Management of acute radiation syndrome after a nuclear detonation

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Disclosures

• Genzyme: Consulting for development of GM-CSF
• Novartis: Consulting and support for cancer research
Outline

• The 10kT ground detonation
• Acute radiation syndrome
  – What we know
  – What we don’t know
  – The unknowable
• Real-life scenarios
10 kT ground-level detonation in a US city

Other common weather patterns include elongated fallout areas that can have potential radiation injuries out to 20 miles (33 km) away. Blast effects noted are 5 psi (major building damage) and 0.5 psi (shattered windows) peak overpressure. Burn distance noted is for 2nd degree burns for individuals within sight of the fireball on a clear day. Radiation levels indicated are 1 Gy-equivalent (light shading) and higher (darker areas).
DHHS evacuation strategy – 2 types of radiation injury

Modified from Weinstock et al. Blood 2008
RTR/AC – 12-48 hours after detonation

- 10,000-100,000 people
- Decontamination
- Family reunification
- Sheltering and food
- Rapid triage
- Stabilization and transport for
  - traumatic injuries
  - chronically ill
- Medical countermeasures
  - SNS
Estimated number of irradiated victims

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Radiation Dose, Gy</th>
<th>Patients, n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All doses</td>
<td>1-kiloton Detonation</td>
</tr>
<tr>
<td>Combined injuries (minimal to intensive care)</td>
<td>20,000</td>
<td>All doses</td>
</tr>
<tr>
<td>Immediate fatalities</td>
<td>All doses</td>
<td>≥10</td>
</tr>
<tr>
<td>Radiation fallout</td>
<td></td>
<td>5–10</td>
</tr>
<tr>
<td>Expectant care</td>
<td></td>
<td>3–5</td>
</tr>
<tr>
<td>Intensive care</td>
<td></td>
<td>1–3</td>
</tr>
<tr>
<td>Critical care</td>
<td>300,000</td>
<td>0.5–1</td>
</tr>
<tr>
<td>Normal care</td>
<td></td>
<td>0.25–0.5</td>
</tr>
<tr>
<td>Ambulatory monitoring</td>
<td></td>
<td>&lt;0.25</td>
</tr>
<tr>
<td>Epidemiologic monitoring</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monitoring for psychosocial well-being without other injury</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* The table depicts projected casualty estimates based on a 1- or 10-kiloton detonation. Assumptions include a city with a population of 2 million people and casualties estimated on the basis of the Hazard Prediction Assessment Capability Program (HPAC), version 3.21 (Defense Threat Reduction Agency, Fort Belvoir, Virginia). Combined injuries consist of radiation injuries in addition to burns or blunt trauma.
Acute radiation syndrome (ARS)

Literature describing ARS

1) Nuclear bombs
2) Therapeutic irradiation
3) Industrial accidents
4) Animal studies
Limitations in the current ARS literature

Nuclear bombs – air blasts, healthcare

Hiroshima before the bomb

Hiroshima after the bomb
Limitations in the current ARS literature

Nuclear bombs – air blasts, healthcare

Hiroshima before the bomb  New York City 2011
Limitations in the current ARS literature

- Therapeutic irradiation – underlying disease, fractionation
Limitations in the current ARS literature

• Industrial accidents – demographics, extensive response
Limitations in the current ARS literature

- Animal models – supportive care, genetic background

<table>
<thead>
<tr>
<th>Species</th>
<th>$LD_{50/30}$ (cGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goat</td>
<td>240</td>
</tr>
<tr>
<td>Swine</td>
<td>250</td>
</tr>
<tr>
<td>Dog</td>
<td>250</td>
</tr>
<tr>
<td>Burro</td>
<td>255</td>
</tr>
<tr>
<td><strong>Human (no care)</strong></td>
<td><strong>350-400</strong></td>
</tr>
<tr>
<td>Guinea pig</td>
<td>450</td>
</tr>
<tr>
<td>Monkey</td>
<td>600</td>
</tr>
<tr>
<td>Hamster</td>
<td>610</td>
</tr>
<tr>
<td>Mouse</td>
<td>640</td>
</tr>
<tr>
<td>Mouse (germ-free)</td>
<td>705</td>
</tr>
<tr>
<td>Rat</td>
<td>714</td>
</tr>
<tr>
<td>Rabbit</td>
<td>750</td>
</tr>
<tr>
<td>Mongolian gerbil</td>
<td>1000</td>
</tr>
</tbody>
</table>
Acute radiation syndrome (ARS)

- Constellation of injury primarily to 4 systems:
  - Gastrointestinal
  - Hematologic
  - Cutaneous
  - CNS/cardiovascular

- Systemic inflammatory response

- Sensitivity differs: Heme (>2Gy) > GI (>3-4 Gy) > CNS (>6 Gy)

- Follows predictable temporal pattern
  - Prodrome
  - Latency
  - Manifest illness
  - Recovery or death
Hypothetical scenario in the Dangerous Fallout zone

- Exposed to radioactive fallout 2 miles from detonation
- Vomiting within 2 hours
- Presents to local hospital the following day after sheltering-in-place
Local medical center – 2-96 hours after detonation

- 5,000-50,000 people
- Decontamination
- Sheltering and food
- Rapid triage
- Stabilization and transport for
  - Traumatic injuries
  - Chronically ill
  - Severe radiation exposure
- Medical countermeasures
  - SNS
  - Pharmacy
Hypothetical scenario in the Dangerous Fallout zone

- Exposed to radioactive fallout 2 miles from detonation
- Vomiting within 2 hours
- Presents to local hospital the following day after sheltering-in-place
  - Vomiting resolved
  - Continued fatigue and lethargy
  - Possible mild confusion
- Lymphocyte count = 1500

What’s his radiation dose?
Estimating radiation dose is difficult

- Geographic dosimetry
- History and physical exam
- Laboratory studies
  - Dicentric chromosomes
  - Lymphocyte count/kinetics
  - Myeloid cells
Estimating radiation dose is difficult.

### Table 5. Biodosimetry Based on Acute Photon-Equivalent Exposures

<table>
<thead>
<tr>
<th>Dose Estimate</th>
<th>Victims with Vomiting</th>
<th>Time to Onset of Vomiting</th>
<th>Absolute Lymphocyte Count†</th>
<th>Rate Constant for Lymphocyte Depletion‡</th>
<th>Dicentrics in Human Peripheral Blood Lymphocytes§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gy</td>
<td>%</td>
<td>h</td>
<td>×10⁹ cells/L</td>
<td>k‡</td>
<td>Per 50 Cells</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>-------------</td>
<td>-----</td>
<td>-------------</td>
</tr>
<tr>
<td>0</td>
<td>-</td>
<td>-</td>
<td>2.45</td>
<td>2.45</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>19</td>
<td>4.63</td>
<td>2.30</td>
<td>2.16</td>
<td>1.90</td>
</tr>
<tr>
<td>2</td>
<td>35</td>
<td>2.62</td>
<td>2.16</td>
<td>1.90</td>
<td>1.48</td>
</tr>
<tr>
<td>3</td>
<td>54</td>
<td>1.74</td>
<td>2.03</td>
<td>1.68</td>
<td>1.15</td>
</tr>
<tr>
<td>4</td>
<td>72</td>
<td>1.27</td>
<td>1.90</td>
<td>1.48</td>
<td>0.89</td>
</tr>
<tr>
<td>5</td>
<td>94</td>
<td>0.99</td>
<td>1.79</td>
<td>1.31</td>
<td>0.69</td>
</tr>
<tr>
<td>6</td>
<td>98</td>
<td>0.79</td>
<td>1.68</td>
<td>1.15</td>
<td>0.54</td>
</tr>
<tr>
<td>7</td>
<td>99</td>
<td>0.66</td>
<td>1.58</td>
<td>1.01</td>
<td>0.42</td>
</tr>
<tr>
<td>8</td>
<td>100</td>
<td>0.56</td>
<td>1.48</td>
<td>0.89</td>
<td>0.33</td>
</tr>
<tr>
<td>9</td>
<td>100</td>
<td>0.48</td>
<td>1.39</td>
<td>0.79</td>
<td>0.25</td>
</tr>
<tr>
<td>10</td>
<td>100</td>
<td>0.39</td>
<td>1.31</td>
<td>0.70</td>
<td>0.20</td>
</tr>
</tbody>
</table>

* Depicted above are the 3 most useful elements of biodosimetry. Dose range is based on acute photon-equivalent exposures. The second column indicates the percentage of people who vomit, based on dose received and time to onset. The middle section depicts the time frame for development of lymphopenia. Blood lymphocyte counts are determined twice to predict a rate constant that is used to estimate exposure dose. The final column represents the current gold standard, which requires several days before results are known. Colony-stimulating factor therapy should be initiated when onset of vomiting or lymphocyte depletion kinetics suggests an exposure dose for which treatment is recommended (see Table 7). Therapy may be discontinued if results from chromosome dicentrics analysis indicate a lower estimate of whole-body dose.

† Normal range, 1.4–3.5 × 10⁹ cells/L. Numbers in boldface fall within this range.

‡ The lymphocyte depletion rate is based on the model \( L_t = 2.45 \times 10^9 \text{ cells/L} \times e^{- k(D) t} \), where \( L_t \) equals the lymphocyte count (×10⁹ cells/L), \( 2.45 \times 10^9 \text{ cells/L} \) equals a constant representing the consensus mean lymphocyte count in the general population, \( k \) equals the lymphocyte depletion rate constant for a specific acute photon dose, and \( t \) equals the time after exposure (days).

§ Number of dicentric chromosomes in human peripheral blood lymphocytes.
### METREPOL dosimetry approach

#### Symptoms

| N | Neurovascular System |
| H | Haematopoietic System |
| C | Cutaneous System |
| G | Gastrointestinal System |

#### Grading (organ specific)

- H: Sensation / itching, Swelling and Edema, Blistering, Desquamation, Ulcer / Necrosis, Hair loss, Onycholysis, Diarrhea
- C: Abdominal Cramps/Pain
- G: Sensation / itching, Swelling and Edema, Blistering, Desquamation, Ulcer / Necrosis, Hair loss, Onycholysis, Diarrhea

#### Grading code

- $N_i$
- $H_i$
- $C_i$
- $G_i$

#### Response Category

- $RC = ?_{x_d}$

#### Example

- $N_2 H_3 C_1 G_2$
- $RC = 3_{2d}$

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**N** = Degree of severity 1-4

**H** = Time point (x) at which RC was established; measured in days (d) after begin of exposure.

**C** = Degree of severity to describe the extent of damage in the neurovascular system.

**G** = An RC equal to 3 was determined on the second day after exposure.
Dose Estimator (Biosimetry Tools) [What Is Biosimetry?]

1. Estimate Exposure Dose -
   Dose Estimator: [
   ● Onset of Vomiting
   ● Lymphocyte Depletion Kinetics
   ● Dicentric Chromosomes
2. Explaining Biosimetry
3. Suggest Hematopoietic Subsyndrome Treatment, Based on Exposure Dose and Event Size
4. Biosimetry Based on Acute Photon-Equivalent Exposures (PDF - 58 KB)

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Dose Estimator - Onset of Vomiting

1. Patient vomited Select Onset Time after the exposure to radiation. Time to Onset of Vomiting and Dose (Illustration)
   
   [Calculate Exposure Dose] [Clear]

2. Estimated Whole-body Radiation Dose: [ ] (Dose shown in units of Gray) (Read-only field)
3. Percent victims with vomiting at this dose: [ ] (Read-only field)
4. Get Suggested Treatment for hematopoietic subsyndrome based on this dose.
Manifet Acute Radiation Syndrome
Gastrointestinal

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Degree of severity 1 to 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhea - frequency</td>
<td>Once to &gt;10 times per day</td>
</tr>
<tr>
<td>Blood in stools</td>
<td>Occult to gross hemorrhage</td>
</tr>
<tr>
<td>Abdominal pain/cramps</td>
<td>Minimal to excruciating</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Once to &gt;10 times per day</td>
</tr>
</tbody>
</table>
Manifest Acute Radiation Syndrome

Cutaneous

<table>
<thead>
<tr>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
</tr>
<tr>
<td>Altered sensation/Itching</td>
</tr>
<tr>
<td>Edema</td>
</tr>
<tr>
<td>Blistering</td>
</tr>
<tr>
<td>Desquamation</td>
</tr>
<tr>
<td>Ulcer/necrosis</td>
</tr>
<tr>
<td>Hair loss</td>
</tr>
<tr>
<td>Onycholysis</td>
</tr>
</tbody>
</table>
## Manifest Acute Radiation Syndrome
### Cardiovascular/CNS

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Degree of severity 1 to 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>Once to &gt;10 times per day</td>
</tr>
<tr>
<td>Anorexia</td>
<td>Able to drink to requiring parenteral nutrition</td>
</tr>
<tr>
<td>Fatigue</td>
<td>Normal activity to prevents activity</td>
</tr>
<tr>
<td>Headache</td>
<td>Minimal to intense</td>
</tr>
<tr>
<td>Neurological deficits</td>
<td>No deficits to unarousable</td>
</tr>
</tbody>
</table>
Multiorgan Acute Radiation Syndrome

- In a review of radiation accident casualties with severe ARS (n=45):
  - 32 had respiratory involvement,
  - 20 had cardiovascular involvement (primarily manifested as heart failure)
  - 25 had liver involvement
  - 32 had urogenital involvement

Fiedner et al. *Stem Cells* 2005
Hypothetical scenario in the Dangerous Fallout zone

- Estimated radiation dose = 4 Gy
- No other injuries
- Over the subsequent 2 days feels well, but then develops:
  - Watery, profuse diarrhea
  - Abdominal cramping
  - Low-grade temperature
  - WBC = 2600; ALC = 200

What should be done?
Neutropenia can be delayed after radiation exposure.
SUPPORTIVE CARE IMPROVES OUTCOME

- In multiple studies in animals and humans, supportive care increases survival:
  - Antibiotics
  - Intravenous fluids
  - Transfusions
  - Wound/skin care

<table>
<thead>
<tr>
<th>Level of care</th>
<th>LD_{50/30} (cGy)</th>
<th>Mean survival times (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No care</td>
<td>350-400</td>
<td>21-28</td>
</tr>
<tr>
<td>Supportive care</td>
<td>600-700</td>
<td>14-21</td>
</tr>
<tr>
<td>Heroic care (e.g. hematopoietic cell transplantation)</td>
<td>?</td>
<td>&lt;7</td>
</tr>
</tbody>
</table>
Why focus on victims with ARS from the fallout zone?

- Large number
- Lack of concomitant traumatic and burn injuries
- Do not require immediate stabilization and evacuation
- Manifest illness after days-weeks
Combined injury worsens outcome in humans

![Graph showing combined injury effects]
Resource demand and availability after a nuclear detonation in Washington DC

<table>
<thead>
<tr>
<th></th>
<th>Symptomatic injured persons or incident demand min - med - max</th>
<th>Single hospital</th>
<th>City</th>
<th>Nation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persons injured (next column) or population of designated area (city, nation)</td>
<td>930,000 – 990,000 – 1,600,000</td>
<td>N/A</td>
<td>592,000</td>
<td>300 million</td>
</tr>
<tr>
<td>Hospital beds (unoccupied)</td>
<td>70,000 – 180,000 – 300,000</td>
<td>165 (40)</td>
<td>3,670 (920)</td>
<td>947,000 (295,000)</td>
</tr>
<tr>
<td>ICU beds (unoccupied)</td>
<td>24,000 – 61,000 – 110,000</td>
<td>20.5 (1.6)</td>
<td>N/A</td>
<td>118,000 (9,400)</td>
</tr>
<tr>
<td>Operating rooms</td>
<td>N/A</td>
<td>6</td>
<td>N/A</td>
<td>30,000</td>
</tr>
<tr>
<td>Burn beds (unoccupied)</td>
<td>0 – 0 – 1,100</td>
<td>N/A</td>
<td>32 (5)</td>
<td>1,760 (580)</td>
</tr>
<tr>
<td>Ambulances</td>
<td>N/A</td>
<td>N/A</td>
<td>38</td>
<td>48,400</td>
</tr>
</tbody>
</table>

Modeling Division of BARDA
Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) Blood and Tissue Requirements Working Group
Gryphon Scientific
Operating conditions change with situation

Incident demand / resource imbalance increases
Risk of morbidity / mortality to patient increases

<table>
<thead>
<tr>
<th>Conventional</th>
<th>Contingency</th>
<th>Crisis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Space</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual patient care space fully utilized</td>
<td>Patient care areas re-purposed (PACU, monitored units for ICU-level care)</td>
<td>Facility damaged / unsafe or non-patient care areas (classrooms, etc) used for patient care</td>
</tr>
<tr>
<td><strong>Staff</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual staff called in and utilized</td>
<td>Staff extension (brief deferrals of non-emergent service, supervision of broader group of patients, change in responsibilities, documentation, etc)</td>
<td>Trained staff unavailable or unable to adequately care for volume of patients even with extension techniques</td>
</tr>
<tr>
<td><strong>Supplies</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cached and usual supplies used</td>
<td>Conservation, adaptation, and substitution of supplies with occasional re-use of select supplies</td>
<td>Critical supplies lacking, possible re-allocation of life-sustaining resources</td>
</tr>
<tr>
<td><strong>Standard of care</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Usual care</td>
<td>Functionally equivalent care</td>
<td>Crisis standards of care</td>
</tr>
</tbody>
</table>

Usual operating conditions

Indicator: potential for crisis standards

Trigger: crisis standards of care

Austere operating conditions

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1) Unless temporary, requires state empowerment, clinical guidance, and protection for triage decisions and authorization for alternate care sites / techniques. Once situational awareness achieved, triage decisions should be as systematic and integrated into institutional process, review, and documentation as possible.

2) Institutions consider impact on the community of resource utilization (consider ‘greatest good’ vs. individual patient needs – for example, conserve resources when possible) but patient-centered decision-making is still the focus.

3) Institutions (and providers) must make triage decisions balancing the availability of resources to others and the individual patient’s needs – shift to community-centered decision-making.
Operating conditions change with situation

Triage under normal conditions

– Sickest first
– Everything for everyone
– Balance of benefit:risk determined in each patient
– No death panels

Triage under disaster conditions

– Salvageable first
– Selective use of resources
– Balance of benefit:risk determined over entire response
Radiation Injury Only

Radiation Dose (Gy)

- > 10 Likely fatal (in higher range)
- 6 - 10 Severe
- > 2 - 6 Moderate
- < 2 Minimal

Resource availability:
- Normal
- Good
- Fair
- Poor

Standard of care:
- Conventional
- Contingency
- Crisis

Coleman CN, Weinstock DM et al. *Disaster Med Health Prep* 2011
Injury severity

≥ Moderate trauma + radiation > 2 Gy

Combined injury (radiation with trauma and/or burns)

Immediate

Delayed

Immediate

Expectant

Delayed

Expectant

Trauma only

Severe trauma

Immediate

Immediate

Delayed

Expectant

Moderate trauma

Delayed

Delayed

Immediate

Immediate

Minimal trauma

Minimal

Minimal

Minimal

Minimal

Resource availability

Normal

Good

Fair

Poor

Standard of care:

Conventional

Contingency

Crisis

Crisis

Coleman CN, Weinstock DM et al. Disaster Med Health Prep 2011

BURN >15% BSA worsens triage category 1 level
Hypothetical case

• Evacuated on day 6 to an academic medical center 1000 miles away
Academic center – 2-30 days after detonation

- 50-5,000 people
- Medical care for ARS
  - Outpatient
  - Inpatient
- Family support
- Medical countermeasures
  - Pharmacy (likely <500 doses)
  - SNS
  - VMI
Hypothetical case

- Evacuated on day 6 to an academic medical center 1000 miles away
- Managed as outpatient at adjacent hotel with daily visit
- Started on G-CSF and prophylactic antibiotics
- On day 10, fever to 102, WBC count = 400
- Admitted for 5 days for intravenous antibiotics
- On day 15, WBC count = 2000 and discharged
Prophylactic antibiotics

• Use standard approaches during neutropenia:
  – Anti-herpes viruses (e.g. acyclovir)
  – Anti-bacterial (e.g. levofloxacin)
  – Anti-fungal (e.g. fluconazole)

• After resolution of neutropenia in victims who received higher doses (>4 Gy), consider:
  – Anti-VZV (e.g. acyclovir)
  – Anti-PCP (e.g. bactrim)
  – Monitoring for CMV reactivation
Myeloid cytokines for neutropenia
Myeloid cytokines for neutropenia

• G-CSF, GM-CSF, PEG-G-CSF
• FDA approved
• Rationale after a nuclear detonation
  – Reduce infection-associated death
  – Prevent or shorten neutropenia to reduce requirement for care
Timing of cytokine administration

- Meta-analysis of G-CSF given after chemotherapy:
  - Reduces death from neutropenia-associated infection 45%
  - Reduces need for hospitalization
  - Reduces length of stay
Timing of cytokine administration

• In rhesus macaques, overall survival is improved if G-CSF is initiated within 24 hours after radiation exposure and continued until resolution of neutropenia
  – Necessity of administration within 24 hours is unclear
  – Early administration will result in some unirradiated persons receiving drug
Myeloid cytokines with “Normal” or “Good” resource availability

<table>
<thead>
<tr>
<th>Radiation dose (Gy)</th>
<th>Radiation alone or with minimal trauma</th>
<th>Moderate trauma</th>
<th>Severe trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;10 Gy</td>
<td>Expectant³</td>
<td>Expectant³</td>
<td>Expectant³</td>
</tr>
<tr>
<td>&gt; 6 – 10 Gy</td>
<td>Immediate²</td>
<td>Delayed²</td>
<td>Expectant³</td>
</tr>
<tr>
<td>≥ 2 – 6 Gy</td>
<td>Immediate¹</td>
<td>Immediate¹</td>
<td>Delayed²</td>
</tr>
</tbody>
</table>

### Myeloid cytokine category

<table>
<thead>
<tr>
<th>Myeloid cytokine category</th>
<th>Recommendation for G-CSF or comparable agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Indicated</td>
</tr>
<tr>
<td>2</td>
<td>Indicated only if supply widely available</td>
</tr>
<tr>
<td>3</td>
<td>Not indicated</td>
</tr>
</tbody>
</table>

**COMBINED INJURY**

Moderate or severe injury + radiation > 2 Gy
Myeloid cytokines with “Fair” or “Poor” resource availability

### Radiation dose
- **>10 Gy**
  - Immediate\(^1\)
  - Expectant\(^3\)
- **> 6 – 10 Gy**
  - Delayed\(^2\)
  - Expectant\(^3\)
- **≥ 2 – 6 Gy**
  - Immediate\(^1\)
  - Immediate\(^1\)

### Radiation only or Minimal trauma
- Moderate trauma
- Severe trauma
  - Expectant\(^3\)

### Radiation only or Minimal trauma

<table>
<thead>
<tr>
<th>Moderate trauma</th>
<th>Severe trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expectant(^3)</td>
<td>Expectant(^3)</td>
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### Resource availability:
- **Fair**
- **Poor**
- **Fair and Poor**

### Myeloid cytokine category
- **1** Indicated
- **2** Indicated only if supply widely available
- **3** Not indicated

### COMBINED INJURY
- Moderate or severe injury + radiation > 2 Gy
Stem cell support after a nuclear detonation

Marrow injury

- Sustained aplasia
- Available donor
- Acceptable pre-transplant condition
- Potentially irreversible marrow injury
- Salvageable
- Minimal combined injury

Stem cell transplant

Expedited HLA typing and donor search

Supportive care

Affected population
Participation may vary

- Correlation between Transfers accepted and HSCT beds: $r = -0.09$
- Correlation between Staff cross-trained and HSCT beds: $r = 0.07$
Participation may vary

1) Altered standards
   - Legal
   - Ethical

2) Financial implications

3) Lack of support for pre-event training
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