CHAPTER 35
EARLY EFFECTS OF RADIATION

Early Effects of Radiation
- A radiation response in human within a few days to months
- It is described as deterministic

Deterministic Radiation Response
- Biologic response whose severity varies with radiation dose
- A dose threshold usually exists

ACUTE RADIATION LETHALITY

Death
- The most devastating human response to radiation exposure

Acute Radiation-Induced Lethality
- It is of only academic interest in diagnostic radiology

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<table>
<thead>
<tr>
<th>Effect</th>
<th>Anatomic Site</th>
<th>Threshold Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Whole body</td>
<td>200 rad/2 Gy\textsubscript{t}</td>
</tr>
<tr>
<td>Hematologic depression</td>
<td>Whole body</td>
<td>25 rad/250 mGy\textsubscript{t}</td>
</tr>
<tr>
<td>Skin erythema</td>
<td>Small field</td>
<td>200 rad/2 Gy\textsubscript{t}</td>
</tr>
<tr>
<td>Epilation</td>
<td>Small field</td>
<td>300 rad/3 Gy\textsubscript{t}</td>
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<tr>
<td>Chromosome aberration</td>
<td>Whole body</td>
<td>5 rad/50 mGy\textsubscript{t}</td>
</tr>
<tr>
<td>Gonadal dysfunction</td>
<td>Local tissue</td>
<td>10 rad/100 mGy\textsubscript{t}</td>
</tr>
</tbody>
</table>

Diagnostic x-ray beams always result in partial-body exposure, which is less harmful than whole-body exposure!

Chernobyl Incident
- April 1986

Three Mile Island Incident
- March 1979

Acute Radiation Syndrome
- Radiation sickness that occurs in human after the whole-body dose of 1 Gy (100 rad) or more of ionizing radiation delivered over a short time

Three Syndromes
- Hematologic Death, Gastrointestinal (GI) Death & Central Nervous System (CNS) Death

Prodomal Period
- The immediate response of radiation sickness
  - Approximate Dose: > 100 rad
  - Mean Survival Time: —
  - Clinical S&S: nausea, vomiting & diarrhea

Latent Period
- The time after exposure during which there is no sign of radiation sickness
  - Approximate Dose: 100-10, 000 rad
  - Mean Survival Time: —
  - Clinical S&S: none

Hematologic Syndrome
- It is characterized by a reduction in white cells, red cells & platelets
  - Approximate Dose: 200-1000 rad
  - Mean Survival Time: 10-60 days
  - Clinical S&S: nausea, vomiting, diarrhea, anemia, leukopenia, hemorrhage, fever & infection
  - Prodomal Period: mild symptoms
  - Latent Period: general feeling of wellness
  - Period of Manifest Illness: vomiting, mild diarrhea, malaise, lethargy & fever
  - Recovery: 2-4 weeks or 6 months (full)
  - Cause of Death: generalized infection, electrolyte imbalance & dehydration

GI Period
- It occurs principally because of severe damage to the cells lining the intestines
  - Approximate Dose: 1000-5000 rad
  - Mean Survival Time: 4-10 days
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- Clinical S&S: same as hematologic plus electrolyte imbalance, lethargy, fatigue & shock
- Prodomal Period: vomiting & diarrhea
- Latent Period: no symptoms present
- Period of Manifest Illness: second wave of nausea & vomiting, followed by diarrhea, anorexia
- Cause of Death: unprevented rapid progression of symptoms

CNS Period
- Its ultimate cause is elevated fluid content of the brain
- Characterized By: increased intracranial pressure, vasculitis & meningitis
- Approximate Dose: > 5000 rad
- Mean Survival Time: 0-3 days
- Clinical S&S: same as GI plus ataxia, edema, systemic vasculitis & meningitis
- Prodomal Period: severe nausea & vomiting
- Latent Period: earlier symptoms disappear
- Period of Manifest Illness: more severe prodomal symptoms, disoriented, loss of muscle coordination, dyspnea, convulsive seizures, loss of equilibrium, ataxia & lethargy

LD$_{50}/60$
- The dose of radiation to the whole body that causes 50% of irradiated subjects to die within 60 days
- It quantitatively measured the acute radiation lethality
- Humans: 350 rad

Acute radiation lethality follows a nonlinear, threshold dose-response relationship!

Mean Survival Time
- Average time between exposure & death
  - Hematologic Syndrome: dose dependent
  - GI Syndrome: remain constant
  - CNS Syndrome: dose dependent

LOCAL TISSUE DAMAGE

Local Tissue Damage
- It follows a threshold-type dose response relationship
- Characteristic: deterministic response

Local Tissues That Can Be Affected Immediately
- Skin
- Gonads
- Bone marrow

Partial-Body Irradiation
- A higher dose is required to produce a response
- It affects organ & tissue
- Effect: cell death
  - Result: shrinkage of the organ or tissue

Atrophy
- The shrinkage of an organ or tissue due to cell death

EFFECT ON SKIN

Skin
- The tissue with which we have had the most experience
- Three Layers
  - Epidermis: outer layer
    - Basal Cells: its lowest layer
  - Dermis: intermediate layer of connective tissue
  - Subcutaneous: layer of fat & connective tissue
- Other Accessory Structures: hair follicles, sweat glands & sensory receptors
- Cells Replacement Rate: 2%/day (50% for GI)
- Skin Effects: nonlinear, threshold dose-response relationship

Basal Cells
- The stem cells that mature as they migrate to the surface of the epidermis

STEWART C. BUSHONG
SUMMARIZED BY: MEYNARD Y. CASTRO
**CHAPTER 35**

**EARLY EFFECTS OF RADIATION**

*Damage to basal cells results in the earliest manifestation of radiation injury to the skin!*

Orthovoltage X-rays
- *Range*: 200-300 kVp

Erythema
- A sunburn-like reddening of the skin
- The first observed biologic response to radiation exposure

Desquamation
- Ulceration & denudation of the skin

Moist Desquamation
- The clinical intolerance for radiation therapy

X-ray-Induced Erythema
- One of the hazards to the patient the early of radiology

Skin-Erythema Dose (SED)
- Dose of radiation, usually about 200 rad, that causes redness of the skin

Epilation/Alopecia/Fox Mange
- Loss of hair

SED<sub>50</sub>
- The dose required to affect 50% of those irradiated
- *Dose*: 500 rad

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<table>
<thead>
<tr>
<th>Potential Radiation Response</th>
<th>Threshold Dose</th>
<th>Approximate Time of Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early transient erythema</td>
<td>200 rad</td>
<td>Hours</td>
</tr>
<tr>
<td>Main erythema</td>
<td>600 rad</td>
<td>10 days</td>
</tr>
<tr>
<td>Temporary epilation</td>
<td>300 rad</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Permanent epilation</td>
<td>700 rad</td>
<td>3 weeks</td>
</tr>
<tr>
<td>Moist desquamation</td>
<td>1500 rad</td>
<td>4 weeks</td>
</tr>
</tbody>
</table>

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**EFFECTS ON GONADS**

Grenz Rays
- It is used to treat tinea capitis (ringworm)
- *Range*: 10-20 kVp

**Testes**
- The male gonads
- It produces spermatogonia & matures into sperm

**Ovaries**
- The female gonads
- It produces oogonia & matures into ovum

**Germ Cells**
- Produced by both ovaries & testes

**Gametogenesis**
- The process of development of germ cells

**Progression of Germ Cell**
- *Male*: Spermatoginia (most radiosensitive) → Spermatocyte → Spermatid → Sperm
- *Female*: Primordial Follicle → Mature Follicle (most radiosensitive) → Corpus Letuem → Ovum

**Oogonia**
- The stem cells of the ovaries
- They multiply in number only before birth & during fetal life

**Primordial Follicles**
- They grow to encapsulate the oogonia

**Oocyte**
- A matured oogonia

**Ovum**
- A mature female germ cell
- *Fertilization*: 400-500 ova
- o Number of years of menstruation times 13 per year
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HEMATOLOGIC EFFECTS

Periodic Blood Examination
- The only monitoring performed on x-ray & radium workers before
- Total cell counts & a white cell differential count

Under no circumstances is a periodic blood examination recommended as a feature of any current radiation protection program!

Hematologic Depression
- Threshold Dose: 25 rad

Hemopoietic System
- Another example of cell renewal system
  - Same with gametogenesis
- Bone marrow
- Circulating blood
- Lymphoid tissue
  - Lymph nodes, Spleen & Thymus
- Principal Effect of Radiation:
  - Depressed number of blood cells in the peripheral circulation

Pluripotent Stem Cell
- Stem cell that has the ability to develop into several different types of mature cells
- It produces lymphocytes, granulocytes, thrombocytes & erythrocyte

Lymphocytes/White Blood Cells
- Blood cells involved in the immune response
- Manufactured by spleen & thymus
- Lifetime in the Bone Marrow: varying (hours or years)
- Lifetime in the Peripheral Blood: varying (hours or years)

Granulocytes
- Scavenger type of cells used to fight bacteria
- Lifetime in the Bone Marrow: 8-10 days
- Lifetime in the Peripheral Blood: couple of days

Spermatogonia
- The stem cells of the testes
- Continually being produced from stem cells progressively through a number of stage to maturity

Spermatocyte
- A matured spermatogonia

Spermatid
- A matured spermatocyte

Spermatid in spermatocytes/matured spermatid in spermatocytes
- A matured spermatocyte
- A mature male germ cell
- Maturation Process: 3-5 weeks

Ovaries
- Irradiation Causes
  - Early Life: atrophy
  - After Puberty: suppression & delay of menstruation
- 10 rad: suppresses menstruation
- 25-50 rad: increased genetic mutations
- 200 rad: temporary sterility
- 500 rad: sterility

The most radiosensitive cell during female germ cell development is the oocyte in the mature follicle!

Testes
- Irradiation Causes: atrophy
- 10 rad: reduce the number of spermatozoa
- 200 rad: temporary sterility
- 500 rad: sterility

Spermatogonial Stem Cells
- The most sensitive phase in the gametogenesis of the spermatozoa

Male Gametogenesis
- A self-renewing system

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- Recovery: 2 months

Thrombocytes/Platelets
- Blood cells involved in the clotting of blood to prevent hemorrhage
- Lifetime in the Bone Marrow: 5 days
- Lifetime in the Peripheral Blood: 1 week
- Recovery: 2 months

Erythrocytes/Red Blood Cells
- Blood cells that are transportation agents for oxygen
- Less sensitive than the other blood cells
  - Rationale: long lifetime in the peripheral blood
- Lifetime in the Bone Marrow: 8-10 days
- Lifetime in the Peripheral Blood: 4 months
- Recovery: 6 months to 1 year

Bone Marrow
- It manufactures most circulating blood cells including lymphocytes
- Child: uniformly distributed throughout the skeleton
- Adult: restricted to flat bones such as ribs, sternum, skull & ends of long bones

HEMOPOIETIC CELL SURVIVAL

Principal Radiation Response of Hemopoietic System
- Decrease in the number of all types of blood cells in the circulating peripheral blood

Lethal Injury
- It causes depletion of mature circulating cells

Lymphopenia
- Reduced in number of lymphocytes

Granulocytosis
- Rapid rise in number of granulocytes

Granucytopenia
- Rapid decrease & slower decrease of granulocytes

Thrombocytopenia
- Depletion of platelets

CYTOGENETIC EFFECTS

Cytogenetics
- The study of the genetics of cells particularly cell chromosomes

Radiation-induced chromosome aberrations follow a nonthreshold dose-response relationship!

Human Peripheral Lymphocytes
- Most often used for cytogenetic analysis

Karyotype
- A chromosome map

Each cell consists of 22 pairs of autosomes & a pair of sex chromosomes – the X-chromosomes from the female & the Y chromosomes from the male!

Chromosomes Structural Radiation Damage
- Single-Hit Chromosome Aberrations
- Double-Hit Chromosome Aberrations

Reciprocal Translocation
- It requires a karyotype for detection

Point Genetic Mutations
- Undetectable even with karyotype construction

Hit
- Radiation interaction with chromosomes

DNA Hit
- It results in an invisible disruption of the molecular structure of the DNA

The lymphocytes & the spermatogonia are the most radiosensitive cells in the body!
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Chromosome Hit
- It produces a visible derangement of the chromosome
- It represents severe damage to the DNA

Single-Hit Chromosome Aberration
- Visualized & recorded during the M phase
- Irradiation During G1 Phase
  - \textit{Cause}: chromatid break
  - \textit{During S Phase}: replicated
  - \textit{During Metaphase}: a chromosome with material missing from the ends of two sister chromatids & two acentric fragments
- Irradiation During G2 Phase
  - \textit{Causes}: single or double chromatid break
  - \textit{During S Phase}: replicated
  - \textit{During Metaphase}: a chromosome with an arm that is obviously missing genetic material & a chromatid fragment

Chromatid Deletion
- The breakage of a chromatid

Isochromatid
- Fragments in chromosome aberrations

Acentric
- Without a centromere

Multi-Hit Chromosome Aberration
- Not uncommon
- Irradiation During G1 Phase
  - \textit{Causes}: ring & dicentric chromosomes
  - \textit{Ring}: when two hits occur on the same chromosome
  - \textit{Dicentric}: when adjacent chromosome each suffer one hit & recombine
- \textit{Irradiation During G2 Phase}: similar to G1 phase but rarer

Stickiness
- A condition in which the mechanism for the joining of chromatids depends

Radiation-Induced Reciprocal Translocation
- Multi-hit chromosome that require karyotype analysis for detection
- \textit{Results in}:
  - No loss of genetic material
  - Simply a rearrangement of the genes

Kinetics of Chromosome Aberration
- \textit{Single-Hit Aberration}:
  - It occurs at very low doses of radiation
  - \textit{Dose-Response Relationship}: linear, nonthreshold
- \textit{Multi-Hit Aberration}:
  - It occurs when the radiation dose exceeds approximately 100 rad
  - \textit{Dose-Response Relationship}: nonlinear, nonthreshold

Radiation Dose-Response Relationship For Cytogenetic Damage
- \textit{Single-Hit}: \( Y = a + bD \)
- \textit{Multi-Hit}: \( Y = a + bD + cD^2 \)

Cytogenetic Analysis
- Biologic radiation dosimeter

Approximate Chromosome Aberration Frequency
- Two single-hit aberrations per rad per 1000 cells
- One multi-hit aberration per 10 rad per 1000 cells