

Medical Response to Radiation: Navigating Emergencies, Enhancing Survival



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Disclosure/Disclaimer

The opinions and assertions expressed herein are those of the author(s) and do not necessarily reflect the official policy or position of the Uniformed Services University or the Department of Defense.

The author has no conflicts of interest to report.

The author will discuss off-label uses of medications and medications currently in various stages of development.

Dr. Winfield Evans, PhD



- Born in January 23, 1923 in Hannah, OK
- Served in the US Army in Italy
- Texas Tech - BS Electrical Engineering (1948)
- MIT - MS Physics (1950)
- U of Oklahoma - PhD Physics (1966)
- Medical physicist at St. Anthony Hospital in Oklahoma City, OK
- 12th President of the SNMMI Southwestern Chapter
- Passed away September 24, 1989 in Hannah, OK

Objectives

- To identify the key signs and symptoms of acute radiation syndrome aiding in prompt patient triage and initial management.
- To describe the protocols for medical response to radiation exposure, including immediate and supportive care measures.
- To evaluate the effectiveness of current radiation prophylaxis and post-exposure treatments in mitigating the health impacts of radiation.

Introduction

**How comfortable do you feel
responding to a potential
radiation emergency?**

Chernobyl, Ukraine (1986)

- Chernobyl nuclear plant explosion
- 50-185 million Ci released
- Many with long-term effects



<https://www.theatlantic.com/photo/2019/06/chernobyl-disaster-photos-1986/590878/>



Goiania, Brazil (1987)

- ^{137}Cs source
- ^{137}mBa γ source
- 112K monitored



https://www-pub.iaea.org/MTCD/Publications/PDF/Pub815_web.pdf



Fukushima, Japan (2011)

- Tsunami-induced power loss
- Hydrogen gas explosions due to lack of cooling
- Deaths from disaster, evacuation and one from radiation



https://en.wikipedia.org/wiki/Fukushima_nuclear_accident



Nuclear Medicine Professionals

- Radiation Knowledge
 - Biology
 - Physics
 - Risks
 - Safety
- Radiation Expertise
 - Detection
 - Dosimetry



Image created by DALL-E

1st Attendance Code

1245

Acute Radiation Syndrome (ARS)

Acute Radiation Syndrome (ARS)

- Large radiation dose (> 0.7 Gy)
- External dose
- Penetrating radiation
- Whole body or $>70\%$ of the body
- Short dose time frame

ARS Phases

Time Course

Prodromal Phase

Nausea and Vomiting

Headache

Diarrhea

Fever

Loss of Consciousness

Latent Phase

Reduced or no symptoms

Manifest Illness

Dose-based Symptoms

- Hematopoietic
- Gastrointestinal
- Cerebrovascular

Recovery/Death

Long term effects

- Stochastic
- Deterministic

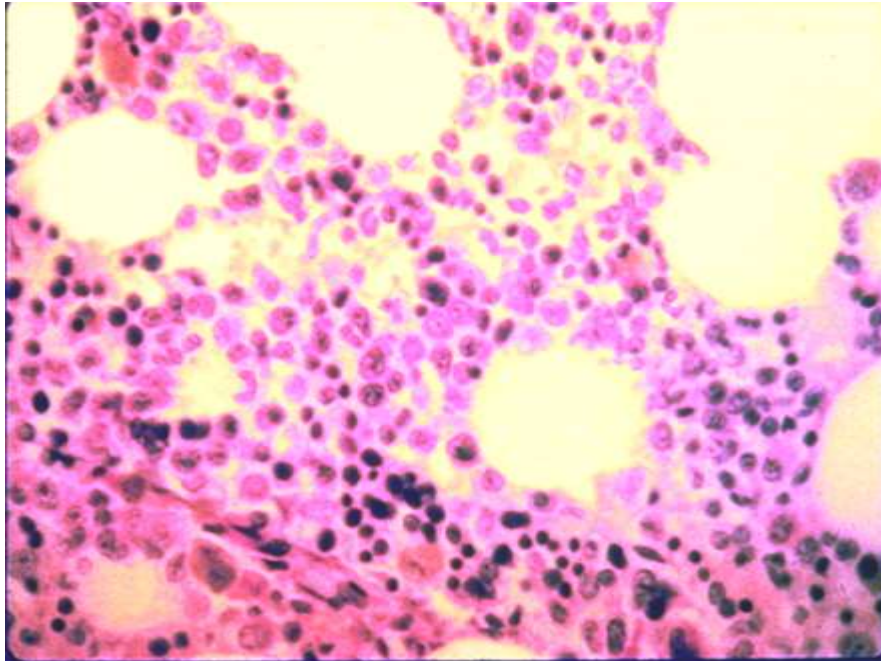
Death

ARS Subsyndromes

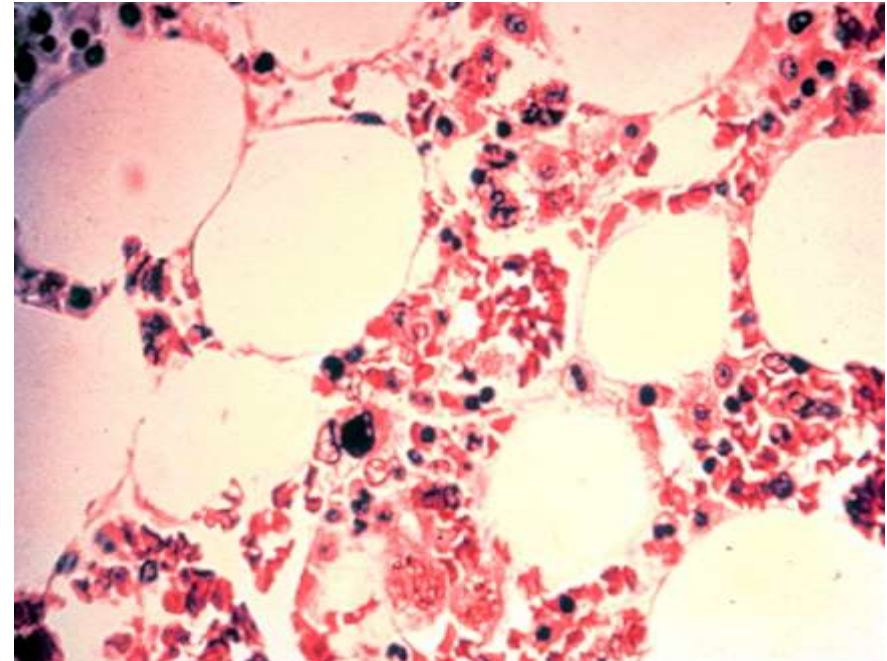
<u>Subsyndrome</u>	<u>Dose</u>	<u>Characteristic Findings</u>
Hematopoietic	0.7 - 5 Gy	Bone Marrow Failure, Pancytopenia
Gastrointestinal	6 - 9 Gy	Severe GI symptoms, GI Bleeding, Electrolyte Abnormalities, Sepsis
Neurovascular	> 10 Gy	Hemorrhagic stroke, Loss of Consciousness, Decreased BP

Hematopoietic Subsyndrome

Normal Marrow

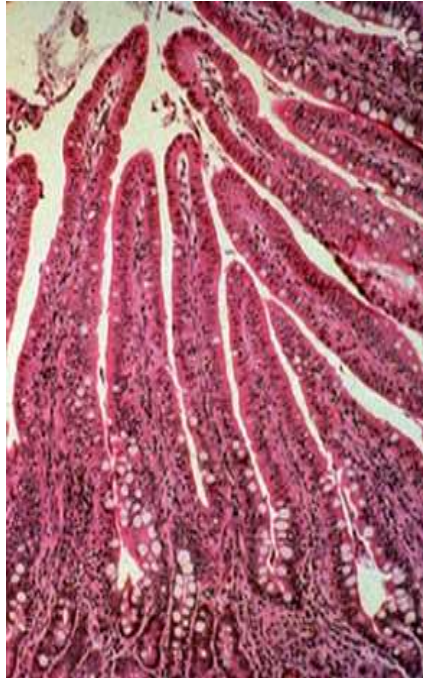


Irradiated Marrow

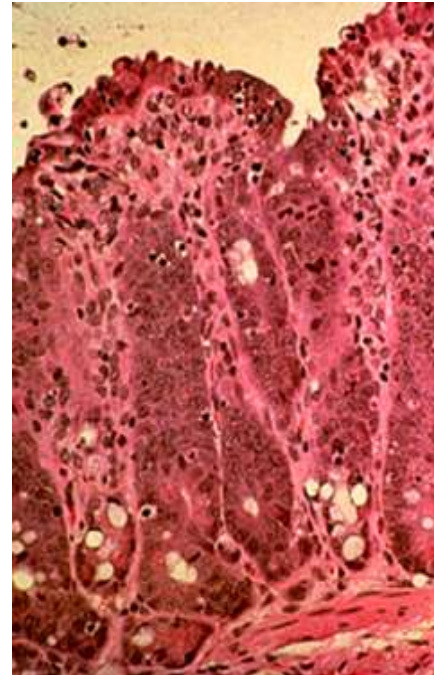


Gastrointestinal Subsyndrome

Normal GI Mucosa



Irradiated GI Mucosa



ARS Triage

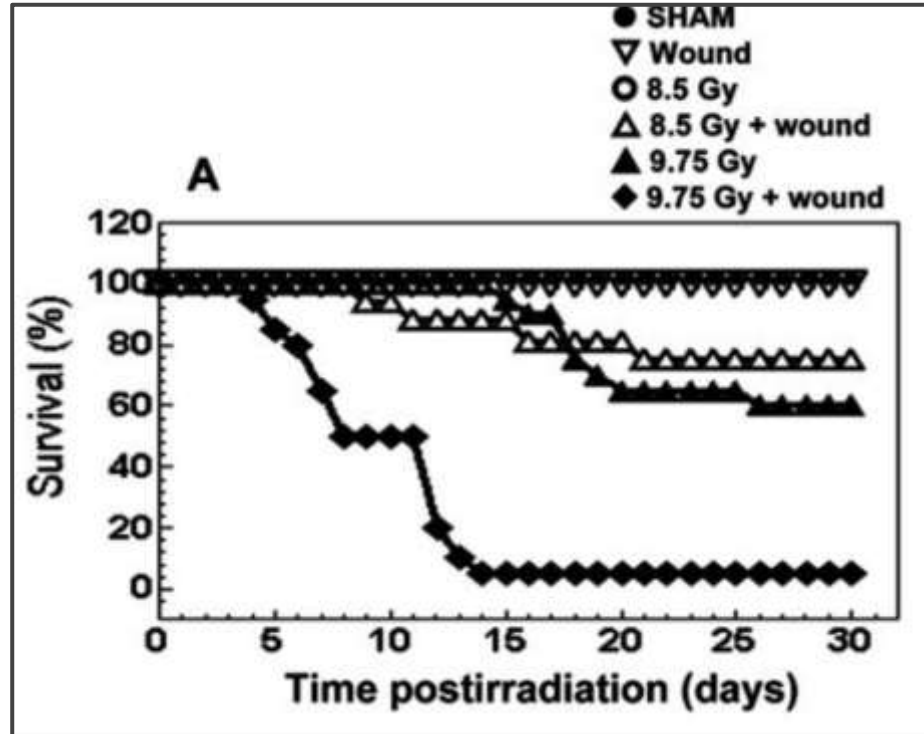
Triage Items

- Life-threatening injuries (ABCs)
- Combined injuries
- Internal contamination
- Time to emesis
- External contamination survey
- Shrapnel
- Lymphocyte depletion statistics



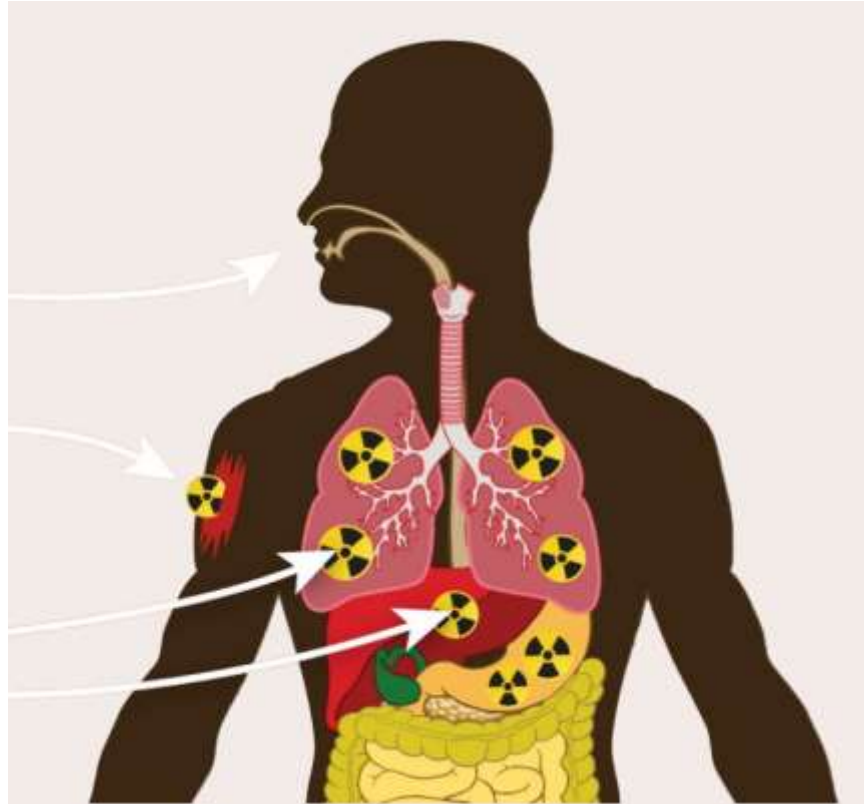
Image created by
DALL-E

Combined Injury



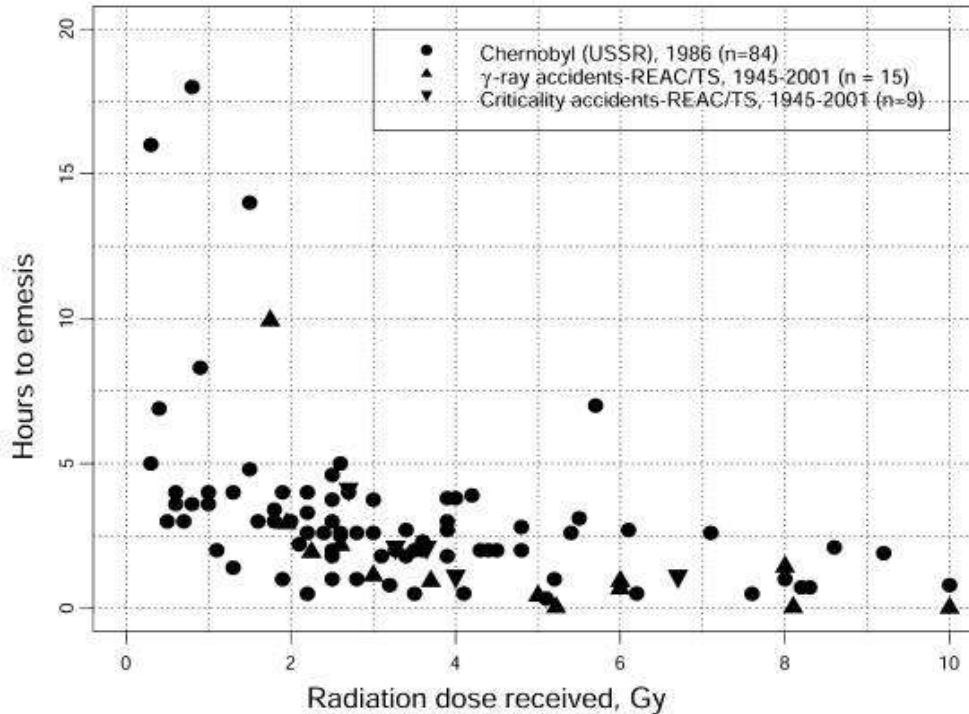
Kiang JG, Jiao W, Cary LH, et al. Radiat Res. 2010 Mar;173(3):319-32.

Internal Contamination



https://www.cdc.gov/nceh/multimedia/infographics/radiation_contamination_vs_exposure.html

Time to Emesis



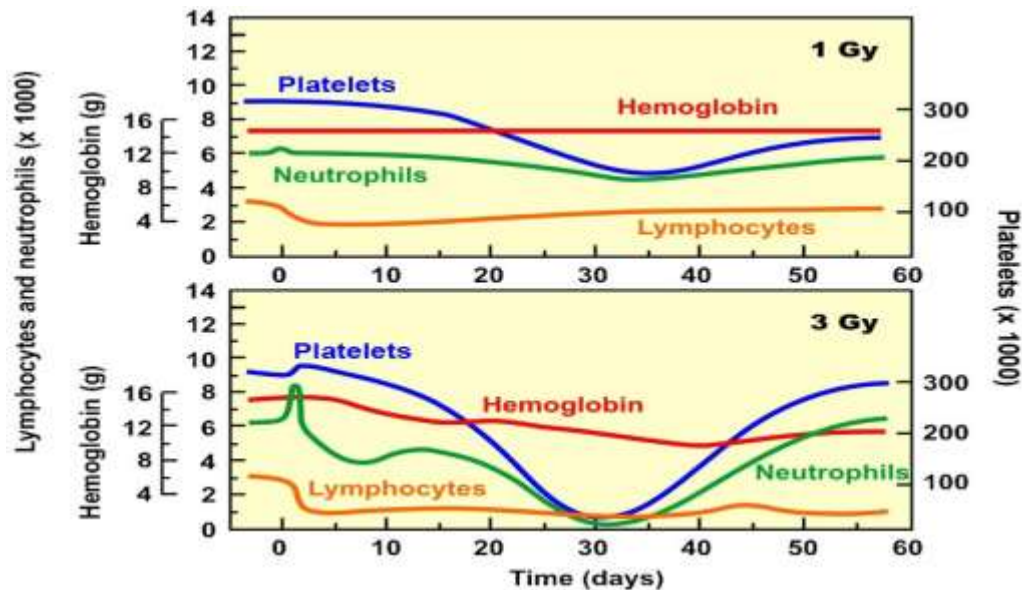
Demidenko E, Williams BB, Swartz HM. Radiat Res. 2009 Mar;171(3):310-9.

Shrapnel



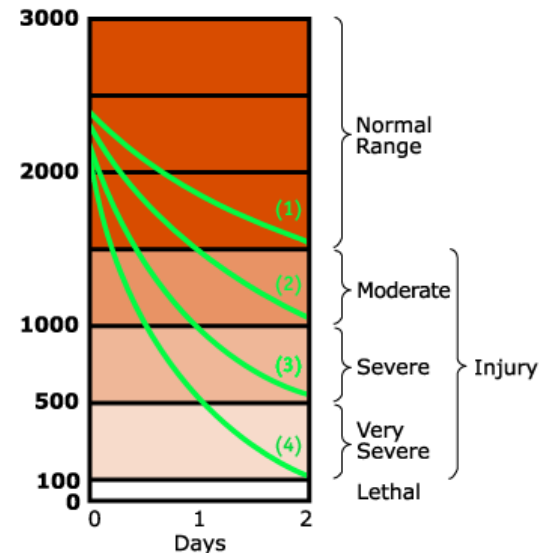
- Most significant radiation risk for providers
- Remove shrapnel with metal tongs/forceps
- Dispose in containers per Radiation Safety Officer

Lymphocyte Depletion



AFRRI research

Patterns of early lymphocyte response in relation to dose.



https://remm.hhs.gov/andrew_slymphocytes.htm

Radiation Emergency Triage

Immediate

- Life-threatening injuries
- Combined injuries
- Internal Contamination

Minimal

- Radiation exposure without injury
- Worried well

Delayed

- Evidence of radiation injury (ARS)
- Time to emesis < 4 hours
- Lymphocyte drop > 50% in 48 hrs

Expectant

- High dose (> 20 Gy)

Triage by Resource Availability

Triage Category and Myeloid Cytokine Recommendation Category^x with Combined Injury (Radiation Exposure ≥ 2 Gy and Trauma/Burn*)

Est. Radiation Dose (gray)	Moderate Trauma	Severe Trauma	Moderate Trauma	Severe Trauma
>10 Gy	Expectant ³	Expectant ³	Expectant ³	Expectant ³
≥ 6 Gy - 10 Gy	Delayed ²	Expectant ³	Expectant ³	Expectant ³
≥ 2 Gy - < 6 Gy	Immediate ¹	Delayed ²	Delayed ²	Expectant ³
	Resource Availability at Medical Venue: "Normal or Good" Standard of Care: Conventional to Contingency		Resource Availability at Medical Venue: "Fair or Poor" Standard of Care: Crisis	

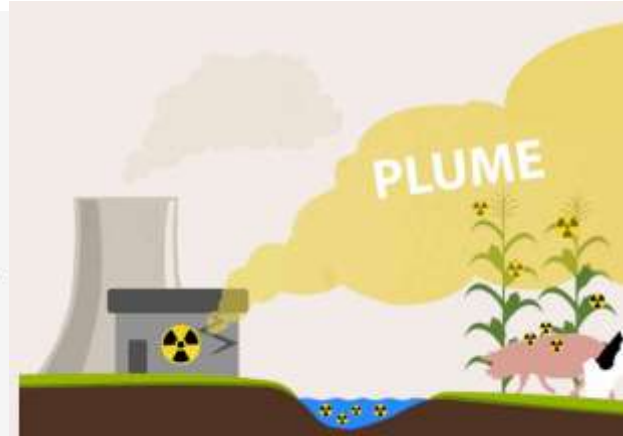
Initial Radiation Injury Management

Resources

- Armed Forces Radiobiology Research Institute (AFRRI)
 - Medical Radiobiology Advisory Team (MRAT)
 - <https://afri.usuhs.edu/>
- Radiation Emergency Assistance Center/Training Site (REAC/TS)
 - <https://orise.orau.gov/reacts/index.html>
- Radiation Emergency Medical Management (REMM)
 - <https://remm.hhs.gov/>
- Radiation Injury Treatment Network (RITN)
 - <https://ritn.net/>
- Centers for Disease Control and Prevention (CDC)
 - <https://www.cdc.gov/nceh/radiation/default.htm>

**Contaminated or Exposed,
how do we know?**

Radiologic Accidents



<https://www.cdc.gov/nceh/radiation/emergencies/resourcelibrary>

Radiologic Terrorism/War



<https://www.cdc.gov/nceh/radiation/emergencies/resourcelibrary>

Provider Protection



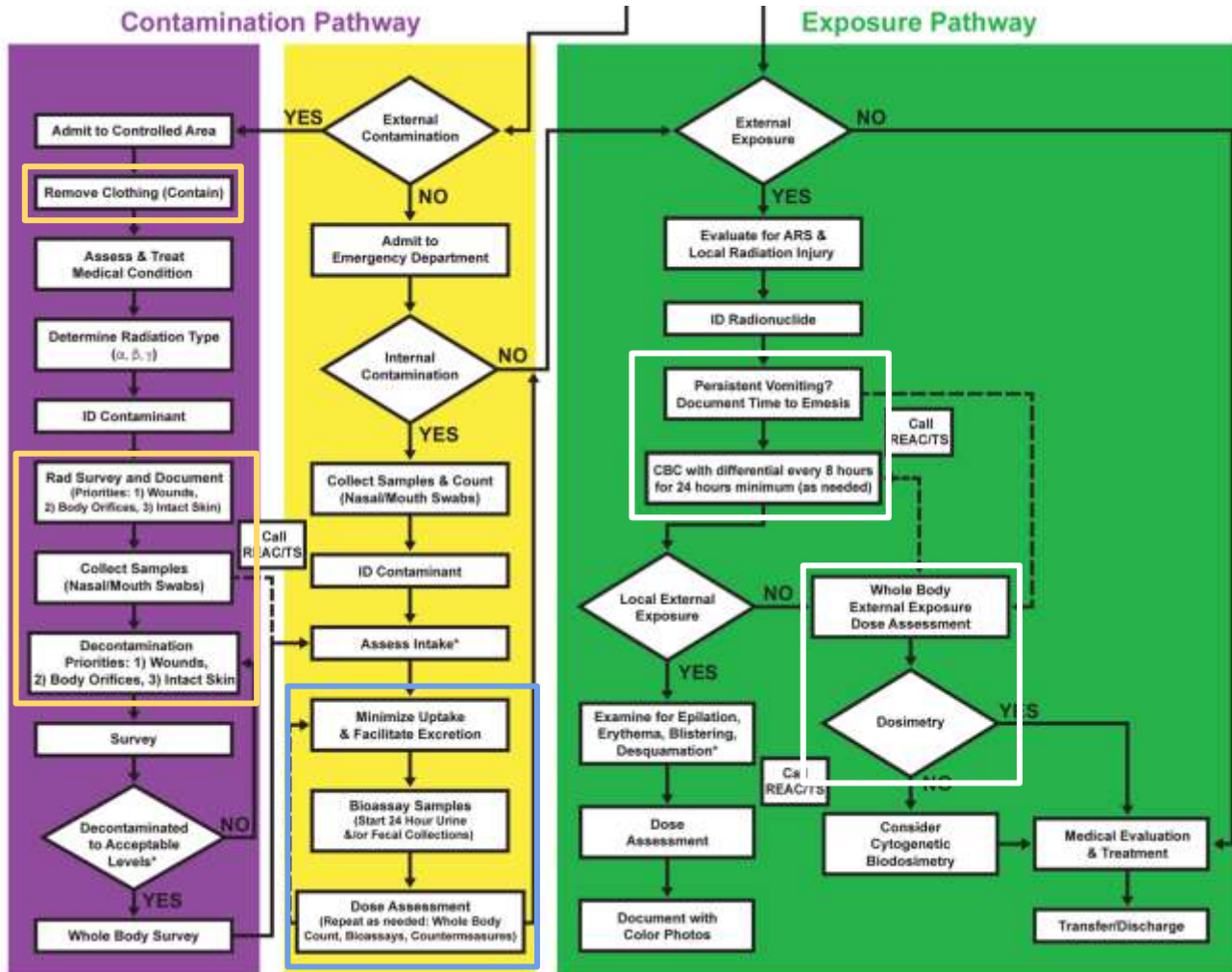
Class C (left)

- Consider for initial decontamination
 - Protects from airborne radioactive material
 - Protects from skin contamination
- Air-purifying respirator
- Face shield

Class D (right)

- Standard isolation PPE
- Utilize after initial decontamination
- Exposure-only concerns

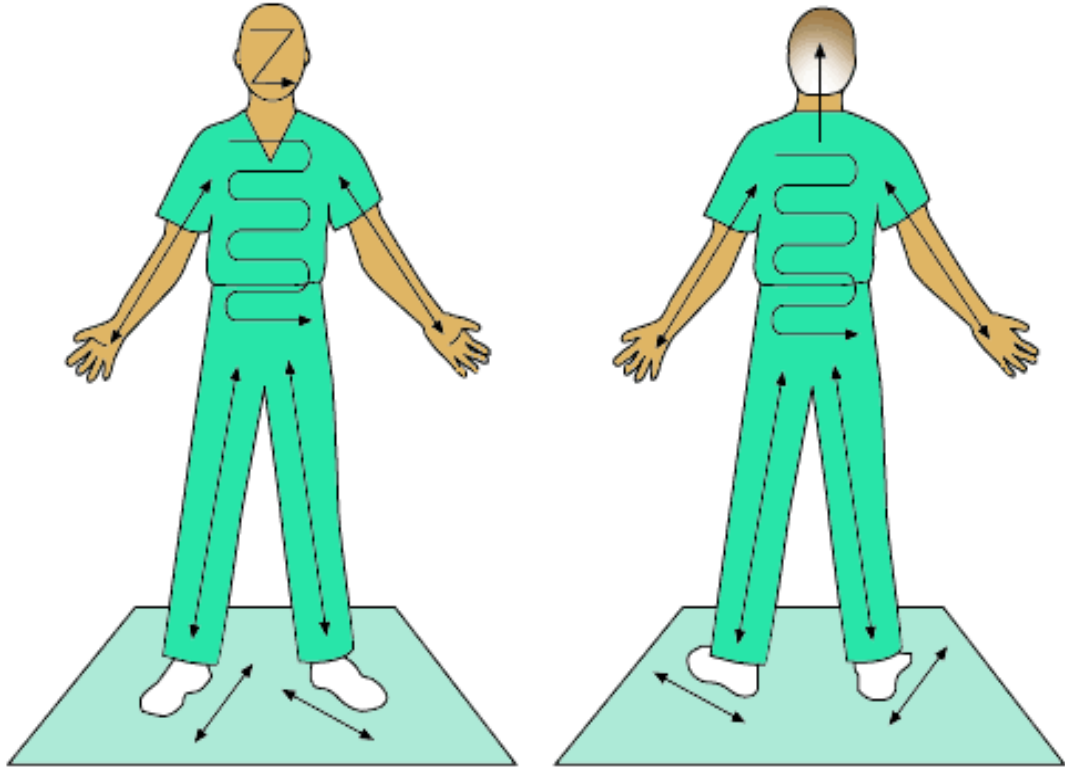




<https://orise.orau.gov/resources/reacts/document/s/radiation-patient-treatment-algorithm.pdf>

Removing a patient's clothing and washing their skin and hair removes >90% of contamination.

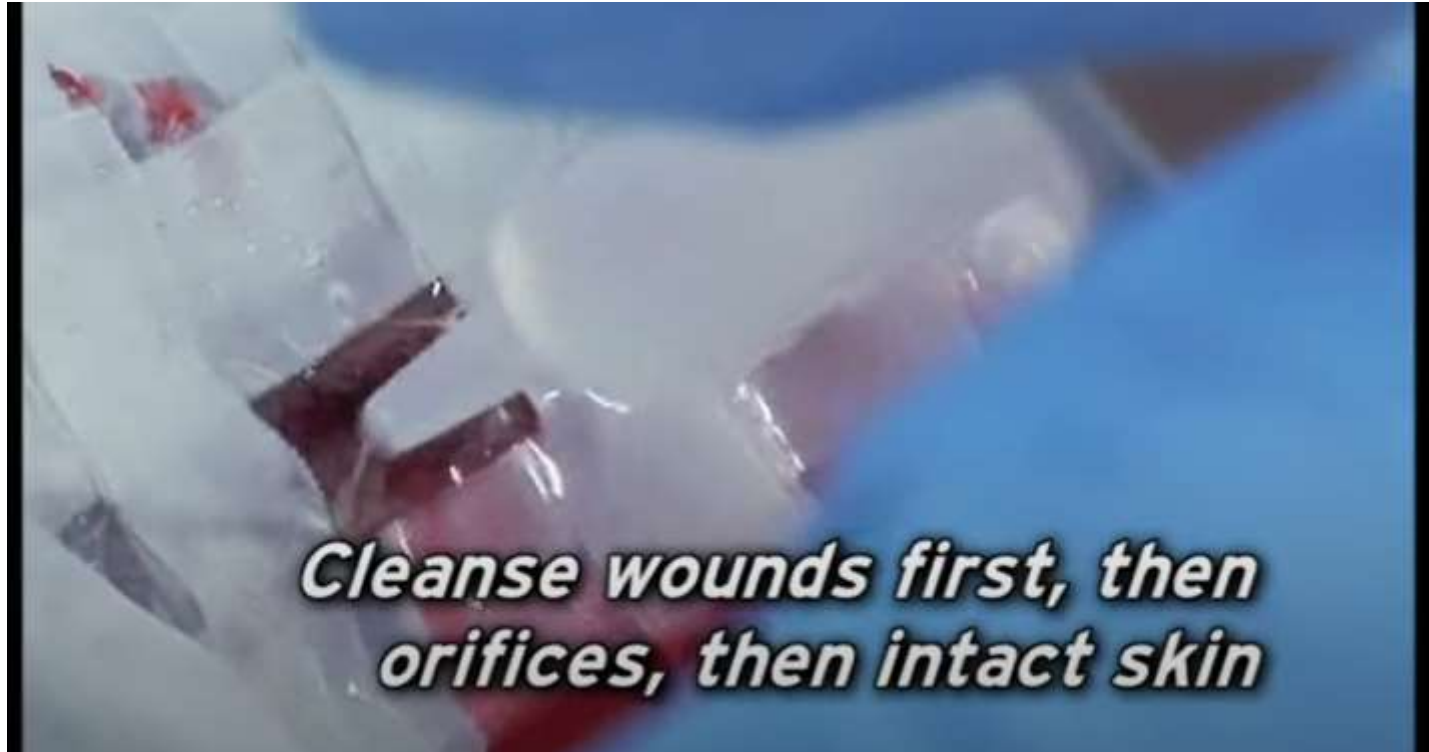
External Contamination Survey



Sample Collection



Prioritized Decontamination

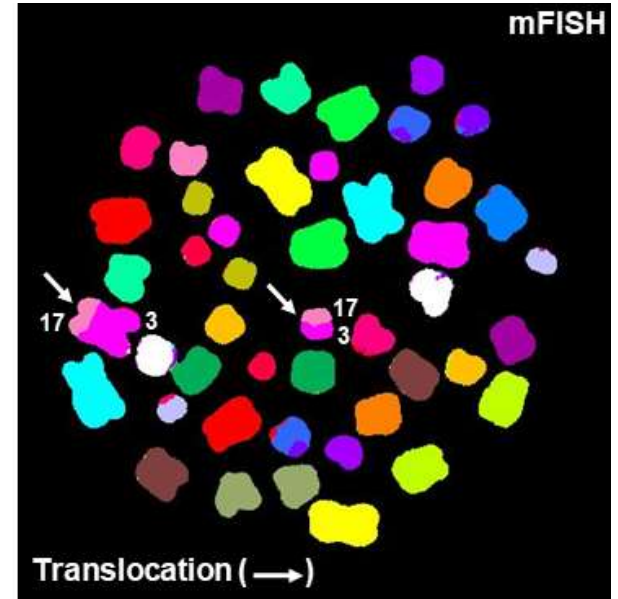
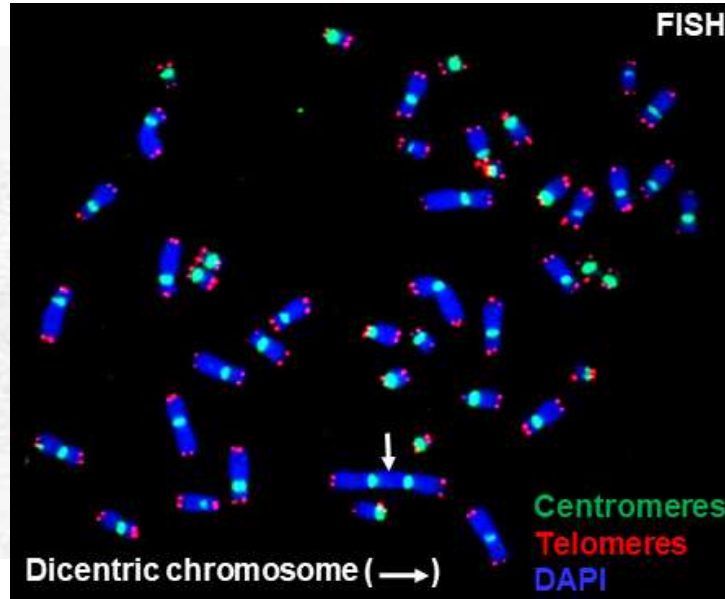
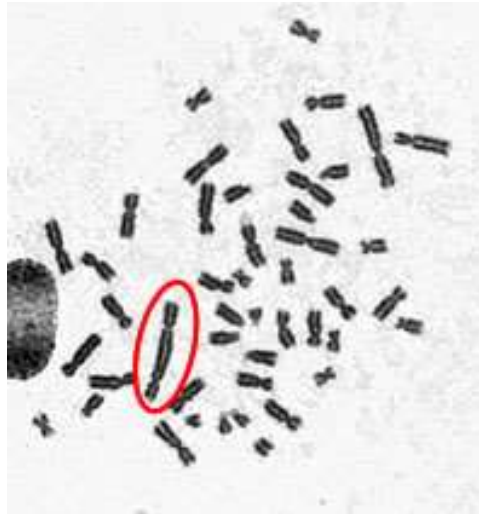


<https://www.cdc.gov/nceh/radiation/emergencies/justintime.htm>

Biodosimetry

- Low resources, rapid assessment
 - Time to emesis (< 4 hours, likely ARS)
- High resources, medium-term assessment
 - NM imaging and dosimetry techniques for internal contamination
- Low resources, 24-48 hour assessment
 - CBC with differential (48 hour lymphocyte depletion by 50%, > 4Gy dose)
- High resources, medium to long-term assessment
 - Dicentric Chromosome Assay (DCA)
 - FISH analysis of chromosome abnormalities
 - Electron Paramagnetic Resonance (EPR)

DCA and FISH



<https://remm.hhs.gov/aboutdicentrics.htm>

<https://orise.orau.gov/reacts/cytogenetic-biodosimetry-laboratory.html>

Medical Radiation Injury Management

Supportive Measures

- Anti-nausea
- IV Fluids and Electrolytes
- Blood Products
 - Irradiated
 - Leukocyte-reduced
- Antimicrobial prophylaxis
 - Neutropenic patients
- Psychological support



Transfusion Guidance

Criteria for Substitution Therapy for Hematopoietic Type Acute Radiation Syndrome

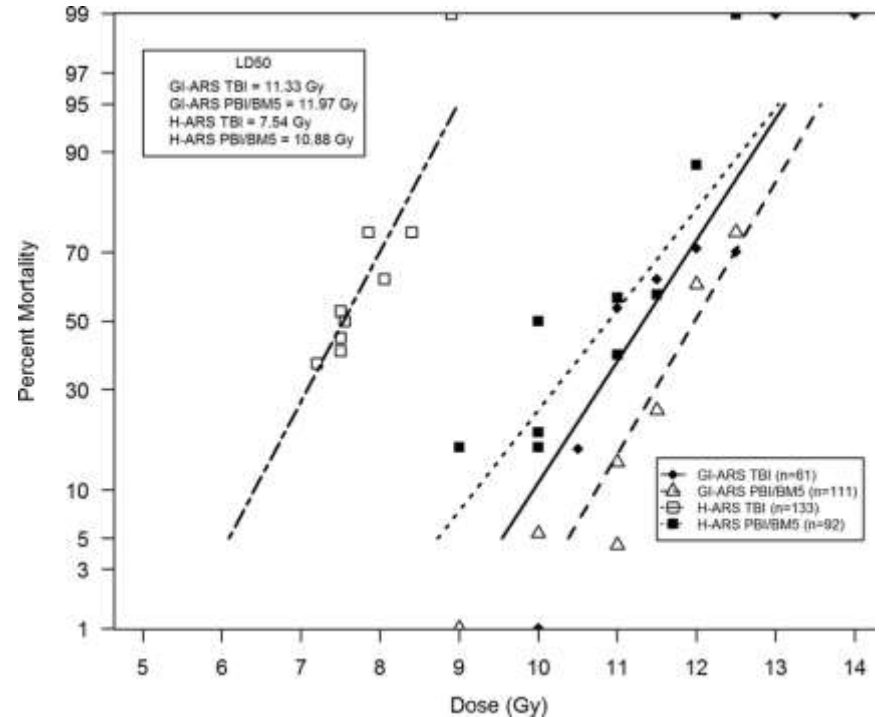
Patient's individual condition	Threshold value	Substitution therapy
Close monitoring possible, no other complication, no bleeding	Platelets: 10,000/ μ L	Irradiated and leukoreduced platelet concentrates
Close monitoring not possible, increased risk of manifest bleeding	Platelets: 20,000/ μ L	Irradiated and leukoreduced platelet concentrates
Additional trauma, surgery, mass transfusion, cerebral edema	Platelets: 50,000/ μ L	Irradiated and leukoreduced platelet concentrates
Anemia	Hemoglobin: 10 g/dL	Irradiated and leukoreduced packed red cells

Internal Contamination

- Radioiodines (^{131}I)
 - Potassium iodide (KI)
- Radiostrontium (^{90}Sr)
 - Calcium, strontium salts
- Tritium (^3H)
 - Fluids and diuretics
- Cesium (^{137}Cs)
 - Prussian Blue ion exchange
- Plutonium (^{239}Pu), Americium (^{241}Am), Curium (^{242}Cm)
 - Chelation (DTPA/EDTA)

Cytokine Countermeasures

- FDA-approved cytokines
 - Filgrastim (Neupogen®)
 - PEGylated filgrastim (Neulasta®)
 - Sargramostim (Leukine®)
- Predominantly promote neutrophils
 - Leukine promotes many cell lineages



MacVittie et al. 2015 Health Physics, 109 (5), 427-439.

Platelet Countermeasures

- FDA-approved thrombopoietin (TPO) receptor activator
 - Romiplostim (Nplate[®])
 - Promotes megakaryocytes and platelets
- Additional platelet promoters are in development, including recombinant TPO, TPO activators, and IL-11.

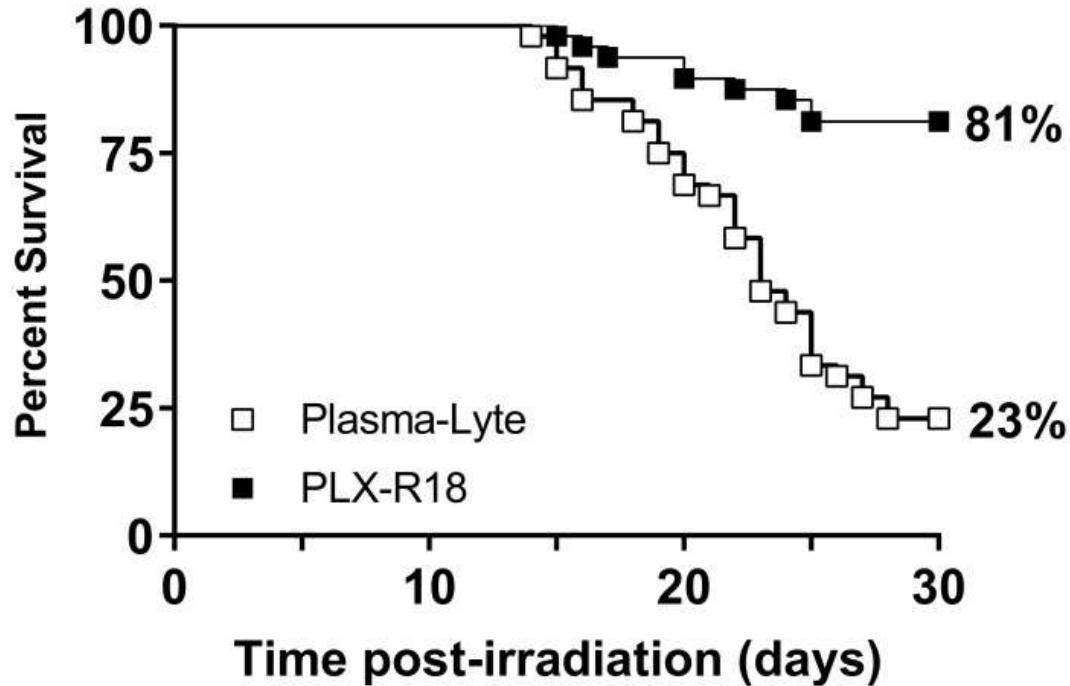
Drug	Irradiation dose	Drug dose (μg/kg)	Injection time post-irradiation (days)	Group size (n=)	Percent mortality	Platelet Nadir (×10 ⁹ /L)	Duration of thrombocytopenia (days)
Vehicle	~LD70/60	Vehicle	1	40*	67.5	12.5	3.8
Nplate	6.8 Gy	5	1	40*	27.5	36.3	1.3
Nplate + PEGfilgrastim		5 and 0.3	1 (both drugs), 8 (only PEGfilgrastim)	40*	12.5	31.5	1.1

MacVittie et al. 2015 Health Physics, 109 (5), 427-439.

Stem Cell Transplant

- Allogeneic and syngeneic stem cell transplants have been attempted in several cases of high radiation exposure.
- In a review of 29 historical bone marrow transplant cases
 - Three patients survived longer than one year
 - Many died from GI subsyndrome conditions, traumatic injuries, or graft vs host disease
 - Engraftment may occur around the same time as the patient's own bone marrow reconstitutes

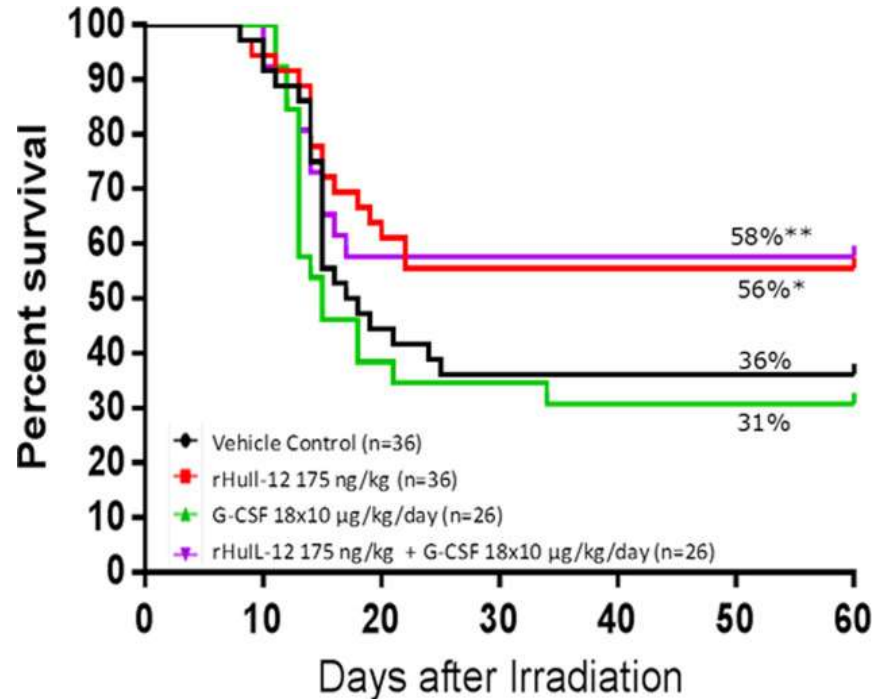
Stromal Cell Therapy



Kumar VP, et al. Genes (Basel). 2022 Sep 28;13(10):1756.

IL-12 Countermeasure

- rhIL-12 (HemaMax[®])
- Pro-inflammatory cytokine
 - Improves hematopoiesis
 - Improves GI function
 - Improves survival



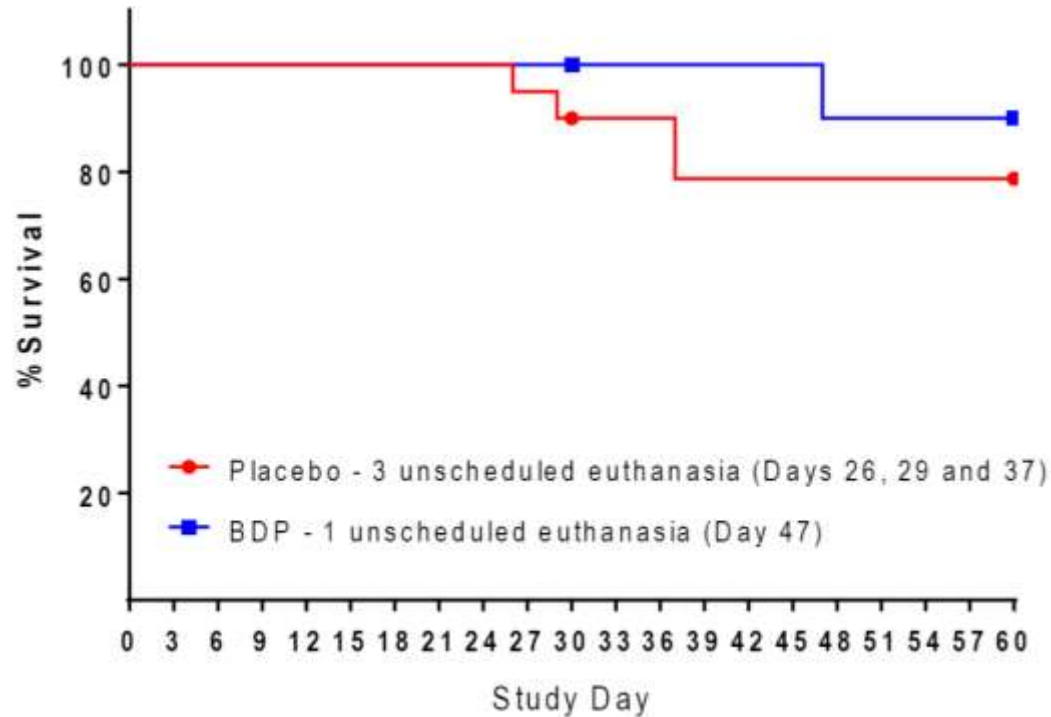
Gluzman-Poltorak Z et al. American journal of hematology. 2014 Sep;89(9):868-73.

BIO300 Countermeasure

- Genistein (BIO300[®])
 - Phytoestrogen that binds ERs
 - Protects progenitor cells from radiation damage
 - Increases cell cycle checkpoints and DNA repair enzymes
 - Captopril combination increases radioprotection
 - Antioxidant properties
 - Mitigates radiation-induced pneumonitis/fibrosis

Singh VK, Seed TM. Expert Opinion on Investigational Drugs. 2020 May 3;29(5):429-41.

OrbeShield® for GI-ARS



Measey T et al. Poster presented at the Radiation Research Society 62 Annual International Meeting, 2016

Prophylactic Medications

- Several prophylactic radioprotectants are in research:
 - Piperazine derivatives
 - Chlorobenzylsulfones (example Ex-RAD)
 - Aminothiols (example amifostine)
 - Enalapril

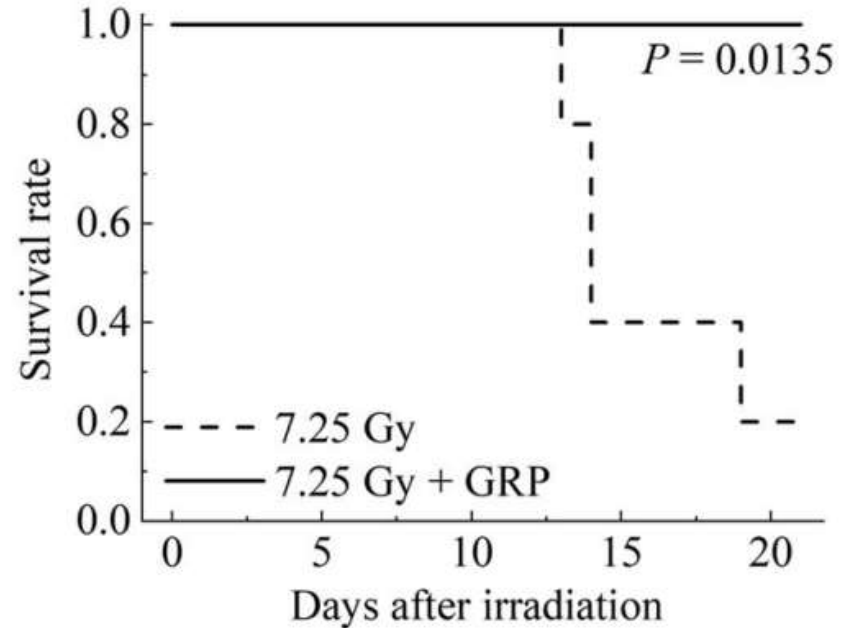


Singh VK, Seed TM. International Journal of Radiation Biology. 2021 Nov 2;97(11):1526-47.

https://www.draeger.com/en-us_us/Safety/Federal-Government-Solutions/Military/NBC-CBRN-Protection

Combination Therapies

- ARS is complicated, impacting many systems.
- Combination therapies likely address the multi-system effects.
- rhG-CSF (Neutrogin[®]) and human TPOR agonist RP (Romiplat[®]) demonstrate improved survival in lethal dose mice models.



Hirouchi T, et al. 2015. Curr Pharm Biotechnol. 17(2):190–199.

2nd Attendance Code

1264

Chronic Radiation Care

- Patients surviving ARS or radiation injury need ongoing patient care for stochastic and deterministic effects.
- Stochastic (more radiation, greater statistical likelihood)
 - Cancer
- Deterministic (more radiation, greater severity)
 - Cataract (most common)
 - Infertility
 - Atherosclerotic disease
 - Pulmonary pneumonitis/fibrosis

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- To identify the key signs and symptoms of acute radiation syndrome aiding in prompt patient triage and initial management.
- To describe the protocols for medical response to radiation exposure, including immediate and supportive care measures.
- To evaluate the effectiveness of current radiation prophylaxis and post-exposure treatments in mitigating the health impacts of radiation.

Questions/Short Survey

- Please feel free to contact me at justin.peacock@usuhs.edu
- Please fill out this short survey about the presentation:

