CHAPTER 4

Radiation Effect for Doses within the Diagnostic Range
LEARNING OUTCOMES

At the end of the lesson, the student should be able to:

- Explain Somatic & genetic
- Explain Stochastic & Deterministic
DETERMINISTIC AND STOCHASTIC EFFECTS OF RADIATION
BIOLOGICAL EFFECTS OF RADIATION
IN TIME PERSPECTIVE

Time scale

Fractions of seconds

Seconds

Minutes

Hours
Days
Weeks
Months

Years

Decades

Generations

Effects

Energy absorption

Changes in biomolecules (DNA, membranes)

Biological repair

Change of information in cell

Cell death

Organ death

Clinical changes

Mutations in a Germ cell Somatic cell

Leukaemia or Cancer

Hereditary effects
Classification of radiobiological effects

- Pathologic
- Gormetic
- Somatic
- Genetic
- Total
- Local
- Early
- Late
- Determined
- Stochastic
Radiation effects

**Early**
(deterministic only)

- **Local**
  Radiation injury of individual organs: functional and/or morphological changes within hrs-days-weeks

- **Common**
  Acute radiation disease
  Acute radiation syndrome

**Late**

- **Deterministic**
  Radiation dermatitis
  Radiation cataracta
  Teratogenic effects

- **Stochastic**
  Tumours
  Leukaemia
  Genetic effects
Deterministic (a) and stochastic (b) effects of radiation
Deterministic Effects

- Deterministic effects develop due to cell killing by high dose radiation, appear above a given threshold dose, which is considerably higher than doses from natural radiation or from occupational exposure at normal operation, the severity of the effect depends on the dose, at a given high dose the effect is observed in severe form in all exposed cells, at higher doses the effect cannot increase.
Stochastic Effects

• Stochastic effects develop due to mutation effect of low dose radiation, the threshold dose is not known accurately; it is observed that cancer of different location appears above different dose ranges, the severity of the effect does not depend on the dose, but the frequency of the appearance of the (probabilistic) effect in the exposed population group is dose dependent, (in most cases) linearly increasing with the dose.
Typical dose-effect relationships for deterministic effects in population

Variation in sensitivities among exposed individuals

Threshold of pathological condition
Threshold doses for some deterministic effects in case of acute total radiation exposure

- **0.2 GY** – increase of number of the chromosomal aberration in bone marrow and lymphocytes
- **0.3 GY** – temporary sterility for man
- **0.5 GY** – depression of haematopoiesis
- **1.0 GY** – acute radiation syndrome
- **2.0 GY** – detectible opacities
- **5.0 GY** – visual impairment
- **2.5 – 6.0 GY** – sterility for woman
- **3.5 – 6.0 GY** – permanent sterility for man
- **3.0 – 10.0 GY** – skin injury
Threshold doses for some deterministic effects in case of radiation exposure for many years

- 0,1 Gy – detectible opacities
- 0,2 Gy – sterility for woman
- 0,4 Gy – visual impairment
- 0,4 Gy – temporary sterility for man
- 0,4 Gy – depression of haematopoiesis
- 1,0 Gy – chronic radiation syndrome
- 2,0 Gy – permanent sterility for man
### Time of onset of clinical signs of skin injury depending on dose received

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Dose range (Gy)</th>
<th>Time of onset (day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>3-10</td>
<td>14-21</td>
</tr>
<tr>
<td>Epilation</td>
<td>&gt;3</td>
<td>14-18</td>
</tr>
<tr>
<td>Dry desquamation</td>
<td>8-12</td>
<td>25-30</td>
</tr>
<tr>
<td>Moist desquamation</td>
<td>15-20</td>
<td>20-28</td>
</tr>
<tr>
<td>Blister formation</td>
<td>15-25</td>
<td>15-25</td>
</tr>
<tr>
<td>Ulceration</td>
<td>&gt;20</td>
<td>14-21</td>
</tr>
<tr>
<td>Necrosis</td>
<td>&gt;25</td>
<td>&gt;21</td>
</tr>
</tbody>
</table>

Acute radiation syndrome (ARS)

- ARS is the most notable *deterministic effect* of ionizing radiation.
- Signs and symptoms are *not specific* for radiation injury but collectively highly characteristic of ARS.
- *Combination of symptoms* appears in phases during hours to weeks after exposure:
  - prodromal phase
  - latent phase
  - manifest illness
  - recovery (or death)
- *Extent and severity* of symptoms determined by:
  - total radiation dose received
  - how rapidly dose delivered (dose rate)
  - how dose distributed in body (whole or partial body irradiation)
Critical organs or tissues after acute whole body radiation exposure

<table>
<thead>
<tr>
<th>Whole body dose, Gy</th>
<th>Critical organ or tissue</th>
<th>Mortality, per cent</th>
<th>Time of death, days</th>
</tr>
</thead>
<tbody>
<tr>
<td>1–2</td>
<td>Bone marrow</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>2–4</td>
<td></td>
<td>5</td>
<td>40–60</td>
</tr>
<tr>
<td>4–6</td>
<td></td>
<td>50</td>
<td>30–40</td>
</tr>
<tr>
<td>6–10</td>
<td></td>
<td>95</td>
<td>10–20</td>
</tr>
<tr>
<td>10–30</td>
<td>Gastrointestinal tract</td>
<td>100</td>
<td>7–14</td>
</tr>
<tr>
<td>&gt; 30</td>
<td>Neurovascular system</td>
<td>100</td>
<td>1–5</td>
</tr>
</tbody>
</table>
Teratogenic effects of radiation as special deterministic effects
The foetus

Typical effects of radiation on embryo:

- Intrauterine growth retardation (IUGR)
- Embryonic, foetal, or neonatal death
- Congenital malformations
# Effects of radiation according to gestational stage

<table>
<thead>
<tr>
<th>Gestational age</th>
<th>Stage</th>
<th>Radiogenic effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 9 days</td>
<td>Preimplantation</td>
<td>All or none</td>
</tr>
<tr>
<td>10 days - 6 weeks</td>
<td>Organogenesis</td>
<td>Congenital anomalies, growth retardation</td>
</tr>
<tr>
<td>6 weeks - 40 weeks</td>
<td>Foetal</td>
<td>Growth retardation, microcephaly, mental retardation</td>
</tr>
</tbody>
</table>
Specific radiation effects on foetus: mental retardation, microcephaly

Cases of mental retardation caused by radiation exposure in Hiroshima and Nagasaki
Frequency of severe mental retardation in prenatally exposed survivors of A-bombing in Hiroshima and Nagasaki
Microcephaly: Hiroshima data

Foetal dose, mSv
Considerations for pregnancy termination

- Threshold dose for developmental teratogenic effects approximately 0,1 Gy
- Normal rate of preclinical loss > 30 %; at 0,1 Gy – increase of 0,1–1 %
- The foetal absorbed dose > 0,5 Gy at 7–13 weeks: substantial risk of IUGR and CNS damage
- 0,25–0,5 Gy at 7–13 weeks: parental decision with physician’s guidance
Cancer induction and genetic effects as examples of stochastic effects of radiation exposure
Stochastic Effects of Radiation Exposure

- Frequency proportional to dose
- No threshold dose
- No method for identification of appearance of effect of ionizing radiation in individuals
- Increase in occurrence of stochastic effects provable only by epidemiological method
Stochastic Effects of Radiation Exposure (continued)

- Stochastic effects observed in animal experiments
- Dose-effect relationship for humans can be studied only in human population groups
- Dose-effect relationship in low dose range (below 100 mSv) not yet verified
- Extrapolation down to zero excess dose accepted only for radiation protection and safety
Carcinogenic Effects

- *Carcinogenic effects* have been known practically since the discovery of radioactivity and since the first case of radiation-induced cancer was described in 1902.

- The epidemiological assessment was made from over 575 cancers and leukaemias for the 80,000 survivors irradiated at Hiroshima and Nagasaki, and about 2,000 cancers of the thyroid in children in the Chernobyl region.

- The actual data does not enable us to show a risk of cancer at greater than 0.1 Gy by acute irradiation. Nevertheless, it is considered that risk of cancer and the relationship dose/risk remains linear for doses below 0.1 Gy.
Phases of Cancer Induction and Manifestation

- Normal Cells
- Initiation
- Mutated Cells
- Elimination Reparation
- Pre-cancer
- Promotion
- Minimal Cancer
- Clinical Cancer
- Spreading
# Human Data on Radiation Cancerogenesis

<table>
<thead>
<tr>
<th>Type or localization of cancer</th>
<th>Population groups</th>
<th>Leukemia</th>
<th>Thyroid gland</th>
<th>Lung</th>
<th>Breast</th>
<th>Bone</th>
<th>Skin</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-bomb survivors</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ra-dial painters</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Early radiologists</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>U-miners</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposed in a nuclear accident</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Risk of Leukaemia depending on Age at Exposure to A-bomb
Age dependency of incidence of leukaemia in British population and radiotherapy patients

Leukaemia per million/yr

AGE, years

General Population

Radiotherapy patients
Cancer Deaths attributable to A-bomb

In 86 572 survivors of Hiroshima and Nagasaki, 7827 persons died of cancer in 1950-90

<table>
<thead>
<tr>
<th></th>
<th>Observed</th>
<th>Expected</th>
<th>Excess</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tumours</td>
<td>7578</td>
<td>7244</td>
<td>334</td>
<td>(4.4)</td>
</tr>
<tr>
<td>Leukaemia</td>
<td>249</td>
<td>162</td>
<td>87</td>
<td>(35.0)</td>
</tr>
<tr>
<td>All cancers</td>
<td>7827</td>
<td>7406</td>
<td>421</td>
<td>(5.4)</td>
</tr>
</tbody>
</table>

Dose dependence of Leukemia in A-bomb Survivors

Leukemia cases, rep 100,000 cent per year

Absorbed dose, Gy
Cancer Mortality of Nuclear Industry Workers

<table>
<thead>
<tr>
<th>Dose ranges, mSv</th>
<th>Observed/Expected deaths</th>
<th>Total number of deaths</th>
<th>Trend test (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10-</td>
<td>2234/462</td>
<td>2228.3</td>
<td>-0.28 (0.609)</td>
</tr>
<tr>
<td>20-</td>
<td>445/479.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-</td>
<td>276/254.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>100-</td>
<td>196/190.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-</td>
<td>161/147.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>400-</td>
<td>56/67.3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

O/E number of deaths from cancers other than leukemia

O/E number of deaths from leukemia other than CLL (chronic lymphocytic leukemia)

The **ERR** (excess relative risk) per **Sv** among the 95,673 nuclear industry workers of Canada, UK and USA (having a mean cumulative dose of 36.6 mSv in the combined cohort for the total period of observation, ie. 34 yrs in the USA and UK, and 29 years in Canada ) is –0.07 for all cancers excluding leukemia, and 2.18 for leukemia excluding CLL.

Childhood Leukaemia around UK Nuclear Facilities

• STUDY GROUP: 46,000 children (followed till the age of 25 yrs) born to parents working in nuclear industry

• FINDINGS: 111 cases of acute leukaemia observed, i.e. fewer than expected in a group of this size and age

• Study found 3 cases of leukaemia in children of male workers who had received a pre-conceptional exposure of 100 mSv or more

• Two of these three cases had already been identified in the 1990 Gardner report (proposed theory that paternal pre-conception radiation leads to increased risk of leukaemia in offspring)

• Conclusions
  – No substantial evidence found to support Gardner’s theory
  – Study did not confirm theory

Lifetime mortality in population of all ages from cancer after exposure to low doses

<table>
<thead>
<tr>
<th>Organ or tissue</th>
<th>Fatal Cancer Probability Coefficient ($10^{-4}$ Sv$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bladder</td>
<td>30</td>
</tr>
<tr>
<td>Bone Marrow</td>
<td>50</td>
</tr>
<tr>
<td>Bone Surface</td>
<td>5</td>
</tr>
<tr>
<td>Breast</td>
<td>20</td>
</tr>
<tr>
<td>Colon</td>
<td>85</td>
</tr>
<tr>
<td>Liver</td>
<td>15</td>
</tr>
<tr>
<td>Oesophagus</td>
<td>30</td>
</tr>
<tr>
<td>Ovary</td>
<td>10</td>
</tr>
<tr>
<td>Skin</td>
<td>2</td>
</tr>
<tr>
<td>Stomach</td>
<td>110</td>
</tr>
<tr>
<td>Thyroid</td>
<td>8</td>
</tr>
<tr>
<td>Remainder$^1$</td>
<td>50</td>
</tr>
<tr>
<td>Total</td>
<td>500*</td>
</tr>
</tbody>
</table>

For general public (all age groups) only

Summary factor of cancer risk for working population taken to be $400 \times 10^{-4}$ Sv$^{-1}$

Reference ICRP, Publ. 60, 1991
## Nominal Probability coefficients for Stochastic Radiation Effects

<table>
<thead>
<tr>
<th>Exposed population</th>
<th>Fatal cancer</th>
<th>Non-fatal cancer</th>
<th>Severe hereditary effects</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult workers only</td>
<td>4.0</td>
<td>0.8</td>
<td>0.8</td>
<td>5.6</td>
</tr>
<tr>
<td>Whole population (all age groups)</td>
<td>5.0</td>
<td>1.0</td>
<td>1.3</td>
<td>7.3</td>
</tr>
</tbody>
</table>

1. Rounded values
2. For fatal cancer, detriment coefficient is equal to probability coefficient

Ref. ICRP, Publ. 60, 1991
Genetic Effects

• Genetic effects might result in lesions of chromosomes in the germinal lineage (ovule and spermatozoid), prone to lead to anomalies in close or distant descendants of the irradiated individual.

• The mutagenic action of radiation was discovered by Nadson and Philipov (1925) and then in the fly was demonstrated by Muller from 1927 onwards.

• As it has not been possible to find any study showing a genetic effect in man, the risk is evaluated from the data obtained from animals.
Genetic Radiation Damage

- Increase of chromosome aberrations in human spermatogonia following radiation exposure of testes has been detected

- Inheritance of radiation damage in human population (including A-bomb survivors) not yet detected
Summary

- Deterministic effects develop due to cell killing by high dose radiation, appear above a given threshold dose, which is considerably higher than doses from natural radiation or from occupational exposure at normal operation, the severity of the effect depends on the dose, at a given high dose the effect is observed in severe form in all exposed cells, at higher doses the effect cannot increase.

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Summary

- Teratogenic effects of radiation: severe mental retardation, microcephaly

- Latency periods of radiation induced cancers occur from 2 to 10 years, risk of cancer depending on age at exposure (reverse dependence), cancer deaths attributable to A-bombs – 5.4 % in 40-yr follow up, cancer mortality studies of nuclear industry workers and offspring – leukaemia probable in workers

- Genetic effects of radiation – not proved in human population
THANKS FOR ATTENTION