Acute Radiation Injury: Whole Body

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Acute Radiation Syndrome

- An acute illness which follows a roughly predictable course over a period of time ranging from a few hours to several weeks after exposure to ionizing radiation.
- It is characterized by the development of groups of signs and symptoms which are manifestations of the reactions of various body systems to irradiation of the whole body or to a significant portion of it.

Acute Radiation Syndromes

- Subclinical ..... 0 – 100 cGy
- Hematopoietic ..... 100 – 800 cGy
- Gastrointestinal ..... 800 – 3000 cGy
- CV / CNS ..... >3000 cGy

Note: 1 Gy = 100 rads
1 cGy = 1 rad

Acute Radiation Syndrome

Diagnosis:

- History of exposure; symptoms (time of onset and severity)
- Hematological profile – CBC with differential every 4-6 hours following exposure; monitor lymphocyte count
- Chromosome analysis – results in one week

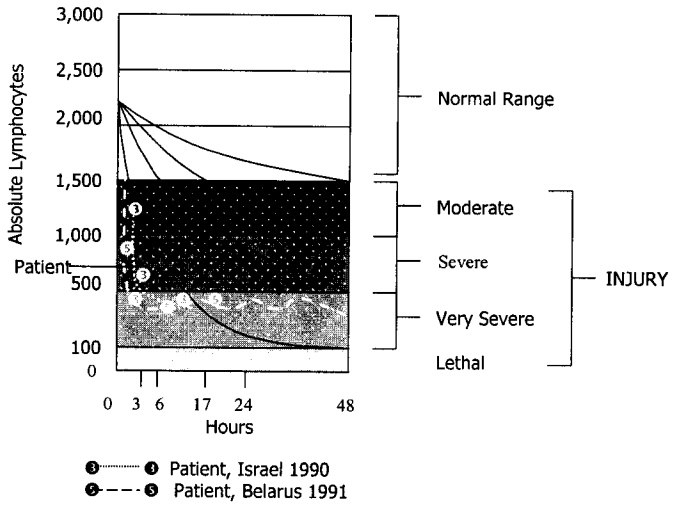
Prodromal Signs and Symptoms

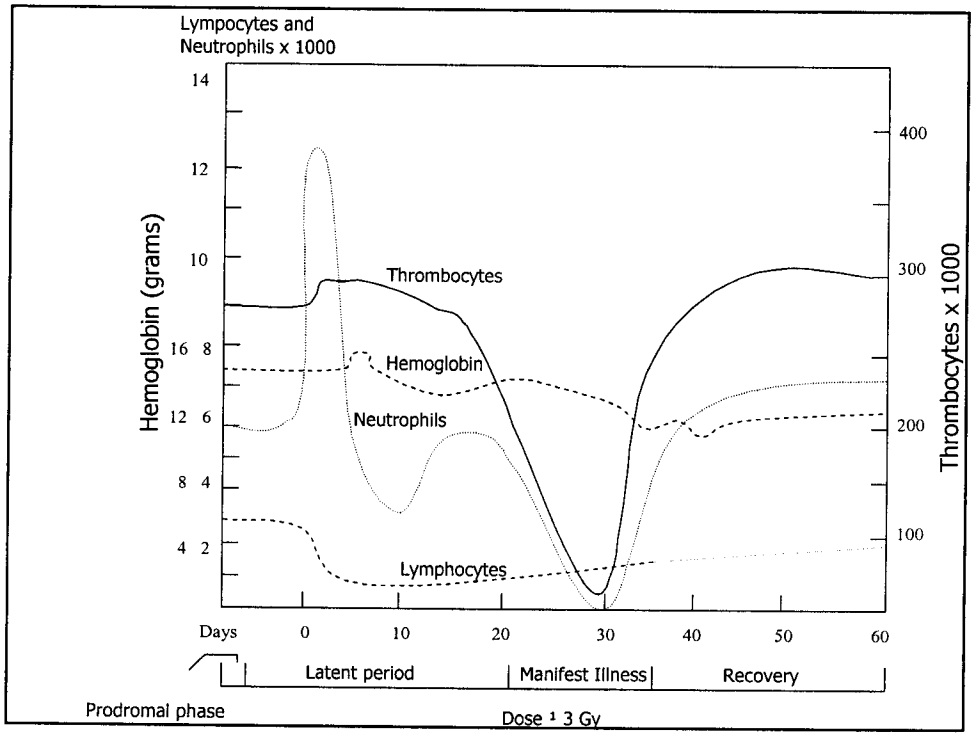
- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Fever
- Conjunctivitis
- Skin erythema

Management of Prodromal Period

- Vomiting – use selective blocking of serotonin 5-HT_3 receptors or use 5-HT_3 receptor antagonists (Zofran® / Kytril®).
- Consider initiating viral prophylaxis.
- Consider tissue, blood typing.
- Treat trauma.
- Consider consultation with hematologist and radiation experts, re: colony stimulating factors, other treatment options, dosimetry and prognosis.

Comparison of Patient Lymphocyte Counts with Values Predicted by Andrews' Model





Acute Radiation Syndrome

- Treatment and supportive care
- Platelet transfusions
- Psychological support
- Infection control
- Stimulation of hematopoietic system

Systemic Effects of Hematopoietic Syndrome

- Immunodysfunction
- Increased infections complications
- Hemorrhage
- Anemia
- Impaired wound healing

Effects of Gastrointestinal Syndrome

- Malabsorption
- Ileus – vomiting; GI distension
- GI bleeding
- Sepsis
  - Fluid and electrolyte shifts
  - Dehydration
  - Acute renal failure
  - Cardiovascular collapse
- GI bleeding
- Sepsis

Cerebrovascular/CNS Syndrome

- Vomiting and diarrhea within minutes
- Confusion and disorientation
- Severe hypotension
- Cerebral edema
- Convulsions – coma
- Hyperpyrexia
- Fatal within 24 to 48 hours

Hospital Care I – Mild (<2 Gy)

- Triage by prodromal symptoms and by lymphocyte depletion kinetics
- Biological and physical dosimetry
- Emergency surgery if indicated during an appropriate time window
- Close observation and frequent CBC with differential
- Outpatient management may be appropriate
- Management of residual skin contamination

Hospital Care II – Moderate (2-5 Gy)

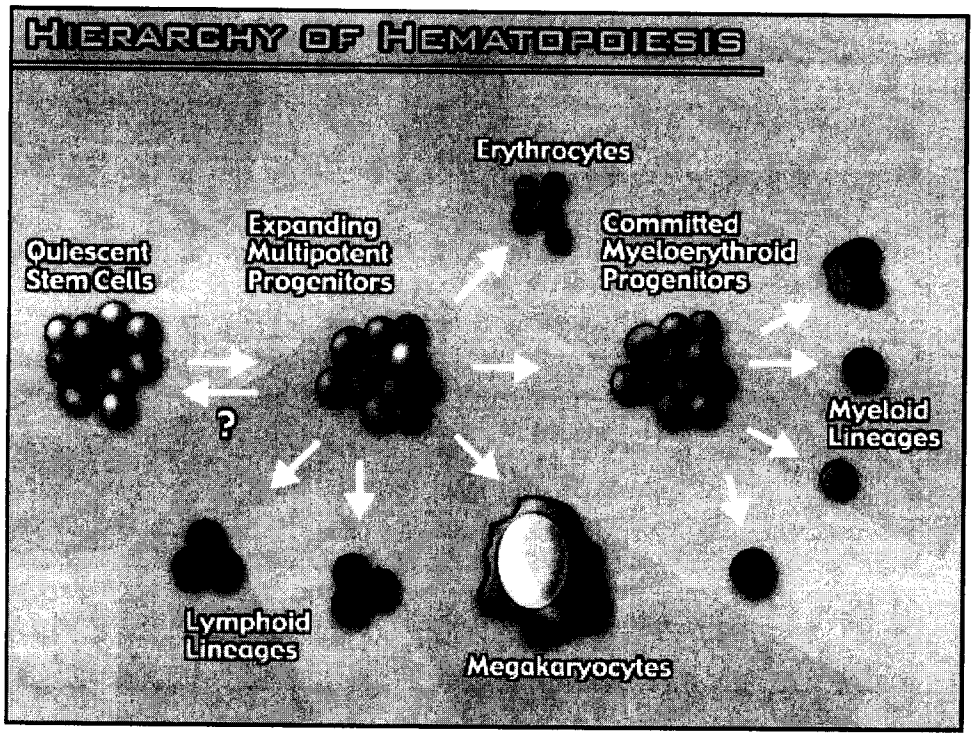
- Reverse isolation
- Gut decontamination
- Growth factor therapy
- Viral prophylaxis
- Antibiotics for febrile neutropenia

Hospital Care III – Severe (5-10 Gy)

- Reverse isolation
- Gut decontamination and viral prophylaxis
- Growth factor therapy with transfusion of peripheral blood progenitor cells (PBPC) or cord/placenta blood progenitor cells (CBPC)
- Clinical problems:
  - Severe thrombocytopenia
  - Absolute neutropenia with or without fever
  - Symptomatic anemia
- Assistance of hematology team knowledgeable in experimental growth factor/ interleukin combinations

New Generation Therapy

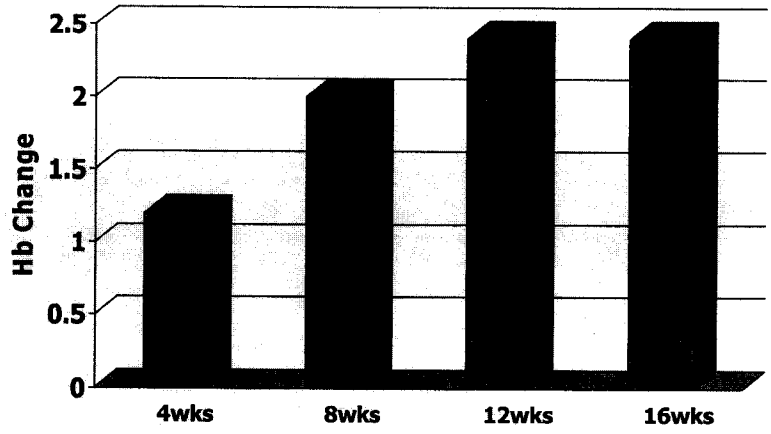
- Peripheral Blood Progenitor Cells (PBPC)
  - Mobilization by cytokines
  - *Ex vivo* expansion by cytokines
  - Au PBPC Tx, Allo PBPC Tx +/- cytokines
- Cord/Placenta Blood Progenitor Cells (CBPC)
  - *Ex vivo* expansion
  - Allo CBPC Tx match, mismatch, child, adult



Hemopoietic Colony-Stimulating Factors

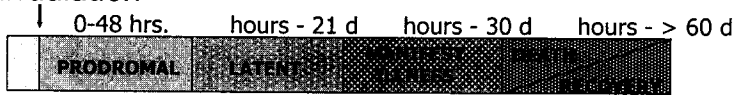
- GM-CSF (Leukine®)
- G-CSF (Neuprogen®)
- IL-6
- IL-11 (Neumega®)
- PIXY321
- MGDF (Megakaryocyte Growth & Development Factor)
- Erythropoietin (Epogen® / Procrit®)

Erythropoiesis



Acute Radiation Syndrome: Clinical Course

Irradiation



- Anorexia
- Nausea
- Vomiting
- Diarrhea
- Fever
- Conjunctivitis
- Erythema
- Lymphopenia
- Granulocytosis

- Prodromata absent or diminished

- Hemorrhages
- Infections
- Immunosuppression
- Electrolyte imbalance
- Vomiting, bl. diarrhea
- Hypotension
- CV/CNS effects

Acute Radiation Injury: Local

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Acute Partial Body Exposure

- In many cases, one portion of the body receives a much higher dose than the rest of the body
- Severe injury to skin and underlying tissues may occur
- Diagnosis is difficult; initial presentation is often misleading
- ARS may or may not be present

Common Sources Inducing Radiation Injury

- Radiography sources, e.g., ^{192}Ir
- Therapy/irradiation sources, e.g., ^{60}Co
- Fission product betas, e.g., Chernobyl
- Medical applicators, e.g., ^{90}Sr
- X-ray machines
- X-ray diffraction units
- X-ray fluorescence units
- Accelerators

Approximate Surface Dose from Common Gamma Emitters

- ^{60}Co – 3100 rad/min/Ci (0.84 Sv/min-GBq)
- ^{137}Cs – 770 rad/min/Ci (0.21 Sv/min-GBq)
- ^{192}Ir – 1200 rad/min/Ci (0.32 Sv/min-GBq)
- ^{226}Ra –1900 rad/min/Ci (0.51 Sv/min-GBq)

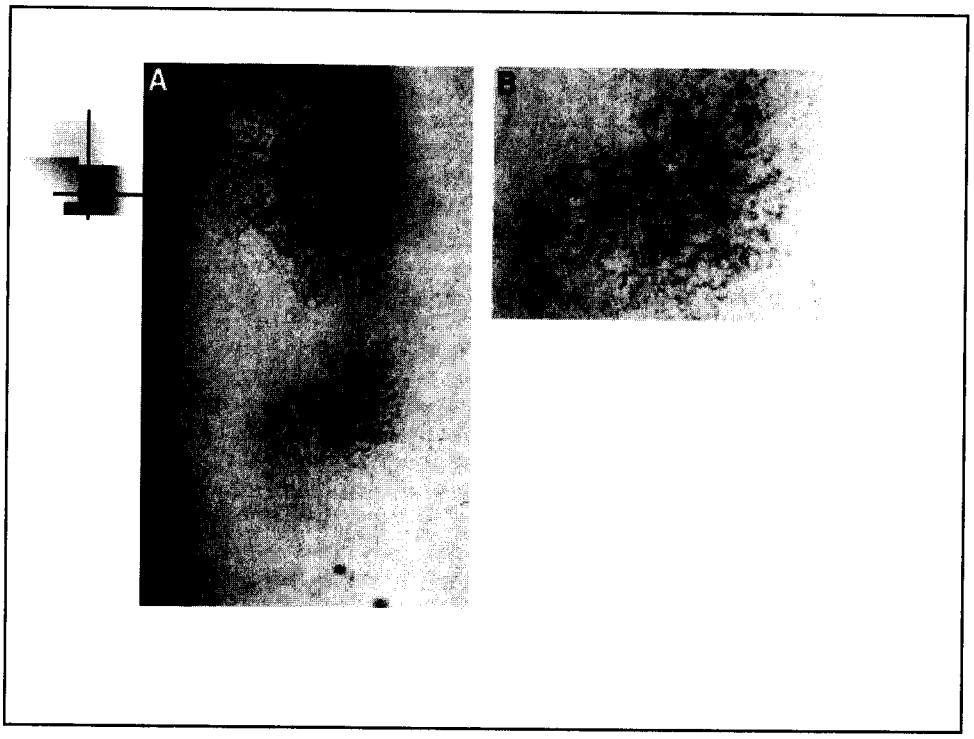
Diagnosis

- History
- Signs and symptoms
- Verify local versus whole body exposure
- Accident mock-up is helpful in dosimetry

Note: During initial assessment, take photographs and obtain baseline information on involved area (ex. slit lamp exam for facial exposure).

External Dose Thresholds for Skin

- 300 cGy – epilation beginning around day 17
- 600 cGy threshold – erythema; distinguish from thermal burn; minutes to weeks post-exposure, depending on dose
- 1,000 – 1,500 cGy – dry desquamation
- 2,000 – 5,000 cGy – wet desquamation, 2-3 weeks post-exposure, depending upon dose
- >>5,000 cGy – radionecrosis, deep ulceration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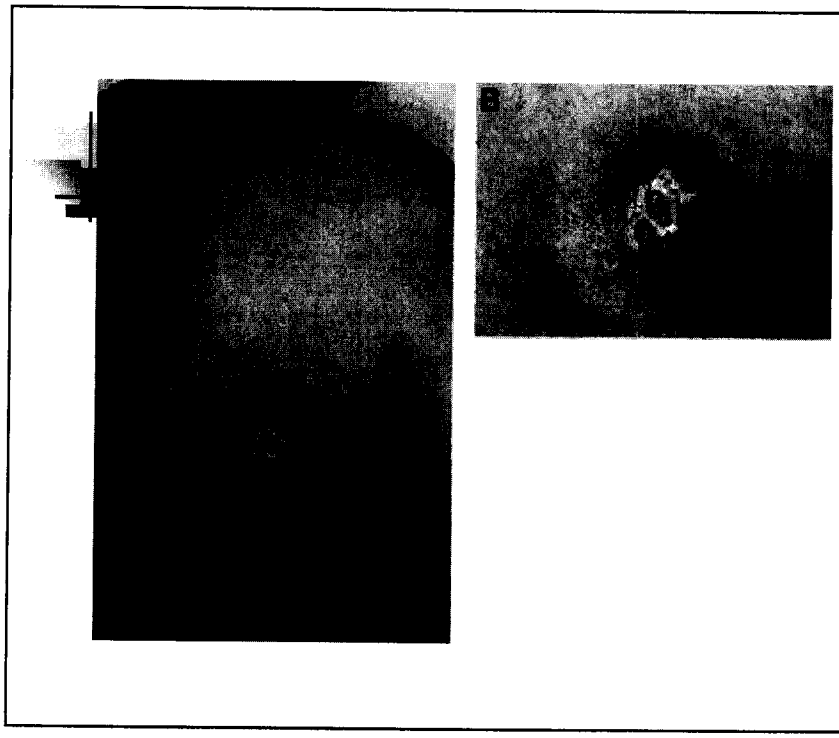
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Management

- Recommendation: consult with experts!
- Protect area
- Avoid nicotine
- Assure nutritional requirements
- Prevent/treat infections
- Cover to control pain
- Consider new techniques in wound management

Problems in Management

- Wounds evolve slowly
- Healing is very prolonged
- Lesions can be intensely painful
- Dosimetry is frequently imprecise
- Healed epidermis if fragile and easily traumatized

Effects on the Vascular Endothelium

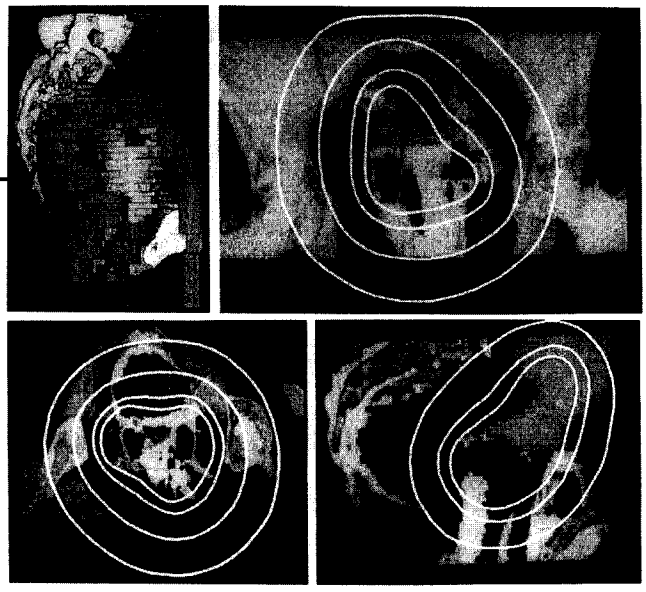
- Endothelial cells swell, pull-up or detach from basement membrane.
- Edema occurs as leaks in denuded areas of microvasculature allow extravasation of fluids and cells.
- Platelets fill in areas of denuded basement membrane and microthrombi form.

Acute Local Radiation Injury: Evaluation and Diagnosis

- History
- Laboratory tests
  - hematological profile; ESR; thermography
- Physical exam
- Radiographic studies as indicated
- Slit lamp ophthalmoscopy
- Serial color photos

Radiation Repair Process in Skin

- Effectiveness of the repair process depends on:
  - severity of injury to the epidermal precursor or stem cells
  - adequacy of the microvasculature
  - structural support of the damaged dermis
  - avoidance of infection and trauma
- The epidermis is renewed by the proliferation of epithelium at the edges of denuded areas, from islands of surviving cells in the damaged zone, and from epithelium of the hair follicles.



COLOR FIGURE 8–9. *(Continued.)* (C) view. (D) Isodose curves in a coronal three-dimensional reconstruction of the pelvis with a Fletcher applicator (*dark blue*) in place. Cross hairs intersect at the cervix with the uterus (*yellow*) above, the rectum (*green*) behind, and the bladder (*red*) anterior. The 3000-, 2000-, and 1000-cGy isodose curves are depicted after ^{137}Cs loading. (E) An axial plane with the cervix at the cross-hairs and the 3000-, 2000-, 1000-, and 500-cGy isodose curves. (F) The sagittal plane as visualized through the three-dimensional virtual simulator. (Images generated with a Picker Varian virtual simulator, courtesy of Dr. A. Wiley and Dr. J. Stephenson, Watson Clinic, Lakeland FL.)

Some New Techniques in Wound Management

- Artificial skin (bi-layered)
- Bioengineered skin (epidermal/dermal constructs)
- Pharmaceutical agents
- Growth factors for topical administration