

Radiation Medical Countermeasures

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Disclosure Statement 3

- This presentation includes a discussion of Neupogen® its use in the treatment of patients diagnosed with Acute Radiation Syndrome (ARS).
- The use of this drug for the treatment of ARS has not been approved by the US Food and Drug Administration (FDA).
- However, in the event of a nuclear/radiological emergency, the Centers for Disease Control and Prevention can distribute Neupogen® from the Strategic National Stockpile under an Emergency Use Authorization approved by the FDA.

Outline

- **Decision-making criteria for using medical countermeasures**
- **Uses and limitations of medical countermeasures**
- **Importance of understanding SNS deployment procedures**
- **Public health prevention measures**

Decision-Making

Two key questions :

1. Is there evidence that victims of a rad/nuc emergency have become internally contaminated?
2. What radioisotopes were released?

Decision-Making

Key Question #1:

Is there evidence of internal contamination?

- Not simple to answer
- Requires sophisticated testing
- Assume when *external* contamination has occurred, some subset may also be *internally* contaminated
- Requires working with health physicists

Decision-Making

Key Question #2:

What radioisotopes were released?

- Optimal treatment depends on radioisotope identification
- Rad/nuc incidents (e.g., dirty bomb detonation) may involve more than one radioisotope
- Nuclear incidents produce & release multiple radioisotopes
- Countermeasures become less effective over time

Decision-Making

- **Partnerships**

- **State & local radiation control professionals**

- **Regional, State, local and tribal public health officials**

Radiation Medical Countermeasures

- **Strategic National Stockpile (SNS)**
 - DTPA (calcium and zinc)
 - Prussian blue
 - Neupogen® (Filgrastim)
- **Non-SNS**
 - Potassium iodide (KI)

Radiation Medical Countermeasures

- **Internal contamination Rx**
 - Potassium iodide (KI)
 - DTPA
 - Prussian blue
- **Acute Radiation Syndrome (ARS) Rx**
 - Neupogen[®]

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Overview**

- **No longer stockpiled in the SNS**
- **FDA-approved blocking agent**
- **Used to prevent adverse health effects caused by internal contamination from radioactive iodine**

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Mechanism of action**
 - Radioactive iodine enters body through lungs or digestive tract
 - Thyroid gland avidly takes up iodine
 - KI temporarily saturates the gland preventing incorporation of radioactive iodine

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Delivery**

- KI comes in two FDA-approved oral formulations: tablet and liquid

- **Treatment Considerations**

- Children under 18 years have the highest risk for thyroid cancer from radioiodine
- Pregnant women should also receive KI

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Window of Effectiveness**
 - **Narrow time window**
 - **KI is ineffective if taken more than 4-6 hours after internal contamination has occurred**

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Summary**

- **Public health officials should**

- **Consider KI a “supplementary public health measure”**
- **Develop primary prevention measures, e.g. issue orders to shelter-in-place when planning to protect the public from release of radioiodine**

Radiation Medical Countermeasures

Potassium iodide (KI)

- **Additional Resources**

- <http://hps.org/documents/kifactsheetdetail.pdf>
- <http://hps.org/documents/kifactsheetbrief.pdf>
- <http://remm.nlm.gov/potassiumiodide.htm#dose>

Radiation Medical Countermeasures

Diethylenetriameneacetate (DTPA)

- **Overview**

- Stockpiled with SNS & also being forward deployed
- FDA-approved chelating agent
- Comes in two forms: calcium & zinc
- Both forms used to treat internal contamination from plutonium, americium, and/or curium

Radiation Medical Countermeasures

DTPA

- **Mechanism of Action**
 - Chelating agent
 - Both forms of DTPA bind to and facilitate a more rapid elimination from the body of
 - *Plutonium*
 - *Americium*
 - *Curium*

Radiation Medical Countermeasures

DTPA

- **Delivery**
 - **Given via intravenous (IV) route once a day**
 - **One or more doses may be required**
 - **Can be delivered via inhaler but there are cautions and caveats**

Radiation Medical Countermeasures

DTPA

- **Window of Effectiveness**
 - Works best if given shortly after internal contamination
 - After 24 hours, chelation is more difficult
 - DTPA can still remove radioisotopes *days to weeks* after internal contamination
 - Do not withhold DTPA even after 24 hours

Radiation Medical Countermeasures

DTPA

- **Additional Resources**

- www.fda.gov/cder/drug/infopage/dtpa/default.htm
- www.emergency.cdc.gov/radiation/dtpa.asp
- <http://orise.orau.gov/reacts/ca-dtpa.htm>
- <http://orise.orau.gov/reacts/zinc-dtpa.htm>

Radiation Medical Countermeasures

Prussian blue

- **Overview**

- **Stockpiled in SNS**
- **FDA-approved binding agent for treatment of internal contamination with radioactive cesium and radioactive (and non-radioactive) thallium**

Radiation Medical Countermeasures

Prussian blue

- **Mechanism of Action**
 - **Binds to radioactive cesium and to radioactive and non-radioactive thallium within digestive tract**
 - **Prevents cesium and thallium from being (re-) absorbed into bloodstream**

Radiation Medical Countermeasures

Prussian blue

- **Delivery**
 - Orally, three times a day
- **Window of Effectiveness**
 - Following a diagnosis of internal contamination, Prussian blue should be given as soon as it becomes available

Radiation Medical Countermeasures

Prussian blue

- **Additional Resources**

- www.fda.gov/cder/drug/infopage/prussian_blue/default.htm
- www.emergency.cdc.gov/radiation/prussianblue.asp
- <http://remm.nlm.gov/prussianblue.htm>
- <http://orise.orau.gov/reacts/files/prussian-blue-pkginsert.pdf>

Radiation Medical Countermeasures

Limitations of Treatment

- **KI, DTPA, & Prussian blue CANNOT**
 - Prevent radioisotopes from entering the body
 - Be used to treat all radioisotopes
 - i.e., countermeasures are specific in their action
 - Treat or reverse adverse effects caused by radioisotopes that have already entered the body
 - Treat Acute Radiation Syndrome (ARS)

Radiation Medical Countermeasures

Acute Radiation Syndrome (ARS)

- **What is ARS?**
 - **Illness caused by high dose, whole-body radiation exposure**
 - **Adverse effects worsen with dose**
 - **Chances for recovery diminish as signs and symptoms of ARS become more severe**

Radiation Medical Countermeasures

Acute Radiation Syndrome (ARS)

- **Physiological Effects**

- **Bone marrow suppression**

- Bone marrow is source of white blood cells, red blood cells, and platelets

- Radiation can wipe out bone marrow starting with the white blood cells

- **Gastrointestinal injury** ☠

- **Neurovascular injury** ☠

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Overview**

- Belongs to a class of drugs known as “colony stimulating factors”
- Used to improve chances of survival for victims of bone marrow suppression

- **Mechanism of Action**

- Stimulates remaining bone marrow to produce mature infection-fighting white blood cells

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Drug Status**

- **Stockpiled with SNS**
- **Not FDA-approved for treatment of bone marrow suppression following acute radiation exposure**
- **Would be administered as an Investigative New Drug (IND) or under Emergency Use Authorization (EUA) from FDA**
- **CDC currently holds both the IND & EUA applications with FDA**

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**

- **Not all radiation exposure victims will benefit**
- **Lower levels of radiation exposure may not completely suppress bone marrow**

- **Such victims can be treated with more common medical interventions**

- Antibiotics
- Antifungals
- Antivirals
- Nutritional and fluid support
- Pain control
- Psych support / counseling

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**
 - **Other victims less likely to benefit from bone marrow stimulation include**
 - **Persons receiving very high doses of radiation**
 - **Persons with combined injury**
 - **Conventional trauma + radiation exposure**

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**
 - **Decision to withhold Neupogen® from victims expected to have a poor prognosis may be based on**
 - **Magnitude of incident**
 - **Total number of victims relative to available resources**
 - **Extent of individual victim's injuries**

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**
 - **Victims with non-survivable ARS or combined injury still require medical treatment**
 - **Pain medication**
 - **Basic medical and nursing care**
 - **Counseling, pastoral, and psychiatric care**

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**
 - Neupogen® distribution determined by epidemiology of radiation incident
 - Radiation doses to victims of RDDs projected to be low
 - Few RDD victims would require treatment with Neupogen®

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**
 - Many more victims of larger scale events will need treatment with colony stimulating factors to improve survival chances
 - IND or nuclear attack generally regarded as less likely to occur
 - Expected need for Neupogen® will be based on how many have been exposed to high doses of radiation

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Treatment Considerations**

- **Measurements of radiation dose can be used to screen who is likely to develop ARS**
- **Public health officials need to collaborate with state and local radiation control program officers to obtain estimated exposure doses**
- **Public health officials can then work with healthcare providers to determine which victims are most likely to benefit from Neupogen®**

Radiation Medical Countermeasures

Neupogen® (Filgrastim)

- **Additional Resources**

- www.emergency.cdc.gov/radiation/neupogenfacts.asp
- www.accessdata.fda.gov/scripts/cder/onctools/labels.cfm?GN=Filgrastim
- www.neupogen.com/pi.html

Treatment Priorities

- Treatment of life-threatening illness and injury takes precedence over treatment of radiation contamination and illness
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Covert Sources

- **Covert sources may go undetected until adverse health effects are identified in the population**

Stockpiled Countermeasures

- **Contact your local SNS coordinator to learn how to**
 - **Request**
 - **Receive**
 - **Distribute**
 - **Dispense**

Prevention Initiatives

- **Public health priorities in rad/nuc**
 - **Prevent / mitigate exposure and contamination**
 - **Protective Action Recommendations**
 - **Shelter-in-place**
 - **Evacuation**
 - **Interdiction of food and drink**

Summary

- **Ask key questions to determine countermeasure needs**
 - Are victims internally contaminated?
 - What radioisotopes were released?
- **Call on colleagues and subject matter experts**
 - Collaborations are critical
 - Regional, state, local and tribal public health officials
 - Radiation control professionals

Summary

- **Plan ahead**
 - **Partner with radiation control program officials**
 - **Pre-establish emergency communication channels**
 - **Formalize radiation medical countermeasure request procedures**