REAC/TS
Radiation Emergency Assistance Center/Training Site
Managed by ORAU for DOE

What Every CHP Should Know About Medical Management of Large, Acute Doses

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NNSA U.S. DEPARTMENT OF ENERGY

Objectives

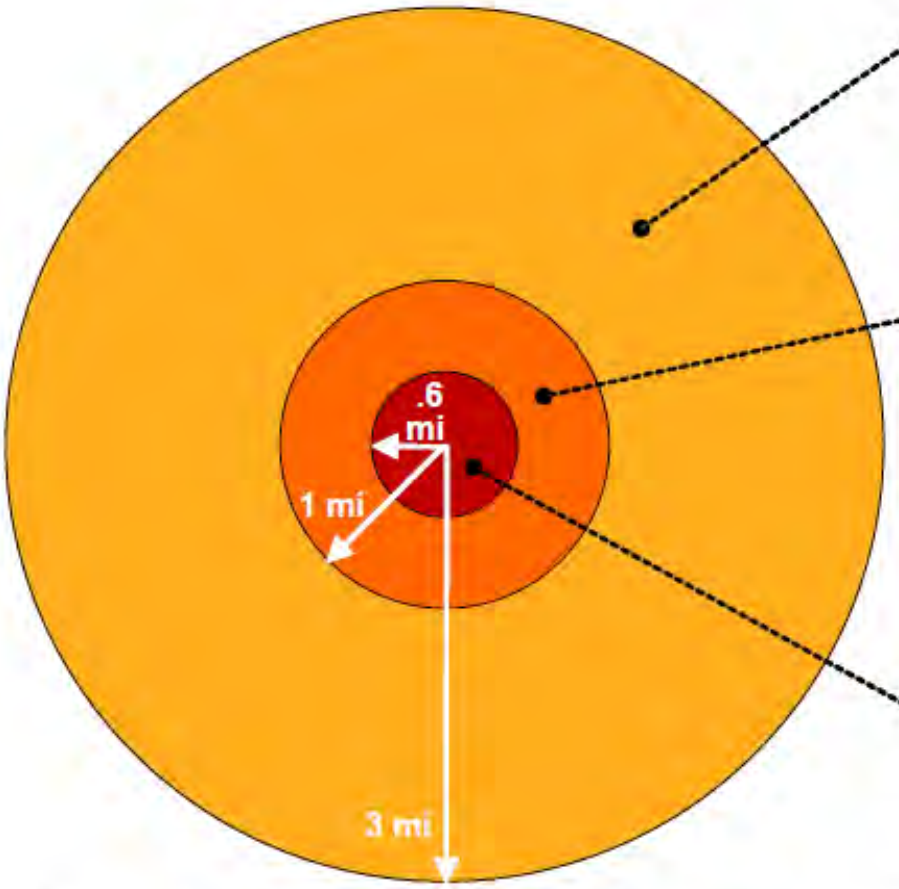
- Consider what to expect at the incident site (first responders) and reception center/emergency department (first receivers) after a large incident
- Understand how to communicate with and inform health care providers
- Determine how the function of health care facilities will change during a mass casualty incident
- Appreciate the diagnosis and clinical management of injury to specific organ systems from a large, acute radiation dose

Introduction

Confucius:

“Success depends on previous preparation, and without such preparation there is sure to be failure”

Damage Varies by Distance from Hypocenter



Light Damage (LD) Zone (1–3 mi): Windows mostly broken, injuries requiring self-care or outpatient care

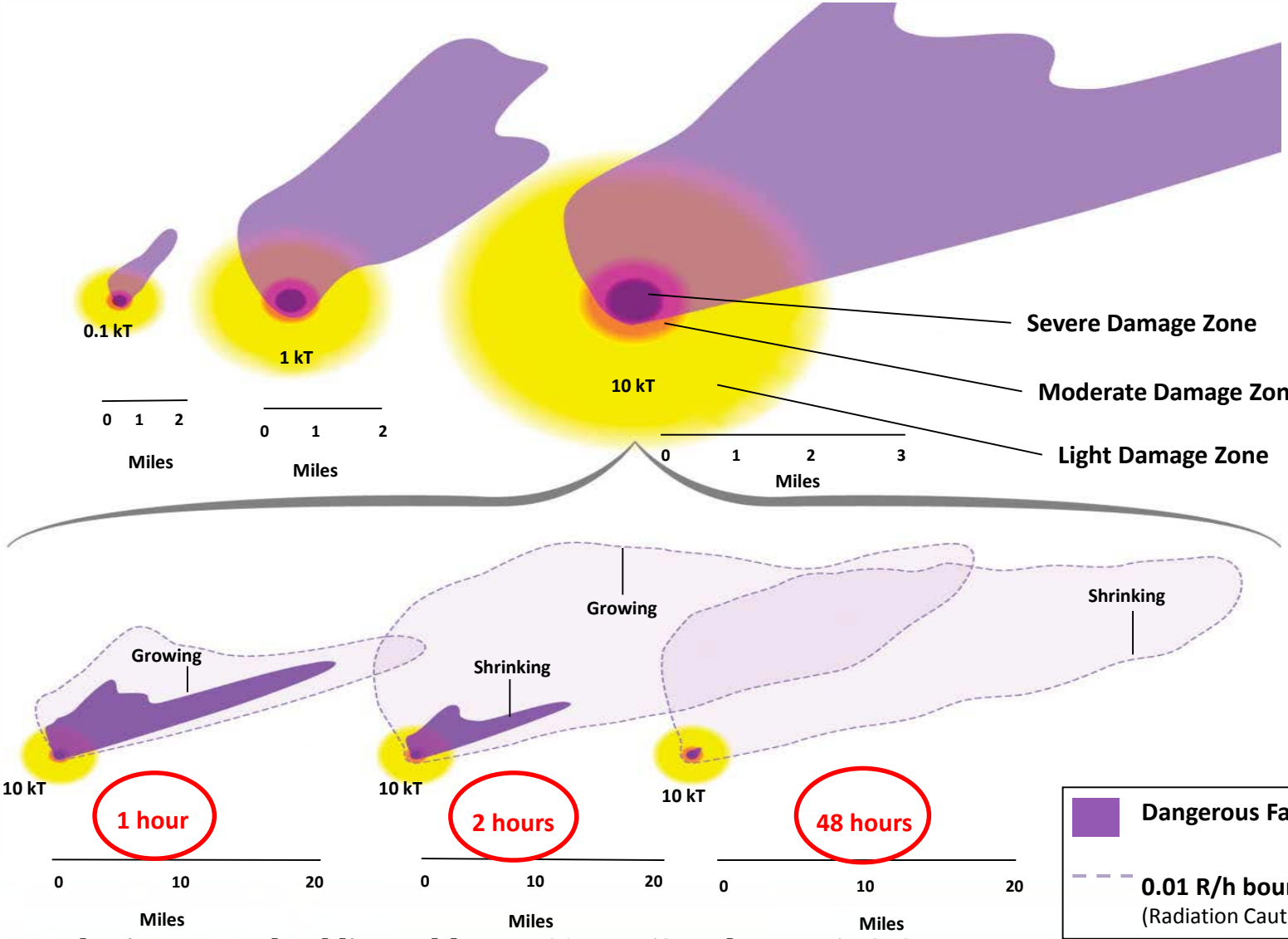
Moderate Damage (MD) Zone (0.5–1 mi): Significant building damage and rubble, downed utility poles, overturned vehicles, fires, many serious injuries, greatest lifesaving opportunities

Severe Damage (SD) Zone (0–0.5 mi): Buildings completely destroyed, radiation prevents entry into the area, lifesaving is not likely

All approximate distances are from the center of detonation site.

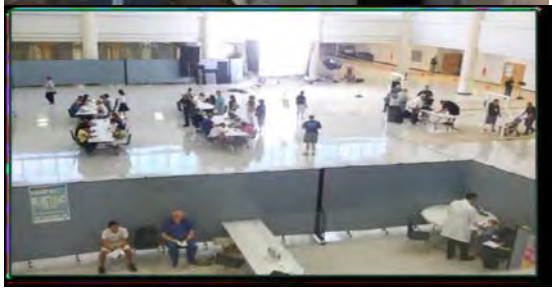
Health and Safety Planning Guide for Protecting Responders Following a Nuclear Detonation, Dec 2016

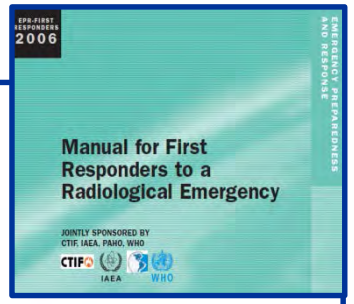
Impact of Environment on Damage and Fallout Zones



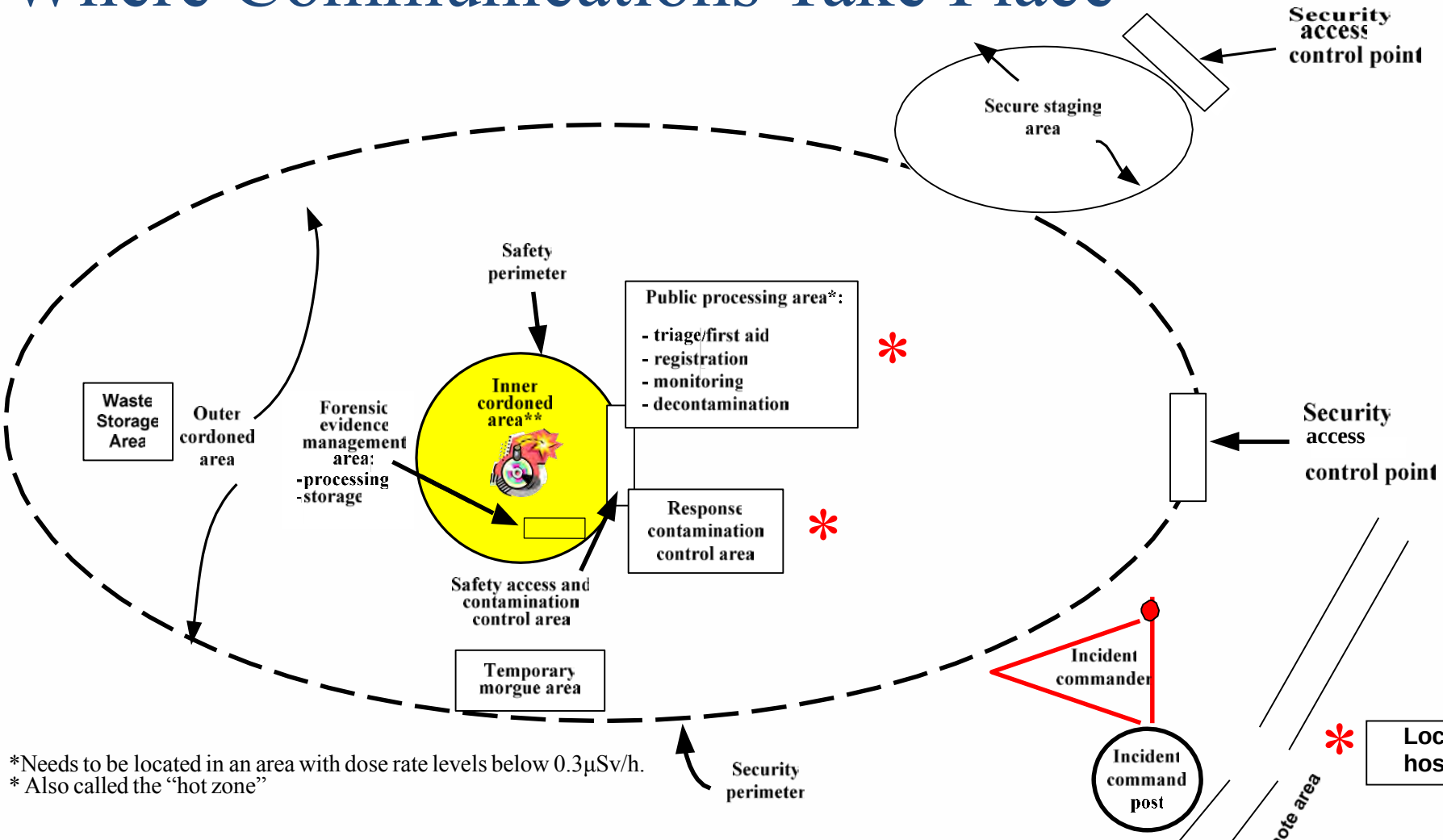
Coleman CN et al, Disaster Med public Health Prep 2011; 5 (Supplement 1): S73

First Responders





Where Communications Take Place



*Needs to be located in an area with dose rate levels below 0.3µSv/h.
* Also called the "hot zone"

Manual for First Responders to a Radiological Emergency, EPR-First Responder, 2006, IAEA

What We Want to Know

- **Clinicians**:
  1. Will I (or other members of my team) become contaminated by interviewing and examining the patient because he/she is contaminated?
  2. Is the patient at risk for acute or chronic diseases because of being exposed to ionizing radiation?

- **Health physicists**:
  1. How will this individual be worked up (blood tests, imaging studies, procedures)?
  2. Where will this individual go (home, hospital, clinic, other)?

Health Physicists Should Avoid Technical Jargon

- Understand how to use annual limit on intake (ALI), committed dose (over 50 years), clinical decision guides (CDGs) and derived reference levels (DRLs) to assess but ***communicate*** dose in terms of ***risk***.

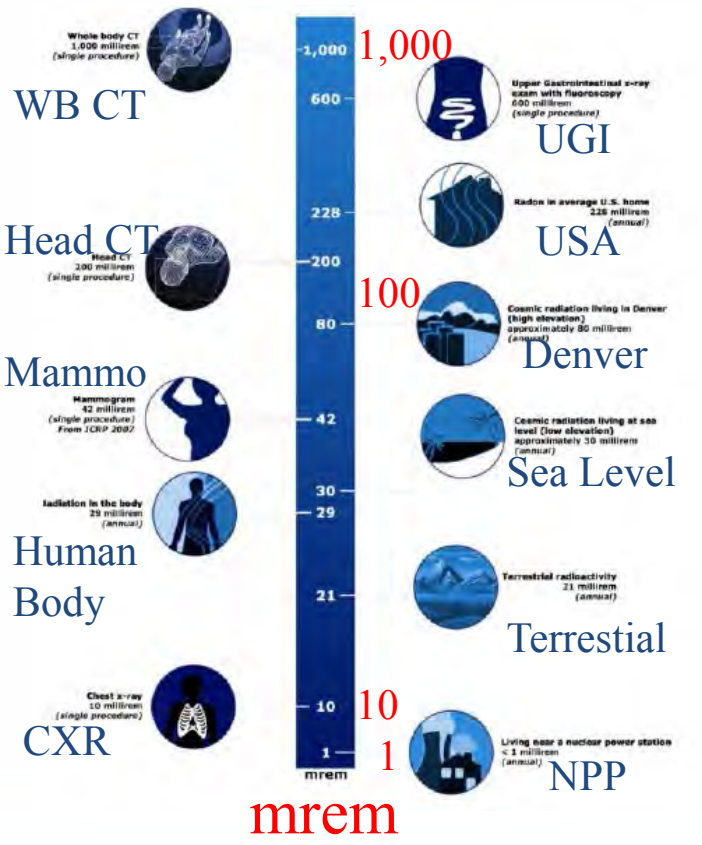
- Do the counts/minute measured over intact skin, wounds, nasal swabs and surfaces translate to a dose rate that places the individual or others ***at risk***?

Examples of Risk Communication

Increase Death by 0.000001 (10-6)

- Smoking 1.4 cigarettes (cancer, heart disease)
- Living 2 mo. with smoker (cancer, heart disease)
- Living 2 days in NYC (pollution)
- Living 2 months in Denver (cosmic radiation)
- Living 5 years at site boundary of NPP (cancer)
- Living 50 years within 5 mi of NPP(cancer)

Rad Levels from Imaging and Activities



Clinicians Should Avoid Abbreviations

- Understand the impact of radiation on organ systems but *communicate* clearly without the use of abbreviations and excess information. Example:
- **"Based on the ALC, this patient is at risk for ARDS and nephrotoxicity, so let's draw blood for gases and RFTs, then move him to the unit where he will be intubated by Dr. 'X' and a triple lumen will be placed for possible HD in the future."**
- Substitutions: *lymphocyte count* for ALC; *lung failure* for ARDS, *kidney failure* for nephrotoxicity; *arterial blood gases* for gases; *renal function tests* for RFTs; *intensive care unit* for unit. Delete extraneous information.
- **"Based on the lymphocyte count, this patient is at risk for lung failure and kidney failure, so let's draw blood for arterial blood gases and renal function tests, then move him to the intensive care unit."**

Impact on Healthcare Facilities

- Damage to **infrastructure** (roadways, railways, etc.) may limit access for victims and suppliers (resulting in shortages), creating need to locate operational facilities and coordinate transportation
- Increased demand will create need to **adapt** by:
  - cancelling elective surgery
  - using ER/DR rooms for emergency surgery
  - discharging patients who may be safely treated at home
  - converting common use space into patient care areas
  - tracking samples, results, interventions, treatments, doses
  - assigning "new" duties to "clinically equivalent" staff

‘New’ Hospital Leadership Structure

Incident Command System

- Incident Commander
  - Operations Section Chief
  - Logistics
  - Planning
  - Financial

  (Directors)
  - Medical Care Branch Director (CMO, CNO)
    - Unit Leaders
      - Inpatient
      - Outpatient
      - Mental Health
      - Clinical Support Services
      - Patient Registration Unit
    - CMO
    - Designated Institutional Officer
    - Department Chairmen
      - Radiology

‘New’ Hospital Functions

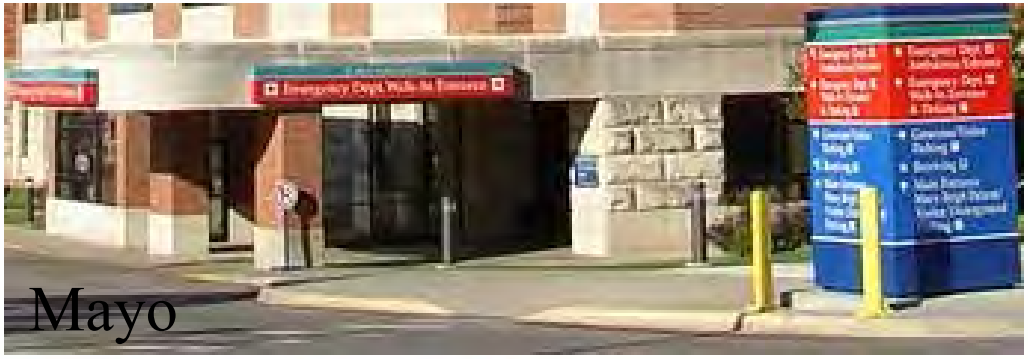
1. Coordinate triage, clinical assessment and patient management among health care facilities
2. Protect health care providers
3. Provide expert advice to government officials for public announcements
4. Provide community support and leadership

First Receivers

National Center for Health Statistics:

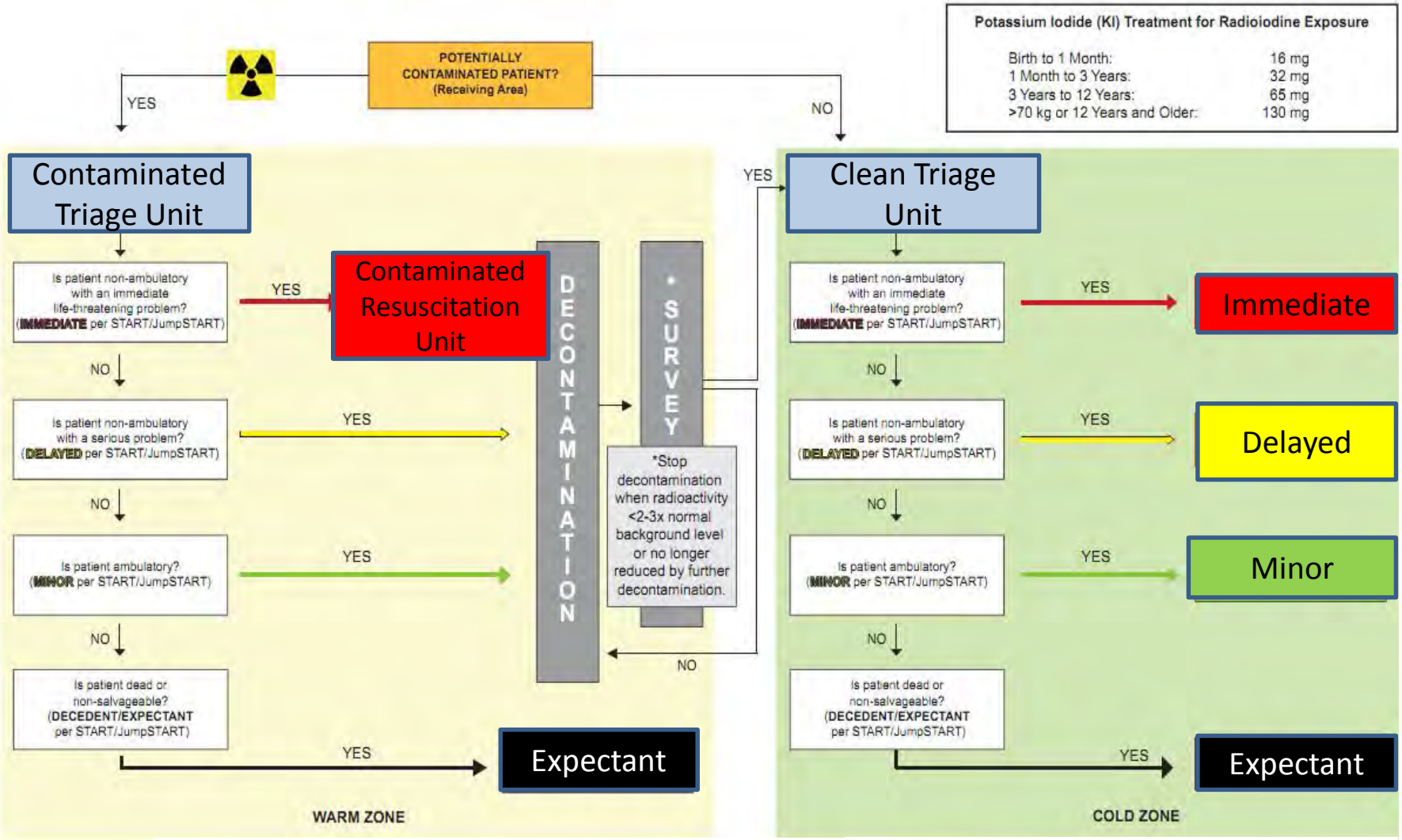
- 130.4 million total visits
- Resulting in 12.2 million admissions (9.3%)
- Pt seen < 15 min - 29.8%

NYU


Mayo


Wikipedia

ED Receiving Areas: Triage, Treatment, Decontamination



Contaminated Casualty Care Area | **Non-Contaminated Casualty Care Area**

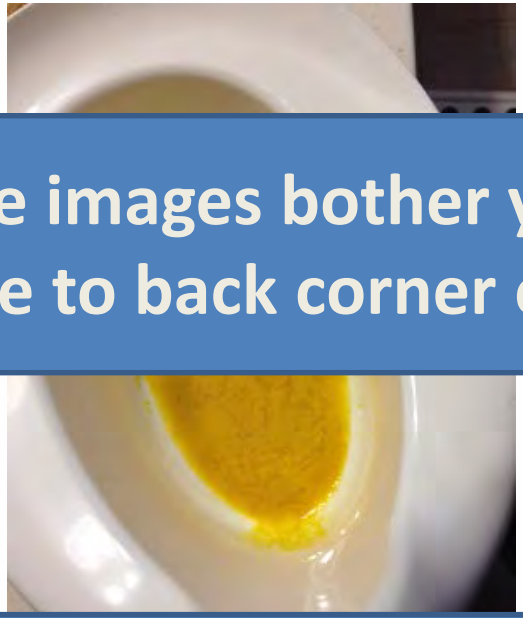
What to Expect in the Emergency Department

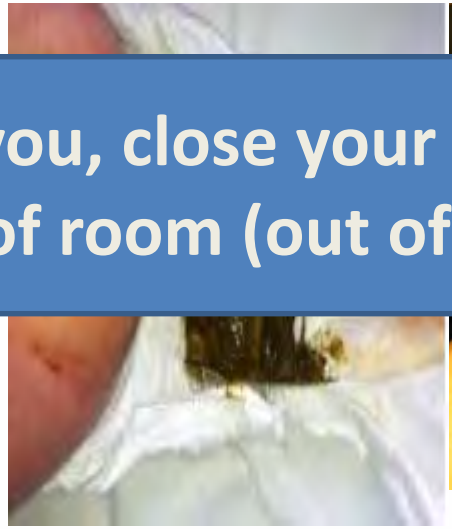
- Smells
- Sights
- Sounds

What to Expect in the Emergency Department

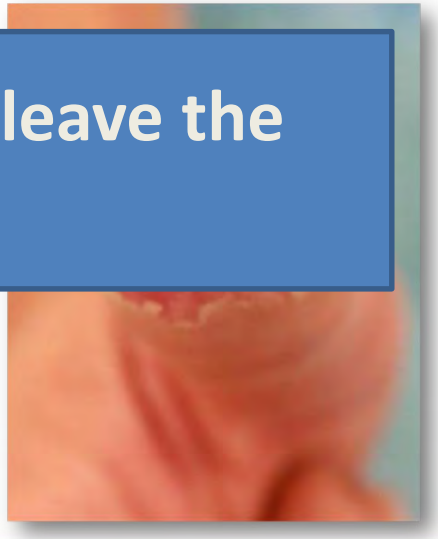
- Sounds

If these images bother you, close your eyes and/or move to back corner of room (out of the way).





If you feel like you will pass out or vomit, leave the room!



Emergency Department Response

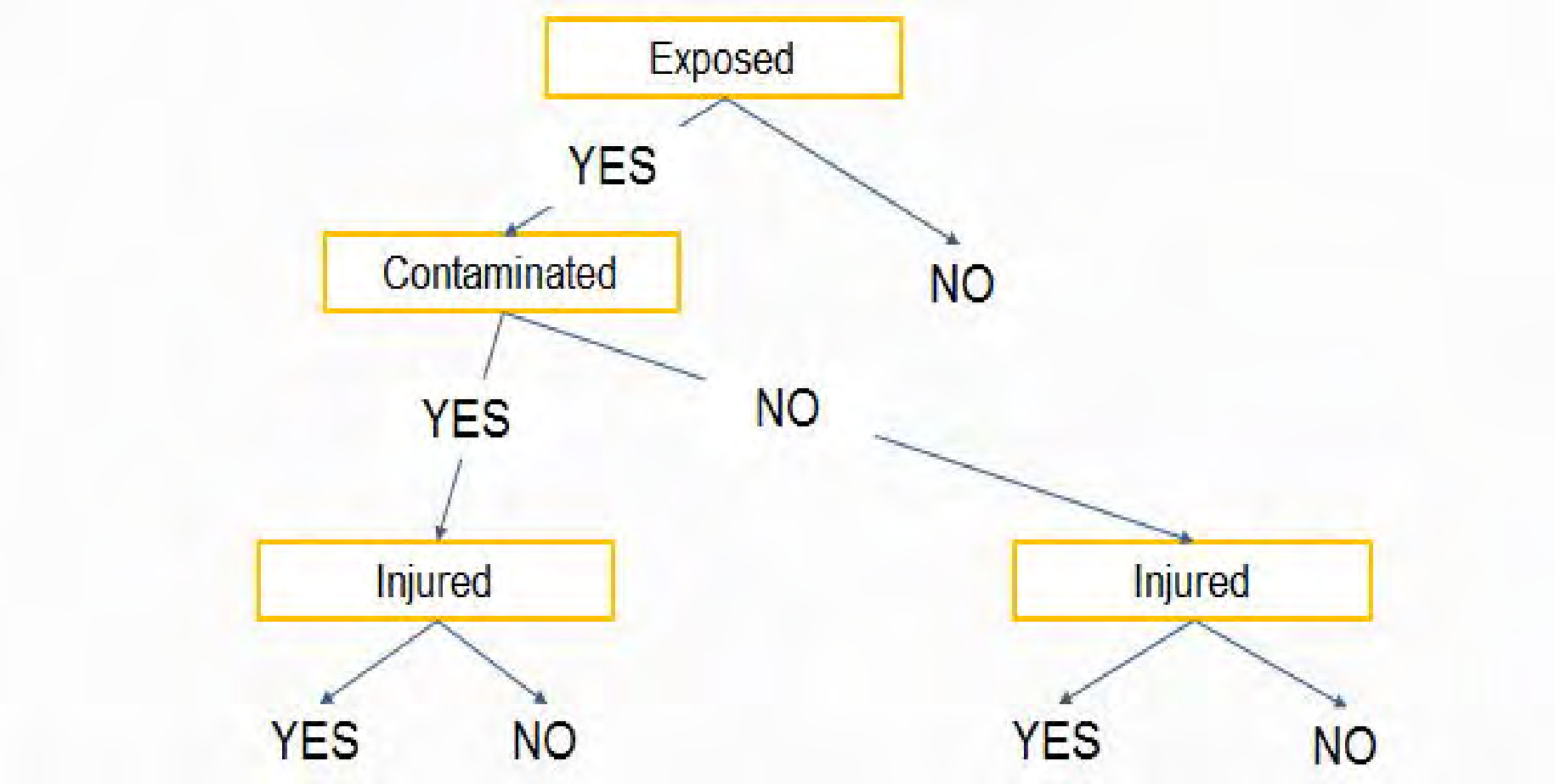
- Classify victims based on exposure, contamination and/or physical injury
- Clinically assess and obtain initial laboratory tests for monitoring
- Decontaminate, if needed
- Triage patients to ambulatory setting, hospital bed (routine care, intensive care, other) or OR

Precautions for Health Care Workers

- Approach patient as though contaminated with human blood, body fluids or sewage
- Use universal precautions (gown, mask, double gloves, cap, shoe covers)
- Change outer gloves frequently to avoid cross-contamination
- Remove protective gear and place in a labeled, sealed plastic container

No health care worker who has adhered to this protocol has become contaminated from handling a contaminated patient

Classification of Victims



Dainiak N et al, Int J Radiat Oncology Biol Phys 2006; 65:16

Triage Measures

1. No Exposure -
    - Consider psychological and social needs of victim, family and friends
2. External Exposure/No Contamination -
    - Process normally in ED and hospital
    - Treat for physical (or other) injury, as required
3. Contamination/ Minor Injury -
    - Decontamination
    - Admit through ED for dose assessment and observation
4. Contamination and Serious Injury
    - Treat life-threatening injury first
    - Decontamination

Estimates of Lethal Dose in Humans

For irradiation in vivo, the 50% lethal dose (LD50) at 60 days after exposure (LD50/60) is:

- 3.5 - 4.5 Gy for healthy, young adults without therapy;
- 6.0 - 7.0 Gy for adults with therapy (antibiotics plus supportive care); and
- Even higher in animals treated with antibiotics, supportive care and growth factors

Gy/Sv is Convenient to Convey Doses for ARS

Dose [Gy]	Onset of vomiting		Lymphocyte count (x10^3/liter) by day						Lymphocyte depletion rate
	%	Time [hr]	0.5	1	2	4	6	8	Rate constant
0	--	--	2.45*	2.45	2.45	2.45	2.45	2.45	--
1	19		2.30	2.16	1.90	1.48	1.15	0.89	0.126
2	35	4.63	2.16	1.90	1.48	0.89	0.54	0.33	0.252
3	54	2.62	2.03	1.68	1.15	0.54	0.25	0.12	0.378
4	72	1.74	1.90	1.48	0.89	0.33	0.12	.044	0.504
5	86	1.27	1.79	1.31	0.69	0.20	0.06	.020	00.63
6	94	0.99	1.68	1.15	0.54	0.12	0.03	.006	0.756
7	98	0.79	1.58	1.01	0.42	.072	.012	.002	0.881
8	99	0.66	1.48	0.89	0.33	.044	.006	<.001	1.01
9	100	0.56	1.39	0.79	0.25	.030	.003	<.001	1.13
10	100	0.48	1.31	0.70	0.20	.020	.001	<.001	1.26

0% deaths

LD 50/60

100% deaths

Waselenko J et al, Ann Intern Med 2004; 140: 1037

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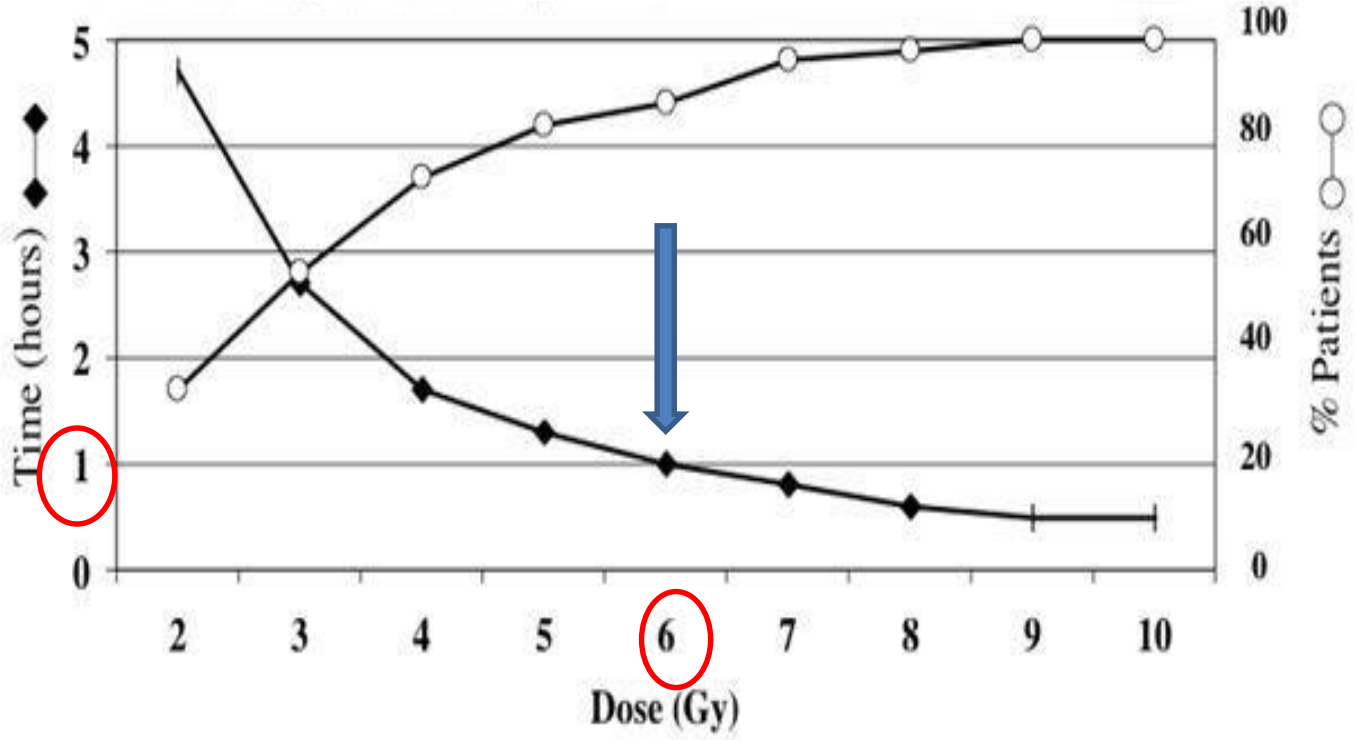

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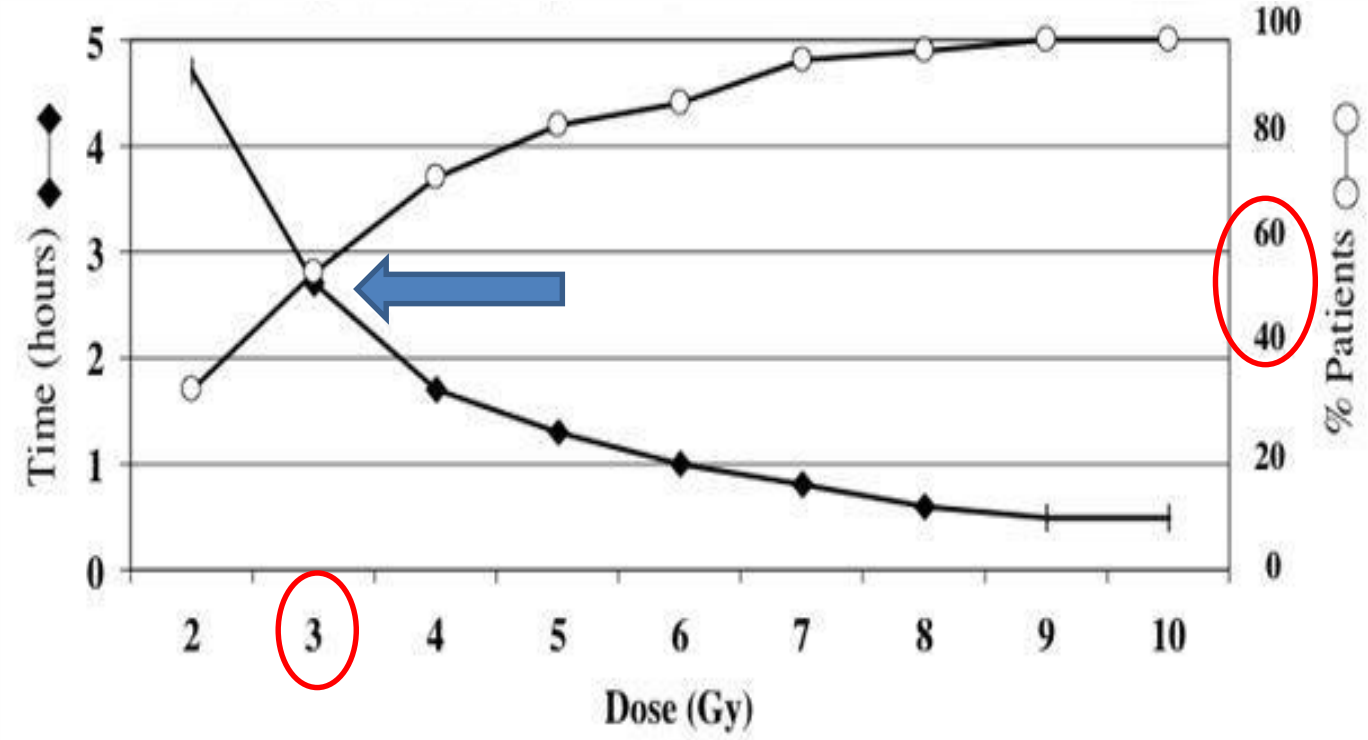

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LD 50/60

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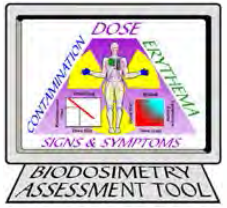
Individual Biodosimetry

1. Time to onset of Vomiting
2. Absolute lymphocyte count
3. Other (C-reactive protein, amylase, Flt-3)

4. Dicentric Chromosome Assay (DCA): **gold standard**, >40 years experience in accidents

Plug results from #1,2,3 into BAT software (W.F. Blakeley): http://www.usuhs.edu/afrri/outreach/biodostools.htm or via REMM website at https://www.remm.nlm.gov



Medical Management of the Acute Radiation Syndrome: Recommendations of the Strategic National Stockpile Radiation Working Group

Jamie K. Waselenko, MD; Thomas J. MacVittie, PhD; William F. Blakely, PhD; Nicki Pesik, MD; Albert L. Wiley, MD, PhD; William E. Dickerson, MD; Horace Tsu, MD; Dennis L. Confer, MD; C. Norman Coleman, MD; Thomas Seed, PhD; Patrick Lowry, MD; James O. Armitage, MD; and Nicholas Dainiak, MD

Table 4. Mass Casualty Scenario for a Nuclear Detonation*

Patient Category	Radiation Dose, Gy	Patients, n	
		1-kiloton Detonation	10-kiloton Detonation
Combined injuries (minimal to intensive care)	All doses	1000–3000	15 000–24 000
Immediate fatalities	All doses	>7000	>13 000
Radiation fallout			
Expectant care	≥10	18 000	45 000
Intensive care	5–10	19 500	79 400
Critical care	3–5	33 000	108 900 *
Normal care	1–3	66 000	70 000
Ambulatory monitoring	0.5–1	82 500	139 000 *
Epidemiologic monitoring	0.25–0.5	106 000	147 000
Monitoring for psychosocial well-being without other injury	<0.25	>150 000	>270 000 *

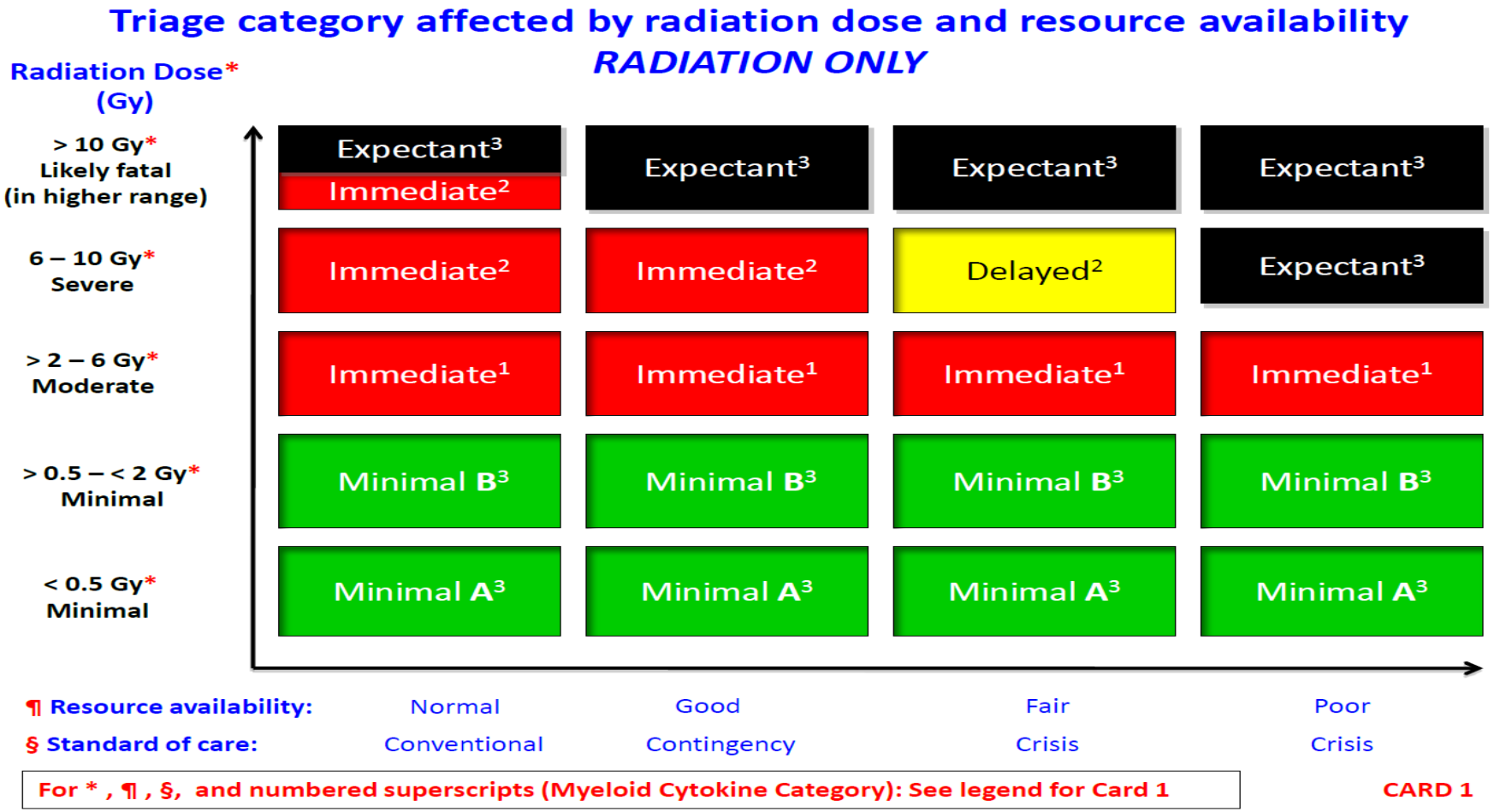
* The table depicts projected casualty estimates based on a 1- or 10-kiloton detonation. Assumptions include a city with a population of 2 million people and casualties estimated on the basis of the Hazard Prediction Assessment Capability Program (HPAC), version 3.21 (Defense Threat Reduction Agency, Fort Belvoir, Virginia). Combined injuries consist of radiation injuries in addition to burns or blunt trauma.

Ann Intern Med. 2004;140:1037-1051.

Psychosocial Needs

- Up to 75% of victims may have some symptoms (insomnia, impaired concentration, social withdrawal)
- Post-traumatic stress disorder may be common among victims, families and friends
- High risk: children, pregnant women, mothers of young children, clean-up workers, victims with prior medical history of psychiatric disorder
- Principle of therapy: establish trust through open communication

Triage by Dose and Resource Availability



Coleman CN et al, Disaster Med Public Health Prep. 2011; Suppl 1:S111-21.

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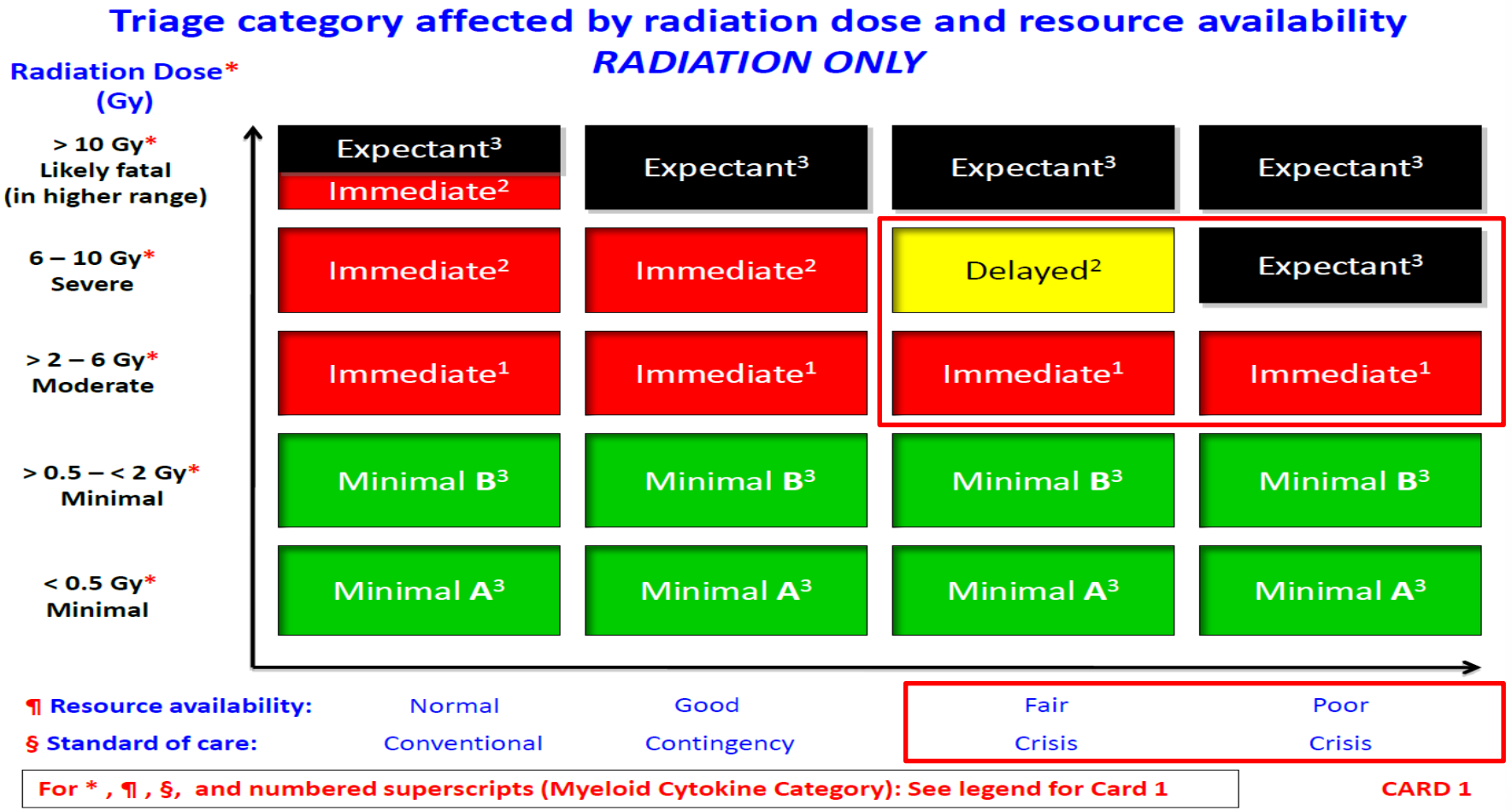

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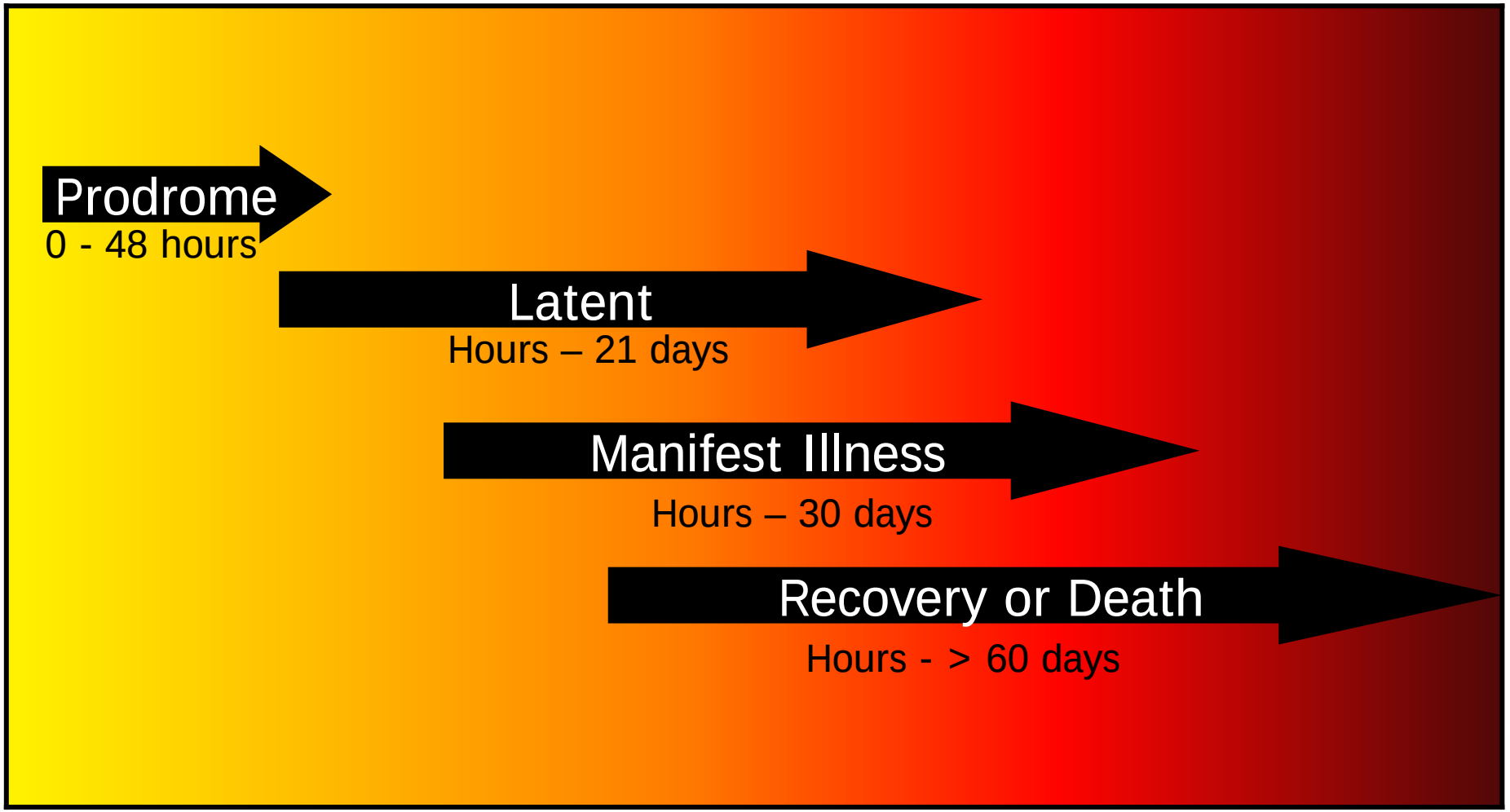
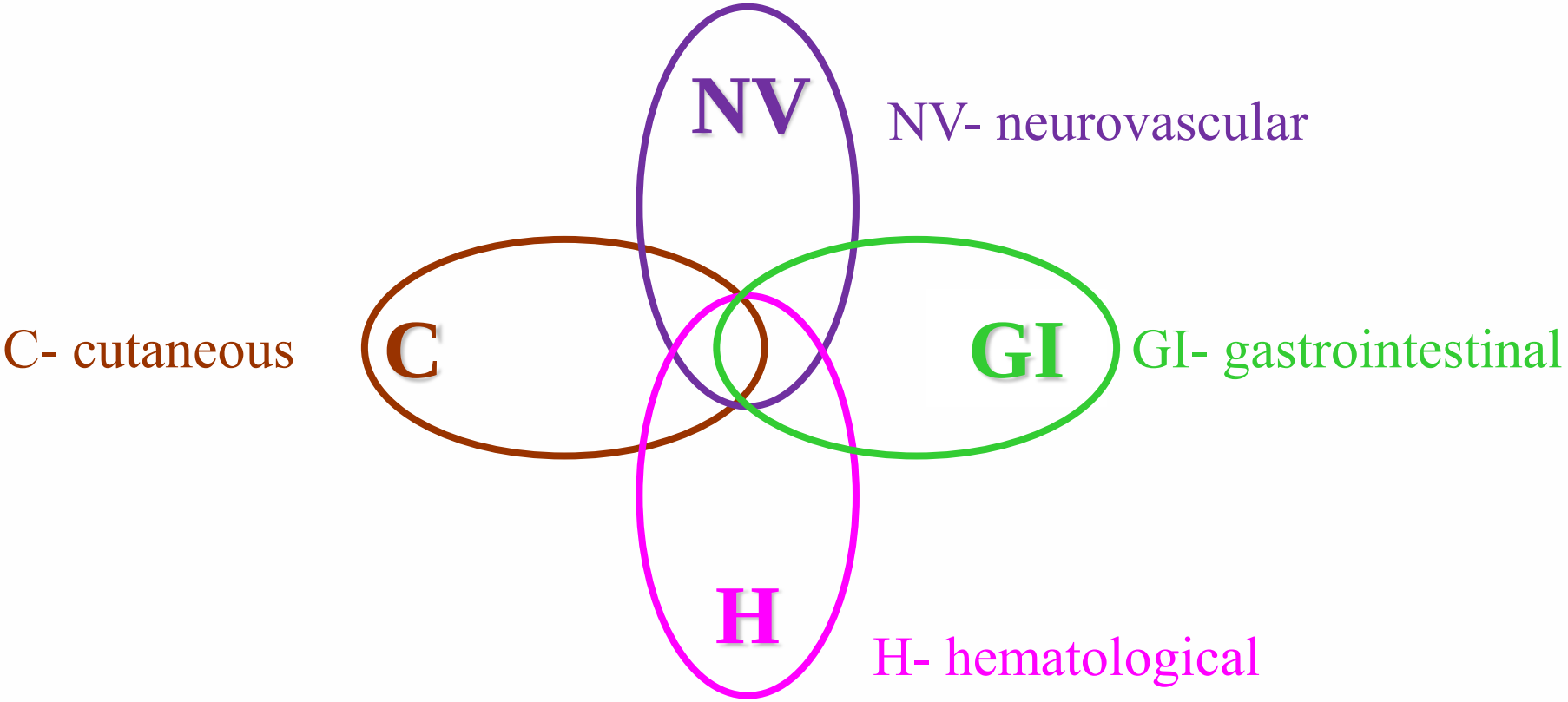
Phases of Acute Radiation Syndrome

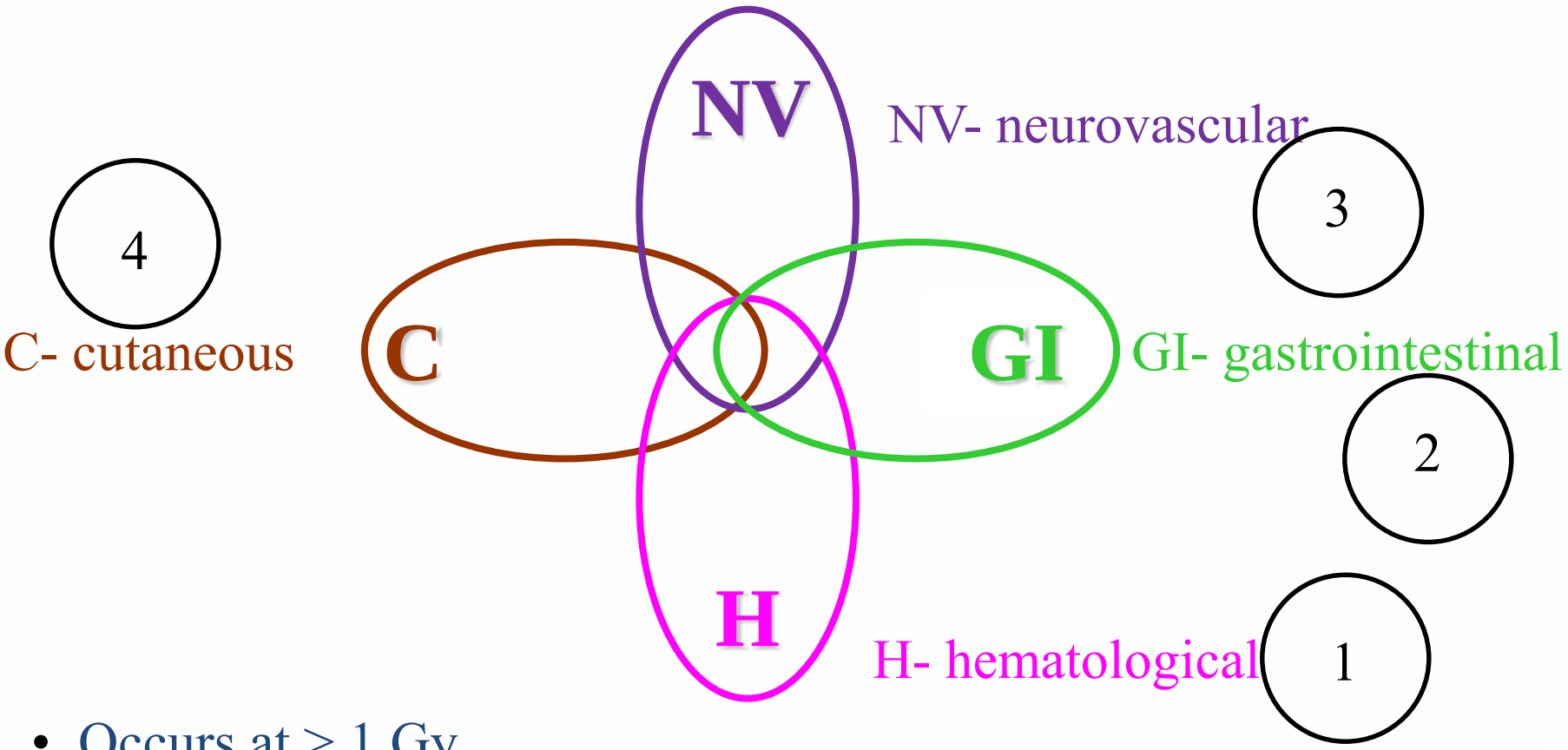


Acute Radiation Syndrome



- Occurs at ≥ 1 Gy
- In general, severity of signs and symptoms correlate with dose

Acute Radiation Syndrome



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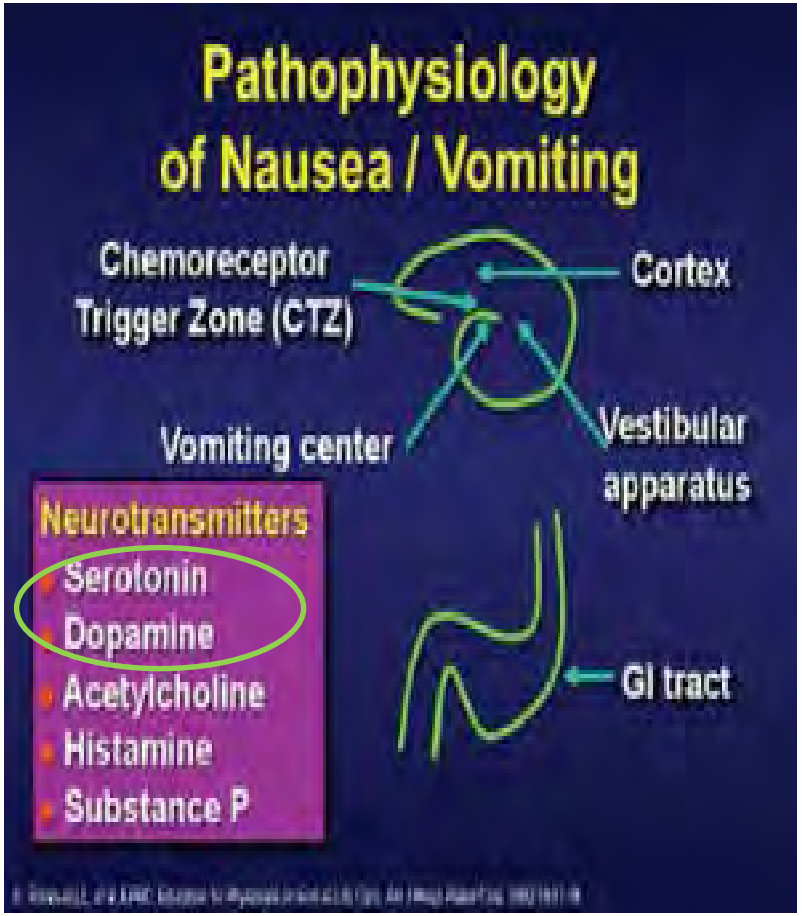
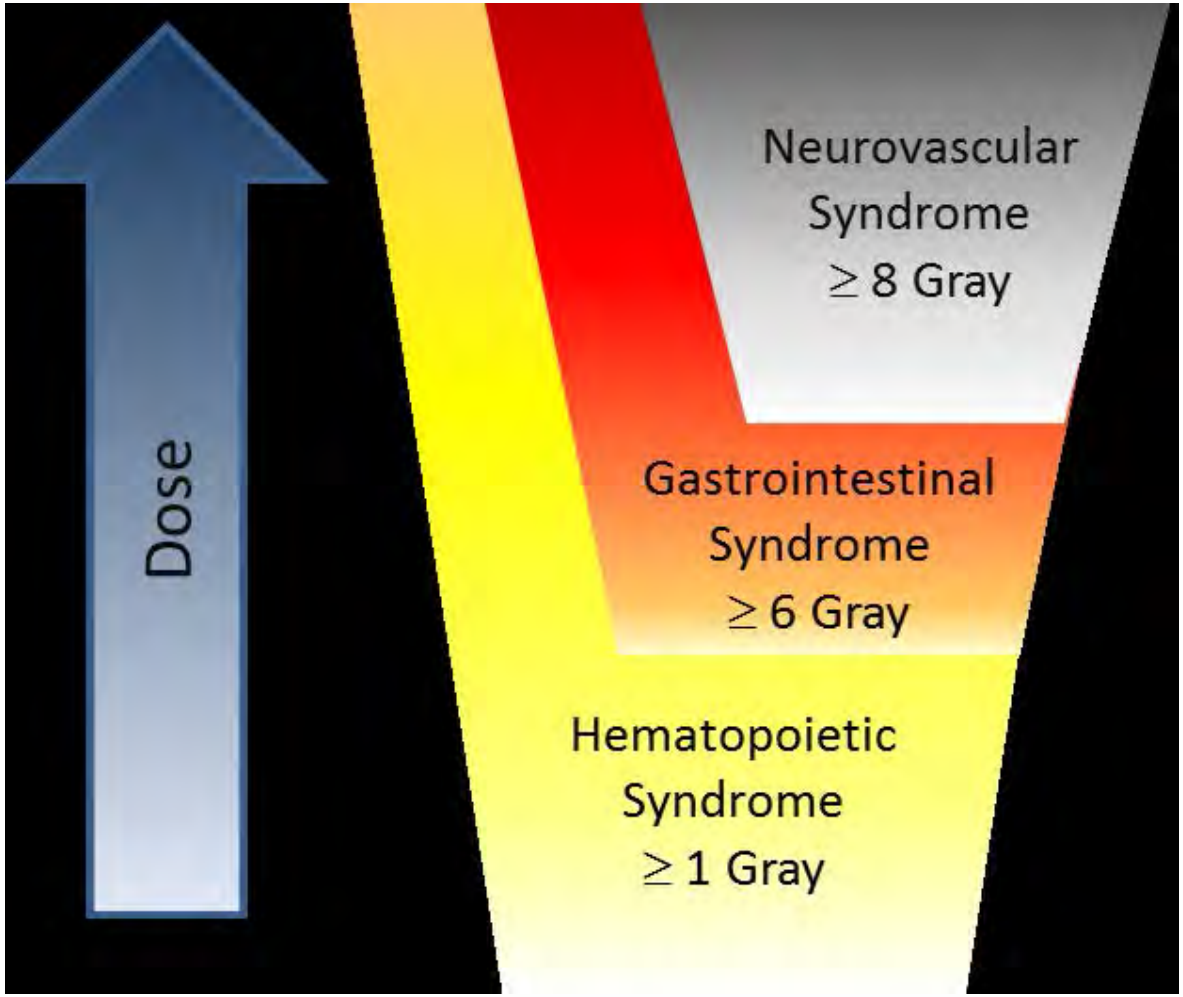
Caveat #1: The Vomiting Center Mediates Early Nausea and Vomiting

- Medullary Chemoreceptor Trigger Zone (CTZ): a neural network at the floor of the 4th ventricle that contains receptors for neurotransmitters whose stimulation causes nausea/vomiting
- Antagonists to receptors (serotonin: *Ondansetron*, and dopamine: metoclopramide) are preferred antiemetics

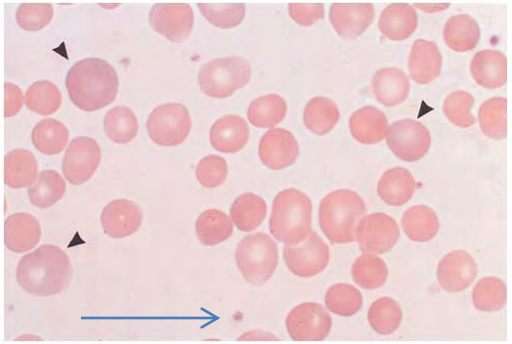


Caveat #2: ARS Component Syndromes are Concurrent (not Sequential)



The Medical Aspects of Radiation Incidents, 2017; 4th Edition, www.orise.orau.gov/reacts

Normal Blood Cell Formation, Functions and Deficiency States (Cytopenias)

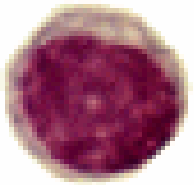


RBCs - carry and deliver oxygen to tissues (Anemia)

Bone Marrow

Stem cells give rise to ***progenitor cells*** that give rise to mature elements of the blood

Neutrophils – engulf/destroy bacteria (Neutropenia)



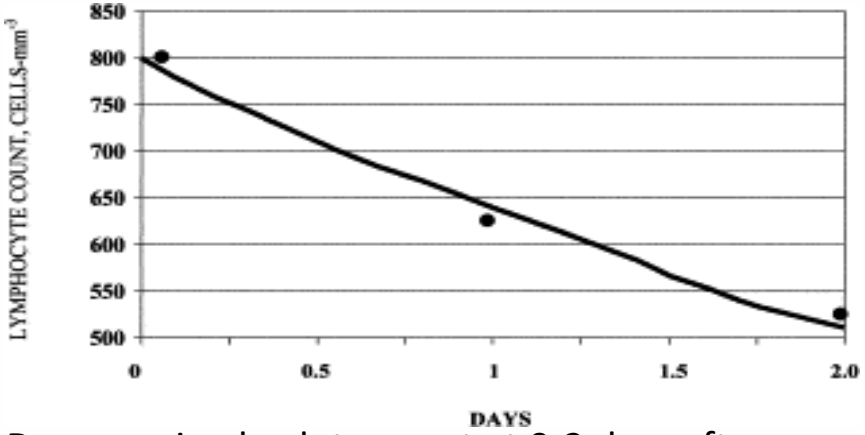
Lymphocytes – produce immune response/Igs (Lymphopenia)

Platelets- plug holes in vessels, form substrate (⟶) for clotting (Thrombocytopenia)

Hematopoietic Syndrome

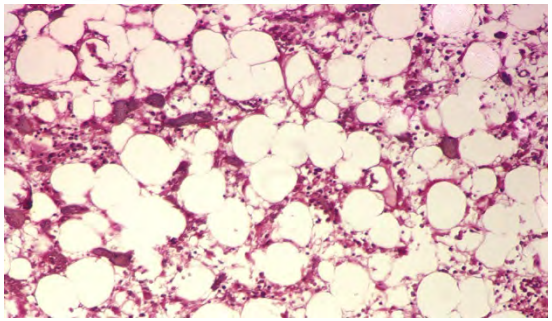
- Occurs at 1-2 Gy or higher
- Lymphopenia is an early (hours to days) indicator of dose. Only Sertoli cells more sensitive to radiation
- Mild cytopenias without marrow damage at 2-3 Gy
- Bone marrow atrophy and pancytopenia over weeks at >3-4 Gy

Lymphocyte Kinetics



Decrease in absolute count at 0-2 days after exposure to 3.5 Gy (mixed neutron-□field). **RE Goans et al. Health Phys 81:446, 2001.**

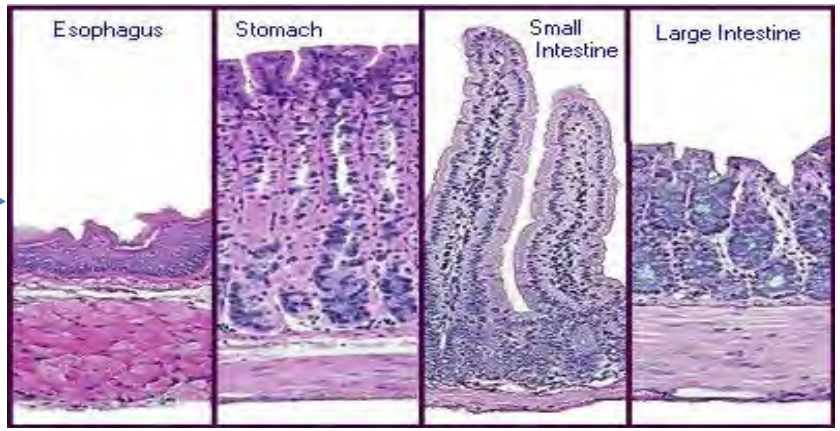
Bone Marrow



Hypocellular marrow from Norwegian patient exposed to 4 Gy. **JV Reitan, Advanced Research Workshop, Ulm, 2003.**

GI Tract Functions and Replacement

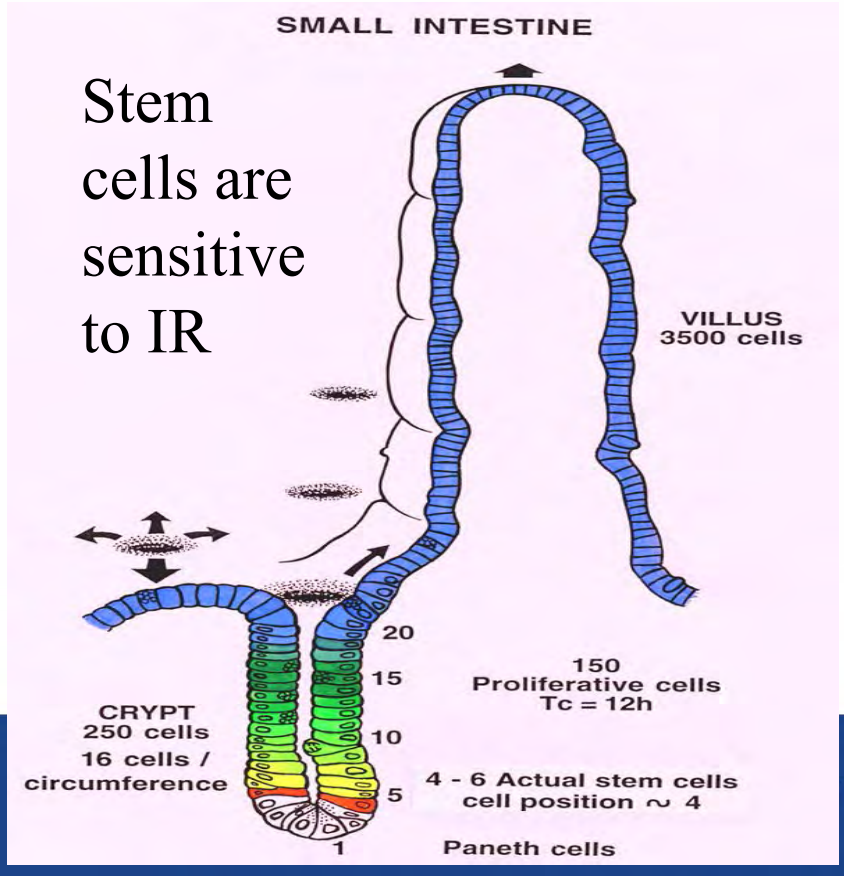
Normal Histopathology



Functions:

1. Absorption of nutrients and secretion of fluids and electrolytes

2. Barrier to bacteria, preventing their passage from bowel lumen to bloodstream



Gastrointestinal Syndrome

- Occurs at 6-8 Gy
- Impaired barrier function due to loss of villous structure (upper fig.), predisposing to infection
- Crypt stem cells cannot replace villus cells that are lost
- Severe complications include necrosis, ulceration and sloughing of bowel (lower fig.)

Extensive small bowel necrosis in autopsy specimen from individual receiving 20 Gy in an accident at Kurchatos Inst Atomic Energy. **A.I. Vorobiev, Stem Cells 15 (suppl 2): 269, 1997.**

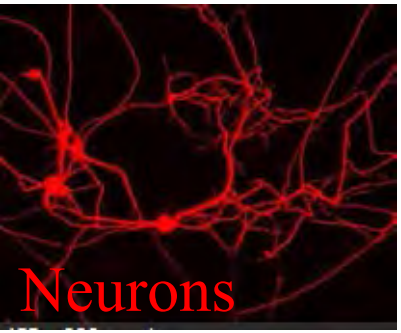
The Neurovascular Unit

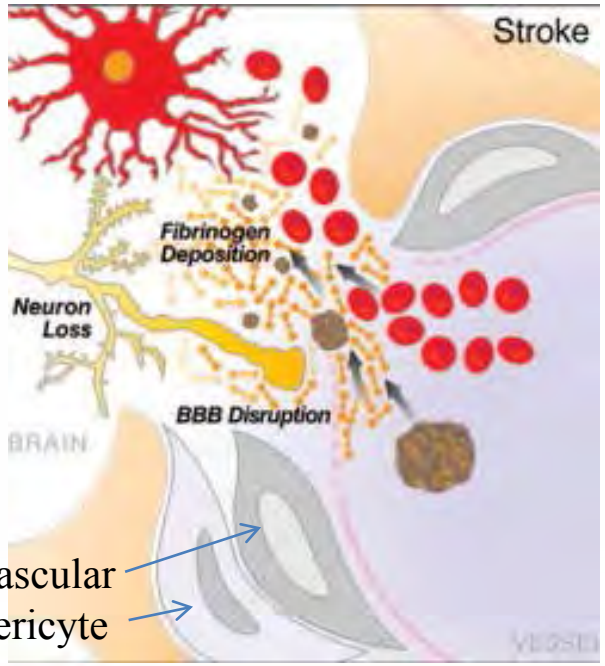
Composed of multiple cell types: glial cells, neurons, pericytes, cerebrovascular cells

Conceptual framework for relationship of neuronal activity and cerebral blood flow

Neurovascular breakdown initiates neurological diseases (stroke and dementia)

Complex interplay of CNS/systemic signs: Pressure, Pulse, Pallor, Pain, Paraesthesias





Neurovascular Syndrome

- Occurs at about 8 Gy or higher
- Presents with fever, hypotension, immediate diarrhea, nausea and vomiting
- During latent period, symptoms may transiently improve
- Ultimately leads to confusion, disorientation and cardiovascular collapse

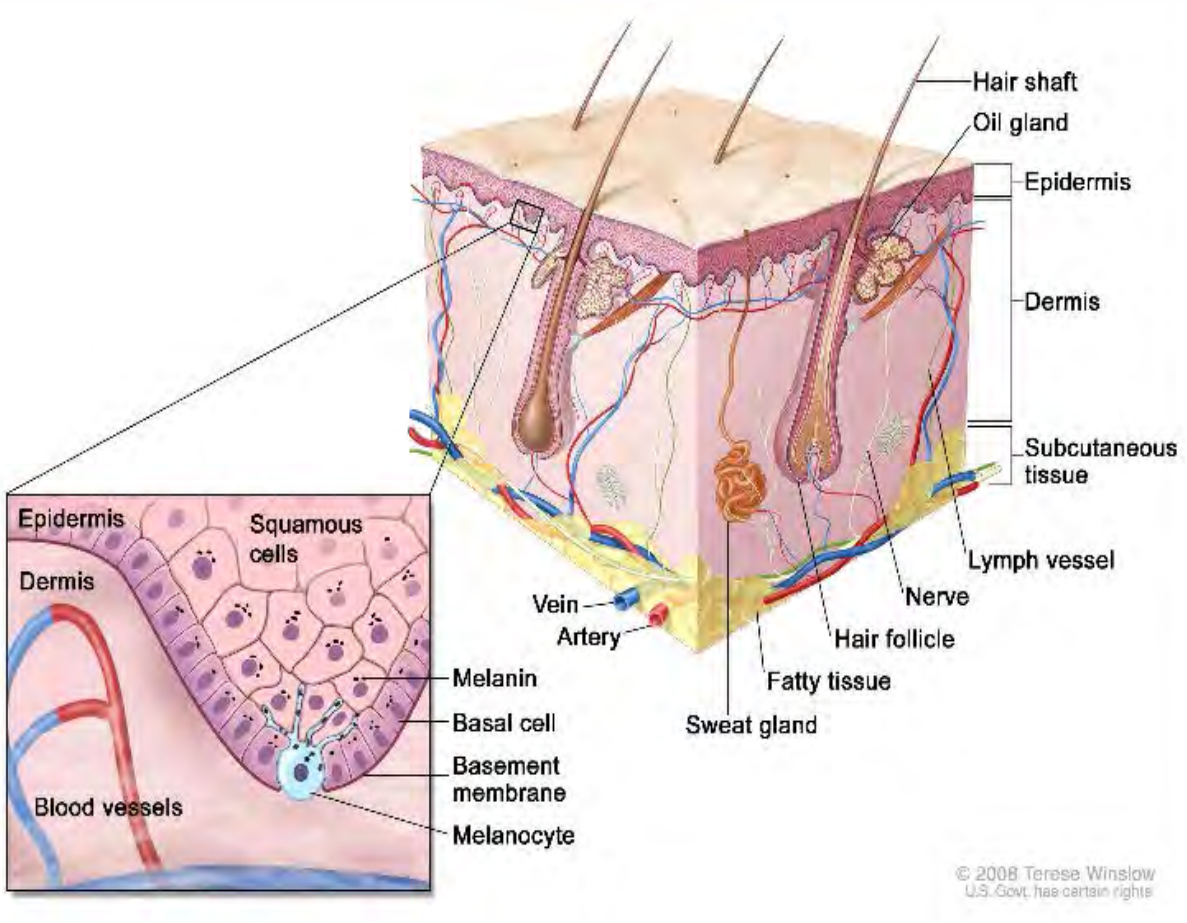
Nonspecific Changes

EEG: spike and wave discharges. IR may cause paroxysmal spike and wave discharges.

CT: dystrophic calcifications along tentorium cerebelli. Nonspecific changes also seen on **MRI** after IR.

Skin Functions and Replacement

- Protects against infectious organisms, dehydration and changes in body temperature
- Disposes wastes, stores water/fat/vitamin D
- Protects internal tissues
- Sensation



Cutaneous Syndrome

- Occurs at >3-6 Gy : epilation (hair loss) and erythema
- Develops within 2-3 weeks and may take years before fully manifest
- May affect multiple levels of the skin (epidermis, dermis, subcutaneous tissue)
- Advanced - ulceration, necrosis, onycholysis and bullae
- Late – fibrosis/scarring

Erythema (6 Gy)

Left:. Early erythema seen 5 days after the exposure to an iridium-192 source (185 GBq, 5 Ci) mounted in a pen-size source holder for industrial radiography which was placed in the pocket of a worker's overall for two hours.

Below: Early Erythema 11 days after exposure.

Cutaneous Lesions

Tense painful bula of the palm on day 20 evolving from erythema with early blistering on day 10 after the contact for a few minutes with iridium-192 source.

Swelling and Onycholysis

Deep <u>infected</u> ulcer on the thigh 6 months after exposure to a 165 Bq (4.4 Ci) cesium-137 source.

Medical Management

- Antibiotics
- Cytokines
- Supportive Care
- Topical Therapy, Skin Grafts/Flaps

Health physicists inform clinicians whose appropriate use of these therapies will increase the LD 50/60, and save lives.

WHO Consultancy

- **Panel of experts:** Co-organizers (ND, VM and ZC) selected 28 SMEs from 4 continents (Europe, North America, South America and Asia). Met on March 16-18, 2009.

- **Virtual scenario:** 100-200 individuals require hospitalization.

- **Pre-Meeting References:** WHO solicited English language references from each expert. References distributed before and during (updated references) meetings.

- **Presentations:** Brief (10-15 min) presentations.

- **Discussion and Ranking:** Recommendations discussed in 1-3.5 hour sessions, followed by ranking of recommendations and assignment of strength of recommendation. Average scores determined for final ranking.

Major Findings

1. No RCTs of medical countermeasures have been completed for individuals treated with ARS.

2. Use of the analysis tool for countermeasures against injury to hematopoietic tissue was restricted by lack of comparator groups in man.

3. Reports of countermeasures for management of injury to non-hematopoietic organ systems often incompletely described.

Summary of Recommendations for Treating Hematopoietic Syndrome in Hospitalized Patients with Whole-Body Exposure to IR

Recommendation	Strength of Recommendation
Administer G-CSF or GM-CSF when ANC < 0.500 x 10^9 cells/L	Strong (B-1a)
Administer ESAs when prolonged anemia is present in order to avoid need for red blood cell infusion	Weak (C-1b)
Administer hematopoietic stem cells after failure of 2-3 weeks of cytokine treatment to induce recovery from marrow aplasia in the absence of non-hematopoietic organ failure	Weak (D-1b)

Strength of recommendation was determined by assignment of quality of the evidence (A-High, B-Moderate, C-Low or D-Very Low) and strong (1a) or weak (1b) recommendation in favor of the practice.

Summary of Recommendations for Treating 100-200 Hospitalized Patients with Whole-Body Exposure to Ionizing Radiation

Syndrome	Recommendation	Strength of Recommendation
Gastrointestinal	Administer fluoroquinolone or similar antibiotic from 2-4 days after radiation exposure	Weak (B-1b)
	Provide bowel decontamination and parenteral antibiotics when indicated, if resources permit	Weak (C-1b)
	Administer a serotonin receptor antagonist prophylactically when suspected exposure is > 2 Gy	Weak (B-1b)
	Administer loperamide PRN for control of diarrhea	Weak (B-1b)
	Provide nutritional support through enteral route	Weak (B-1b)

Summary of Recommendations for Treating 100-200 Hospitalized Patients with Whole-Body Exposure to IR

Syndrome	Recommendation	Strength of Recommendation
Neurovascular	Provide supportive care with a serotonin receptor antagonist, mannitol, furosemide and analgesics	Strong (A-1a)
Cutaneous	Topical antibiotics, topical steroids, topical antihistamines	Strong (A-1a)
	Surgical excision with skin grafts/flaps and amputation	Strong (A-1a)
	Mesenchymal stem cells for intractable neuropathic pain	Proof of Concept

Summary

- Your role at the incident site and emergency department will be to work with clinicians to inform medical management and save lives
- Although you understand ALIs, CDGs and DRLs, you will need to communicate dose to clinicians and government officials in terms of radiation risk
- The functions of healthcare facilities will change profoundly in an acute, large scale incident, as they operate within an unfamiliar Incident Command System, and extend operations to other facilities, government officials and the community at large
- ARS develops at 1 Gy, includes 4 subsyndromes (hematologic, gastrointestinal, neurovascular and cutaneous), and is treated with antibiotics, cytokines, supportive care, topical therapy and placement of skin grafts/flaps

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