Chapter 4

TREATMENT OF INTERNAL RADIONUCLIDE CONTAMINATION

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INTRODUCTION

Military and civilian providers of medical care must be prepared to deal with the medical aftermath of a nuclear detonation or accident. With the earth's increasing nuclear arsenal and the growing use of nuclear energy systems, our biosphere is threatened by the production and release of large quantities of radioisotopes. The accidents at Chernobyl, USSR, in 1986 and at Goiânia, Brazil, in 1987 have stressed the importance of knowing how to manage the radioactive contamination of persons in military and civilian settings. Such management requires knowledge of the metabolism of various radionuclides in humans and methods to increase their elimination from the body.

Many aspects of medical management are based on judgments and evaluations that are difficult to instruct. Treatment information is sparse and often subjective. This chapter discusses difficult treatment decisions, with the understanding that considerable latitude exists in medical evaluation.

In a nuclear explosion, over 400 radioactive isotopes are released into the biosphere.¹ About forty are considered to be potentially hazardous to humans because of either their organospecificity or their long half-life. Both early and delayed radioactive fallout will be deposited in our external environment, which could result in internal contamination with radionuclides.

INITIAL MANAGEMENT

The medical staff providing the initial management of radionuclide-contaminated patients will have varying responsibilities, depending on the isotopes involved, radiation-monitoring capabilities, location, and available facilities. Thorough evaluation and estimates of internal contamination may take days or weeks, however, so these decisions may have to be based only on historical information and superficial measurements. Medical personnel must proceed quickly to obtain information and make treatment decisions based on available early estimates of possible exposure. Treatment risks must be weighed against the presumed risks of untreated exposure. Damage from the latter may not be manifested until 20-30 years after internalization.

Initial management may be divided into four applications: (a) uptake and clearance, (b) sampling of radioactivity, (c) on-site management, and (d) hospital management.¹⁻³

Uptake and Clearance

Internal contamination occurs by three main routes (listed in order of importance): *inhalation, ingestion,* and *wound contamination.* A fourth and infrequent route is *percutaneous absorption*, which applies almost exclusively to the radioisotope tritium and its association with water. The uptake and retention of a radionuclide

are influenced by its portal of entry, chemistry, solubility, metabolism, and particle size.¹⁻⁴ Of the three main routes, inhalation poses the biggest threat, especially in a fallout environment.^{1-3,5,6} The size of the radioactive particle determines if it will be deposited in the lungs, because particles greater than 10 microns in diameter cannot pass by the nasal hairs. *Clearance time* (time required for particles to be removed from the lungs) depends on which respiratory compartment receives the deposit,¹⁻³ and time will be an important factor in treatment decisions. Times for respiratory clearance into the next higher compartment are as follows: trachea, 0.1 hour; bronchi, 1 hour; bronchioles, 4 hours; and alveoli, 100-1,500 or more days.^{1,3} Soluble particles that are deposited into the alveoli may be systemically absorbed at the alveolar-blood interface, and may thereby become incorporated into target organs. Insoluble particles also pose a threat, especially if plutonium from unspent fuel or industrial accidents is present. Prolonged exposure of the alveolar epithelium to high-LET alpha emitters, like plutonium, has been related to increased incidence of malignancy.^{2,6}

In 1955, the International Commission on Radiological Protection adopted a model for evaluating the hazards of inhaled radioactive particles.⁶ According to this model, 25% of inhaled radioactive particles are immediately exhaled, and the remaining 75% are deposited along the respiratory tree. About half of the particles are deposited in the upper bronchial tree, where they are moved by the ciliary epithelium to the nasopharynx. In the nasopharynx, they are propelled by the mucociliary swallowing reflex into the digestive tract, where they enter the gastrointestinal path.²

Ingestion is usually secondary to inhalation and the mucociliary swallowing response. However, in a fallout environment, direct ingestion from contaminated foodstuffs is also probable. The degree of intraluminal gastrointestinal exposure depends on transit time through the gut, which will vary widely from person to person.^{1,3} The mean clearance times of the human digestive tract are stomach, 1 hour; small intestine, 4 hours; upper large intestine, 13-20 hours; and lower large intestine, 24 hours, resulting in a total mean emptying time of 42 hours. The much slower rate of movement in the large intestine places its luminal lining at higher risk for damage from nonabsorbable radionuclides. Gastrointestinal transit time may be shortened by use of emetic and/or purgative agents.

Some relatively soluble radionuclides may not be absorbed due to acidic or caustic properties that fix them to tissue proteins.^{1,2,7,8} Systemic absorption through the intestine varies widely, depending on the radioisotope and its chemical form. Clear differences exist between radioiodine, which is rapidly and completely absorbed, and plutonium, which is almost nonabsorbed (0.003%). Furthermore, nonabsorbable alpha emitters apparently do not cause gastro-intestinal injury, even in large amounts. Nevertheless, the gastrointestinal tract is the critical target organ for the many insoluble radionuclides that travel its length almost unabsorbed.

Wounds contaminated by fallout and shrapnel may provide continuous irradiation of surrounding tissues and increase the likelihood of systemic incorporation.^{13,5,911} This hazard remains until the contaminant is removed by cleansing, surgical debridement, or radionuclide decay. The last process may take a few days or millions of years, depending on the contaminant.

Sampling of Radioactivity

Since the identification of radionuclide contaminants is important for treatment, it may be necessary to know whether beta-gamma or alpha emitters are present. Health-physics personnel should be able to provide this information even with limited radiation-detecting equipment. Separate swabs of the nares should be taken to determine radioactivity and possible inhalation contamination before decontaminating the skin by showering or washing. The nasal swab should be taken at the site and sent in a sealed, clean container to higher-care facilities along with the patient. Although skin decontamination should be done as quickly as possible, the stability of an injured patient is vital, and first aid must be the primary concern.

On-Site Management

Contamination of the skin with radionuclides is usually not immediately life threatening to either the patient or medical personnel, unless the contamination is from a gamma emitter and the dose rate is several Gys per hour. Partial or complete emergency decontamination should be done at the site before a patient is transported to a higher-care facility. Discarding contaminated clothing will remove up to 85% of external contaminants; following this with showering or washing will remove more than 95% of surface contamination.^{1,3,5} A combined nuclear-chemical war may present many problems for decontamination procedures. A light wash-down and vacuuming or brushing of protective clothing may be all that can be done.

Hospital Management

Hospital emergency plans should provide for the proper management of incoming contaminated casualties. The National Council on Radiation Protection and Measurements provides a universal outline guide that can be adapted for most facilities.¹ A designated decontamination area should be prepared, and traffic in this area should be one-way to prevent contaminating "clean" areas of the facility. Ideal decontamination facilities should have equipment to wash ambulatory and injured patients, shielding to use with high-level beta-gamma contamination, and a floor plan that minimizes cross-contamination of clean areas.¹⁻³ Medical personnel should be rotated through the decontamination area to ensure that their radiation exposure is kept to a minimum. Clothing and other contaminated materials should be discarded at a contained location away from the health-care facility. At many hospitals, the morgue or autopsy room is an excellent

decontamination area. It has contained liquid systems, a table easily adapted to wash a contaminated patient, and often a heavily lined area that can be used to store contaminated materials. Other possibilities include physiotherapy areas and cast rooms. Table 4-1 lists the supplies that are recommended for a decontamination room.¹

The initial evaluation of a patient should include a complete history of the contamination incident, a physical examination to uncover conventional injuries (but which usually provides no evidence of radionuclide contamination), and laboratory tests, including a complete blood count with platelets and a routine urinalysis. The incident history should provide some background for predicting possible internalization of radionuclides. The internalization may be from fallout; handling a damaged, undetonated nuclear weapon; accidental ingestion of (or external contamination by) a specific radioactive substance; or radionuclide-contaminated wounds. The patient should then be placed into the emergency- plan triage system and treated accordingly.

MEASUREMENT OF RADIOACTIVE CONTAMINATION

Generally, health physicists at large medical facilities will be responsible for radiation monitoring. However, all medical personnel should be aware of the various monitoring techniques in order to understand their reliability, limitations, and sources of possible error. The determination of surface contamination will require monitoring for alpha and beta-gamma emissions.

Alpha particles have limited penetration, and a patient will be protected by an intact epidermis. Alpha contamination does not become hazardous unless it is internalized through inhalation, ingestion, or wounds.^{1,6,11} Alpha particles are the most difficult radiocontaminant to detect, and negative monitoring results are not always reliable. Due to the high absorption of alpha particles even in air, it is important to keep the radiation monitor close to the measured surface. Direct contact readings are preferred. Proportional counters are the most common device for detecting alpha radiation in the laboratory, and they are capable of discriminating between alpha and beta-gamma emitters. However, the counters are not yet available for military field use. Scintillation counters are currently used for determining radioactivity contamination while in the field, but they are less sensitive than proportional counters. Surface monitoring with swipes may also be used to test for transferable alpha material. Textured paper (such as filter paper) is wiped across the test surface and then measured in a laboratory scintillation counter. Results may identify contamination with transferable alpha (plutonium) or weak beta (tritium) radiation. The nose swipe is also used for alpha emitters. A cotton swab or narrow strip of filter paper moistened with distilled water is gently wiped around the naris opening (one per naris). After the swab or paper is dry, the radioactivity is determined.

Beta and gamma radiations are often emitted simultaneously by decaying radioisotopes. These types of radiation present internal and external hazards. Instruments for measuring either type of radiation are similar, but the Geiger-Mueller (GM) counter is the most common detection device. Unfortunately, high radiation levels can saturate GM counters and give false or even zero readings. Ionization chambers can measure higher dose rates. Both are sensitive to extremes of heat and humidity, and both may fail in a corrosive chemical environment. Shielding the probe of the detection device will provide a relatively pure reading of the gamma component, and the difference between the shielded and unshielded readings provides the beta (and often soft gamma) component.

All medical personnel need to be alert to possible mixed external-internal contamination. A patient may have inhaled contaminated steam or dust during the cleanup of an accident, as happened in the 1986 nuclear reactor accident at Chernobyl.^{12,13} If the internalized materials are beta- or gamma-emitting substances, they may provide radiation readings on the monitoring devices used for external decontamination. Of course, internalized alpha particles will not register on monitoring devices, but their presence may be suggested by the incident history or by the detection of external alpha particles.

If patients are few and there is a need to know (or closely estimate) the total internal radiation dose, all body effluents must be collected for an extended time. Careful measurements of all excreted radiation will provide data for calculating a close estimate of the total internal body burden.¹ Depending on the radioisotope involved and its physicochemical characteristics, the collections may have to be made for months.

Many pitfalls exist in the interpretation of excretion data analyses. Variations in excretion rates from person to person will interfere, and the time of exposure, possible interim therapy with chelators, and data on the excretion of inhaled contaminants may complicate the estimate.

A nuclear detonation or accident may result in alpha, beta, gamma-ray, X-ray, and neutron emissions. Devices that are available to detect exposure to gamma, X, and neutron radiations include dosimeters, film badges, and thermoluminescent detectors.

TREATMENT DECISIONS

Early information on the history of the exposure incident may identify the major isotopes involved and provide some dosimetry information. Patients will likely present with no clinical symptoms other than possible conventional trauma. Therefore, critical decisions on the initial treatment may have to be based on knowledge of human physiology, the pharmacology of agents to be used, the metabolism of the radioisotopes, and the historical information. Treatments for internal contamination should begin within hours of exposure.^{1-5,7,14} Emergency

planning will pay off by reducing the time for dosimetric evaluations and will result in more informed initial decisions. After the initial treatment, there will generally be time to assess the situation as data from monitoring become available. Later, dose estimates will determine if further treatment and evaluation are needed, or if the treatment involves risks.

Usually no immediately life-threatening hazard is associated with radiation contamination, especially after the removal of clothing and washing. The probability that a patient will incur radiation-induced health problems is low, and any incidence may be decades in the future. Risky decontamination procedures (such as lung lavage or surgery) that could lead to internalization should be carefully evaluated, and a decision may require assistance by expert consultation.^{1,15}

Physicochemical properties of radiocontaminants play a significant role in determining treatment. The solubility of the material containing the contaminant may determine its distribution within the body, or even its accessibility into the body. As no material is completely insoluble, some small fraction may rapidly become internalized from the lung or through a wound. In contrast, normally soluble materials may be present in an insoluble form, or may be made insoluble under systemic physiological conditions. Therefore, treatment begun as early as possible after exposure will significantly increase the probability of successful internal decon-tamination.^{1-3,5,7,10}

Medical personnel should be aware of the possible presence of mixed-fission products (MFP), which are groups of radionuclides likely to be found together after nuclear reactor or detonation incidents. The appropriate treatment regimen is based on the time of exposure after the nuclear event. Some MFP groups are plutonium with associated americium, curium, and neptunium, and uranium with thorium, radium, and their decay products. Treatment is determined by the particular radioisotopes.

In a complete nuclear detonation, over 400 radionuclides are released. However, only about forty of these are potentially hazardous to humans.¹⁻³ The most significant radioisotopes from unspent nuclear fuel are tritium, plutonium, and uranium. Of particular interest are the radioisotopes whose organospecificity and long half-lives may result in irreversible damage or induction of malignant alterations. Radioisotopes of immediate medical significance are listed in Table 4-2, with descriptions of properties, target organs, and treatment.

THERAPEUTIC MANAGEMENT

Skin decontamination has two goals: (a) to remove radiocontaminants and thereby reduce the total dose, and (b) to prevent possible internalization. If done appropriately, skin decontamination will also contribute to a more accurate determination of the internal contamination. If the radioactive contaminant is

resistant to an initial washing with soap or detergent and water, further decontamination should be supervised by a physician. The physician needs to understand the basic physical and physiological principles involved. The contaminant's half-life, energy level, and dose rate must be weighed against continued and harsher decontamination procedures, which may abrade the intact skin or decrease the distance to the important dermis basal layer. Because the skin regenerates every 10-14 days, contamination would eventually be shed naturally. Signs of excessive decontamination efforts will be more evident 24 hours later, and two or three less intensive decontamination efforts are less traumatic to the skin than one major effort. If necessary, further cleansing may include mild abrasives, chelating agents, and bleach. Chemical techniques are rarely needed.

After first aid to control hemorrhage and shock, the next steps are to determine if wounds are contaminated and then to locate any other contamination.^{1-5,10,11,14} Alpha emitters and possibly weak beta emitters are difficult to locate around wounds. A simple film of irrigation fluid, blood, or tissue fluid can entirely mask this contamination, which then may internalize via the circulatory or lymph systems. Once the surface contaminant is located, irrigation should be sufficient to remove it, although some wounds may need debridement that is deeper than conventional injuries require. This debridement involves a certain risk of translocation or absorption (especially when working with possible alpha emitters, like americium or plutonium); therefore, the chelating agent DTPA should be given systemically and the wound should be irrigated with DTPA before debridement.

If limb wounds have high concentrations of beta-gamma contaminants, medical personnel must limit their exposure by frequently rotating shifts or by working with shields. Amputation of the limb may have to be considered if (a) the wound is highly contaminated and decontamination attempts cannot be made or are not successful, (b) the contamination is so intense that extensive radiation-induced necrosis is likely, or (c) the injury is so severe that functional recovery is unlikely.

TREATMENT OF INTERNAL CONTAMINATION

The goals of internal decontamination are to reduce absorption and to enhance elimination and excretion. Treatment is most effective if it is started as soon as possible after exposure.

Clearance of the Gastrointestinal Tract

Gastric absorption can be reduced by stomach lavage, emetics, purgatives and laxatives, ion exchangers, and aluminum antacids. Other less effective treatments are alginates, barium sulfate, and phytates, which currently are not recommended for internal decontamination of radionuclides.

Stomach lavage is useful only if the ingested dose is known to be large, and if the intake is recent and still in the stomach. Lavaged material must be monitored for radioactivity and the patient must be kept in a head-low position to prevent aspiration.

The most common emetic agents are apomorphine (5-10 mg, subcutaneous) and ipecac (1-2 g in capsule or 15 ml in syrup), which should be given concomitantly with 200-300 ml of water. Caution should be used not to induce emesis in an unconscious patient.

Laxatives or purgatives (such as castor oil) will stimulate intestinal motility, and saline cathartics will increase water movement into the intestine and induce removal of contents within 3-6 hours. The selection of purgatives or laxatives should be based on their speed of action (slowly acting drugs, like bulk-forming and wetting agents, are not appropriate). These agents are contraindicated if the patient has abdominal pain of unknown origin, or if surgery is a possibility.

Prussian blue, an ion exchanger, was used to treat victims in the 1987 cesium-137 contamination incident in Goiânia¹⁶ and has been well tolerated in humans (1 g given orally with water three times per day).^{1, 2} It may be continued for 3 weeks or longer, as indicated. However, Prussian blue is not approved by the Food and Drug Administration (FDA), and emergency approval for an investigational drug would have to be obtained. Ion-exchange resins, like sodium polystyrene sulfonate (for adults, 15 g, 4 level teaspoons of resin suspension), have an assumed but untested usefulness for inhibiting the uptake of radionuclides in the gut.

Aluminum antacids are an effective treatment for reducing the uptake of radioactive strontium. A dose of 100 ml of aluminum phosphate gel, given immediately after exposure, decreases the absorption of radioactive strontium in the gut by about 85%. Aluminum hydroxide, given in a single dose of 60-100 ml, reduces uptake by about 50%. Both forms are nontoxic. This is the treatment of choice for contamination with radiostrontium.^{1,2}

Prevention or Reversal of Radionuclide Interaction with Tissues

Blocking and Diluting Agents. Blocking and diluting agents decrease the likelihood of absorption by decreasing the availability of the radionuclide. A blocking agent, such as potassium iodide (300 mg/day for 7-14 days) for radioiodine, blocks the uptake of a radioisotope by significantly increasing the availability of the stable isotope. Diluting agents simply dilute the radioisotope, which statistically decreases the opportunity for absorption. Water is a diluting agent in the treatment of tritium contamination. For maximum efficacy, the stable isotopes that are used as the blocking or diluting agents must be as rapidly absorbed or metabolized as the radioisotopes are.

Mobilizing Agents. Mobilizing agents are compounds that enhance and increase the natural turnover processes and thereby induce the release of radioisotopes from tissues. They are most effective when given immediately, but they may retain some effectiveness for up to 2 weeks after exposure. Included in this group are antithyroid drugs, ammonium chloride, diuretics, expectorants and inhalants, parathyroid extract, and corticosteroids. These agents require experienced consultation, treatment, and management.^{1,9}

Chelating Agents. Chelators are substances that bind with some metals more strongly than others to form a stable complex that, when soluble, can be more readily excreted by the kidneys. The effectiveness of chelation therapy is influenced by many physiological factors, including plasma proteins, blood pH, enzymes, and even nucleic acids. The most commonly known chelating agent is EDTA, normally given as the calcium salt. However, for treatment of the heavy-metal multivalent radio-nuclides expected from a nuclear yield, the powerful chelator DTPA is generally more effective. DTPA-chelated complexes are more stable than EDTA complexes, and are therefore less likely to release the radionuclide before excretion. The calcium and zinc forms of DTPA have both been approved by the FDA as investigational new drugs (IND) for the chelation of plutonium, berkelium, californium, americium, and curium. Physicians finding a need for DTPA should contact the Radiation Emergency Assistance Center/Training Site (REAC/TS) to become a coinvestigator (see address in reference note).¹⁷ REAC/TS usually responds to nuclear accidents and incidents and will arrive at the site within 48 hours. It is doubtful that DTPA will be available in combat.

DTPA is administered as an intravenous solution of 1 g dissolved in 250 ml of saline or 5% glucose, infused over 1 hour per day for up to 5 days.^{1,15} As an irrigation solution, 1 g CaDTPA and 10 ml of 2% lidocaine are dissolved in 100 ml normal saline for plutonium and americium contamination.⁵ If the contaminants have an atomic number greater than uranium's 92, the treatment is simple: DTPA is used for all contaminants except uranium. The use of DTPA is contraindicated for treatment of uranium contamination because of the added risk of renal damage.¹⁸ Uranium contamination has been treated with oral sodium bicarbonate, regulated to maintain an alkaline urine pH, and accompanied by diuretics.¹

Other chelating agents are dimercaprol, penicillamine, and deferoxamine (DFOA). Dimercaprol is a highly toxic chelator that has been effective in treating mercury poisoning. Penicillamine and CaEDTA are significantly less toxic and more effective for mercury poisoning. (Radiomercury, however, is not a likely hazard of nuclear detonation.) Penicillamine is an amino acid derived from penicillin, but it has no antibacterial properties. It has been used to treat contamination with many metals, mainly copper, mercury, and lead. It does not appear to be especially promising for the treatment of internal radionuclide contamination. DFOA has been used to treat iron poisoning. In combination with DTPA, it has an increased affinity for iron. DFOA appears to be more useful than DTPA in treat-

ing plutonium contamination, but until it is approved by the FDA for this purpose its use cannot be recommended.

Lung Lavage. Lung lavage has been successful in decreasing radiation-induced pneumonitis in laboratory animals.¹ It has been used in human therapy for chronic obstructive lung diseases.¹⁹ However, the procedure requires general anesthesia, and a careful risk-benefit assessment must be made before it is used for radionuclide decontamination. Endoscopy is the procedure most similar to lung lavage, and it has a mortality rate of 0.08%-0.85% in patients judged to be in good condition. Considering that the risk from lung lavage is immediate and that the possible effects from internal radionuclides are decades away, medical personnel will have to weigh the benefit to the patient carefully. Unless the lung burden is so great that it will result in acute radiation injury, lung lavage is not recommended.¹⁻³

SUMMARY

A plan for medical care must be available to deal with the contingency of a nuclear event. The first priority is basic first aid, followed by decontamination in a predesignated area. The level and type of radiation exposure must be calculated as accurately as possible. Contamination may be internalized via inhalation, ingestion, and absorption through wounds and skin. Treatment is determined by the particular radiation to which the patient has been exposed. Internal decontamination must be started in the first few hours after exposure if radionuclides could have been internalized.

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