Radiation Injury Treatment Network: Planning for the worst, using experience from hematology & transplantation

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Radiation Injury Treatment Network

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Radiation Injury Treatment Network (RITN)

Purpose:

To provide surge capacity and management guidance for radiation casualties with bone marrow suppression
Voluntary network of 51 academic medical centers
6 blood donor centers & 7 umbilical cord blood banks
Radiation Injury Treatment Network (RITN)

- Expertise in management of bone marrow suppression
- Organized by National Marrow Donor Program (NMDP) & American Society of Blood and Marrow Transplantation (ASBMT)
- Supported by the US Office of Naval Research
- Coordinated with the Office of the ASPR, DHHS
Not RITN

Steps in developing our Contingency Plans

Review radiation hazards
Outline clinical protocol
  similar to Phase II trial
Build a network
Plan for performance evaluation
  similar to protocol interim analysis
BAD THINGS CAN HAPPEN

IND

RDD

PPA

CFW

OMG
BAD THINGS CAN HAPPEN

IND

*Improvised Nuclear device*

RDD

*Radiological Dispersal Device*

PPA

*Power Plant Accident*

CFW

*Contamination of Food or Water*

OMG
BAD THINGS CAN HAPPEN

IND

*Improvised Nuclear device*

RDD

*Radiological Dispersal Device*

PPA

*Power Plant Accident*

CFW

*Contamination of Food or Water*

OMG

*Oh My God!*
Irradiation from accident, military or terrorist event

Differs from Medical Therapeutic Irradiation

- High dose rate
- Mixed isotopes
- Accompanying trauma or burns
- Variable partial body shielding
Cytokine & HCT support considered

Depending on dose, rate
Volume exposed

Other injuries
*Number of casualties; chaos*
Acute radiation syndromes

- Hematopoietic
- Gastrointestinal
- Cerebrovascular
- Cardiovascular
- Neurologic

BMT expertise
Evaluation & Management of Acute Radiation Syndrome
Radiation or Toxins may injure marrow
Without any immediate big disaster

Individuals with modest (incomplete) marrow irradiation

< 3 Gy  recover with medical support

4-10 Gy (may not be total) body irradiation

>10 Gy unlikely to recover
Radiation or Toxins may injure marrow
Without any immediate big disaster

Individuals with modest (incomplete) marrow irradiation

< 3 Gy recover with medical support
\[ \text{ANC} > 2500 \text{ at 7 days}; > 1500 \text{ at 14 days} \]
\[ \text{Platelets} > 150,000 \text{ at 14 days} \]

4-10 Gy (may not be total) body irradiation

>10 Gy unlikely to recover
Radiation or Toxins may injure marrow
Without any immediate big disaster

Individuals with modest (incomplete) marrow irradiation

< 3 Gy recover with medical support

4-10 Gy (*may not be total*) body irradiation
- Myelosuppression
- Variable immunosuppression
- Variable skin, mucosal or GI toxicity
  - *Exacerbated by other injuries*

> 10 Gy unlikely to recover
Potential for life-threatening exposure during clean-up.

Casualty impact from radiation events
Estimated number of irradiated casualties

Table 4. Mass Casualty Scenario for a Nuclear Detonation*

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Radiation Dose, Gy</th>
<th>1-kiloton Detonation</th>
<th>10-kiloton Detonation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combined injuries (minimal to intensive care)</td>
<td>All doses</td>
<td>1000–3000</td>
<td>15 000–24 000</td>
</tr>
<tr>
<td>Immediate fatalities</td>
<td>All doses</td>
<td>&gt;7000</td>
<td>&gt;13 000</td>
</tr>
<tr>
<td>Radiation fallout</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expectant care</td>
<td>≥10</td>
<td>18 000</td>
<td>45 000</td>
</tr>
<tr>
<td>Intensive care</td>
<td>5–10</td>
<td>19 500</td>
<td>79 400</td>
</tr>
<tr>
<td>Critical care</td>
<td>3–5</td>
<td>33 000</td>
<td>108 900</td>
</tr>
<tr>
<td>Normal care</td>
<td>1–3</td>
<td>66 000</td>
<td>70 000</td>
</tr>
<tr>
<td>Ambulatory monitoring</td>
<td>0.5–1</td>
<td>82 500</td>
<td>139 000</td>
</tr>
<tr>
<td>Epidemiologic monitoring</td>
<td>0.25–0.5</td>
<td>106 000</td>
<td>147 000</td>
</tr>
<tr>
<td>Monitoring for psychosocial well-being without other injury</td>
<td>&lt;0.25</td>
<td>&gt;150 000</td>
<td>&gt;270 000</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.
Remote management of few many (possible) victims

Regional screening of thousands—exposure history, brief assessment
GI symptoms; Other
CBC (date/time; subject retain copy of result)
Investigational Biodosimetry Measures
New radiation mitigators
Triage for urgent care; Evacuate; Advise for later followup
Ground Zero
Evacuation
Victim collection points
Decon
Triage
Trauma centers
Specialty care & treatment centers

Radiation Injury Treatment Network

- Transplant Centers
- Donor Centers
- Cord Blood Banks

Evacuation
 Victim collection points
Decon
Triage
Trauma centers
Specialty care & treatment centers
Triage that incorporates resource availability

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
Triage that incorporates resource availability

**Downgrade 1-2 levels by combined injury (+ trauma/burns)**

<table>
<thead>
<tr>
<th>Radiation Dose (Gy)</th>
<th>Immediate</th>
<th>Delayed</th>
<th>Expectant</th>
<th>Minimal</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 10 Likely fatal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 - 10 Severe</td>
<td>Immediate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 2 - 6 Moderate</td>
<td>Immediate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 2 Minimal</td>
<td>Minimal</td>
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Resource availability:
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RITN ARS Treatment Guidelines

• Follow standard approaches for patients with bone marrow toxicity from chemotherapy

• Based on severity of cytopenias and presence of complications (e.g. neutropenic fever)
  – Irradiated, leukoreduced transfusions
  – Antibiotics
  – IV fluid and other support
  – G-CSF
  – Hospitalization when indicated
  – Opportunity to apply new mitigation approaches
RITN Pre-event planning and training

- Standard Operating Procedures at each center
- Site readiness assessments
- Annual tabletop exercise
- Annual training/education requirement:
  - >2,600 RITN staff completed Basic Radiation Training since 2006
  - >2,300 medical staff have attended RITN ARS medical Grand Rounds training since 2008
  - >150 participated in REAC/TS training in Oak Ridge, TN since 2008
Pre-event national integration

• **Readiness exercises/events**
  – Annual RITN directed tabletop exercise
  – Top Officials IV (TOPOFF) (2007) - DHS
  – Pinnacle 07 (2007) – DHHS-ASPR
  – ConvEX 2008 – IAEA
  – National Level Exercise 2010 (NLE 2010)

• **Emergency communications equipment at each center**
  – Government Emergency Telecommunication Service (GETS) calling cards
  – Satellite telephones
Post-event response

- Surge capacity
- National guidance – online, teleconsult
- Coordination of patient management
  - Treatment guidelines (www.ritn.net)
  - Template admission orders (www.remm.nlm.gov)
  - HLA typing of 6,000 – 10,000 casualties/week during an emergency
  - Product harvesting and transport
Surge capacity based on 2010 tabletop exercise

Total patients accepted

Planning includes RITN management of up to 30,000 irradiated casualties
RITN initiatives to address existing gaps

• **Reimbursement**
  • Non-NDMS hospitals
  • Hospitalization > 30 days
  • Out-patient care

• **Shortages**
  • Blood products
  • Medications
    • Strategic national stockpile
    • Vendor-managed inventory
    • User-managed inventory
User-managed inventory

- Establish stockpiles within RITN centers of key agents with dual use
  - G-CSF
  - Antibiotics
  - Cellular therapies?
- Rotate products into clinical pharmacies to avoid expiration
- Cost-efficient and strategically located
RITN initiatives to address existing gaps

• Research
  • Modeling
  • Patient access
  • HSCT registries
  • Exercises
Established RITN Protocols

Defined eligibility for donor search and HCT
Defined donor matching and selection process
Defined regimen and GVHD prophylaxis
Suitable for broad use
Permit future reassessment and modification
Defined supportive care

Defined data collection plans

*to learn and do it better next time*
RITN HSCT approach for ARS - similar to BMT CTN 0301

- Cyclophosphamide 50 mg/kg
- Fludarabine 30 mg/m²
- Anti-thymocyte globulin (Thymoglobulin®) 3 mg/kg

Allograft infusion

- Cyclosporine or tacrolimus, days -3 to +100
- Mycophenolate, d-3 to +30
- G-CSF

Minimal myelosuppression and mucositis = minimal additional resource allocation

Weinstock et al. Blood 2008