Pharmacotherapy

1. Internal Contamination

a. Time-dependent phenomenon

b. Related to physical properties of isotope

c. Incorporation can occur rapidly

2. Internal Contamination: Diagnosis

a. Exposure history

b. Physical exam

c. Laboratory studies
- Complete blood count
- Urinalysis

3. Treatment for Internal Contamination

a. Gastric lavage and catharsis
- Recommended treatment for cobalt 60, phosphorus 32, and radium 226
- Radium 226 ingestion – 10% magnesium sulfate solution

b. Activated charcoal
- May have limited or no significant efficacy in radionuclide GI decontamination

c. As necessary
- Anti-emetics
- Anti-diarrheals
- Replace fluids and electrolytes

d. Decisions may have to be based on:
- History only suggestive of exposure
- Incomplete laboratory data

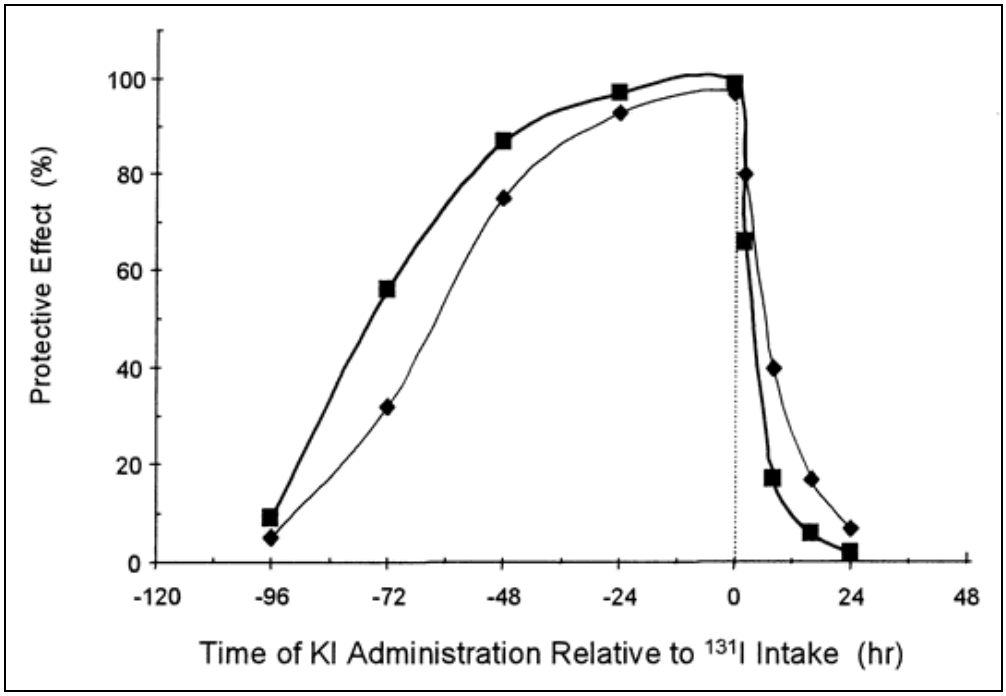
e. Treatment modalities:
- Prevent incorporation
- Remove radioactive isotopes

f. Pharmacotherapy
- Potassium Iodide or KI
- Prussian Blue
- Diethylenetriaminepentaacetate (DTPA)
- Granulocyte colony stimulating factor, filgrastim

g. Mass Casualty Implications
- Demand for drugs may exceed initial supplies
- Quantities - Strategic National Stockpile
- Not all individuals exposed will be candidates for drug therapy

4. Potassium Iodide

a. IOSAT™; ThyroSafe™; Thyro-Block™
b. ThyroShield™ solution for children
c. Orally administered radioactive iodine blocking agent
d. Prevents radioactive iodine uptake in thyroid gland by competing for binding sites
e. Radioactive iodine release scenarios
   - Nuclear power plant incident
   - Detonation of improvised nuclear device
   - "Dirty bomb" is unlikely source
f. Blockade of radioactive iodine uptake is time-dependent
   - KI is 80% effective at 2 hours post-exposure; 40% effective at 8 hours



Source: Potassium Iodide as a Thyroid Blocking Agent in Radiation Emergencies [2001]. http://www.fda.gov/cder/guidance/4825fnl.pdf

g. Thyroid of fetus and young children more sensitive to carcinogenic effects of radioiodine
   - Radioiodine uptake inversely proportional to thyroid size

h. Administration guidance available from US Food and Drug Administration (FDA)

5. Additional guidance on KI

http://www.fda.gov/cder/guidance/4825fnl.pdf

6. Prussian Blue

a. Ferric (III) hexacyanoferrate (II) (Radiogardase®)

b. Orally administered decorporation agent (capsules)

c. Promotes fecal excretion of radioactive cesium and thallium

d. Binds isotopes in gastrointestinal tract via ion-exchange, adsorption, and mechanical trapping; limits entero-hepatic recirculation

e. Does not treat complications of radiation exposure
   - Need concomitant supportive care
     - antibiotics
     - antiemetics
     - nutritional support
     - IV fluids
     - irradiated blood products/filtered transfustions

f. Recommended for internal contamination ≥ 10 times the annual limit of intake

g. Requires a Health Physicist to assess

h. Treat until body burden ≤ 1 annual limit of intake

i. Initiate treatment as soon as possible

j. Treat for minimum of 30 days
   - Duration based on level of contamination

7. Additional guidance on Prussian Blue

http://www.fda.gov/cder/drug/infopage/prussian_blue/default.htm
http://www.bt.cdc.gov/radiation/prussianblue.asp
http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202737.html
http://www.orau.gov/reacts/prussian.htm

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8. DTPA - Diethylenetriaminepentaacetate

a. Calcium (Ca) and zinc (Zn) salts
b. Intravenous chelating agents for plutonium, americium, curium
c. DO NOT USE for uranium, neptunium
d. Ca-DTPA
   - Within 6 hours of exposure is most effective
   - Initially 10x more effective than Zn-DTPA
   - At 24 hours post-exposure Zn-DTPA and Ca-DTPA have equal efficacy
   - With chronic use, Ca-DTPA causes depletion of zinc and magnesium
   - Use Ca-DTPA during first 24 hours, then replace with Zn-DTPA
e. Ca-DTPA contraindications
   - Minors, pregnant women, serious kidney disease, bone marrow suppression
   - Check renal function prior to each administration
   - Discontinue if
     - proteinuria
     - hematuria
     - casts

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9. Additional Guidance on DTPA

http://www.fda.gov/cder/drug/infopage/dtpa/default.htm
http://www.orau.gov/reacts/calcium.htm
http://www.orau.gov/reacts/zinc.htm
http://www.bt.cdc.gov/radiation/dtpa.asp

10. Filgrastim -Colony Stimulating Factors (CSF)

a. Endogenous glycoproteins

b. Induce hematopoietic progenitor cells of bone marrow to proliferate and differentiate into specific mature blood cell types

c. Filgrastim [Granulocyte-CSF (G-CSF)]
- Genetically engineered protein
- Daily IV or IM administration
- Minimal effect on hematopoietic cell types other than neutrophil progenitors

d. FDA-approved for treatment of neutropenia resulting from myelosuppressive cancer therapy

e. Not approved for treatment of ARS

f. Recommended for adults with moderate to severe ARS

g. Discontinue use when absolute neutrophil count rebounds to 1,000 cells per µL

h. Has been used as investigational drug for persons with unintentional radiological exposures

i. Side effects
- Allergic reactions (< 1 in 4,000 patients)
  - Good response to antihistamines, steroids, bronchodilators and/or epinephrine
  - ~50% have recurrence on re-exposure
- Fatal and non-fatal splenic rupture
- Severe sickle cell crises in patients with sickle cell disease

11. Additional Guidance on Filgrastim

http://www.bt.cdc.gov/radiation/neupogenfacts.asp
http://www.accessdata.fda.gov/scripts/cder/onctools/labels.cfm?GN=Filgrastim

12.SUMMARY

a. Pharmacotherapy must be administered quickly after exposure
b. May need to begin treatment in the absence of a definitive diagnosis
c. Match the treatment to the exposure
d. Guidance is available from the FDA and CDC concerning appropriate administration

From "*Medical Management of the Acute Radiation Syndrome: Recommendations of the Strategic National Stockpile Radiation Working Group*"
http://www.annals.org/cgi/reprint/140/12/1037.pdf

"Barriers to the provision of optimal care [in a radiation mass casualty event] include limitations of resources, loss of infrastructure, a high volume of victims, and presence of combined injury.

Allocation of potentially limited resources should be determined by the number of victims and their long-term prognosis.

Estimation of individual radiation dose is recommended for determining survivability of patients in a range of doses that indicate predisposition to the acute radiation syndrome.

Treatment recommendations are based on this dose range, which becomes increasingly narrower as the number of casualties increases and with the occurrence of combined injuries."

Source: "Radiological and Nuclear Terrorism: Medical Response to Mass Casualties," a self-study training program for clinicians, developed by the Centers for Disease Control and Prevention, 2006.

For copies of this product, email cdcinfo@cdc.gov.

To learn more about responding to a radiological incident, visit http://www.bt.cdc.gov/radiation