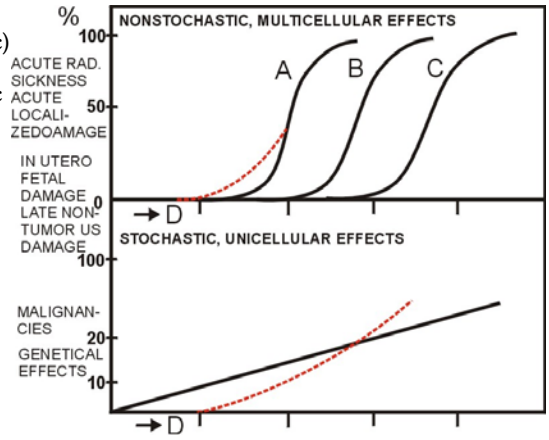
Example: Radiation damage of the blood forming organs (see practicals)

Cytokinetic parameters of a tissue determine its reaction to irradiation (radiosensitivity of the cells, dynamics of depopulation and recovery); mitotic fraction of a given tissue → time needed to the manifestation of tissue damage. Non-dividing cells are not sensitive in the $LD_{50/30}$ region. Stem cells – a key position in the recovery of self-renewal cellular systems

Disturbance of the function of a tissue has a delay – the mature compartment is intact, it takes some time for the failure of proliferative compartments to „arrive“ to the periphery; life span of cells → the slope of the decline in the periphery (RBC 120 days, granulocytes and platelets 10 days)

5. Effects on organismic level

Fig 9 Deterministic (non-stochastic) and stochastic effects of the ionizing radiation



5.1 Deterministic effects

- acute radiation sickness
- acute localized damage
- damage to the embryo/foetus in utero → loss of „formative mass" (microcephalia, microphtalmia etc.)
- late non-tumorous damage: cataract, chronic radiation dermatitis, pulmonary fibrosis etc.

Loss of large numbers of cells, large doses, S-shaped dose /effect curves (Fig. 9, upper part): dose threshold and plateau. Typical clinical presentations. Tissue recovery

Acute radiation sickness:

Radiosensitivity of tissues → the dose needed for depopulation (bone marrow, gut, brain)

Transit time → delay (timing) of effects (brain, gut, bone marrow)

Acute localized damage:

- Radiation dermatitis
- Germinative epithelium → sterility, premature menopause

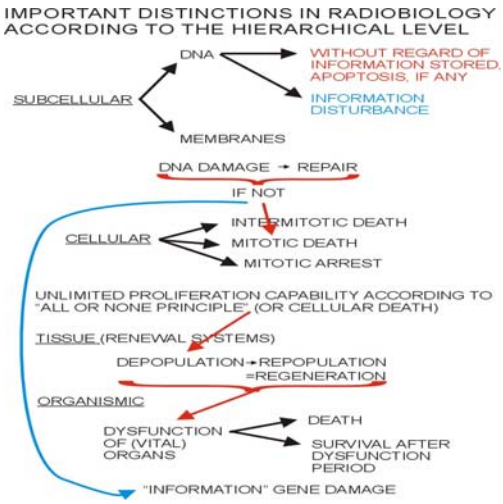
5.2 Stochastic effects

- malignant tumors (esp. lungs, mamma, thyreoid, bones)
- genetic damage (germinative cells → progeny: abortus, perinatal mortality, congenital malformations); quantitatively less important than tumor induction

One cell (mutation, malignant transformation), low doses, dose/effect curves as in Fig. 9 (bottom): uncertainity about the effect of low doses (threshold? linear? hormesis?). Doses are additive

Stochasticity: causal connection with radiation cannot be proved in individual cases; no dependency of the disease intensity on the dose

Fig. 10 A hierarchy of radiation effects



6. Radiation hygiene

In practice: linear character of the dose/response curve in the region of small doses is presupposed → ALARA principle: As low as reasonably possible

Natural radiation background + medical radiation sources → the vast majority of exposures