National Center for Disaster Medicine and Public Health

Radiation Disaster Issues in Children:

An Approach to the Patient

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Drug Disclaimer

Drugs with potential therapeutic value are mentioned in this primer. For the purposes of this primer, the following drugs are considered FDA off-label for radiation disaster induced neutropenia:

- Pegfilgrastim
- Filgrastim
- Sargramostin.

A Strategic National Stockpile (SNS) Radiation Working Group has recommended these drugs for use in radiation disaster induced neutropenia, and FDA advisory committees are evaluating this for further consideration as a label change. To follow this evolving preparedness effort, please see http://www.fda.gov/AdvisoryCommittees/Calendar/ucm341085.htm.

The following drugs may be off-label for pediatric radiation disaster patients depending on the age of the patient not due to the indication:

- Prussian Blue
- Cefepime

- Gancyclovir
- Valacyclovir
- Granisetron
- Loperamide
- Ciprofloxacin
- Levofloxacin
- Fluconazole.

Intended Audience

This primer is designed for health care providers.

Objectives

At the conclusion of this activity, the participant will be able to:

1. Apply basic concepts of ionizing radiation to pediatric disaster patients.

2. Describe unique pediatric management priorities after ionizing radiation incident exposures.

3. Develop an appropriate clinical management plan for the pediatric radiation disaster patient and manage the case in collaboration with appropriate consultants.

Competencies

If you are using a competency-based approach for your professional development, or using this document as part of a competency-based education or training program, the following information is provided to assist you in relating this document to competency development.

This document supports learning related to the following competencies, *with regard to radiation issues in pediatric disaster patients: **

Core Competencies and Subcompetencies for Disaster Medicine and Public Health by Walsh, et al. [1]

> Subcompetency 4.1 "Identify authoritative sources for information in a disaster or public health emergency"
>
> Core Competency 7.0 "Demonstrate knowledge of principles and practices for the clinical management of all ages and populations affected by disasters and public health emergencies, in accordance with professional scope of practice"
>
> Subcompetency 7.1 "Discuss common physical and mental health consequences for all ages and populations affected by a disaster or public health emergency"
>
> Core Competency 11.0 "Demonstrate knowledge of short- and long-term considerations for recovery of all ages, populations, and communities affected by a disaster or public health emergency"
>
> Subcompetency 11.1 "Describe clinical considerations for the recovery of all ages and populations affected by a disaster or public health emergency" [1(pp 50-51)]

* There are many published competency sets within the field of disaster health. For additional information, see: Disaster-related competencies for healthcare providers. Disaster Information Management Research Center, National Library of Medicine at: http://disaster.nlm.nih.gov/dimrc/professionalcompetencies.html

Disclaimers

1. The views expressed are those of the author and do not reflect the official policy or position of the National Center for Disaster Medicine and Public Health, the Uniformed Services University of the Health Sciences, the Department of Defense or the United States Government.
2. Medication doses expressed as dose/kilogram (kg) or dose/meter squared (m^2) are pediatric doses unless otherwise specified.
3. This Primer references unlabeled or unapproved drugs that may be considered for use in pediatric patients of radiation disasters—for a more detailed discussion please see the next section titled "Drug Disclaimer".
4. Information about drugs and dosages current as of July 2013.
5. Health care providers should consider the specific circumstances of each patient encountered during an emergency, the resources available at that time, and use his/her best clinical judgment when providing care.
6. The information in this Primer is meant to supplement principles of good clinical management.

Drug Disclaimer

Drugs with potential therapeutic value are mentioned in this primer. Indications (FDA on-label) and dosages can be challenging during routine daily clinical care of pediatric patients. In the context of a radiation disaster, this is even more challenging.

As they assess and care for their patients, clinicians caring for pediatric radiation disaster casualties should check product information, the FDA website, published literature, and remain attuned to Federal and State emergency policy declarations, such as "emergency use authorizations" and public health emergency declarations which may alter their obligations to inform patients in such a disaster or contingency setting. Because of the evolving nature of a radiation disaster, such as the detonation of an improvised nuclear device, clinicians should anticipate a fluid legal and policy situation in the immediate response and recovery phases (first 4 weeks after detonation).

For the purposes of this primer, and in compliance with continuing health education requirements, the following drugs are considered FDA off-label for radiation disaster induced neutropenia:

- Pegfilgrastim
- Filgrastim
- Sargramostin.

A Strategic National Stockpile (SNS) Radiation Working Group has recommended these drugs for use in radiation disaster induced neutropenia, and FDA advisory committees are evaluating this for further consideration as a label change. To follow this evolving preparedness effort, please see http://www.fda.gov/AdvisoryCommittees/Calendar/ucm341085.htm .

The following drugs may be off-label for pediatric radiation disaster patients depending on the age of the patient not due to the indication (they should otherwise be considered on-label when used to treat secondary morbidities from radiation exposure such as infection):

- Prussian Blue
- Cefepime
- Gancyclovir
- Valacyclovir
- Granisetron
- Loperamide
- Ciprofloxacin
- Levofloxacin
- Fluconazole.

Should the clinician feel the risk/benefit ratio warrants use of aforementioned drugs in pediatric radiation disaster patients, then she should inform the child's parents or legal guardians of the need and seek their consent.

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1.0 .Introduction

The risk for radiation exposure in humans comes from various sources, some natural, some accidental, and some intentional. Depending on the dose, radiation effects can range from no effect to significant, and possibly lethal, short-term and/or long-term effects. Most of these effects have been determined from the study and management of historical human exposures. This publication will focus on the medical effects that radiation exposure has on children. Because children undergo more rapid growth and development, radiation exposure can present unique health challenges compared to adults. Much of what is known currently is extrapolated from adult information and experience. An excellent resource for more information, videos, and algorithms for many of the topics discussed in this publication can be found on the U.S. Department of Health and Human Services' Radiation Emergency Medical Management (REMM) website which provides guidance on the diagnosis and treatment for health care providers dealing with radiation exposures and can be found at http://www.remm.nlm.gov/wheretostart.htm.

Accidently exposed children occur mainly as a result of medical procedures exposure or secondary to parental occupational exposure/contamination. Non-accidental (intentional) exposure from the use of nuclear weapons, improvised nuclear devices (INDs) and dirty bombs (radiological dispersion devices, RDDs) will be a real threat for the foreseeable future. Since children are likely to receive radiation exposures from intentional acts, and are a more vulnerable population in some ways, it is important to understand their differences from adults when considering disaster management scenarios. Once immediate lifesaving measures are performed and the child undergoes successful decontamination, the management of the pediatric patient exposed to ionizing radiation requires the following information:

1. Total dose
2. Dose rate
3. Type of radiation exposure
4. Mode of exposure
5. External and/or internal exposure
6. Isotopes involved
7. Co-injuries (burns, trauma, etc.)
8. Co-morbidity
9. Biodosimetry

With this knowledge a problem-based estimate of the health impact of the radiation exposure and a patient-based management plan can be developed.

With any radiation exposure it is important to verify the source, type, and duration of exposure. It is also important to know how the exposure occurred and if additional injuries are present.

2.0 Radiation Biology

Ionizing radiation affects cells in the living organism by directly damaging DNA, RNA, and proteins, and by the production of damaging free radicals by its interaction with substances such as water (the body is comprised of about 85% water), which cause similar cellular damage. Each cell and tissue type responds and reacts to this damage in different ways. Some tissues are able to withstand radiation damage better than other tissues. For example, rapid-turnover cells, such as gastrointestinal mucosa, are more sensitive to radiation exposure than tissue such as cortical bone. Damage occurs to mucosa at lower radiation doses than for bone. The most sensitive cells to radiation are spermatogonia, lymphocytes, hematopoietic stem cells, and intestinal crypt cells. Least sensitive are nerve and muscle cells. In addition to varying tissue tolerance of radiation exposure for different cells, specific organ tolerance of radiation exposures may differ depending on the age of the patient. For example, younger children have less myelination of the central nervous system than adolescents and adults and are therefore more sensitive to certain side effects of radiation exposure at a given dose. Depending on the dose and the cell's or tissue's susceptibility, the damage caused to organs by radiation can lead to cell death (lethal), or can be sub-lethal. Sub-lethal damage can lead to the cell fully repairing itself, or can leave the cell with impaired function and an abnormal ability to reproduce itself (mutation).[2, 3]

When ionizing radiation damages the DNA of a cell, it causes breaks in the DNA strands. When the DNA strand attempts to naturally repair itself, it forms new bonds in a chromosome that results in swapping parts with other chromosomes. This recombination leads to aberrant combinations that can be viewed under the microscope and appear as dicentric chromosomes (instead of the normal monocentric chromosomes). These dicentrics, which rarely form spontaneously, can be quantified resulting in an estimated radiation exposure dose. The ability to perform a dicentric assay to estimate radiation dose is a form of biodosimetry. **Biodosimetry** is an important tool for health care providers following radiation exposure to determine the expected care and outcome for an individual affected patient. **Forms of radiation biodosimetry include**:[2, 4]

-Signs and symptoms (such as timing of vomiting after exposure)

-Measurements of radioactivity of the exposed with personal and area dosimetry

-Hematologic parameters from a CBC with differential for serial lymphocyte counts

-Dicentric determination with cytogenetics

-Bioassay sampling as appropriate (nares and other mucous membranes, blood tests such as serum amylase, CRP, citrulline level, etc.)

It is necessary to utilize multiple parameters when determining exposure/risk depending on the situation, population, and capabilities as an occurrence progresses over time. These parameters can be used together to determine triage and to guide medical treatment. The Armed Forces Radiobiology Research Institute (AFRRI) has a **Biodosimetry Assessment Tool (BAT)** available as a software application. It is available on request for download from AFFRI at:

http://www.usuhs.mil/afrri/outreach/request.htm

3.0 Types of Radiation Incidents

Most causes of radiation exposures today occur from medical, research, and industrial sources. They can involve a single person or many people, depending on the situation. These are mostly accidental and can involve other injuries, such as burns and/or wounds. Common radioactive sources involved include technetium-99, indium-111, gallium-67, iodine-131, iodine-125, iridium-192, cobalt-60, cesium-137, and radium-226.[3]

Other accidental radiation exposures occur through nuclear reactor explosions and nuclear fallout (with or without explosion). These exposures usually involve multiple people, including whole local populations. Large scale decontamination and medical response measures add to the complexity of these situations. These radioactive agents include fission products, iodine-131, and long-term isotopes, such as cesium-137 and strontium-90.[3]

Terrorism including radioactive ("dirty") bombs and weapons (improvised nuclear devices, INDs) represent intentional exposures and are a real threat in today's world. Radioactive agents of concern include enriched uranium, depleted uranium, plutonium, tritium, and radium. Some of these agents are high energy, or have extremely long decay half-lives. When weaponized, these agents become internalized through wounds, burns, and blast injuries that make the surgical and medical management more complicated.

4.0 Isotopes Likely

Ionizing radiation exposures can occur as a result of accidental or non-accidental exposures. Commonly used isotopes and isotopes used in past episodes of radiation exposures and some of their characteristics are listed in Table 5. *(Also available on REMM:* **http://www.remm.nlm.gov/isotopestable.pdf**)

5.0 Types of Contamination

When exposed to radiation without contamination from fallout, the individual does not become radioactive. The radiation energy passes through the individual. When the radioactive substance is attached to the individual's clothing or skin, however, there is external contamination, and the individual is in fact radioactive until this external contamination is removed. Because fallout is like coarse dust or ash, just walking through a radiation area affected by fallout will lead to external contamination. When the radioactive substance is ingested, inhaled, or lodged in tissue (i.e., through a wound), the individual has internal contamination. Internal and external contamination can occur together in the same setting. A helpful algorithm for assessing contamination and related radiation exposure can be found at http://www.remm.nlm.gov/contamonly.htm#skip.

5.1 External Contamination

External contamination occurs when clothing, hair, or skin becomes contaminated with radioactive material. If this occurs because of fallout, the highest levels of radioactivity on the exposed individual will be closer to the ground. Thus, children and crawling infants are more likely to come in contact with fallout through skin exposure. **External contamination of the skin can lead to ingestion or inhalation of the radioactive substance leading to internal contamination.** External contamination with alpha emitters does not cause significant external injury, since they are blocked by the outer layer of skin. They can be ingested or inhaled, though, and result in internal organ damage. Children are more likely to ingest these in an exposure through placing contaminated hands in their mouth, nose picking, etc. Beta emitters, however, cause significant injury to skin and tissue with external contamination, and need to be removed as soon as possible. If the source of external contamination is a gamma emitter, full body radiation exposure can occur resulting in acute radiation sickness (described later). When external contamination occurs, at least 90-95% of the radioactivity can be removed just by removing the contaminated clothing and shoes and washing off with soap and water, part of the decontamination process.[5, 6] A video resource developed originally for chemical decontamination, can be applied to this setting of children externally contaminated with radiation-- http://www.youtube.com/watch?v=ctt6RJGMV9Y. While this is a chemical decontamination video and the methods will differ for radiation, it brings up valuable points for pediatric patients. Another recommended method of removing external contamination is simply brushing off the patient if environmental or other local factors make washing less feasible.

An important concept in the care of patients externally contaminated by radioactive material is their assessment and care pose little to no risk to medical personnel. There have been no case reports of a medical provider harmed or injured because of caring for a radioactively contaminated patient. Health care personnel responding to, and involved in, a

radiation exposure situation should wear personal protective equipment (PPE, as discussed below), but should not let the donning of PPE interfere with emergency, life saving care of radioactively contaminated patients. Contaminated patients should have any life-threatening injuries or illnesses addressed before decontamination occurs. Emergency care should never be delayed for decontamination. When the patient is stable, decontamination can occur in the emergency setting. It is important to decontaminate the patient as soon as possible after care for life-threatening injuries has been provided to minimize the radiation dose. ***Remember that simply removing the clothing and shoes reduces significantly the radiation from external contamination.***[3, 7] Further details on decontamination for external contamination can be found at the REMM website at http://www.remm.nlm.gov/ext_contamination.htm.

Part of the radiation dosimetry process requires sampling of externally contaminated patients to assist in determining the extent and route of exposure. See NCRP Composite Glossary for additional information on related terminology: http://www.ncrponline.org/PDFs/NCRP Composite Glossary.pdf). Swipes of the skin and swabs of all exposed orifices (nose, mouth) should be collected (individual swab for each nostril), labeled, and individually wrapped for radiation assay. Nasal swabbing is useful to determine risk for inhalation exposure, particularly if done soon after the exposure. Any bandages should be saved as well for dosimetry analysis. If radiation detection, indication, and computation (RADIAC) equipment is available, areas contaminated by radioactivity ("hot") can be detected and these areas can be swiped for assay.[3, 7] Additionally, place clothes and shoes from contaminated patients in a separate, labeled plastic bag for radiation testing as you would also save swabs, swipes, and removed bandages.

5.2 Internal Contamination

Internal contamination occurs when a radioactive material enters the body. This can occur by ingestion, inhalation, or through wounds in collateral injuries. Internal contamination also can occur with aggressive external decontamination procedures, such as vigorous scrubbing of contaminated skin, which can lead to abrasions that allow internalization of radioactive substances. Children are more prone than adults to ingestion from external contamination by placing unwashed hands in their mouth.

Acute medical effects of internal contamination are less common than chronic radiation injury to target organs depending on the ingested agent and its metabolism. If a high energy gamma emitter is internalized, it can result in whole body radiation exposure and lead to acute radiation syndrome (discussed below).

Inhaled radioactive agents, such as alpha emitters, can lead to pulmonary fibrosis. Once the agent is inhaled it may be absorbed into the lymphatics or blood stream, where it may cause other organ damage. In these instances, collect any sputum for radioactivity assay.[3, 7]

Ingested agents may cause some gastrointestinal damage if they are of high enough energy. Insoluble agents pass through the GI tract and are excreted. If they are alpha emitters they usually do not cause damage. Beta or gamma emitters can cause significant injury. Soluble radioactive agents are more problematic because they can cause significant organ toxicity once they are absorbed systemically. In these cases, collect any emesis for radioactivity assay.

Radioactive agents also can be internalized through the skin. Intact skin prevents the absorption of most compounds, but some radioactive agents, such as tritium-water and radioactive iodine, can be passively absorbed. Skin that has been damaged because of trauma, burns, abrasions, etc., can lead to internalization of external contamination. Radioactive material also can be weaponized in bombs and projectiles, which are internalized through wounds. For the reasons outlined, broken skin and wounds in a radioactive contamination situation should be carefully and fully evaluated for radioactivity. **To decrease continued radiation exposure, wounds should be fully irrigated and foreign materials removed to the extent possible and saved for dosimetric analysis.**

Internal contamination with soluble radioisotopes affects different organs depending on the isotope involved. Specific agents and their management will be discussed below. In addition to the survey and sample collections described above for external contamination, patients known or suspected of internal contamination should have all wounds assayed for radioactivity by RADIAC survey or swipes. As indicated and where available, whole body RADIAC equipment, such as whole body scanners, should be utilized. In addition urine (spot urine and 24 hour collection) and stool must be collected and assayed for radioactivity. Blood samples for complete blood count serum chemistries/additional labs should be collected to determine radiation exposure extent and to monitor effects on certain target organs, such as the liver, kidney, or thyroid, as indicated (see example order template for these patients with suggested lab tests at http://www.remm.nlm.gov/adult_and_pediatric_orders.pdf). Any foreign bodies from radioactive wounds should be saved for radioactivity assay as well (as discussed above for biodosimetry). For guidance on technique on assessing for external contamination using a hand held device (Gieger counter), see http://www.remm.nlm.gov/remm_RadPhysics.htm#survey. Additional information on various RADIAC devices and their uses can be found at http://www.remm.nlm.gov/civilian.htm.

6.0 Differences between Children and Adults

6.1 Biological Considerations

Children are more vulnerable than adults in many clinical situations, including radiation exposures. Children metabolize various compounds differently than adults. This difference in

metabolism can lead to enhanced organ toxicity from certain agents. One example is the effects of radioactive iodine exposure on the developing thyroid gland. In addition, children are undergoing relatively rapid growth compared to adults and many of their organs are not fully developed. Radiation exposure to organs such as the central nervous system, the developing gonads, and the heart will have more deleterious effects than on those same organs in adults at the same radiation doses.[5]

Children have thinner skin than adults and therefore encounter more significant damage at the same level of thermal injury. In addition, because of their larger body surface area related to mass, they are more susceptible to increased fluid losses secondary to burns, vomiting, diarrhea, and decreased oral intake. Their smaller physical mass also makes them less tolerant of radiation doses in general than adults, and more likely to have significant injury from the same blast and thermal exposure.[5]

Children have a faster respiratory rate and may receive more absorbed dose of radiation from inhaled radioactive agents than adults during the same exposure. As mentioned above, children may also be more likely to ingest radioactive agents through hand-to-mouth action. For younger children and infants in a fallout situation, their closer proximity to the ground may lead to greater exposure through skin contamination and greater body exposure due to greater radiation levels at ground level. Children are also less able to escape dangerous situations than adults because of decreased mobility, fear, and immature decision making, so may receive a greater radiation dose secondary to prolonged exposure.[5]

6.2 Family Considerations

Children respond better in disaster situations if they have family members present with them, particularly their parents. Long-term psychological damage (such as post-traumatic stress disorder (PTSD)) can be lessened with family involvement. Every effort should be made to keep family units together. Also, identifying co-morbid conditions, medications being taken, and other medical historical information is greatly facilitated if family is present.[6] An excellent website that discusses family emergency preparation for radiation disasters can be found at the Centers for Disease Control, Radiation Emergencies website at: **http://www.bt.cdc.gov/radiation/**

6.3 Psychosocial Considerations

In any disaster situation, it is important to educate children about disasters without overly alarming them. Preparing for the possibility of disasters is important for every family. Including in this preparation is discussing with children the possibility of disasters and what to do if they occur based on their individual developmental age. Use the following guidelines:[8]

- Tell children that a disaster is something that could hurt people or cause damage.
- Explain how important it is to make a family disaster plan.
- Teach children
  - How to call for help

- When to call each emergency number
- To call the family contact if separated
- To keep personal identification information in their possession at all times

Once a radiation disaster has occurred the psychological effects can be apparent for years. One of the most common disabling consequences is chronic fear and anxiety. This can lead to significantly more social isolation and negative life events for these children and their families.[9] Individuals who have experienced even the threat of radiation exposure, such as those living near nuclear power plants where accidents have occurred demonstrate a high level of psychosomatic complaints and have higher levels of neuroendocrine stress hormones that can last for years following the event.[9] If the radiation exposure event is associated with witnessed injuries or deaths, the emotional effects are enhanced. Reported behavioral consequences in these instances have resulted in disruption of interpersonal relationships, attitude, and social outlook that, if chronic, can lead to health effects, such as hypertension.[9] Psychobehavioral disturbances are further magnified when disasters are accompanied by loss of home, family members, or lack of timely information.[9]

Management of the psychological harm to children after a radiation disaster requires that pediatricians provide advice to parents and supportive counseling to children and families. Pediatricians should screen children closely for the presence of adjustment reactions and stress responses after a disaster has occurred. They should additionally assist parents in identifying the early signs of adjustment reactions, particularly in toddlers and other children who may have difficulty verbalizing their feelings. Finally, children should be referred for mental health services in a timely manner when behavioral disturbances are found.[9]

6.4 Special Needs Children

Depending on the specific disorder or need, special needs children will be even more vulnerable than otherwise well children in any disaster situation. Mobility issues can be significant with non-mobile, larger children. Special equipment may be needed for certain children, such as those with tracheostomies who are ventilator dependent.[6]

7.0 Clinical Management Considerations for Children

Patients exposed to radiological agents generally do not pose a danger to healthcare personnel. Necessary medical and surgical treatment to prevent loss of life or limb should not be delayed for decontamination of the radioactively contaminated patient. Emergency medical care should be the same initially for these patients as for patients who are not contaminated with radioactivity---the ABC's, now CAB's (for circulation, airway, breathing) in the new Pediatric Advanced Life Support (PALS) standards-- should be assessed and addressed first. [10] Following this, the patient can be evaluated for radioactivity and decontaminated.[2] A sample set of inpatient orders for patients admitted with radiation exposure can be found at

http://www.remm.nlm.gov/adultorderform.htm and serve as a prototype for items to consider depending on the specific patient and incident being managed.

7.1 Assessment/Decontamination

(Algorithm on REMM helpful for further guidance at http://www.remm.nlm.gov/contamonly.htm#skip)

Patients with radiation exposure will often be asymptomatic early after the exposure, so a careful history must be taken to help with the determination of the likely radiation dose. Three key parameters provide critical information for determining dose:

- time of exposure
- distance from the radiation source
- duration of exposure.

Timing of symptom onset can be an important clue on the radiation dose received. Nausea and vomiting can occur minutes to days following exposure. **The earlier vomiting occurs, the higher the dose of radiation absorbed by the patient. Dose estimates based on the onset of vomiting have been suggested for adult patients, but there is no estimate for pediatric patients.** Thus, adult estimates should be cautiously applied to children.

7.1.1 Internal vs. External Contamination

External decontamination must be addressed before internal contamination. RADIAC surveys should be done frequently until decontamination is complete and care should be taken not to contaminate the RADIAC equipment itself with radioactivity**. Removal of clothing will remove about 90% of external contamination. Careful and gentle washing of the skin and hair will remove the majority of the rest.** Following decontamination RADIAC equipment can help guide the areas of skin that need to be swiped and further decontaminated. Contaminated wounds also need to be swiped as do bilateral nares. Radiation activity found on nasal swabs is indicative of potential dose to the lungs. **Swabs of nares** should be done as early as possible since radiation levels will be cleared from the nares by normal respiratory processes. Urine and stool should also be collected and assayed for radioactivity for indication of ingested radioactive agents.[3, 7]

7.1.2 Biodosimetry/Biomarkers

The REMM website is an excellent resource for a variety of radiation related information. A useful tool for estimating radiation dose exposure using basic biodosimetry measures (onset of vomiting or progressive lymphocyte counts) can be found at:

http://www.remm.nlm.gov/ars_wbd.htm

A more extensive tool (the Biodosimetry Assessment Tool (BAT)) is available on request for download from AFFRI at:

http://www.usuhs.mil/afrri/outreach/request.htm

7.2 Combined Injuries

Injuries suffered during radiation exposures involving blasts or weapons can include open or penetrating wounds and burns. These areas can be contaminated with radioactivity, which must be assessed and considered with treatment. Burns that are superficial can be decontaminated by washing and irrigation. Full thickness burns should be treated per standard burn protocols. Any radioactivity in the burn eschar will slough off with the dead tissue over time. Since there is no blood flow through this damaged tissue, the radioactivity in the eschar will not become systemic.[2, 6]

Wounds should be flushed with copious amounts of fluids, including wounds of skin, abdomen and chest. If radioactivity remains in the wound, it will be removed with the normal debridement of the wound if needed. Eye contamination should also be removed with copious flushing of the appropriate fluids. Radioactive wash fluids should be collected and processed separately.[2]

In significant whole body radiation exposures (discussed further below in the Acute Radiation Sickness section), **the presence of wounds and burns complicate the care and decrease the survival of patients** because of healing complications and infection risks.

8.0 Internal Contamination

Extra vigilance for internal contamination is warranted in children. Consider internal contamination if the RADIAC readings remain persistently high after decontamination or if your history suggests it. Nose and mouth contamination may indicate inhalation or ingestion. Gastric lavage, cathartics, laxatives, and antacids can assist in clearing ingested agents.

8.1 Medical Effects/Issues

With internal contamination, several factors are important to consider in determining the overall risk for acute and long-term effects of radiation exposure. These factors include the amount of internal contamination of the patient, the radiation characteristics, radiation biological half-life, and target organs for the particular isotope or type of radiation.

The biological half-life is different than the radioactive decay half-life of the radioisotope. **The biological half-life refers to the time it takes for half of the radioactive substance to be removed from the body after being internalized**. For example, even though the radioactive decay half-life of cesium-137 is 30 years, the biological half-life ranges from 12-

165 days, and is shorter in infants than in adults. Tritium (hydrogen-3) has a radioactive decay half-life of 12 years, but a biological half-life of 10-12 days.[3]

The radiation agent characteristics are important to consider for dose effects. A weak beta emitter such as tritium would require a large internal contamination dose to cause many medical issues, but internal contamination from a strong gamma emitter, such as the iridium-192 used for radiation therapy probes, can cause whole body gamma irradiation exposure and result in not only local injury, but also acute radiation syndrome.[6]

Target organs for specific radioactive isotopes can have high levels of damage because of metabolism characteristics and the accumulation of the isotope in specific organs. Strontium-90 and radium-226 both mimic calcium and are absorbed in bone. Radioactive iodines (iodine-131) are taken up by the thyroid gland, and uranium targets the kidney (and bone).[6]

Treatment of internal contamination with specific agents depending on the radioisotope involved can reduce the radiation dose absorbed and decrease the risk of future biological effects. Agents are used that block the uptake of the radioisotope by the target organ, dilute the radioisotope to decrease effective dose, or chelate the radioisotope so it can be more readily excreted (mainly in the urine or stool). Discussed below are a few agents and their treatment.

8.2 Key Isotopes of Concern for Internally Contaminated Pediatric Patients

8.2.1 Radioactive Iodine: Potassium Iodine

Internal contamination with **radioactive iodine** (e.g. iodine-131, iodine-125) occurs when either isotope is preferentially taken up by the **thyroid gland**, which results in **hypothyroidism** and an **increased risk for thyroid nodules and cancer**. Hypothyroidism causes significant and devastating neurodevelopmental damage and delay if not treated in the infant and young child. The fetus (after 12 weeks gestation), neonate, and child are at increased risk because the smaller, less developed thyroid gland concentrates the radioactive iodine to a greater extent than that of adults. The main routes of internal contamination from radioactive iodine are inhalation and ingestion of contaminated food, milk, or water. For neonates, radioactive iodine is excreted in breast milk. Radioactive iodines are commonly expected to be released in accidents involving nuclear power plants.

It is important to give timely and appropriate dosing of **oral stable potassium iodide (KI)** before or shortly after an exposure to radioactive iodine, because it can greatly reduce the uptake of radioactive iodine by the thyroid gland. The potential side-effects of taking KI include transient hypothyroidism, gastrointestinal upset, and rashes, but it is generally well tolerated. Repeated dosing is expected to increase the incidence of side-effects. KI doses are age-

dependent, and timing of the dosing is of critical importance to be effective. By giving KI before or within one hour of exposure to radioactive iodines, >90% of uptake can be blocked. After 4-5 hours, there is only 50% blockage and after 12 hours, the blockage is minimal. A single dose gives protection for 24 hours. KI dosing should be stockpiled in areas where radioactive iodine release is possible (around nuclear power plants). For ongoing exposures, repeated daily dosing may be required---this should be determined in conjunction with public disaster response leadership. KI pills are available over the counter. There is a liquid preparation, SSKI (1,000mg/ml) for younger patients available by prescription.[6, 3] For dosing see Table 2 below.

For neonates receiving KI, thyroid function testing should be performed 2-4 weeks following administration to detect hypothyroidism. If recurrent use is needed, monitor thyroid function tests in all children. If evidence of low thyroid function is detected, the infant/child should be placed on thyroid hormone replacement and closely monitored.[6]

Table 1: Threshold Thyroid Radioactive Exposures and Recommended Doses of KI for Different Risk Groups

	Predicted Thyroid gland exposure (cGy)	KI dose (mg)	Number or fraction of 130 mg tablets	Number or fraction of 65 mg tablets	Milliliters (mL) of oral solution, 65 mg/mL***
Adults over 40 years	≥ 500	130	1	2	2 mL
Adults >18 through 40 years	≥ 10	130	1	2	2 mL
Pregnant or Lactating Women	≥ 5	130	1	2	2 mL
Adolescents, 12 through 18 years*	≥ 5	65	½	1	1 mL
Children over 3 years through 12 years	≥ 5	65	½	1	1 mL
Children 1 month through 3 years	≥ 5	32	Use KI oral solution**	½	0.5 mL
Infants birth	≥ 5	16	Use KI oral	Use KI oral	0.25 mL

through 1 month			solution**	solution**	

* Adolescents approaching adult size (≥ 150 lbs) should receive the full adult dose (130 mg)

** Potassium iodide oral solution is supplied in 1 oz (30 mL) bottles with a dropper marked for 1, 0.5, and 0.25 mL dosing. Each mL contains 65 mg potassium iodide.

From: US Food and Drug Administration, 10/22/2012
http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm072265.htm

8.2.2 Radioactive Cesium and Thallium: Prussian Blue

For internal contamination with **radioactive cesium and thallium**, the treatment is **Prussian blue** (ferric hexacyanoferrate) given orally. In prior accidental exposures, this has resulted in a 40-45% reduction in whole body effective biological half-life for children and adolescents. Prussian blue is not absorbed by the GI tract and serves as an ion exchanger in the enterohepatic circulation. Side effects are rare and consist mainly of constipation. Treatment should be started as soon as possible after the contamination and continued for a minimum of 30 days. For adults and adolescents, the dose is three grams orally three times a day (TID). For children age 2-12, the dose is one gram orally TID. Prussian blue comes as 500 mg capsules and is available from the US Strategic National Stockpile and the Radiation Emergency Action Center/Training Site (REAC/TS) in Oak Ridge, Tennessee.[6]

8.2.3 Radioactive Plutonium, Americium, Curium: *DTPA*

Diethylenetriaminepentaacetate (DTPA) is a salt that chelates radioactive rare earth heavy metals such as **plutonium, americium, and curium**, transports them in the circulation, and enhances excretion in the urine. **DTPA comes in calcium (Ca) and zinc (Zn) salt forms**, and both are used for therapy. Begin treatment if any of these agents are suspected based on clinical suspicion or history suggestive of internal contamination. Continued treatment is based on accurate dose assessments using biodosimetry methods including urine excretion levels. Ca-DTPA is used for the first day of therapy, because it is more effective on the first day than Zn-DTPA. After the first day, both are equally effective. Zn-DTPA is used after the first day since it has less risk of causing metabolic abnormalities than Ca-DTPA. Initial adult dose is one gram Ca-DTPA intravenously (IV) on day one, then one gram IV daily of Zn-DTPA as daily maintenance doses. Pregnant mothers should only be given the Zn-DTPA form for treatment and nursing mothers should not breastfeed if they have internal contamination. For children less than 12 years old, the dose of either agent is 14 mg/kg/day IV daily, starting the first day with Ca-DTPA, then using Zn-DTPA for subsequent days. Side effects include nausea, vomiting, chills, fever, itching, and muscle cramps. Ca-DTPA and Zn-DTPA are available from the US Strategic National

Stockpile and the Radiation Emergency Action Center/Training Site (REAC/TS) in Oak Ridge, Tennessee.[6]

Additional resources are found on the clickable, hyperlinked table in Attachment 1 and also at the Food and Drug Administration, Radiation Emergencies, Drug Information Related to Radiation Emergencies website at: http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm063807.htm

8.2.4 Uranium: Bicarbonate

As described above, DTPA will also chelate uranium, but should **NOT** be used for internal contamination with uranium since it can lead to renal toxicity. Instead, **uranium internal contamination is treated with alkalinization** of the urine with sodium bicarbonate. Internal contamination with uranium leads to renal damage by causing acute tubular necrosis. Alkalinization of the urine makes the uranium isotope less nephrotoxic as it is excreted. Any retained uranium metal in wounds should be removed whenever possible, because uranium is absorbed into the bloodstream and deposited in the kidneys if these fragments remain in the body.[6]

9.0 Acute Radiation Syndrome

(REMM algorithm for evaluation and management of ARS can be found at http://www.remm.nlm.gov/exposureonly.htm#skip)

Acute Radiation Syndrome (ARS) occurs when a significant part of the body, usually >60%, is exposed to a high-level radiation exposure. This is usually from an external source exposure, less likely from an internal contamination source. The dose of radiation exposure determines the level of cellular damage caused in specific organ systems. This dose also determines the typical clinical course that can be expected for the exposed individual. Depending on the dose of radiation, this clinical course occurs over a matter of hours to weeks. For the purpose of significant high-dose whole body exposure to radiation that results in ARS, a dose of 1 Gy (100 rads) received at a high dose rate (a short period of time) is a threshold of radiation exposure that leads to a well-defined clinical course, which requires some level of support to the affected patient. These definitions are the same whether dealing with adult or pediatric patients. Important historical information that is significant to know regarding the whole-body or significant partial-body exposure includes how long the patient was exposed to the radiation, if there was any shielding of all or part of the patient, or if the exposure was fractionated (received over multiple exposures).[2, 11]

ARS follows a clinical course based on the dose of radiation exposure (see REMM table at http://www.remm.nlm.gov/nato-doserate.htm for further details). A subclinical phase of

ARS occurs at doses of 0.2 – <1 Gy. At these doses, there is bone marrow suppression with lymphopenia, but no clinically apparent acute illness in most patients. **A dose of 1-4 Gy** results in injury to the **hematopoietic system** resulting in depression of the bone marrow---the higher the dose, the more severe the depression. At **doses >3-4 Gy, the gastrointestinal (GI) system** develops significant dysfunction leading to death in patients with no medical support. This defines the $LD_{50/60}$ in humans, the dose of total body radiation that causes death in 50% exposed at 60 days. With extensive medical support, patients with ARS from doses of up to 6-8 Gy may survive. Patients with a whole body radiation exposure of >8 Gy are not likely to survive long-term despite extensive medical support. Whole-body exposures of **>20 Gy** results in endothelial damage to the blood vessels throughout the body, including the heart and brain, leading to rapid deterioration of the patient and death within days in almost all cases.[2, 11,6]

ARS has a prodromal phase, a latent phase, a phase of well-defined illness, and a period of recovery or death depending on the radiation dose received. Based on the description in the paragraph above, ARS has three clinically relevant subsyndromes: **Hematopoietic, Gastrointestinal, and Cerebrovascular**. If radiation exposure details are not known, radiation dose can be estimated early in the post-exposure period by various biodosimetry measures including clinical history and lymphocyte depletion kinetics. In general, **if vomiting starts >4 hours after the incident, there is no significant change in serial lymphocyte counts within 48 hours, and there are no other significant injuries, the prognosis for recovery from the ARS is good. If the patient has coma or seizures, vomiting occurs <4 hours after the incident, serial lymphocytes drop more than 50% within 48 hours, the patient has bloody stools or emesis, or there are other serious injuries (burns, wounds), the prognosis for recovery from the ARS is poor.**[2, 11, 6] A useful algorithm for evaluation and management of ARS can also be found at http://www.remm.nlm.gov/exposureonly.htm#skip.

9.1 Hematopoietic Syndrome[2,11,12,6]

The hematopoietic syndrome of ARS typically occurs in the 1-8 Gy exposure range; the higher the dose, the more severe the syndrome. At these doses, the bone marrow stem cells are affected and the patient's blood counts, including hemoglobin, white blood cell count, and platelet counts are all adversely affected. The **prodrome** for this syndrome include nausea, vomiting, anorexia, malaise, and possible diarrhea starting 3-16 hours after exposure and lasting less than 48 hours. The onset, severity, and duration of the symptoms during this prodrome depend on the actual dose received by the patient as whole-body, or significant partial-body, exposure irradiation. Following the prodromal period, the **latent period** will be mostly asymptomatic for most patients except for mild weakness that may last 3-4 weeks. If the dose received in >3 Gy, the patient may have hair loss around two weeks after the exposure. Since the bone marrow of patients exposed to >2 Gy may be significantly affected,

these patients will have neutropenia and lymphopenia resulting in immunosuppression. Keeping the patient in a clean environment, even in a HEPA-filtered, negative flow room, may be considered for the more immunosuppressed patients, as they will be at risk of developing life-threatening bacterial, viral, fungal, and other infections. For this reason, children exposed to >2 Gy of whole-body or significant partial-body radiation should receive treatment with **neutrophil cytokine therapy** within the first 24-72 hours following exposure for treatment of expected neutropenia.[12] Treatment with cytokine therapy will not prevent the onset of neutropenia, but will shorten the duration and, by doing so, reduce the risk of infection. **Granulocyte Stimulating Factor (G-CSF)** can be dosed as a one-time subcutaneous shot of pegfilgrastim at a dose of 6 mg for children and adults weighing at least 45 kg and 100 micrograms/kg for children weighing <45 kg. Because of the complex of PEG (polyethylene glycol) to the G-CSF, the drug lasts in the body until the neutrophil count recovers, requiring only one dose. Regular, un-pegylated G-CSF (filgrastim) is dosed at 5 micrograms/kg daily subcutaneously until neutropenia count reaches >1,000, usually about 2 weeks after starting daily dosing. Also available is GM-CSF (sargramostim), granulocyte-monocyte colony stimulating factor, dosed at 250 micrograms/m^2/day subcutaneously until neutrophil increases to >1,000. The absolute neutrophil count (ANC) is calculated using the following equation:

ANC = White Blood Cell Count in thousands (WBC) X (the percentage of Neutrophils + Bands)

Example:

CBC shows a WBC of 1.0 (1,000) and differential shows 24% Neutrophils and 1% Bands

ANC = 1,000 X (0.24 + 0.01) = (1,000 X 0.25) = 250---Neutropenic patient

If a **patient develops a fever** and is neutropenic with an absolute neutrophil count (ANC) of < 500, the patient needs to be placed on empiric broad-spectrum antibiotic coverage after blood cultures have been drawn. Fever is defined as a single temperature of > 38.3^0 C (101^0 F) or $\geq$ 38.0^0 C (100.4^0 F) for $\geq$ 1 hour. Other cultures should be considered and obtained as indicated by the history and physical exam, such as urine culture, throat culture, wound culture, etc. Antibiotic coverage should at a **minimum cover for gram-positive and gram-negative bacteria**. If the patient is clinically stable and showing no signs of sepsis, single agent coverage can be considered with cefepime at 50 mg/kg/dose IV every 8 hours or ceftazidime at 50 mg/kg/dose IV every 8 hours. Consider adding Vancomycin IV at 10 mg/kg/dose IV every 6 hours if there is an additional suspicion for gram-positive bacteria based on history or physical examination. If any signs or symptoms of sepsis or clinical instability are present (such as toxic appearance, low blood pressure, mental status changes or other) broadening the gram-negative coverage to include a second antibiotic, such as gentamicin at a dose of 2-2.5 mg/kg/dose IV every 8 hours, should be strongly considered. These antibiotic regimens are widely used for patients with

fever and neutropenia, but are only a suggestion. Local practice guidelines may vary and should be considered in selecting the actual antibiotics used. Also consider any allergies the patient may have when making antibiotic selections. Modifications of antibiotics can be made based on clinical condition of the patient and results of cultures obtained. If **fever persists** or the patient clinically worsens despite broad spectrum antibiotics, consider the addition of **antifungal therapy** with amphotericin B or other antifungal agent. If **viral infection** is suspected, such as CMV or herpes, antiviral therapy with **gancyclovir** (for CMV) or **valacyclovir** (for herpes) is indicated. Antibiotics, antifungals, and antivirals may be indicated as prophylaxis in certain clinical situations or environments.

In addition to depression of the WBC count, patients may experience anemia and/or thrombocytopenia depending on the radiation dose received. Support of patients with blood product replacement for anemia and thrombocytopenia may be necessary. **All blood products (PRBC's and platelets included) given to immunosuppressed patients, such as patients with ARS, should be irradiated and leukocyte reduced prior to transfusion.** Irradiation of the blood products prevents transfusion of immunocompetent T-lymphocytes from the donor unit into the immunocompromised patient, preventing transfusion-acquired graft versus host disease, a fatal condition in these patients. Leukocyte reduction also removes WBC's that can transmit cytomegalovirus (CMV) to immunocompromised patients.

Packed red blood cells (PRBC's) can be given for significant or symptomatic anemia. NOTE: any blood product transfused to an immunocompromised patient, including those exposed to significant doses of whole-body radiation, must be irradiated (prevents fatal transfusion acquired graft vs host disease) and leukocyte reduced (to avoid CMV transmission) prior to transfusion. Most children will tolerate a hemoglobin (Hgb) level down to 7-8 g/dl before requiring transfusion if otherwise clinically stable. If the Hgb drops below this level, or the patient is having signs or symptoms of anemia, such as excessive fatigue, significant tachycardia, dizziness, etc., a transfusion with PRBC's that have been irradiated and leukocyte reduced at a dose of 10-15 cc/kg slow IV over 2-3 hours. The frequency for monitoring the patient's Hgb level is based upon their clinical situation and the serial CBC results. There is no specific frequency. These CBC results will determine the need for further PRBC transfusions. In individuals with prolonged anemia, consideration for giving erythropoietin to stimulate red cell production can be considered. If used, iron supplementation should also be considered. See Table 3 for a summary of guidance for use of bone marrow growth factor use in ARS.

Platelet transfusions are indicated for patients with thrombocytopenia who are excessively bruising or bleeding. This typically happens when the platelet count drops to < 20,000 K/UL. Platelet transfusion may also be necessary if the platelet count is <50,000 and the patient needs to undergo a procedure. If the patient has a history of intracranial trauma or

bleeding, the platelet count may need to be > 100,000 to protect from extra bleeding. Patients with low platelet counts (<100,000) should not receive non-steroidal anti-inflammatory (NSAIDS) medications or other drugs that interfere with platelet function. Platelet transfusions of apheretic platelet concentrates, which have been irradiated and leukocyte reduced, at a dose of 10-15 cc/kg IV over one hour are usually well tolerated and successful at increasing the platelet count to a safe range to stop bleeding. If using single-donor pooled platelets, the dose is 1-2 units/m^2 for body surface area (BSA). Monitoring of the platelet count and patient clinical condition will determine the need for further platelet transfusions.

Hematopoietic stem cell transplantation (bone marrow, peripheral blood, or umbilical cord blood stem cells) may be considered in patients who have a reasonable chance of survival with ARS. Patients receiving > 4-5 Gy but less than 8 Gy whole-body exposure are patients to consider as candidates if suitable donors are available. Patients receiving less than 4-5 Gy can usually be treated with supportive care as outlined above until their own bone marrow recovers. Patients receiving > 8 Gy are not expected to survive because of additional tissue and organ damage that occurs as discussed below.

Additional **supportive measures** to consider include control of symptoms. Nausea and vomiting from radiation exposure may respond to serotonin-receptor antagonists such as ondansetron (0.15 mg/kg/dose q 8 hours IV or PO) or granisetron. Maintaining nutrition by maximizing GI support with enteral feeding as tolerated by the patient is best to maintain intestinal health. Loperamide for control of diarrhea not related to GI infection may be helpful.

Table 2: Summary of Recommendations for Treating Hematopoietic Syndrome in Hospitalized Patients with Whole-Body Exposure to Ionizing Radiation

Summary of Recommendations for Treating Hematopoietic Syndrome in Hospitalized Patients with Whole-Body Exposure to Ionizing Radiation
Recommendation
Administer G-CSF or GM-CSF when ANC <0.500 X 10^9 cells/L
Administer Erythropoiesis-stimulating agents when prolonged anemia is present to avoid need for red blood cell infusion
Administer hematopoietic stem cells after failure of 2-3 weeks of cytokine treatment to induce recovery from marrow aplasia in absence of nonhematopoietic organ failure

Adapted from: Dainiak N, Meineke V. First global consensus for evidence-based management of the hematopoietic syndrome resulting from exposure to ionizing radiation. *Disaster Med Public Health Prep*. 2011:. 5; 202-212.

9.2 Gastrointestinal Syndrome [2, 11, 13, 6]

In addition to the hematologic syndrome described above, patients who receive **>5-6 Gy** whole-body or significant partial-body irradiation have damage to their gastrointestinal (GI) system secondary to effects on the GI stem cells and small blood vessels in the intestines. The prognosis for patients exposed to >6 Gy is very poor and doses **>8 Gy are generally fatal**. This damage results in significant GI signs and symptoms and a clinical course known as the gastrointestinal syndrome. The **GI prodromal signs and symptoms** include severe nausea and vomiting, possible watery diarrhea and cramps, and fever starting at 1-4 hours following exposure and lasting about 48 hours. For **GI antibacterial prophylaxis**, a fluoroquinolone antibiotic (such as ciprofloxacin or levofloxacin) should be administered within 2-4 days following significant radiation exposures, and addition of prophylaxis with an antifungal agent such as fluconazole should be considered as well. The latent period of the GI syndrome lasts about 5-7 days and is characterized by malaise and weakness. As the GI damage progresses, the intestines are unable to absorb water and nutrients, and intravascular fluids/water are lost into the GI tract. The denuded intestinal mucosa is a significant risk factor for bacterial infection, requiring appropriate antibiotic coverage for invasive intestinal organisms. Patients develop severe vomiting and diarrhea with fever that progresses to bloody diarrhea, shock, renal failure, and death within 8-14 days following exposure. At doses of >8 Gy, survival may be prolonged with aggressive fluid replacement and intensive care management, but death usually eventually occurs from multiple organ failure.

9.3 Cerebrovascular Syndrome[2, 11, 13, 6]

At doses of whole-body or significant partial-body irradiation of **>20 Gy** patients experience the **cerebrovascular syndrome**, which results from the endothelial cell injury of small blood vessels, especially in the brain. This leads to capillary leakage resulting in edema, including cerebral edema. The cerebrovascular **prodromal signs and symptoms** include a burning sensation of the skin within minutes of the exposure, vomiting and diarrhea less than 30 minutes after the exposure, and loss of balance, confusion, and possible loss of consciousness. Patients may experience a latent period where they appear to improve for a few hours, or even a couple of days, where they can appear very oriented and alert, even euphoric, but weak. Following this **short latent phase**, patients manifest illness with severe central nervous symptoms including reduced consciousness and possible seizures. Development of watery diarrhea, blood pressure instability, and respiratory distress leads to cardiovascular collapse and death, usually within 2-3 days.

10.0 Cutaneous Radiation Injury[2, 11, 13, 6]

Local radiation injury of the skin of 3 Gy or more results in erythema and other changes depending upon the dose absorbed. The **prodrome signs and symptoms** include erythema, itching, and heat sensation. This prodrome lasts for minutes to hours depending on the dose.

Within 2-3 weeks, the injury manifests as secondary erythema, edema, and blisters, hair loss, followed by dry (8-12 Gy) or moist desquamation (15-20 Gy), ulcers, and necrosis. These changes are painful and can cause fever. Recovery from these changes leads to scarring, pigment changes, and atrophy. The obliterative vasculitis and nerve damage that occurs can lead to chronic pain. Long term (10-30 years later), exposed areas are susceptible to squamous or basal cell carcinoma. Acute management of these burns includes infection control, high-level wound care, and appropriate pain control measures, including opioids. Topical glucocorticoid steroids may decrease inflammatory damage. Antihistamines (systemic and/or topical) may help with itching and swelling. Topical antibiotics may decrease infection of burn areas. Surgical debridement and reconstruction may be necessary with extensive and deep injuries, and should be used to remove necrotic material. See Table 4 for summary of recommendation considerations for hospitalized patients with ARS.

Table 3: Summary of Recommendations for Treating Hospitalized Patients with Whole-Body Exposures to Ionizing Radiation

Summary of Recommendations for Treating Hospitalized Patients with Whole-Body Exposures to Ionizing Radiation	
Syndrome	**Recommendation**
Gastrointestinal	Administer fluoroquinolone or similar antibiotic 2-4 d after radiation exposure
	Provide bowel decontamination and parental antibiotics when indicated, if resources permit
	Administer a serotonin-receptor antagonist prophylactically when suspected exposure >2Gy
	Administer loperamide as needed to control diarrhea
	Provide nutritional support through enteral route if possible
Cutaneous	Administer topical class II-III steroids, topical antibiotics, and topical antihistamines to radiation burns, ulcers, and blisters
	Surgically excise and graft radiation ulcers or localized necrosis with intractable pain
Neurovascular	Provide supportive care with a serotonin receptor agonist, mannitol, furosemide, and analgesics
Critical Care	Administer fluid and electrolyte replacement therapy and sedatives when significant burns, hypovolemia, and/or shock occur
	Administer mechanical ventilation with a lung-protective strategy for acute respiratory failure
	Maintain average blood glucose of 140-180 mg/dL for majority of critical care patients
	Administer H_2 blocker or proton pump inhibitor

Adapted from: Dainiak N, Meineke V. Literature review and global consensus on management of acute radiation syndrome affecting nonhematopoietc organ systems. Disaster Med Public Health Prep. 2011: 5; 183-201.

11.0 Surgical Considerations

Pediatric patients exposed to radiation may have associated injuries including blast injury, open wounds, burns, and foreign bodies. In addition to good debridement of wounds to reduce ongoing radiation exposure if contaminated with radioactive material, expedient wound management may be indicated. **If a patient has experienced a dose of radiation that will lead to the hematologic syndrome of ARS, any surgical procedures, including wound closures, foreign body removal, or abdominal procedures need to be completed within a 24-36 hour window to allow for initial surgical wound healing before the patient becomes neutropenic.** Neutropenia results in poor wound healing and the development of infections that may be difficult to treat despite appropriate antimicrobials.[6, 3]

12.0 Pregnancy Effects

The fetus is very sensitive to radiation. The dose to the fetus is usually less than the mother receives unless the radiation is from internal contamination. In this situation, if radioactivity concentrates in the bladder, the fetus is exposed at a greater level due to the proximity of the uterus to the bladder. Also, the fetal thyroid gland is very iodine avid after 12 weeks gestation and will concentrate radioactive iodine to a higher level than an adult typically will. Depending on the gestation of the fetus, exposure to radiation may have different effects. A health physicist should be consulted to determine the biodosimetry exposure. Consultation with a maternal-fetal specialist and geneticist would be useful to determine ultimate fetal risks and effects based on dose received.[6]

13.0 Long-term Effects

Potential late effects of radiation exposure depend on which part of the body receives radiation therapy, the age or the patient, and any other chronic conditions. These late effects may include problems with soft tissue or bone growth, vision problems, changes in endocrine function (low hormone levels), learning disabilities or brain injury, and increased risk for developing cancer. An extensive resource for the late effects of radiation exposure outlined by organ system in the radiation field or whole-body exposure can be found in the Children's Oncology Group Long Term Effects Follow-up Guidelines at http://www.survivorshipguidelines.org/pdf/LTFUGuidelines.pdf.

13.1 Malignancy

Children exposed to radiation are at risk of developing cancers depending on the type, dose, and location of radiation exposure. **Thyroid cancer** is a frequent late complication of

ionizing radiation, with an excess relative risk/Gy exposure of 7.7 for developing this disease for patients receiving an exposure to ionizing radiation prior to the age of 15 years old.[14] Radioactive iodine exposure in an unblocked thyroid gland can result in hypothyroidism as well. Other cancers often seen include leukemias, breast cancers, central nervous system tumors, and bone cancers.[6]

13.2 Neurodevelopmental

Significant radiation to the developing brain that has not been fully myelinated results in cognitive impairment and other dysfunction based on dose and age. The younger the patient, the more significant the damage. In addition, a significant radiation dose to the hypothalamic area will result in significant neuroendocrine dysfunction, which can cause maturational sexual delay or failure and growth retardation. Thyroid dysfunction can result from decreased TSH production.[6]

13.3 Growth

Growth failure can result from hypothalamic radiation exposure or from radiation exposure to immature skeletal growth plates. If the radiation exposure is unilateral, growth failure and disfigurement may result from unequal growth of affected bones.[6]

14.0 Summary

Following exposure to ionizing radiation, certain aspects of care needs to be considered in the pediatric patient that may differ from adult victims with the same exposure. Once immediate lifesaving measures are taken and the child undergoes successful decontamination, the management of the pediatric patient exposed to ionizing radiation requires the following information:

1. Total dose
2. Dose rate
3. Type of radiation exposure
4. Mode of exposure
5. External and/or internal exposure
6. Isotopes involved
7. Co-injuries (burns, trauma, etc.)
8. Co-morbidity
9. Biodosimetry

With this knowledge a problem-based estimate of the health impact of the radiation exposure and a patient-based management plan can be developed.

15.0 APPENDIX 1: Radiation Facts

Radiation is defined as energy transmitted through space in the form of particles or waves/rays. It exists as two types: **non-ionizing and ionizing**. [3]

Non-ionizing radiation refers to electromagnetic energy that causes excitation of atoms and molecules, but does not have enough energy to ionize an atom or molecule, that is to displace, an electron from the atom. Examples of non-ionizing radiation are microwaves, radio waves, visible light, and near ultraviolet light.

Ionizing radiation is electromagnetic energy that has enough energy to displace one or more electrons or other particles from an atom or molecule, thus producing an ionized product that is reactive. Examples of ionizing radiation include X-rays, gamma rays, and many naturally occurring elements (such as uranium and radium) or man-made products (such as radioactive cesium and cobalt). Ionizing radiation has many applications not only in medicine and industry, but also as part of nuclear weapons and other devices. This publication will focus on ionizing radiation exposures and its medical effects on children.

The **energy** of a radioactive agent is known as its **activity**, which is expressed as **radiation being emitted per unit time** (disintegrations per second), usually expressed in **curies (Ci)**. Different elements have different activities, which determine the damage they cause per unit time during an exposure.[6]

Radioactive elements lose energy through the spontaneous transformation from an unstable nucleus to a more stable nucleus, a process known as radioactive decay. For each different element, this decay is at a **half-life** that is unique for each element. **The half-life of decay is the time required for the radioactivity of a given element to be reduced by half**. Knowledge of the half-life of the radiation source is important to determine when the danger from a radiation source exposure is over. Some elements have a decay half-life expressed in terms of seconds, others in days, years, decades, or millennia (thousands of years).[3]

See Table 5: Isotopes of Interest: Properties, Treatment, and Fact Sheets
(Also available on REMM: **http://www.remm.nlm.gov/isotopestable.pdf**)

15.1 Types of Radiation

Some ionizing radiation exposure is a common part of life. This exposure occurs through natural sources, such as cosmic radiation, environmental radon and thorium, and also through common exposures through medical tests and procedures, as well as from certain occupational exposures. The naturally occurring ionizing radiation sources vary depending on geography and occupation. The average annual background radiation exposure in the United

States from all these common sources is approximately 0.62 rem (see definition for rem in table below) per year. [6]

Ionizing radiation occurs in a variety of energies with differing pathological effects based on various exposure parameters (e.g., type, route, duration, dose, etc.). This radiation comes from different locations in the atom or molecule. Atoms have a nucleus comprised of protons and neutrons, which is surrounded by electrons. Four types of radiation are medically important. These include **alpha and beta particles, gamma and X-rays, and neutrons**.

15.1 Alpha, Beta, Gamma, etc.

A REMM video for brief explanation of types of radiation energies http://www.youtube.com/watch?v=mySIzIk3ZUM.

Alpha particles are helium nuclei ejected by certain unstable radioactive substances such as Americium 241 found in home smoke detectors. Alpha particles are relatively high energy and heavy. These characteristics make them potentially very damaging to tissue, but also very easy to shield. Alpha particles do not travel far and do not penetrate intact outer layer of skin, clothing, or paper. They in general have little external hazard, but can have significant internal toxicity, particularly from wound absorption and inhalation.[6]

Beta particles exist when an electron is ejected from the nucleus of an atom. Cobalt 60 is an example of a common beta particle emitter and is used in medical/research applications. Beta particles are high energy particles that can travel a short distance through tissue, but can be shielded by plastic and aluminum. Beta particles can produce damage either directly or through secondary weak x-rays produced (through a process known as bremstrahlung) from beta particle passage through dense materials, such as lead. Passage through less dense materials, such as plastic or aluminum, results in less bremstrahlung production, and so they are the appropriate shielding for beta particles. Because beta particles do penetrate into tissue, they cause significant damage with external and internal exposure to the surface of the tissue affected.[6]

X-rays and gamma rays are types of photon ionizing radiation. They are both nearly massless bundles of energy, which allows them to deeply penetrate through tissue. Exposure to them can result in whole body radiation exposure and damage to body organs. X-rays are produced when energy is lost from an electron of an atom, while gamma rays are produced when a nucleus loses energy. Otherwise they both have similar energy properties and characteristics. They are often produced when a radioactive element undergoes alpha or beta particle decay. When Cobalt 60 undergoes beta particle decay to yield the stable element Nickel 60, it also emits two powerful gamma rays. Shielding of x-rays or gamma particles requires thick lead or concrete.[6, 3]

Neutrons are radioactive particles rarely produced by the natural decay of elements. They are typically produced through the process of nuclear fusion or nuclear fission. Neutrons have no charge, so they can readily interact with the nucleus of an atom, possibly being absorbed into it. This can result in another unstable, radioactive atom. Neutrons are deeply penetrating as well and must be shielded by thick concrete. Neutrons can cause much greater tissue damage than gamma rays. [6, 3]

15.2 Radiation Units

As described above, the activity of a particular radioactive element is expressed in curie (Ci). Quantifying the exposure that occurs during a radiation incident is defined as the amount of charge, or ions (from photons, i.e., X and gamma rays), produced per unit of air. The unit for expressing this energy is the **roentgen (R)**. This unit of ionization (R) is often what is measured by the Geiger counter or ion chamber devices used to monitor radiation activity in an area when radioactive material is present. **One roentgen (R) is approximately equal to one rad** (described below).[6, 3]

Quantifying the amount of radiation to which the body and various tissues have been subjected determines the exposure. This exposure and its effects on the body are expressed in terms of the absorbed dose**. The units of energy used to quantify the amount of energy of any type of ionizing radiation that is transferred to the body are the rad (radiation absorbed dose) or Gray (Gy). The International System unit for expressing absorbed dose is the Gy. As defined, 100 rad = 1 Gy**.[3]

Different types of radiation (gamma rays, alpha particles, beta particles, etc.) impart different energies to tissue on exposure at any given absorbed dose. These differences in energy to a tissue on exposure are defined as equivalent doses, using a quantifying factor for each type of radiation. **The dose in rads multiplied by the quantifying factor defines the rem (radiation equivalent, man, abbreviated as rem) with one rad approximately equal to one rem**. The International System unit for quantifying the dose equivalent for a radiation exposure in any material is the sievert (Sv). The quantifying factor for X-rays and gamma rays is defined as one. So, as an example, if an individual is exposed to an absorbed dose of 100 rad (1 Gy) of X-rays the dose equivalent is 1 Sv**. In general, for acute medical effects the most useful units to use for exposure are the rad or Gy. The rem or Sv is used more often in determining the long-term effects on a given tissue, such as the risk of radiation-induced cancer.** On review, one R = one rad = one rem (approximately).[3] See Table 1 for comparison of radiation units used to describe radiation energies.

Table 4: Radiation Units of Measure

Unit	Abbreviation	Definition	Comment
Roentgen	R	The amount of energy absorbed in air	For x-rays and gamma rays only
Radiation absorbed dose	rad	The energy absorbed per gram of material 1 rad = 100 ergs/gram	Important because it represents the amount of energy that is absorbed by the material of interest- e.g., person, organ, tissue, cells
Roentgen equivalent man	Rem	The product of the amount of energy absorbed (rad) times the efficiency of radiation in producing damage rem = rad x (W_r)	Accounts for the different degrees of damage produced by equal doses of different radiations, for example: **Radiation** **Radiation Weighting Factor (W_r)** x rays gamma rays 1 beta particles neutrons range 2-20 alpha particle 20
Gray*	Gy	1 Gy = 100 rad	1 Gy = 1 joule/kilogram
Sievert*	Sv	1 Sv = 1 Gy x W_r	1 Sv = 100 rem
Curie	Ci	The number of radioactive decays (disintegrations)/ unit of time	1 Ci = 2.2 x 10^{12} disintegrations/minute 1 Ci = 3.7 x 10^{10} disintegrations/second
Becquerel*	Bq	The number of radioactive decays (disintegrations)/ unit of time	1 Bq = 60 disintegrations/minute 1 Bq = 1 disintegration/second

* International units (SI) of Bequerel, Gray and Sievert are the currently favored expressions.

Adapted from:

Program on Technology Innovation: Evaluation of Updated Research on the Health Effects and Risks Associated with Low Dose Radiation (PDF – 903 KB) (Electric Power Research Institute [EPRI] document 1019227, Table 2-1, page 42, November 2009)

16.0 References

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Additional Useful Websites:

Centers for Disease Control, Radiation Emergencies
http://www.bt.cdc.gov/radiation/

Food and Drug Administration, Radiation Emergencies, Drug Information Related to Radiation Emergencies
http://www.fda.gov/Drugs/EmergencyPreparedness/BioterrorismandDrugPreparedness/ucm063807.htm

Children's Oncology Group Long Term Follow-up Guidelines (Version 3.0), Radiation Exposure Long-Term Effects, pp 47-117.
http://www.survivorshipguidelines.org/pdf/LTFUGuidelines.pdf

NCRP Composite Glossary
http://www.ncrponline.org/PDFs/NCRP Composite Glossary.pdf

Radiation Injury Treatment Network
http://ritn.net/

Table 5: Isotopes of Interest: Properties, Treatment, and Fact Sheets.

Table Source: http://www.remm.nlm.gov/isotopestable.pdf Accessed August 21, 2013. Please check this link for any updates to this table.

Isotopes of Interest: Properties, Treatment, and Fact Sheets

Information in this table adapted from:

- Management of Persons Contaminated with Radionuclides: Handbook (NCRP Report No. 161, Vol. I), National Council on Radiation Protection and Measurements, Bethesda, MD, 2008.
- Tochner ZA, Glatstein E, *Internal Contaminant Radionuclides: Properties and Treatment* (Table 216-1) in "Chapter 216: Radiation Bioterrorism," in Harrison's Principles of Internal Medicine, 17th Edition, Fauci AS, Longo DL, Kasper DL, Braunwald E, Jameson JL, Loscalzo J, Hauser SL, eds., pp. 1358-1364, McGraw Hill, 2008.

Isotope	Ionizing radiation decay mode	Radioactive half-life	Biological half-life	Major exposure pathways	Focal accumulation	Treatment: References for use	Fact sheets (CDC, ATSDR, EPA, Argonne Natl. Lab)
Americium (Am-241)	α	458 years	73,000 days	Inhalation Skin	Lungs Liver Bone Bone marrow	DTPA† *	CDC ATSDR EPA Argonne (PDF - 39 KB)
Californium (Cf-252)	α, γ	2.6 years	N/A	Inhalation Ingestion	Bone Liver	DTPA*	Argonne (PDF - 39 KB)
Cesium (Cs-137)	β, γ	30 years	70 days	Inhalation Ingestion	Follows potassium; renal excretion	Prussian blue, insoluble† *	CDC ATSDR EPA Argonne (PDF - 39 KB)
Cobalt (Co-60)	β, γ	5.26 years	9.5 days	Inhalation	Liver	Succimer (DMSA)§ (DailyMed) DTPA* EDTA§ N-Acetyl-L-cysteine§	CDC ATSDR EPA Argonne (PDF - 38 KB)

Curium (Cm-244)	α, γ, neutron	18 years	Liver: 7,300 days Bone: 18,250 days	Inhalation Ingestion	Liver Bone	DTPA† *	Argonne (PDF - 42 KB)
Iodine (I-131)	β, γ	8.1 days	138 days	Inhalation Ingestion Skin	Thyroid	Potassium iodide† * Saturated solution of potassium iodide§ Propylthiouracil§ Methimazole§ Potassium iodate§	CDC ATSDR EPA Argonne (PDF - 38 KB)
Iridium (Ir-192)	β, γ	74 days	50 days	N/A	Spleen	Consider DTPA* Consider EDTA§	CDC Argonne (PDF - 95 KB)
Isotope	**Ionizing radiation decay mode**	**Radioactive half-life**	**Biological half-life**	**Major exposure pathways**	**Focal accumulation**	**Treatment: References for use**	**Fact sheets (CDC, ATSDR, EPA, Argonne Natl. Lab)**
Phosphorus (P-32)	β	14.3 days	1,155 days	Inhalation Ingestion Skin	Bone Bone marrow Rapidly replicating cells	Hydration + Phosphate drugs • Sodium glycerophosphate§ • Sodium phosphate§ • Potassium phosphate§ • Calcium carbonate§ • Aluminum hydroxide§	

						• Aluminum carbonate§ • Sevelamer§ (DailyMed)	
Plutonium (Pu-239)	α	2.2 x 10^4 years	73,000 days	Inhalation (limited absorption)	Lung Bone Bone marrow Liver Gonads	DTPA§ DFOA§ EDTA§ DTPA + DFOA§	CDC ATSDR EPA Argonne (PDF - 58 KB)
Polonium (Po-210)	α	138.4 days	60 days	Inhalation Ingestion Skin	Spleen Kidneys Lymph nodes Bone marrow Liver Lung mucosa	Gastric Lavage Dimercaprol (BAL)* Succimer (DMSA)§ (DailyMed) D-Penicillamine§ (DailyMed)	CDC Argonne (PDF - 41 KB) HPS (PDF - 492 KB) NRC More references
Radium (Ra-226)	α, β, γ	1,602 years	16,400 days	Ingestion	Bone	Aluminum hydroxide* Barium sulfate* Sodium alginate§ Calcium phosphate§	ATSDR EPA Argonne (PDF - 52 KB)
Strontium (Sr-90)	β	28 years	18,000 days	Inhalation Ingestion	Bone	**Inhalation:** Calcium gluconate§ Barium sulfate§ **Ingestion:** Rx is the same as for radium (see above). Additional Rx may include stable strontium compounds: Strontium lactate§ Strontium gluconate§	CDC ATSDR EPA Argonne (PDF - 39 KB)

Isotope	Ionizing radiation decay mode	Radioactive half-life	Biological half-life	Major exposure pathways	Focal accumulation	Treatment: References for use	Fact sheets (CDC, ATSDR, EPA, Argonne Natl. Lab)
Thorium (Th-232)	α	1.41 x 10^{10} years	Bone: 8,030 days Liver/total body: 700 days	Inhalation Ingestion	Bone	Consider DTPA*	ATSDR EPA Argonne (PDF - 49 KB)
Tritium (H-3)	β	12.5 years	12 days	Inhalation Ingestion Skin	Whole body	Water diuresis*	EPA Health Protection Agency (UK)
Uranium (U-235)	α	7.1 x 10^{8} years	15 days	Ingestion	Kidneys Bone	Sodium bicarbonate* For high level intake consider off-label diuretics and/or dialysis§	CDC ATSDR EPA Argonne (PDF - 46 KB)
Yttrium (Y-90)¶	β	64 hours	N/A	Inhalation Ingestion	Bone	DTPA* EDTA§	Argonne ¶ (PDF - 39 KB)

References for use

† **FDA approved:** Countermeasures so marked have been approved as treatment for internal contamination with the listed radioisotope by the US Food and Drug Administration (FDA).

* **NCRP preferred:** Countermeasures so marked have been listed as preferred treatments for internal contamination with the listed radioisotope by the National Council on Radiation Protection and Measurements [Management of Persons Contaminated with Radionuclides: Handbook (NCRP Report No. 161, Vol. I)]. Except where noted, use of these countermeasures has not been approved by the US Food and Drug Administration (FDA).

§ **NCRP suggested:** Countermeasures so marked have been listed as suggested treatments for internal contamination with the listed radioisotope by the National Council on Radiation Protection and Measurements [Management of Persons Contaminated with Radionuclides: Handbook (NCRP Report No. 161, Vol. I)]. Use of these countermeasures has not been approved by the US Food and Drug Administration (FDA).

See also:

- Summary of Radioactive Properties for Selected Radionuclides (PDF - 145 KB) (Human Health Fact Sheet, Argonne National Laboratories, 2005)
- Radiological and Chemical Fact Sheets to Support Health Risk Analyses for Contaminated Areas (PDF - 2.34 MB) (Argonne National Laboratories, 2007)

More Polonium-210 references

- Understanding Radiation - Topics: Polonium 210 (Health Protection Agency)
- Individual Monitoring Conducted by the Health Protection Agency in the London Polonium-210 Incident (Health Protection Agency)
- Jefferson RD, Goans RE, Blain PG, Thomas SH. Diagnosis and treatment of polonium poisoning. Clin Toxicol (Phila.) 2009 May; 47(5):379-92. [PubMed Citation]
- Harrison J, Leggett R, Lloyd D, Phipps A, Scott B. Polonium-210 as a Poison. J Radiol Prot. 2007 Mar;27(1):17-40. [PubMed Citation]
- Scott BR. Health risk evaluations for ingestion exposure of humans to polonium-210. Dose Response. 2007;5:94-122. (PDF - 175 KB)

¶ For Yttrium-90 radioactive properties and health concerns, see Strontium-90 Human Health Fact Sheet

For further information on Emergency Use Authorizations:
http://www.fda.gov/emergencypreparedness/counterterrorism/ucm182568.htm

http://www.emergency.cdc.gov/training/eua/index.html

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