Acute Somatic Effects of Radiation

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Acute Somatic Effects

- **Acute**: immediate, or soon after, as opposed to delayed effects such as carcinogenesis.
- **Somatic**: cells of the body, as opposed to germ cells leading to genetic or heritable effects.

Deterministic Effect

- Threshold in dose.
- Severity of effect increases with dose above a threshold.
- Caused by damage to many cells.
- Examples include a cataract, fibrosis, effects on fertility or lethality due to total body exposure.
Total Body Irradiation – Radiological Terrorism

Eric J. Hall, D.Phil., D.Sc.

Total Body Irradiation

- Prodromal Syndrome, which leads into...
- Cerebro-vascular Syndrome, or
- Gastro-intestinal Syndrome, or
- Hematopoietic Syndrome
- About 400 ARS cases worldwide

<table>
<thead>
<tr>
<th>Radiation Exposure</th>
<th>Prodromal Syndrome</th>
<th>Latent Period</th>
<th>Manifest Illness</th>
<th>Recovery or Death</th>
<th>Time</th>
</tr>
</thead>
</table>

Prodromal Syndrome

- Symptoms to be expected at about 50% Lethal Dose:
  - Neuromuscular – Easy fatigability.
  - Gastrointestinal – Anorexia, vomiting.
- Additional symptoms to be expected after a Supralethal Dose:
  - Neuromuscular – Fever & hypotension.
  - Gastrointestinal – Immediate diarrhea.
## Expected Temporal Distribution of Symptoms Following Whole Body Irradiation

<table>
<thead>
<tr>
<th>Midline Tissue Dose</th>
<th>Symptom</th>
<th>Percentage</th>
<th>Time Post Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1.0 Gy (50-100 rad)</td>
<td>Anorexia</td>
<td>15-50</td>
<td>3-18 hrs</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>5-30</td>
<td>3-20 hrs</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>15-20</td>
<td>4-16 hrs</td>
</tr>
<tr>
<td>1-2 Gy (100-200 rad)</td>
<td>Anorexia</td>
<td>50-90</td>
<td>1-48 hrs</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>30-70</td>
<td>4-30 hrs</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>20-50</td>
<td>6-24 hrs</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>35-60</td>
<td>1-72 hrs</td>
</tr>
<tr>
<td></td>
<td>Weakness</td>
<td>25-50</td>
<td>3-48 hrs</td>
</tr>
<tr>
<td></td>
<td>Bleeding (mild)</td>
<td>10</td>
<td>1-5 wks</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>10-50</td>
<td>2 days-5 wks</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>10-50</td>
<td>1-5 wks</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>&lt;5</td>
<td>5-6 wks</td>
</tr>
</tbody>
</table>

Table courtesy of James Conklin, M.D.

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<th>Percentage</th>
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</tr>
</thead>
<tbody>
<tr>
<td>2-3.5 Gy (200-350 rad)</td>
<td>Anorexia</td>
<td>90-100</td>
<td>1-48 hrs</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>70-90</td>
<td>1-48 hrs</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>50-80</td>
<td>3-24 hrs</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>10</td>
<td>4-8 hrs</td>
</tr>
<tr>
<td></td>
<td>Fatigue (moderate)</td>
<td>60-90</td>
<td>2 hrs-6 wks</td>
</tr>
<tr>
<td></td>
<td>Weakness (moderate)</td>
<td>50-80</td>
<td>2 hrs-6 wks</td>
</tr>
<tr>
<td></td>
<td>Bleeding</td>
<td>10-50</td>
<td>1-5 wks</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>10-80</td>
<td>1-5 wks</td>
</tr>
<tr>
<td></td>
<td>Infection</td>
<td>10-50</td>
<td>2-5 wks</td>
</tr>
<tr>
<td></td>
<td>Ulceration</td>
<td>30</td>
<td>3-5 wks</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>5-50</td>
<td>4-6 wks</td>
</tr>
</tbody>
</table>

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<th>Time Post Exposure</th>
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</thead>
<tbody>
<tr>
<td>3.5-5.5 Gy (350-550 rad)</td>
<td>Anorexia</td>
<td>100</td>
<td>1-72 hrs</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>90-100</td>
<td>1-72 hrs</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>80-100</td>
<td>3-24 hrs</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>10</td>
<td>3-8 hrs</td>
</tr>
<tr>
<td></td>
<td>Fatigue</td>
<td>90-100</td>
<td>1 hr-6 wks</td>
</tr>
<tr>
<td></td>
<td>Weakness</td>
<td>90-100</td>
<td>1 hr-6 wks</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>50</td>
<td>4-24 hrs</td>
</tr>
<tr>
<td></td>
<td>Bleeding</td>
<td>50-100</td>
<td>6 days-6 wks</td>
</tr>
<tr>
<td></td>
<td>Fever &amp; Infection</td>
<td>80-100</td>
<td>6 days-6 wks</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>50-99</td>
<td>3.5-6 wks</td>
</tr>
</tbody>
</table>

Table courtesy of James Conklin, M.D.
**Expected Temporal Distribution of Symptoms Following Whole Body Irradiation**

<table>
<thead>
<tr>
<th>Midline Tissue Dose</th>
<th>Symptom</th>
<th>Percentage</th>
<th>Time Post Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-5.75 Gy (550-750 rad)</td>
<td>Anoxia</td>
<td>100</td>
<td>1-72 hrs</td>
</tr>
<tr>
<td></td>
<td>Nausea</td>
<td>100</td>
<td>1-48 hrs</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>100</td>
<td>4-6 hrs</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>10</td>
<td>4-30 hrs</td>
</tr>
<tr>
<td></td>
<td>Fatigue &amp; Weakness (severe)</td>
<td>100</td>
<td>1 hr-2 wks</td>
</tr>
<tr>
<td></td>
<td>Dizziness &amp; disorientation</td>
<td>100</td>
<td>10-14 days</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>60</td>
<td>4-30 hrs</td>
</tr>
<tr>
<td></td>
<td>Bleeding, fever, infection, hypotension</td>
<td>100</td>
<td>30-50 hours</td>
</tr>
<tr>
<td></td>
<td>Death</td>
<td>100</td>
<td>2-3 wks</td>
</tr>
</tbody>
</table>

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**Cerebrovascular Syndrome**

- Cerebrovascular Syndrome is caused by whole body exposure to about **100 Gy** (10,000 Rads) of gamma rays – and results in death in **30-50 hours**.
- Cause of death may be changes in permeability of small blood vessels in the brain, i.e. damage to the microvasculature leading to edema.

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**Cerebrovascular Syndrome: Case Report**

In 1964, a 38-year old man, working in a 235U recovery plant, was involved in an accidental nuclear excursion. He received a total body dose estimated to be about 8800 rads, made up of 2000 rads due to neutrons and 6600 rads do to γ rays. He recalled seeing a flash, and was hurled backwards and stunned; he did not lose consciousness and was able to run to a building 200 yards away. Almost at once he complained of abdominal cramps, headache, vomited, and was incontinent of diarrheal stools which were bloody. He died 49 hours after the accident.
Total Body Irradiation – Radiological Terrorism

*Eric J. Hall, D.Phil., D.Sc.*

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**Self Renewal Tissue**

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**Turnover Time in Various Tissues**

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Cell Type</th>
<th>Turnover Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>RBC</td>
<td>120 days</td>
</tr>
<tr>
<td></td>
<td>Granulocytes</td>
<td>10 hours</td>
</tr>
<tr>
<td></td>
<td>Platelets</td>
<td>16 days</td>
</tr>
<tr>
<td></td>
<td>Lymphocytes</td>
<td>up to many years</td>
</tr>
<tr>
<td>Gastrointestinal, Tract</td>
<td>Oral Cavity</td>
<td>5 days</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>3-9 days*</td>
</tr>
<tr>
<td></td>
<td>Small Intestine</td>
<td>2 days</td>
</tr>
<tr>
<td></td>
<td>Colon</td>
<td>4-6 days</td>
</tr>
<tr>
<td>Skin</td>
<td>Epithelium</td>
<td>13-100 days*</td>
</tr>
<tr>
<td>Respiratory Tract</td>
<td>Tracheal epithelium</td>
<td>50 days</td>
</tr>
<tr>
<td></td>
<td>Lung alveolar cells</td>
<td>10-30 days</td>
</tr>
<tr>
<td>Urinary Bladder</td>
<td>Epithelium</td>
<td>50 days</td>
</tr>
<tr>
<td>Testes</td>
<td>Male germinal Epithelium</td>
<td>14 days</td>
</tr>
<tr>
<td>Eye (cornea)</td>
<td>Epithelium</td>
<td>7 days</td>
</tr>
</tbody>
</table>

* Depending on site

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**Gastrointestinal Syndrome**

- Gastrointestinal Syndrome results from whole-body exposure to about 10 Gy (1000 Rads).
- **Death** occurs in about 9 days in the human due to depopulation of the epithelial lining of the gastrointestinal tract.
Villus in Intestinal Epithelium

Regenerating Crypts
Gastrointestinal Syndrome: Case Report

1946, a 32-year old white male of 1100 to 2000 rads, total-body exposure. The man's hands received as much as 30,000 rads. The patient vomited several times within the first few hours of the exposure. On admission his temperature and pulse rate were slightly elevated; the remainder of his physical examinations were normal.

His general condition remained relatively good until the sixth day, when signs of several paralytic ileus developed which could only be relieved by continuous gastric suction. Within 24 hrs, 10 liters of gastric aspirate were removed. On the seventh day, liquid stools which were guaiac-positive off occult blood were noted. The patient developed signs of circulatory collapse and died on the ninth day post-irradiation. At the time of death, jaundice and spontaneous hemorrhages were observed for the first time.

Gastrointestinal Syndrome: Case Report (cont'd)

At autopsy, the small intestine showed the most striking change. It was distended, flabby, and filled with dark brown semiliquid material. Vascular congestion and numerous petechial hemorrhages were present on the serosal surface. The mucosal surface was edematous and deeply erythematous, and in addition the jejunum was covered by a membranous exudate.

Microscopically, there was complete erosion of the epithelium of the jejunum and ileum as well as loss of the superficial layers of the submucosa. The duodenal epithelium was lost except in the crypts, while the colon epithelium was somewhat better preserved. The denuded surfaces were covered everywhere by a layer of exudate in which masses of bacteria were seen, and in the jejunum the bacteria had invaded the intestinal wall. Blood cultures at postmortem yielded E. coli.

Hematopoietic Syndrome

- Hematopoietic Syndrome results from whole body exposure to 3 to 8 Gy (300 to 800 rads).
- Radiation sterilizes some or all of the mitotically active precursor cells. Symptoms result from lack of circulating blood elements weeks later.
- LD₅₀ for the human, is 3 to 4 Gy (300 to 400 Rad) for young adults without medical intervention.
- Some individuals who would otherwise die, may be saved by antibiotics, platelet infusions, or bone marrow transplants.
Whole Body Radiation Lethality

Management of Hematopoietic Syndrome

- Platelets for local hemorrhage.
- Antibiotic screen during nadir of peripheral blood count.
- Barrier nursing.
- Bone marrow transplants.
- Growth factors to stimulate hematopoiesis.

Comparison of Granulocyte Counts in the Y-12 Patients and in 4 Victims of the Vinča Accident
Comparison of Platelet Counts in the Y-12 Patients and in 4 Victims of the Vinča Accident

The "Fallout" from Chernobyl

Chernobyl – On Site

- 2 Immediate deaths.
- 203 Acute irradiation syndrome.
- 35 Severe bone marrow failure.
- 41 Severe skin burns.
- 13 Died by September.
Chernobyl

- 13 received bone marrow transplants ± HLA.
- 6 received fetal liver transplants (all died early, some a G.I. Death).
- 2 survived, one rejected the transplant, one maybe saved by the transplant (questionable).

Hematopoietic Syndrome: Case Report

26 year-old male involved in a criticality accident at Los Alamos in March 1945 – the first person to die of ARS. Total body dose 6.35Sv. Right hand, 200Gy. Left hand, 30 Gy.
Red blood count changed little up to the time of death
Platelets dropped-Transfusion-dropped again
Granulocytes; initial rise falling to zero at time of death
Day 1. Nausea, anorexia and vomiting
Day 2. Greatly improved, except for numbness in hand
Day 5. Rise of temperature
Day 10. Nauseated, cramps
Day 24. Comatose, 106 ºF, Died, no white cells.
Total Body Irradiation – Radiological Terrorism

Eric J. Hall, D.Phil., D.Sc.

42 hours post-exposure

3½ days Post-exposure

12 days post exposure
Total Body Irradiation – Radiological Terrorism

Eric J. Hall, D.Phil., D.Sc.
Effects of Radiation
On the Developing
Embryo and Fetus

Moderate doses of radiation can
produce catastrophic effects on the
developing embryo and fetus.
The effects depend on the stage of
gestation, the dose, and dose rate.

Radiation Effects on the
Embryo & Fetus

Gestation is divided into three periods -
(times given are for human gestation):

- Preimplantation 0-9 days
- Organogenesis 10 days - 6 weeks
- The Fetal Period 6 weeks to term
Growth Retardation

- Not observed following irradiation during preimplantation.
- Early organogenesis - most intra-uterine growth retardation expressed as weight reduction at term. Can recover later.
- Early fetus - largest degree of permanent growth retardation.

Growth Retardation at Hiroshima by In Utero Irradiation

- 80% of 1,613 children exposed in utero followed to age 17 years.
- Those exposed within 1500 m of the hypocenter compared with those more than 3000 m:
  - 2.25 cm - shorter.
  - 3.0 kg - lighter.
  - 1.1 cm - smaller head diameter.

* Average kerma 25 rads (0.25 Gy).
  (BEIR III Report)
Total Body Irradiation – Radiological Terrorism

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Mouse Embryo & Fetus Deformities

Reduced Head Diameter in Japanese Exposed in Utero to A-Bomb Radiation

*Microcephaly*
Japanese Irradiated *In Utero*

**IQ**
- Test for irradiation at 8-15 weeks.
- Loss of 21 to 29 points at 1 Gy.
- Normal score 107 points.

**Japanese Irradiated *In Utero***
- MRI studies indicate **MASSIVE** impairment of cells to migrate from proliferation zones.
- A typical distribution of gray matter often associated with mental retardation –
  - But then it is usually unilateral.
  - Radiation produces bilateral changes.
- Maximum effect at 8-15 weeks.
Journal Article – 2004

Effect of Low Doses of Ionising Radiation in Infancy on Cognitive Function in Adulthood: Swedish Population Based Cohort Study

Per Hall, Hans-Olov Adami, Dimitrios Trichopoulos, et. al.
British Medical Journal 328(1Jan), 2004.

4577 Boys < 18 Mo.
R/T for Haemangioma

- Decrease in % attending high school.
  Doses > 100 mGy (10 rad)
- Dose response (20-250 mGy) for cognitive tests.
  Concept discrimination
  General instruction
  Technical comprehension
  NOT spatial recognition

Summary of Radiation Effects In Utero
End