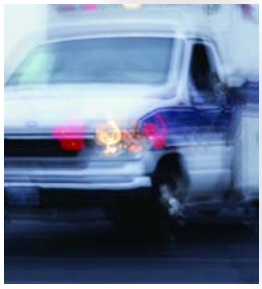
Terrorism and Disaster

WHAT CLINICIANS NEED TO KNOW




Radiation Attack

RUSH UNIVERSITY MEDICAL CENTER

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* Faculty member has nothing to disclose.

**Faculty disclosure: Owner of stock shares in Pfizer.

*** Faculty disclosure: CBCE Speaker's Core for SuperGen.

Radiation Attack

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INSTRUCTIONS

The questions that appear throughout this case are intended as a self-assessment tool. For each question, select or provide the answer that you think is most appropriate and compare your answers to the key at the back of this booklet. The correct answer and a discussion of the answer choices are included in the answer key.

In addition, a sign is provided in the back of this booklet for posting in your office or clinic. Complete the sign by adding your local health department's phone number.

Radiation Attack

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INTENDED AUDIENCE

Internal medicine, family medicine, and emergency medicine physicians and other clinicians who will provide evaluation and care in the aftermath of a terrorist attack or other public health disaster

LEARNING OBJECTIVES

Upon completion of this case, participants will be able to:

- Identify individuals requiring treatment for radiation exposure and define necessary medical interventions.
- Describe guidelines for decontamination of victims of radiation exposure and strategies for ensuring healthcare worker safety.
- Outline the rationale and initial management of patients who believe they have been exposed to radiation, including patient interview, risk identification, and triage, using 3 key elements of biodosimetry.
- Discuss the role of potassium iodide (KI) in a radiation incident and when it should be employed.

CASE HISTORY

You are a primary care physician in an urban area. You receive word that an explosion has occurred in the downtown metro station in your city approximately 45 minutes ago. Early reports suggest this was an intentional simultaneous detonation of 2 radiological dispersal devices (RDDs) on a subway that was traveling in an underground tunnel. Partial collapse of the tunnel has occurred, and at least 22 persons are dead at the scene. Many of these patients suffered crush injuries. Fire department and local police and FBI officials are on the scene.

A radiological survey performed by the Metro Hazmat team reveals low levels of surface contamination, with a radiation field near the train debris of approximately 5 milliRad/hour. This radiation exposure rate is approximately 1,000 times the natural background for the area, but is still relatively low.

We are exposed to radiation from natural sources all of the time. Natural background doses vary throughout the country. For comparison, one chest x-ray is equivalent to the amount of radiation exposure one experiences from natural surroundings in 10 days.

COMMENT: RADIOLOGICAL DISPERSAL DEVICES

Contemporary nuclear threats can be divided into 5 likely scenarios: [1]

1. An attack on nuclear power plants
2. A malevolent attack using simple radiological devices
3. Terrorist use of a radiological dispersal device or dirty bomb
4. Detonation of an improvised nuclear device
5. Detonation of a sophisticated nuclear weapon

A radiological dispersal device (RDD), commonly referred to as a "dirty bomb", is an explosive device that when detonated disperses an attached radioactive source. An RDD is not a sophisticated nuclear weapon. The radiation risk from an RDD detonation is actually very low, but blast injuries arising from detonation of the weapon may occur. Many radioisotopes have a high dose rate when the patient is near the source, but generally there is a significant drop-off in radiation dose rate with distance.

An RDD detonation will cause significant psychological trauma, and a number of people will seek medical attention for concern of radiation exposure. The healthcare worker plays an essential role in minimizing fear in these low risk patients, as well as colleagues. Healthcare workers must recognize that patients who are exposed to radiation but not contaminated pose no threat to hospital personnel.

One stainless steel capsule, that was attached to an undetonated explosive located a half meter behind the train conductor's seat, was recovered from the wreckage. A health physics survey at the site supports that the capsule contained the radionuclide Cesium-137 (Cs-137). Additionally, some of those who died in the explosion appear to be imbedded with radioactive pellets, also likely Cs-137. All subway trains have been halted, and traffic in the city has come to a standstill.

COMMENT: FIRST RESPONDER PROTECTION

First responders should be monitored for their radiation exposure and should use caution, but they must not let the risk of exposure to radiation interfere with rapid triage and removal of trauma victims from the field of injury.

Protection against radiation depends on the time near the source of radiation, the distance from the source of radiation, and the amount of shielding from the source. To reduce exposure from a radiation source, first responders should consider the following three points: time, distance, and shielding from the radiation source.

- Time – limit time near the radiation source by working in short, rotating shifts.
- Distance – increase distance from the radiation source by remaining behind a protective barrier and returning immediately to a safe area when shifts are finished.
- Shielding – increase shielding by wearing personal protective equipment and returning to an area behind protective barriers (walls) as soon as possible, and placing bags of contaminated waste in secure concrete walled areas away from the immediate work area.

You are paged that one of your patients has presented to the emergency department (ED). The patient is a 27-year-old female subway employee, who was driving the train involved in the explosion. The patient was in front of the undetonated RDD for the 3 hours of her shift. She was brought in by air ambulance 45 minutes after detonation of the 2 RDDs.

RADIATION BASICS[2]

Non-ionizing radiation is associated with commonly used objects including television, radio, microwaves, and cell phones.

Ionizing radiation can injure living tissue through transference of energy to cells in the body. The result of this exposure can impair the cells' ability to repair itself or can lead to permanent alteration in the cells' functioning or genetic material, which can be a precursor to development of cancer.

Additional terms and definitions are provided in a glossary provided by the CDC: http://www.bt.cdc.gov/radiation/glossary.asp

RADIATION EXPOSURE VS. CONTAMINATION

EXPOSURE

- occurs after being in the presence of a radioactive source
- no health hazard to healthcare worker
- no decontamination necessary

CONTAMINATION

- is the presence of radioactive material on (external) or in (internal) the patient
- hazard to healthcare worker until removed – external contamination may not be seen or smelled but may be measured by a Geiger counter
- decontamination is necessary

Note: In the setting of an explosion, the patient may be both exposed and contaminated, as in this case study.

COMMENT: HOSPITAL PREPAREDNESS

Every medical facility should have a disaster plan that includes specific plans to manage potentially irradiated casualties. Hospital personnel must be familiar with their disaster plans, including specific radiation disaster plans, and these plans must be practiced by running drills. In preparing to receive victims of a radiological incident, hospitals should take the following steps:[3]

- Initiate hospital disaster plan
- Gather information about the incident and track updates
- Mobilize hospital radiation experts and request radiation monitoring and survey instruments
- Request extra security for the ED
- Identify separate areas on hospital grounds for incoming "walking wounded" and people who fear radiation exposure
- Prepare the ED by identifying areas where contamination will be tolerated and requesting extra containers for waste, extra gloves, and other necessary supplies
- Prepare the ED staff by providing appropriate personal protective equipment (PPE)

For more information on hospital triage and management of radiation emergencies, review the Radiation Emergency Assistance Center/Training Site at http://www.orau.gov/reacts/.

QUESTION 1

As you prepare to take care of ED patients who have been involved in this disaster and have been decontaminated, what PPE should you wear?

a. N-95 respirator, gown, shoe covers, and gloves
b. Powered Air Purifying Respirator (PAPR), gown, shoe covers, and double gloves
c. Hazmat suit
d. Surgical face mask, gown, shoe covers, and double gloves

Reminder: You can find the Answer Key & Discussion on page 14.

The patient arrives at your institution, and her initial vital signs are a pulse of 110, a blood pressure of 150/90, a respiratory rate of 20, a weight of 60 Kg, with a normal temperature. The patient is conversant but feels nauseous.

The patient was externally decontaminated at the scene by the city Hazmat team. Her clothes were removed and placed in a bag, she was showered and given a clean robe to wear. At the hospital, secondary survey of the patient reveals several head lacerations and facial ecchymosis, and mild erythema of her lower back, buttocks, and perineum. There is no evidence of imbedded shrapnel. This patient poses little to no health threat to hospital personnel.

COMMENT: DECONTAMINATION & TRIAGE

Hospitals preparing to receive contaminated victims must establish a decontamination zone near the ED. This decontamination area will go from the hot zone, where patients are presenting for decontamination and hospital personnel must wear hazmat suits, to the cold zone where patients present after being decontaminated and hospital personnel must wear PPE including gown, mask, shoe covers, and double gloves. A radiation survey is done on each patient after decontamination. Once this survey reveals that radiation levels are reduced to less than 2 times the background level, healthcare worker PPE can be removed.

Patients must be medically stabilized from their traumatic injuries first, which should take priority over decontamination. Note that part of a full body assessment of a trauma patient will involve removal of the patient's clothing, which will also remove the majority of external contamination. The "golden hour" has been widely recognized by surgeons to be an hour of opportunity in which the lives of severely injured people may be saved if they are rapidly triaged by first response personnel and treated by trauma specialists.

Hospital personnel must know how to triage, decontaminate, and expand to meet the needs of a large number of low-risk patients who will present with concerns of radiation exposure. The goal of triage is to evaluate and prioritize individuals by immediacy of treatment needed. Triage should include a radiologic survey to assess dose rate, documentation of prodromal symptoms, and collection of blood work. As in traditional triage, ABCs (airway, breathing, circulation) apply, and life-threatening injuries should be addressed immediately. Management of life-threatening injuries takes precedence over radiological surveys and decontamination.

During triage, sites of erythema should be carefully documented, as this may be transient and would heighten concern for subsequent local radiation injury of the skin and underlying tissues. It is important to determine the patient's physical proximity and duration near any source of the radiation. The position of patient, relative to the source at the time of exposure, and the presence of any shielding should also be noted.

COMMENT: EXTERNAL AND INTERNAL CONTAMINATION

Both internal and external contamination of the patient should be considered. External contamination occurs when radioactive debris is deposited on the body and clothing. **Removing the clothing of those externally contaminated usually eliminates more than 90% of contamination.**[2] Most of the remaining surface radioactivity on the hair and skin is eliminated with soap and water. The skin is an important barrier to radioactive material and should not be abraded during decontamination.[2]

Focal tissue damage and necrosis are the result of localized exposure to radiation. The injury will appear to be burns, but is actually an intense area of local tissue injury that will take several months to heal.[2]

Internal contamination can occur if patients are imbedded with radioactive fragments disseminated through the explosive device. All patients with contaminated wounds or imbedded fragments will need to be assessed for internal contamination. The type of monitoring and the need for intervention is based on the radionuclide present, and the appropriate course of action would be determined after consultation with the institution's radiation safety officer. Radioactive shrapnel may yield significant radionecrosis of the skin and underlying tissue 3-4 weeks post-accident, and these pellets should be removed cautiously and quickly.

When non-emergent surgery is necessary in an irradiated patient, it should be carried out within 36 hours, and not later than 48 hours after exposure. Additional surgery, if required, should not be performed until at least 6 weeks post-exposure, in order to assure recovery from the period of cytopenia and immunosuppression, which would otherwise seriously add to the risk of developing surgical complications (ie, infection, poor wound healing).

In cases where removal of radioactive fragment are involved, surgeons must consult their local radiation safety officer immediately. Fortunately, monitoring and protective barriers are often available in hospitals. For example, brachytherapy shielding may be found in the operating room and may afford some protection. Pregnant personnel should be excluded and ideally the surgical team would rotate to minimize exposure to their hands. Ring dosimeters can be worn on both hands (or the dominant hand

HEALTHCARE WORKER PROTECTION

When treating patients who have been exposed, healthcare workers should take universal precautions. When treating patients who have been contaminated, healthcare workers should wear standard disposable surgical attire (gown, mask, shoe covers, and double gloves) until a Geiger counter reveals that radiation levels are reduced to less than 2 times the background level or level from natural sources in the environment.

Hospital radiation safety officers or physicists should always be consulted when healthcare workers are treating patients with radiation exposure.

as a minimum) and are available in nuclear medicine. However, these are not usually read in-house. An electronic pocket dosimeter, taped to the forearms, under the gown, at a set distance from the fingers, can be used to calculate the provider's dose to her hands. All patients with contaminated wounds or imbedded fragments will need to be assessed for internal contamination.

Unfortunately, the 27-year-old female subway employee was seated just in front of one of the radioactive capsules, which has resulted in a high-level dorsal exposure. Even with partial shielding, her dorsal exposure may result in significant damage to the hematopoietic system due to the predominance of active bone marrow in the spine and dorsal ribs and pelvis. Recognizing her high level dorsal exposure, you are concerned that she may develop acute radiation syndrome.

COMMENT: ACUTE RADIATION SYNDROME

Irradiation of human cells has acute and delayed effects which may affect every major organ system. Radiation damage results from the sensitivity of cells to radiation, with the most replicative cells being the most sensitive to acute effects. The inherent sensitivity of these cells results in a constellation of clinical syndromes that occur with radiation exposure, within a predictable range of doses after whole-body or significant partial-body exposure.

The energy that radiation deposits in tissue is called the dose, or absorbed dose. The units of measure for absorbed dose are the gray (1 joule per kilogram of tissue) or the rad (1/100 of a gray). Acute radiation syndrome (ARS) occurs after whole-body or significant partial-body irradiation of greater than 1 gray (Gy) delivered at a relatively high dose rate.[1] Clinical components of ARS include hematopoietic, cutaneous, gastrointestinal, and cerebrovascular systems, which are described further in Table 1. Each syndrome can be divided into 4 phases:

1. Prodromal phase: Usually occurs in the first 48 hours, but may develop up to 6 days after exposure.
2. Latent phase: A short period that is characterized by improvement of symptoms, as the person appears to have recovered. Unfortunately, this effect is transient lasting for several days to a month.
3. Manifest illness: This stage may last for weeks, and is characterized by intense immunosuppression and is the most difficult to manage. If the person survives this stage, recovery is likely.
4. Recovery or death.

Symptoms are dependent on the absorbed dose and may appear within hours to weeks and follow a somewhat predictable course. Individuals suffering from a lethal dose of radiation may experience a compression of these phases over a period of hours, resulting in early death. The mean lethal dose of radiation required to kill 50% of humans at 60 days ($LD_{50/60}$) is a whole-body radiation dose between 3.25 - 4 Gy in persons managed without supportive care, and 6-7 Gy when antibiotics and transfusion support are provided. The lethal dose may be somewhat higher with early initiation of colony stimulating factors (CSFs). A significant partial-body or whole-body dose >10 Gy is considered lethal.

Because of the inherent radiosensitivity of the hematopoietic system, irradiation of bone marrow results in exponential rate of death. Pancytopenia predisposes victims to infection, bleeding, and poor wound healing. Importantly, radioresistant cells exist and may survive exposure up to 6 Gy, albeit with a reduced capacity of self-renewal. Radioresistant cells and bone marrow spared from partial shielding during exposure may support reestablishment of hematopoiesis.

Table 1. Grading System for Response of Neurovascular, Gastrointestinal, and Cutaneous Systems and Levels of Hematopoietic Toxicity*

Symptom or Sign	Degree 1	Degree 2	Degree 3	Degree 4
Neurovascular System				
Nausea	Mild	Moderate	Intense	Excruciating
Vomiting	Occasional (once per day)	Intermittent (2-5 times per day)	Persistent (6-10 times per day)	Refractory (>10 times per day)
Anorexia	Able to eat	Intake decreased	Intake minimal	Parenteral nutrition
Fatigue syndrome	Able to work	Impaired work ability	Needs assistance for activity of daily living	Cannot perform activity of daily living
Temperature, ˚C	<38	38-40	>40 for <24 h	>40 for >24h
Headache	Minimal	Moderate	Intense	Excruciating
Hypotension	Heart rate >100 beats/min; blood pressure >100/170 mm Hg	Blood pressure <100/70mm Hg	Blood pressure <90/60 mm Hg; transient	Blood pressure <80/? mm Hg; persistent
Neurologic deficits†	Barely detectable	Easily detectable	Prominent	Life-threatening, loss of consciousness
Cognitive deficits‡	Minor loss	Moderate loss	Major impairment	Complete impairment
Gastrointestinal System				
Diarrhea				
Frequency, stools/d	2-3	4-6	7-9	10
Consistency	Bulky	Loose	Loose	Watery
Bleeding	Occult	Intermittent	Persistent	Persistent with large amount
Abdominal cramps or pain	Minimal	Moderate	Intense	Excruciating
Cutaneous System				
Erythema§	Minimal, transient	Moderate (<10% body surface area)	Marked (10%-40% body surface area)	Severe (>40% body surface area)
Sensation or itching	Pruritus	Slight and intermittent pain	Moderate and persistent pain	Severe and persistent pain
Swelling or edema	Present, asymptomatic	Symptomatic, tension	Secondary dysfunction	Total dysfunction
Blistering	Rare, sterile fluid	Rare, hemorrhage	Bullae, sterile fluid	Bullae, hemorrhage
Desquamation	Absent	Patchy dry	Patchy moist	Confluent moist
Ulcer or necrosis	Epidermal only	Dermal	Subcutaneous	Muscle or bone involvement
Hair Loss	Thinning, not striking	Patchy, visible	Complete, reversible	Complete, irreversible
Onycholysis	Absent	Partial	Partial	Complete
Hematopoietic Toxicity				
Lymphocyte changes_	≥1.5 x 10^9 cells/L	1-1.5 x 10^9 cells/L	0.5-1 x 10^9 cells/L	<0.5 x 10^9 cells/L
Granulocyte changes¶	≥2 x 10^9 cells/L	1-2 x 10^9 cells/L	0.5-1 x 10^9 cells/L	<0.5 x 10^9 cells/L
Thrombocyte changes#	≥100 x 10^9 cells/L	50-100 x 10^9 cells/L	20-50 x 10^9 cells/L	<20 x 10^9 cells/L
Blood loss	Petechiae, easy bruising, normal hemoglobin level	Mild blood loss with <10% decrease in hemoglobin level	Gross blood loss with 10%-20% decrease in hemoglobin level	Spontaneous bleeding or blood loss with >20% decrease in hemoglobin level

*Modified from Waselenko, MacVittie, Blakely, et al.[1]
† Reflex status (including corneal reflexes), papilledema, seizures, ataxia, and other motor signs or sensory signs.
‡ Impaired memory, reasoning, or judgment.
§ The extent of involvement is decisive and should be documented for all skin changes.
_ Reference value, 1.4-3.5 x 10 9 cells/L
¶ Reference value, 4-9 x 10 9 cells/L
# Reference value, 140-400 x 10 9 cells/L

The patient states she has been healthy otherwise and denies the possibility of pregnancy. Approximately 1 hour and 45 minutes post-exposure, she begins to develop emesis. One milligram of Granisetron (anti-emetic, 5HT3 serotonin receptor blocker) is administered intravenously. She undergoes repairs of her lacerations. Her heart rate is 98, her blood pressure is 132/78, and her initial complete blood count with differential is normal. Her B-HCG returns as negative.

COMMENT: BIODOSIMETRY

Individual radiation exposure dose (biodosimetry) is essential for predicting the clinical severity, treatment, and survivability of exposed individuals.[1] The three most important measures for calculating the exposure dose are:

- time to onset of vomiting
- the rate of lymphocyte depletion
- the presence of chromosome aberrations (chromosome dicentrics)

Annotation of any vomiting, with the time of onset, must be included on the patient's medical chart. Once the exposure dose is estimated, treatment and illness manifestations, as well as prognosis, can be estimated. Serial CBCs with differential (to derive the absolute lymphocyte count) are required to predict the rate at which the patient's lymphocytes will be depleted. Serial CBCs are performed every six hours. If the second CBC is abnormal, this result is used to calculate the rate or slope of decline. If the second CBC is normal, then a third CBC must be drawn to calculate the rate or slope. These data can be analyzed using the Biodosimetry Assessment Tool (BAT), which is available at no cost at http://www.afrri.usuhs.mil. This instrument will allow for a prediction of the patient's absorbed dose, which can then be used to establish the role, if any, for the use of colony-stimulating factors (CSFs) and other therapies. Table 2 demonstrates the data elements of biodosimetry to calculate a dose estimate. Biodosimetry should be used by the clinician, in conjunction with hematology/oncology expertise, to plan for treatment of the patient.

QUESTION 2

What historical and laboratory information is essential to estimate the radiation exposure rate?

a. Time to onset of fever, frequency of diarrhea, and chromosome dicentrics assay.
b. Time to onset of vomiting, serial CBCs, and chromosome dicentrics assay.
c. Time to onset of skin erythema, time to onset of vomiting, and the rate of granulocyte depletion.
d. Time to onset of fever, the degree of hypotension, and the early development of thrombocytopenia.

Based on the BAT calculation, and time to onset of vomiting of 1 hour and 45 minutes, the patient's exposure is estimated at 4 Gy. (Please refer to Table 2). After you discuss treatment options with the patient, she chooses to begin daily granulocyte-colony stimulating factor (G-CSF) injections at 300 µg subcutaneously while awaiting analysis of her decline in lymphocyte counts (lymphocyte depletion kinetics).

Eight hours later, after the patient's second CBC with differential returns, the data is analyzed using the BAT program. The program does not compute the exposure dose, because the lymphocyte number still falls in a normal range. A repeat

CBC in 6 hours is ordered. The third CBC with differential is analyzed and suggests a 4.2 Gy whole-body exposure, which is consistent with the time to onset of emesis and the dose estimate based on physical reconstruction (1/2 meter away from a Cs-137 source for three hours), which is ~ 3.96 Gy.

Twenty-four hours after the exposure, chromosome dicentrics, the gold standard test, has been drawn and submitted for further dose analysis. While the erythema previously noted on her back and buttocks has resolved, concern for ARS and local radiation injury is considered.

Table 2. Biodosimetry Based on Acute Photon-Equivalent Exposures*

Dose Estimate	Victims with Vomiting	Time to Onset of Vomiting	Absolute Lymphocyte Count†						Rate Constant for Lymphocyte Depletion‡	Dicentrics in Human Peripheral Blood Lymphocytes§	
			Day 0.5	Day 1	Day 2	Day 4	Day 6	Day 8		Per 50 Cells	Per 1,000 Cells
Gy	%	h	x10 ^{9} cells/L						k‡	n	
0	–	–	**2.45**	**2.45**	**2.45**	**2.45**	**2.45**	**2.45**	–	0.05-0.1	1-2
1	19		**2.30**	**2.16**	**1.90**	**1.48**	1.15	0.89	0.126	4	88
2	35	4.63	**2.16**	**1.90**	**1.48**	0.89	0.54	0.33	0.252	12	234
3	54	2.62	**2.03**	**1.68**	1.15	0.54	0.25	0.12	0.378	22	439
4	72	1.74	**1.90**	1.48	0.89	0.33	0.12	0.044	0.504	35	703
5	86	1.27	**1.79**	1.31	0.69	0.20	0.06	0.020	0.63	51	1024
6	94	0.99	**1.68**	1.15	0.54	0.12	0.03	0.006	0.756		
7	98	0.79	**1.58**	1.01	0.42	0.072	0.012	0.002	0.881		
8	99	0.66	**1.48**	0.89	0.33	0.044	0.006	<0.001	1.01		
9	100	0.56	1.39	0.79	0.25	0.030	0.003	<0.001	1.13		
10	100	0.48	1.31	0.70	0.20	0.020	0.001	<0.001	1.26		

* Depicted above are the 3 most useful elements of biodosimetry. Dose range is based on acute photon-equivalent exposures. The second column indicates the percentage of people who vomit, based on dose received, and time to onset. The middle section depicts the time frame for development of lymphopenia. Blood lymphocyte counts are determined twice to predict a rate constant that is used to estimate exposure dose. The final column represents the current gold standard, which requires several days before results are known. Colony-stimulating factor therapy should be initiated when onset of vomiting of lymphocyte depletion kinetics suggests an exposure dose for which treatment is recommended (see Table 3). Therapy may be discontinued if results from chromosome dicentrics analysis indicate a lower estimate of whole-body dose.

† Normal range, 1.4–3.5 x 10^9 cells/L. Numbers in boldface fall within this range.

‡ The lymphocyte depletion rate is based on the model Lt = 2.45 x 10^9 cells/L x e-k(D)t, where Lt equals the lymphocyte count (x 10^9 cells/L), 2.45 x 10^9 cells/L equals a constant representing the consensus mean lymphocyte count in the general population, k equals the lymphocyte depletion rate constant for a specific acute photon dose, and t equals the time after exposure (days).

§ Number of dicentric chromosomes in human peripheral blood lymphocytes.

COMMENT: TREATMENT/MANAGEMENT

Several well-designed prospective trials have examined a variety of colony-stimulating factors (CSFs) and schedules in irradiated non-human primates and canine models. These studies have demonstrated not only an enhancement in neutrophil recovery in those animals treated with early CSFs (<24 hours post-exposure), but more importantly, they have demonstrated a survival advantage, which serves as the justification for the current treatment recommendations.

CSFs should be initiated in any adult with a whole-body or significant partial-body exposure of >3 Gy. People at the extremes of age (ie, children <12 years of age and adults >60 years) may be more susceptible to irradiation and have a lower $LD_{50/60}$. Therefore, a lower threshold dose (2 Gy) for initiation of CSF therapy is appropriate in these populations and in those suffering from major trauma and/or burns.

Based on the patient's radiation exposure of ≥3 Gy, this level of exposure places her at risk of radiation-induced aplasia arising from ARS. The only hematopoietic CSFs which have marketing approval for the management of treatment-associated neutropenia are the recombinant forms of granulocyte-macrophage colony-stimulating factor (GM-CSF), G-CSF, and its pegylated form (PEG-G-CSF or pegfilgrastim). Currently, none of these cytokines has approval by the Federal Drug Administration for the management of radiation-induced aplasia. The optimal dose in this setting is unknown, so the doses of CSFs recommended are the standard doses employed in patients who have treatment-related neutropenia. All CSFs and most antimicrobials are class C drugs, so pregnant patients must be counseled prior to use of these agents. Tables 3 and 4 outline the treatment guidelines and recommended doses of cytokines.

While there may be an initial granulocytosis followed by significant neutropenia, the CSF should be continued throughout this entire time period, which may be prolonged. The CSF may be discontinued when the absolute neutrophil count (ANC) reaches a level of >1,000 cells/mm^3 after recovery from the nadir. Reinstitution of CSF may be required if the patient has a significant neutrophil decline (<500 cells/mm^3) after its discontinuation.

If resources allow, transplantation should be considered for people exposed to a dose of 7-10 Gy who are not suffering from significant burns or other major organ toxicity and who have an appropriate donor. A lower exposure may be considered in those patients with a genetically identical donor or previously stored autograft.

Transfusion of cellular components such as packed red blood cells and platelets are required for patients with severe bone marrow damage. All products must be leukoreduced and irradiated. Leukoreduction affords some protection against platelet alloimmunization, as well as protection against acquiring cytomegalovirus infections. Irradiation of the products will prevent the development of transfusion-associated graft versus host disease, a fatal complication that can arise in immunocompromised patients given products with alloreactive lymphocytes. Although the benefit of epoetin and darbepoetin have not been established in radiological events, their use should be considered for patients with anemia. Response time is delayed by 3-6 weeks and iron supplementation may be required.

Prophylaxis of vomiting is not recommended as its development and time of onset has merit as a biodosimetric tool. Prolonged antiemetic therapy is not warranted in this situation as it usually abates in 48-72 hours. However, serotonin receptor antagonists are very effective prophylaxis for patients who have received therapeutic radiation. Another therapeutic option, neuroleptic derived antiemetics, can be employed for breakthrough nausea or employed if the former is not available.

COMMENT: ROLE OF POTASSIUM IODIDE (KI)

It is a common misconception that potassium iodide (KI) should be used as a prophylaxis in all cases of radiation exposure. In fact, KI is indicated only for treatment of radionuclide containing iodine. Individuals, especially those who are iodine avid such as children, adolescents, and pregnant women, are particularly prone to developing malignancy of the thyroid gland and may be afforded some protection with KI if exposed to radioiodines.

Table 3. Guidelines for Treatment of Radiologic Victims*

	Proposed Dose (Gy) Range for Treatment with	Proposed Dose (Gy) Range for Treatment with	Proposed Dose (Gy) Range for Referral for SCT Consideration
Small-volume scenario (£100 casualties)			
Healthy person, no other injuries	3-10‡	2-10§	7-10 for allogeneic SCT; 4-10 if previous autograft stored or syngeneic donor available
Multiple injuries or burns	2-6‡	2-6§	NA
Mass casualty scenario (>100 casualties)			
Healthy person, no other injuries	3-7‡	2-7§_	7-10 for allogeneic SCT_; 4-10 if previous autograft stored or syngeneic donor available_
Multiple injuries or burns	2-6_	2-6_	NA

* Consensus guidance for treatment is based on threshold whole-body or significant partial-body exposure doses. Events are due to a detonation of a radiologic dispersal device resulting in £100 casualties and those due to detonation of an improvised nuclear device resulting in >100 casualties have been considered. These guidelines are intended to supplement (and not substitute for) clinical findings based on examination of the patient. NA = not applicable; SCT = stem-cell transplantation; ANC = absolute neutrophil count

† Prophylactic antibiotics include a fluoroquinolone, acyclovir (if patient is seropositive for herpes simplex virus or has a medical history of this virus), and fluconazole when absolute neutrophil count is <0.500 x 10^9 cells/L.

‡ Consider initiating therapy at lower exposure dose (2 Gy) in non-adolescent children and the elderly. Initiate G-CSF or GM-CSF treatment in victims who develop an ANC <500 cells/mm^3 and are not already receiving a CSF.

§ ANC <500 cells/mm^3 . Antibiotics should be continued until neutrophil recovery has occurred. Follow Infectious Diseases Society of America guidelines for febrile neutropenia if fever develops while on prophylaxis.

_ If resources are available.

Table 4. Recommended Doses of Cytokines. *

Cytokine	Adults	Pediatrics	Pregnant Women†	Precautions
G-CSF or filgrastim	5 ug/kg of body weight per day as a SC injection started as early as possible and continued until ANC >1,000 cells/mm^3	5 ug/kg of body weight per day as a SC injection started as early as possible and continued until ANC >1,000 cells/mm^3	Class C	Sickle cell hemoglobinopathies, significant coronary artery disease, ARDS. Consider discontinuation if pulmonary infiltrates develop at neutrophil recovery.
Pegylated G-CSF or Pegfilgrastim	6 mg SC x 1 dose	For adolescents >45 kg: 6 mg SC x 1 dose	Class C	
GM-CSF or Sargramostim	250 ug/m^2 of body weight per day as a SC injection started as early as possible and continued until ANC >1,000 cells/mm^3	250 ug/m^2 of body weight per day as a SC injection started as early as possible and continued until ANC >1,000 cells/mm^3	Class C	

* Abbreviations: absolute neutrophil count (ANC), subcutaneous (SC), acute respiratory distress syndrome (ARDS), granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF).

† Experts in biodosimetry need to be consulted. Any pregnant patient with radiation exposure should be evaluated by a health physicist to have the fetal exposure assessed. Class C refers to U.S. Food and Drug Administration Pregnancy Category C, which indicates that studies have shown animal, teratogenic, or embryocidal effects, but there are no adequate controlled studies in women; or no studies are available in animals or pregnant women.

QUESTION 3

Potassium iodide (KI) prophylaxis prevents which of the following?

a. Bone marrow suppression arising form ionizing radiation
b. Thyroid cancer arising from ionizing radiation
c. Thyroid cancer arising from radioiodine exposure
d. Acute radiation syndrome arising from ionizing radiation

The patient's chromosomal dicentrics revealed an exposure dose of 4.1 Gy. She experienced pubic hair loss 2 weeks post-exposure, which was the extent of her cutaneous injury. She developed significant neutropenia (<500 cells/mm^3) approximately 18 days after the incident and was started on prophylactic levofloxacin at 500 mg/day, diflucan at 400 mg/day, and acyclovir 400 mg twice daily. Prophylaxis against fungal and viral pathogens is warranted, analogous to those patients undergoing stem cell transplantation for hematological malignancies. She received leukoreduced and irradiated products to support her through her aplastic phase. She developed febrile neutropenia, and she was started on cefepime, and her levofloxacin was discontinued. A fever work-up failed to reveal a focus of infection, but she defervesced.

COMMENT: TREATMENT OF COMPLICATIONS/INFECTIONS

Susceptibility to infection results from a breech of the body's natural line of defense, including the skin and/or mucosal barriers as well as immune suppression consequent to a decline in lymphohematopoietic elements. Irradiated animals and patients are uniquely susceptible to sepsis from a smaller innoculum of bacteria.

In patients experiencing significant neutropenia, ANC <500 cells/mm^3, broad-spectrum prophylactic antimicrobials should be given during the potentially prolonged period of neutropenia. Prophylaxis should include a fluoroquinolone with streptococcal coverage or a fluoroquinolone without streptococcal coverage plus penicillin (or a congener of penicillin), antiviral drugs (acyclovir or one of its congeners), and antifungal agents (fluconazole). Antimicrobials should be continued until they are clearly not effective (ie, the patient develops neutropenic fever) or until the neutrophil count has recovered with an ANC >500/mm^3.

Focal infections that develop during the neutropenic period require a full course of antimicrobial therapy. Therapy of patients with neutropenic fever should be guided by the recommendations of the Infectious Diseases Society of America. Use of additional antibiotics is based on treatment of concerning foci, and these complicated issues should be addressed in consultation with your infectious disease team.

The patient demonstrates evidence of count recovery at day 27. Her cefepime, fluconazole, and acyclovir were discontinued as her cultures remained negative. In spite of her neutrophil recovery, her CD4 count on day 30 was 124 and she was started on *Pneumocystis jirovecii* pneumonia (formerly *Pneumocystis carini* pneumonia or PCP) prophylaxis, which is to be continued until her absolute CD4 count is >200 cells/mm^3.

COMMENT: LONG-TERM MANAGEMENT

The patient's CD4 count should be monitored every 3 months and her *Pneumocystis* prophylaxis should continue until her CD4 count is >200 cells/mm^3. Based on her cytomegalovirus seropositivity, her immunosuppression, and the undefined risk of reactivation in this setting, monitoring every week for CMV antigenemia until approximately day 100 post-exposure is recommended. The patient should see an immunologist 12 months post-exposure to assess for waning immunity against poliovirus, tetanus, diphtheria, and measles.

Additionally, significant radiation to the spleen may result in functional hyposplenism, although unlikely at this dose. However, vaccination for *Hemophilus influenzae* type B, *Streptococcal pneumoniae*, and *Neisseria meningitidis* should be considered in the appropriate setting. Avoidance of live vaccines for at least 24 months would be prudent. Long-term surveillance for subsequent myelodysplasia and secondary malignancies is requisite. The patient should also be counseled regarding additional modifiable risks, such as smoking cessation, if applicable.

CONCLUSION

The medical management of irradiated patients is complex and resource demanding. While the loss of life may be considerable, especially if a more sophisticated device were employed, the benefit of supportive care is significant. Maximal deployment of finite resources will require appropriate triage, so that one may enhance the survival of as many victims as possible.

ANSWER KEY & DISCUSSION

QUESTION 1

As you prepare to take care of ED patients who have been involved in this disaster and have been decontaminated, what PPE should you wear?

a. N-95 respirator, gown, shoe covers, and gloves
b. Powered Air Purifying Respirator (PAPR), gown, shoe covers, and double gloves
c. Hazmat suit
d. Surgical face mask, gown, shoe covers, and double gloves.

ANSWER: The correct answer is d. All healthcare providers should undertake simple precautions such as wearing PPE. In the hospital setting, this will include gown, face mask, shoe covers, and double gloves. The inner gloves should be taped to the gown so that they are not pulled off when the exterior gloves are removed, as frequent changing of outer gloves are required. This will prevent self-contamination and prevent contamination spread throughout the hospital environment.

QUESTION 2

What historical and laboratory information is essential to estimate the radiation exposure rate?

a. Time to onset of fever, frequency of diarrhea, and chromosome dicentrics assay.
b. Time to onset of vomiting, serial CBCs, and chromosome dicentrics assay.
c. Time to onset of skin erythema, time to onset of vomiting, and the rate of granulocyte depletion.
d. Time to onset of fever, the degree of hypotension, and the early development of thrombocytopenia.

ANSWER: The correct answer is b. Time to onset of vomiting and the rate of lymphocyte depletion have been shown to correlate with whole-body and significant partial body ionizing radiation. These, along with chromosome dicentrics, are currently the best biodosimetry indicators for the clinician charged with large numbers of casualties and the need to make decisions expeditiously. Early onset fever and diarrhea may indicate a lethal exposure, but they have not been shown to be predictive in a biodosimetry model. Early transient skin erythema suggests radiation damage to the skin has occurred and suggests a dose of more than 2 Gy, but does not accurately predict whole-body dose.

QUESTION 3

Potassium iodide (KI) prophylaxis prevents which of the following?

a. Bone marrow suppression arising form ionizing radiation
b. Thyroid cancer arising from ionizing radiation
c. Thyroid cancer arising from radioiodine exposure
d. Acute radiation syndrome arising from ionizing radiation

ANSWER: The correct answer is c. KI affords some protection against the long-term sequelae of thyroid malignancy, resulting from exposure to radioiodines. It must be given as soon as possible and is particularly important for iodine avid individuals such as, infants, children, and pregnant women. KIs role in radiation exposure is limited to thyroid protection and is only beneficial if radioiodine is present. It does not protect the thyroid from the effects of ionizing radiation nor does it have any impact on marrow suppression.

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