Radiation Biology: Deterministic Effects of Radiation

Bushong, Chapter 33

Somatic & Genetic Damage Factors

- Amount of biologic damage a human undergoes as a result of radiation exposure depends on several factors.
- Ionizing radiation produces the greatest amount of biologic damage in the human body when a large dose of densely ionizing (high-LET) radiation is delivered to a large or radiosensitive area of the body.

Somatic and Genetic Damage Factors

1. The quantity of ionizing radiation to which the subject is exposed
2. The ability of the ionizing radiation to cause ionization of human tissue
3. The amount of body area exposed
4. The specific body parts exposed

Somatic Effects

Classified as:

- _____
  - Deterministic (non-stochastic)
  - Effects are cell-killing and directly related to the dose received
  -

Somatic Effects

- _____
  - Stochastic (probabilistic)
  - Mutational or randomly occurring somatic changes independent of dose
  - Late radiation effects result as a consequence of low doses delivered over a long interval of time

Somatic Effects

-

- High dose effects include:
  - nausea, fatigue,
  - erythema (diffuse redness over an area of skin after irradiation),
  - epilation (loss of hair),

Somatic Effects

- blood disorders, intestinal disorders, fever,
- dry and moist desquamation (shedding of the outer layer of skin),
- depressed sperm count in the male, temporary or permanent sterility in the male and female, and
- injury to the central nervous system (at extremely high radiation doses).

Early Deterministic Somatic Effects

- Epidermis – Outermost layer
  - Basal cells are stem cells that mature as they migrate to the surface
  - Slowly lost and replaced by new cells
  - Skin cells replaced at a rate of about 2% per day

Early Deterministic Somatic Effects

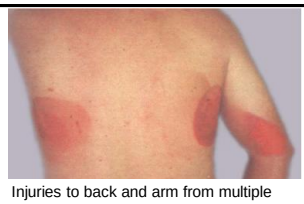
Ken Graham Photography

Early Deterministic Somatic Effects

_____:

- Shedding of the outer layer of skin
  - Dry
  - Wet (ulcerations)

http://breastcancerchronicles.files.wordpress.com/2007/07/radiation-burn.jpg



Injuries to back and arm from multiple prolonged electrophysiological and ablation procedures with bi-plane fluoroscopy. Wounds on back healed into scarred areas while injury on arm required grafting.
Date 5 July 2012
Source http://www.biij.org/2007/2/e22/
Author LK Wagner, PhD; Vlietstra et a

Acute Radiation Syndrome (ARS)

- Collection of symptoms that occur in the body after a high-level radiation exposure
- Three (3) syndromes:
  -
  -
  -

Acute Radiation Syndrome (ARS)

Four (4) major response stages:

-
-
-
-

Prodromal Period

-

- May last a few hours to several days
- Severity of the symptoms is dose related (higher dose = more severe symptoms)

Prodromal Period (con't)

Characterized by:

-
-
-
-
-

Latent Period

- Immediately follows the prodromal period
-
-
- If the dose is not lethal, recovery begins in 2 to 4 weeks

Manifest Illness

- Period which affects on the following systems become visible
- Three systems
  -
  -
  -

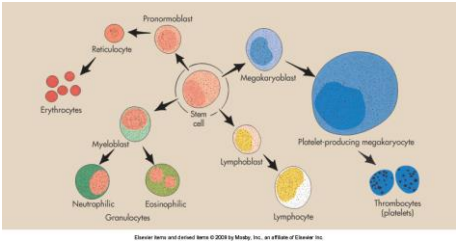
Hematologic (Hematopoietic) Syndrome

- "Bone Marrow Syndrome"
-

Hematologic (Hematopoietic) Syndrome

- Characterized by:
  - Decrease in bone marrow stem cells
    - Erythrocytes (red blood cells)
    - Lymphocytes (white blood cells)
    - Granulocytes (white blood cells)
    - Thrombocytes (platelets)

Hematologic Syndrome



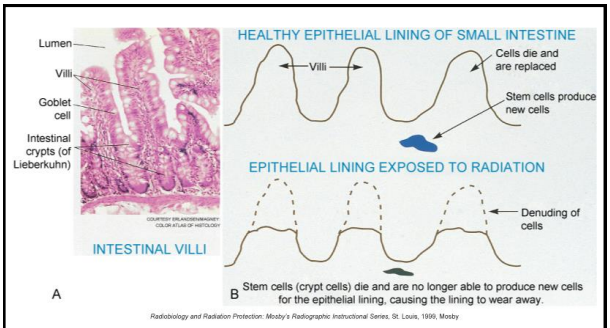
All blood cells develop from a pluripotent stem cell

Hematologic Syndrome

- Survival time shortens as the radiation dose increases
- The body becomes more susceptible to infection from its own intestinal bacteria
- The body also becomes more prone to hemorrhage
- When death occurs, it is a consequence of bone marrow destruction

Gastrointestinal Syndrome

- Radiation doses of 10-50 Gy (1000-5000 rads)
- Prodromal period
  - A few hours after exposure
  - Severe nausea, vomiting, diarrhea for about 24 hours
- Latent period
  - Lasts about 3 to 5 days



Radiobiology and Radiation Protection: Mosby's Radiographic Instructional Series, St. Louis, 1999, Mosby

Gastrointestinal Syndrome

- Manifest illness
  - Nausea, vomiting, diarrhea
  - Anorexia
  - Hemorrhage (gastrointestinal bleeding)
  - Electrolyte imbalance
  - Emaciation
- Death is usually due to catastrophic damage to epithelial cells lining the GI tract

Central Nervous System (CNS) Syndrome

- Radiation doses of 50 Gy (5000 rads) or more
- Can cause death within a few hours to 3 days after exposure
- Severe nausea and vomiting within a few minutes

Central Nervous System (CNS) Syndrome

Prodromal period:

- Excessive nervousness
- Confusion
- Diarrhea
- Loss of vision
- Burning sensation of the skin
- Loss of consciousness

Central Nervous System (CNS) Syndrome

Latent period:

- Lasting up to 12 hours
- Lessening of symptoms

Central Nervous System (CNS) Syndrome

Manifest illness:

- Symptoms of prodromal period return
- Disoriented
- Shock
- Periods of agitation alternating with stupor
- Ataxia
- Cranial vault edema

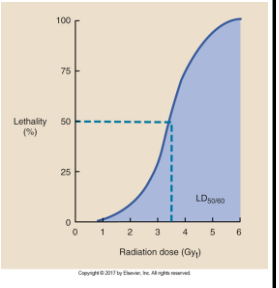
Central Nervous System (CNS) Syndrome

- Manifest illness (con't):
- Loss of equilibrium
- Fatigue
- Lethargy
- Convulsive seizures
- Meningitis
- Prostration
- Respiratory distress
- Vasculitis
- Coma

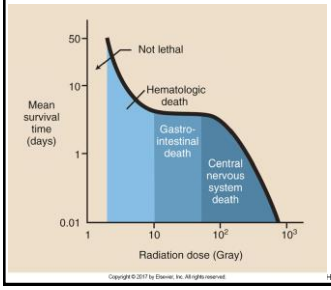
Lethal Dose (LD)

LD $_{50/60}$

- Dose of radiation that can be lethal to 50% of the exposed population within 60 days (measure of lethality)
- Acute radiation lethality follows a nonlinear, threshold dose-response relationship
- S-shaped curve



Mean Survival Time



- As the whole-body radiation dose increases, the average time between exposure and death decreases

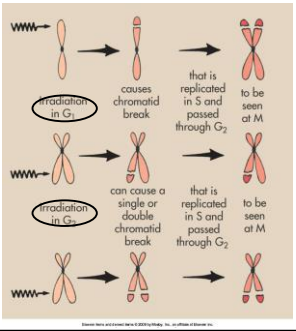
Chromosome Anomalies

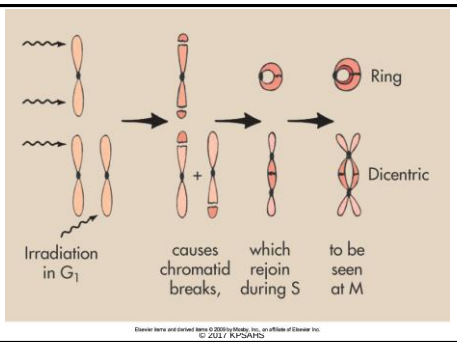
Two types of anomalies:

- *Chromosome aberrations*
  - Irradiation in interphase during G1 before synthesis
  - Identical strand produced during synthesis
  - Chromosome aberration in which both sister chromatids exhibit break

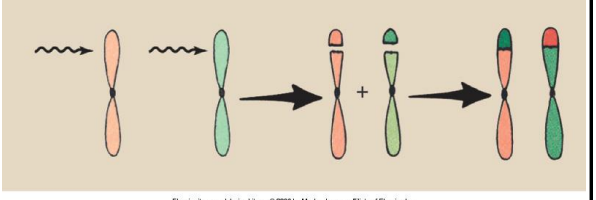
Chromosome Anomalies

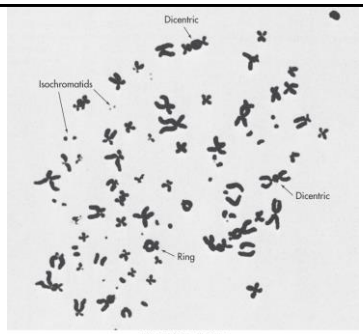
- *Chromatid aberrations*
  - Occurs in late interphase (after S), so only 1 daughter cell is affected
- Hit
  - Radiation interacting with a chromosome (direct or indirect)
  - A chromosome hit produces a visible derangement of the chromosome





Multiple hit in G_1 with interaction on two different chromatids causing reciprocal translocations





[Courtesy Neil Weir, University of Pittsburgh.]