 Topics

Acute Radiation Syndrome (ARS)
• Definition and diagnosis
• Treatment

External and Internal Contamination
• Definition and diagnosis
• Treatment

Examples, Follow-Up Care and Research
Radiation Injury

• EXPOSURE
  – Acute Radiation Syndrome (Hematopoietic / GI / CV-CNS / Cutaneous Subsyndromes)

• EXTERNAL CONTAMINATION

• INTERNAL CONTAMINATION
Radiation Injury

EXPOSURE DUE TO CONTAMINATION

EXTERNAL

S

Partial Whole Body

Modified from AFRRI
Radiation Injury

EXPOSURE DUE TO CONTAMINATION

EXTERNAL

INTERNAL

inhalation

Modified from AFRRI
Radiation Injury

EXPOSURE DUE TO CONTAMINATION

EXTERNAL  INTERNAL

ingestion

Modified from AFRRI
Radiation Injury

EXPOSURE DUE TO CONTAMINATION

EXTERNAL

INTERNAL

S

Partially Whole Body

trauma, injection, absorption

Modified from AFRRI
Medical Effects

Acute:
Usually none. ARS possible with large intake or high energy isotopes (e.g. Polonium)

Chronic:
Carcinogenesis, chronic radiation injury in target organ, e.g. kidney, lung, bone
Alexander Litvinenko

Died Nov 2006 from Polonium-210

Photo Source: www.msnbc.msn.com
Major Pathways of Release

- Inhalation ($\gamma, \alpha, \beta$)
- Cloud Shine ($\gamma$)
- Ground Shine ($\gamma$)
- Skin ($\beta$)
- Deposition

Release from resuspended material

Courtesy: F. Harper
Contamination with Cutaneous Radiation Injury

Superficial & partial thickness: Increased permeability

Full thickness contamination: Remains in burn eschar
Major Pathways of Release

- Inhalation ($\gamma, \alpha, \beta$)
- Cloud Shine ($\gamma$)
- Section (β)
- Ground

Courtesy: F. Harper
Amount of Internal Hazard (acts as a poison)

- Amount of radionuclide
- Radiation characteristics
- Target organ
- Radiation biological half-life
# Possible Contaminating Agents

<table>
<thead>
<tr>
<th>Nuclide</th>
<th>Primary Radiation Type (half-life)</th>
<th>Primary Form</th>
<th>Application that Forms the Basis for Size of Source</th>
<th>Deposition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sr-90</td>
<td>Beta (28.6 y)</td>
<td>Ceramic (SrTiO₃)</td>
<td>Large radioisotopic thermal generator (RTG)</td>
<td>Bone</td>
</tr>
<tr>
<td>Cs-137</td>
<td>Beta + Ba-137m Gamma (30.17 y)</td>
<td>Salt (CsCl)</td>
<td>Irradiator</td>
<td>Whole body</td>
</tr>
<tr>
<td>I-131</td>
<td>Beta, Gamma (8.02 d)</td>
<td>Salt</td>
<td>Fission product, nuclear weapons testing, nuclear medicine</td>
<td>Thyroid</td>
</tr>
<tr>
<td>H-3</td>
<td>Beta (12.3 y)</td>
<td>Gas/liquid</td>
<td>Gun sights, nuclear warheads</td>
<td>Kidney</td>
</tr>
<tr>
<td>U-238</td>
<td>Alpha (4.5x10¹² y)</td>
<td>Metal</td>
<td>Depleted munitions</td>
<td>Kidney</td>
</tr>
<tr>
<td>Pu-238</td>
<td>Alpha (87.75 y)</td>
<td>Ceramic (PuO₂)</td>
<td>RTG used for the Cassini Saturn space probe</td>
<td>Lung (inhaled) Bone</td>
</tr>
<tr>
<td>Am-241</td>
<td>Alpha (432.2 y)</td>
<td>Pressed ceramic powder (AmO₂)</td>
<td>Single well-logging source</td>
<td>Liver Bone</td>
</tr>
<tr>
<td>Ra-226</td>
<td>Alpha (1600 y)</td>
<td>Salt (RaSO₄)</td>
<td>Old medical therapy sources</td>
<td>Bone</td>
</tr>
</tbody>
</table>
Large source scenarios

Modified from AFRRI
Biological Half-Life

**Definition:**
The time for half the atoms of a substance to be removed from the body.

**Examples:**
- Cesium ($^{137}\text{Cs}$): 12 – 165 days (shortest in infants)
- Tritium ($^3\text{H}$): 10 - 12 days
- Plutonium (Pu): bone = 100 yrs, liver = 40 yrs
- Uranium (U): bone = 300 days, kidney = 15 days, lung = 120-1470 days (size/solubility)

Inhalation Pathway

- Most efficient route
- Inhale radiation-emitting particulate matter (we do not “inhale radiation”)
- Particle size — key factor (0.1 – 5 microns)
- Secondary source for ingestion
- Solubility — important
# Clearance Times from the Respiratory Tract

<table>
<thead>
<tr>
<th>Structure</th>
<th>Clearance Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trachea</td>
<td>6 min</td>
</tr>
<tr>
<td>Bronchi</td>
<td>1 hr</td>
</tr>
<tr>
<td>Bronchioles</td>
<td>4 hr</td>
</tr>
<tr>
<td>Terminal Bronchioles</td>
<td>10 hr</td>
</tr>
<tr>
<td>Alveoli</td>
<td>100 - 1500+ days</td>
</tr>
</tbody>
</table>

Topics

Acute Radiation Syndrome (ARS)
- Definition and diagnosis
- Treatment

External and Internal Contamination
- Definition and diagnosis
- Treatment

Examples, Follow-Up Care and Research
Initial Patient Management

• First address life-threatening conditions / injuries — the ABC’s

• Initial survey (frisk with RADIACs)
• Nasal swabs-do early

Health care workers have never been hurt caring for contaminated patients
First Steps:

External Decontamination

1. Remove patient’s clothing.
2. Wash patient with mild soap and water (or take a shower).

95+% EFFECTIVE
General Management to Reduce Internal Dose (Consider as a Poison)

a. Reduce intake, uptake, deposition
b. Increase excretion
c. Decide “Risk versus Benefit” for treatment
Classes of Some Drugs for Treatment of Internal Contamination

- Blocking agents, e.g. potassium iodide
- Chelating agents, e.g. DTPA
- Diluting agents, e.g. water
- Ion exchange resins, e.g. Prussian Blue
Potassium Iodide (KI) for Radioactive Iodine (RAI) Protection

• **Indication**: Protection against RAI to reduce risk of thyroid cancer
• **Contraindication**: Iodine hypersensitivity
• **Availability**: over the counter
• **Possible side effects**:
  — Allergic reaction, GI upset, thyrotoxicosis
  — Hypothyroidism in neonates: Get TSH
• **Use**:
  — Administer NLT 4 hours after exposure to RAI
  — Prioritize sheltering for pregnant and lactating females and those allergic to KI

Threshold Thyroid Radioactive Exposures and Recommended Doses of Potassium Iodide (KI)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Predicted Thyroid Exposure</th>
<th>KI dose daily mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults &gt; 40 yrs</td>
<td>&gt; 500 cGy (5 Gy)</td>
<td>130</td>
</tr>
<tr>
<td>Adults 18-40 yrs</td>
<td>&gt; 10 cGy</td>
<td>130</td>
</tr>
<tr>
<td>Pregnant / lactating females</td>
<td>&gt; 5 cGy</td>
<td>130</td>
</tr>
<tr>
<td>Age 3 - 18 yrs</td>
<td>&gt; 5 cGy</td>
<td>65 (130 if large)</td>
</tr>
<tr>
<td>1 month – 3 yrs</td>
<td>&gt; 5 cGy</td>
<td>32</td>
</tr>
<tr>
<td>Birth – 1 month</td>
<td>&gt; 5 cGy</td>
<td>16</td>
</tr>
</tbody>
</table>

Potassium Iodide (KI)

- 130 mg/tablet
- 65 mg/ml
- 1000 mg/ml
Chelating Agents: e.g. DTPA

Diethylenetriaminepentaacetate (Trisodium Calcium / Zinc Salts)

• FDA approved, 2004
  – For plutonium (Pu), americium (Am), curium (Cu)
  – Available in Strategic National Stockpile (SNS)
  – Prescription, injection

• May remove 60-90% of soluble plutonium
  – When started early
Other Chelating Agents

- Deferasirox (FDA 2005, oral for Fe*)
- Deferoxamine (Fe*, Pu)
- Dimercaprol (As*, Au*, Hg*, Cr Ni, Pb)
- EDTA (Pb*, other metals)
- Penicillamine (Cu*, Au, Hg, Pb)
- Sevelamer (P*)
- Succimer (Pb*)

* FDA approved for these indications only
Ion Exchange Resins: e.g. Prussian Blue (ferric ferrocyanide)

- FDA approved, 2003
  - Prescription drug available in Strategic National Stockpile
- Indicated for Cesium and Thallium
- Dosage
  - Oral, adults 3 grams tid (18 capsules) per day; ages 2-12, 1 gram tid (6 capsules) per day, possibly for weeks
- Side Effect: Possible constipation
- Reduces $^{137}\text{Cs}$ biological half-time to <30% previous value
DILEMMAS

- Rapid diagnosis
  - Where to send specimens?
  - Location and use of whole body counters?
- When to treat? 5-10 x Annual Limit?
- When to stop treatment?
- Special populations, e.g. children, pregnant females, elderly
<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium Iodide (KI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prussian Blue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Remember FDA Indications?

<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>DTPA</td>
<td>Plutonium</td>
<td>Rx SNS*</td>
</tr>
<tr>
<td></td>
<td>Americium</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Curium</td>
<td></td>
</tr>
<tr>
<td>Potassium Iodide (KI)</td>
<td>Radioiodides</td>
<td>OTC SNS</td>
</tr>
<tr>
<td>Prussian Blue</td>
<td>Cesium</td>
<td>Rx SNS</td>
</tr>
<tr>
<td></td>
<td>Thallium</td>
<td></td>
</tr>
</tbody>
</table>

* SNS is the Strategic National Stockpile
Treatment of Fission Products?

- No specific drug since there may be dozens of isotopes present
- Prevent inhalation and ingestion
- Shelter in place
- External decontamination
- Consider irrigation, cathartics and laxatives
Topics

Acute Radiation Syndrome (ARS)
- Definition and diagnosis
- Treatment

External and Internal Contamination
- Definition and diagnosis
- Treatment

Examples, Follow-Up Care, Research Areas
Examples of Medical Response to Radiation Accidents

- 1986 Chernobyl, Ukraine (former USSR)
- 1987 Goiânia, Brazil
- 1999 Tokaimura, Japan
CHERNOBYL
April 1986
Worst Radiation Accident in History

Photo: Monitoring Chernobyl Reactor from Helicopter

Adapted from AFRRI
Chernobyl
Medical Response

• 500 personnel hospitalized
  – > 100 personnel received > 1 Gray
• Intensive Supportive Care
  – Clean environment / isolation
  – Prophylactic and therapeutic antimicrobials
  – Transfused RBC and platelets
  – “High rate of survival up to 6 Gray”

Chernobyl: Bone Marrow Transplants

- 13 transplants for victims with doses 5.6 – 13 Gy
- 2 survivors (as of 1989 after doses of 8.7 & 5.6 Gy)
- **Causes of Death**
  - Burns 5
  - Interstitial pneumonitis 3
  - Graft versus Host Disease 2
  - Renal failure & ARDS 1
  - **11 deaths**

- **Conclusion**: No clear evidence that bone marrow transplants were beneficial

Chernobyl at 20+ Years

- About **50 deaths** due to radiation injury
- **4000+ childhood thyroid cancer**
- Long-term **psycho-social impact**
  - Evacuation of 135,000
  - Victim mentality
  - Expecting medical problems
  - Socio-economic problems

Chernobyl Forum, 2005.
Goiânia, Brazil, September 1987

“Worst radiation accident in the Western Hemisphere”

Source: Science, 1987

~ 2.5 cm diameter
~ 1400 Ci, Cesium-137 as CsCl salt (powder)
Goiânia Cesium-137 Incident: Dirty bomb scenario?

• 130,000 people (10%) came to ER /temporary screening locations
• 250 (0.2%) were contaminated
• 20 (0.01%) required treatment
Goiânia Cesium-137 Incident: Dose/Therapy Information

- 20 patients, ARS dose exposure: 1 - 7.1 Gy
- Internal contamination: + urine
  + stool
  + perspiration
- Treatment
  Chelation therapy: Prussian Blue
  Infection/sepsis: antibiotics, antifungal, antiviral
  Bone marrow stimulation: GM-CSF
- Outcome: 4 deaths (4-6 Gy)

IAEA Pub “The Radiological Accident in Goiania”, 1988
available at www-pub.iaea.org
Tokaimura, Japan 1999

Incident: Criticality accident
Tokaimura, Japan: Patient A

- Patient A holding funnel
- Estimated dose 16-25 Gy-Equivalent
- Rapid loss of consciousness
- Suffered from cutaneous radiation burns, and intestinal, renal and respiratory impairment
- Numerous problems with vascular hyperpermeability

Adapted from AFRRI
Patient A Interventions

- Cytokines (G-CSF)
- Peripheral stem cell transfusion from HLA-identical sibling
- Digestive tract decontamination
- Crypt cell stimulation with L-glutamine
- High dose pentoxyphylline to control vascular injury
- Expired 84 days after exposure from cardiac event
Tokaimura, Japan: Patient B

- Patient B pouring uranium
- Estimated dose 6-10 Gy-Equivalent
- GI tract decontamination
- Crypt cell stimulation with L-glutamine
- G-CSF cytokine bone marrow stimulation
- Cord blood cell transfusion
- Vascular injury control with high-dose pentoxiphylline

Adapted from AFRRI
Patient B Interventions (contd)

- Severe cutaneous burns required multiple skin grafts
- Developed radiation pneumonitis and pulmonary hemorrhage
- Expired 7 months after incident in April 2000
Long Term and Follow-Up Care

• Multiple Organ Dysfunction: pulmonary, hepatic, renal and cardiac failure

• Possible late effects
  – Malignancies: Leukemia early, then breast, intestinal, lung, thyroid etc.
  – Cataracts, sterility
  – In-utero and childhood effects
  – Psychosocial

• Need long term screening
Research Areas

• Biodosimetry
  – Genomic and proteomic predictors of dose
  – High through-put screens

• Radiation mitigators and protectants
  – Amifostine - no
  – Improved chelating agents
  – Captopril, statins, vitamins, etc.
Summary of Topics Covered:

Acute Radiation Syndrome (ARS)
- Definition and diagnosis
- Treatment

External and Internal Contamination
- Definition and diagnosis
- Treatment

Examples, Follow-Up Care, Research Areas

Questions?