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CHAPTER 13

Internal Contamination with Medically Significant Radionuclides

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In a nuclear explosion, over 400 radioactive isotopes are released in the biosphere (1). Of these, about 40 radionuclides are of potential hazard to man. Of particular interest to the field of medicine are the isotopes whose organospecificity and long half-life present a danger of irreversible tissue damage or the induction of malignant alterations.

Some incorporated radionuclides are partly diminished in the processes of radioactive decay and biological elimination, but other isotopes have a long half-life and are incorporated in firm tissue. These latter isotopes must be therapeutically removed from the contaminated individual.

The radiation effects of an internally deposited radionuclide depend on its chemical nature, solubility, half-life, type of radioactive decay, the tissue of incorporation, and the physiological factors determining its metabolic fate. High organospecificity of certain fission products will result in radiation damage to selective tissues; in contrast, other radionuclides that are uniformly distributed in the body fluids will result in the relatively uniform exposure of various organs to the radiation. Some radionuclides produce detectable tissue damage soon after their incorporation in tissues of high radiosensitivity, whereas other radioisotopes may result in induced somatic and genetic changes as late effects.

From the biomedical point of view, an approach to the problem of internal contamination should focus on radionuclide organospecificity, physical characteristics, and chemical characteristics. The fate of radioisotopes will depend on various factors, including their chemical and physical natures, solubility, particle size, homeostasis, type of decay, biological deprecation, and elimination from the contaminated individual.

Radioisotopes that have no specific target organs will be rapidly eliminated by the processes of natural clearance. But that is not true for the organospecific
radioisotopes. Some highly organospecific radioisotopes (e.g., iodine) are concentrated in their natural target organs (thyroid), and other radionuclides that are not normally present in nature (e.g., plutonium) also show high organospecificity, with osteotropic characteristics (due to their metabolic pathways) similar to the normal constituents of the calcified tissue. Incorporation of such radioisotopes in their target organs can result in considerable tissue damage. This is because some of those isotopes have extremely long half-lives and involve decay by the particulate (alpha and beta) radiation, resulting in a high probability of malignancy in the target organs that are radiosensitive.

Radioisotopes that are produced by nuclear fission are distributed in the organism by the bloodstream after they enter the organism by ingestion, by inhalation, or through wounds. The amount that enters depends on the radioisotope’s physical properties and its solubility in body fluids. The ultimate size of the deposit in tissue is determined by the radioisotope’s chemical properties.

Various radioisotopes use different portals of entry into the individual. Some are preferentially absorbed in gastrointestinal mucosa, others gain access to the bloodstream via the respiratory tract, and still others preferentially enter the body fluids through wounds or by direct intravascular administration. The length of retention of the radioisotope in the body is determined by its effective half-life, mechanism of entry, quantity, target organ, and the processes of elimination.

Some fission products are preferentially absorbed in the intestine (calcium, strontium, iodine, cesium, etc.), whereas others (e.g., actinides) are hardly absorbed by ingestion and are primarily incorporated by inhalation or through contaminated wounds. Most of the fission products are rapidly eliminated from the body after the initial fallout from a nuclear detonation. The main biomedical hazard is due to the radioisotopes of high organospecificity and long half-life (such as $^{137}$Cs, $^{90}$Sr, $^{90}$Y, $^{14}$C, $^{3}$H, $^{131}$I, and transuranic elements), which invariably produce pathologic changes (including malignant tumors, spontaneous and induced mutations) as their genetic effects in the contaminated individual.

I. ROUTES OF ENTRY AND DISTRIBUTION

The four main routes of internal contamination are (1) ingestion and gastrointestinal absorption, (2) inhalation and transalveolar transfer to the bloodstream, (3) percutaneous absorption, and (4) through wounds or by direct injection into the bloodstream.

A. INGESTION

Gastrointestinal absorption of the nuclear fission products differs for the various radionuclides. Some of the ingested radioactive isotopes preferentially enter...
the bloodstream via the intestinal mucosa, whereas other isotopes are not absorbed in any significant amount. Of those isotopes whose principal route of entry is gastrointestinal absorption, the most significant are the isotopes of cesium (\(^{137}\text{Cs}\)), strontium (\(^{90}\text{Sr}\)), cobalt (\(^{60}\text{Co}\)), iodine (\(^{131}\text{I}\)), phosphorus (\(^{32}\text{P}\)), mercury (\(^{197}\text{Hg}\) and \(^{203}\text{Hg}\)), radium (\(^{226}\text{Ra}\)), and tritium (\(^{3}\text{H}\)).

Gastrointestinal absorption is an important route of entry of the osteotropic alkaline earth isotopes such as \(^{90}\text{Sr}\). Gastrointestinal absorption is particularly important as a consequence of the delayed fallout hazards because of the contaminated biosphere and the food contaminated by nuclear fission products (farm produce and dairy products). However, the homeostatic mechanisms that govern the transfer of radioactive isotopes across the intestinal mucosa can discriminate against some of the radioisotopes that are foreign to the organism, thus favoring absorption of their homologs, which are involved in the normal homeostasis.

Over 90% of the entire process of discrimination of strontium takes place in the gastrointestinal tract, where calcium is preferentially absorbed. This phenomenon constitutes one of the methods of therapeutic removal of radioactive strontium via the intestinal tract.

Other sites where discrimination processes against radioactive strontium occur include the renal tubules, the mammary gland, and the placenta, where calcium reabsorption is favored. These biological membranes represent the sites of homeostatic protection against potentially hazardous radionuclides.

The mechanism of preferential absorption of calcium in relation to strontium in the intestinal mucosa was partly addressed by the processes of diffusion and active transport for calcium, whereas the transfer of strontium from the intestinal lumen to the circulation is mainly via diffusion (2). The ingestion of \(^{137}\text{Cs}\) results in its rapid entry into the bloodstream. Numerous cases have been reported of accidental contamination with \(^{137}\text{Cs}\) in humans (3, 4).

Intestinal absorption of radioactive iodine (\(^{131}\text{I}\)) is an important route of accidental contamination because the transfer of contamination from the biosphere to the human body takes place via the food chain (from pasture to dairy product to man). Numerous reports in the literature (5, 6) describe protective measures against the accidental ingestion of \(^{131}\text{I}\) (including disposal of contaminated cattle feed and dairy products). In all cases of accidental ingestion of \(^{131}\text{I}\), a thyroid bioassay should be made, and therapeutic management of the contaminated patients should begin immediately. Periodic monitoring for the evidence of hypothyroidism should be performed for several years (7).

The intestinal absorption of radium (\(^{226}\text{Ra}\)) is an important cause of inducing skeletal malignancies. Over 30% of \(^{226}\text{Ra}\) is absorbed in the intestine after accidental ingestion, and it is almost entirely deposited in the skeleton (8–10). Ingestion of \(^{226}\text{Ra}\) has been reported in the classic work on internal contamination in dial painters who ingested luminous paints containing \(^{226}\text{Ra}\) (11, 12). Various pathological consequences followed the ingestion of \(^{226}\text{Ra}\), including
osteogenic sarcoma, fibrosarcoma, paranasal and mastoid carcinoma, aplastic anemia, and leukemia (13, 14).

Other radionuclides that enter the circulation via the gastrointestinal tract include tritium (H) which penetrates intestinal mucosa in the form of tritiated water (15) and uranium isotopes (234U, 235U, and 238U). The uranium isotopes present a high biomedical hazard because of their long half-lives, nephrotoxicity (238U), and retention in the skeletal tissue (234U and 235U), with a high potential of inducing malignancy in the bone and hematopoietic tissues.

B. Inhalation

The kinetics of (1) the deposition of radionuclides in the bronchial tree and alveoli and (2) the passage of radionuclides across the alveoli into the bloodstream is extremely complex, from the viewpoints of physiology and radiation toxicology (16). Inhaled radioactive particles are deposited in the upper bronchial tree on the alveolar surfaces, or, if soluble, they are absorbed into the systemic circulation.

Classic reports on the quantitative data concerning deposition of the radioactive particles in the bronchoalveolar tree were reported over 35 years ago (17, 18). Since then, many reports have been published concerning the pathways of various radioisotopes in the respiratory system. To evaluate the radiation hazard of inhaled radioactive particles, a general model of their metabolic behavior in the respiratory system was adopted by the International Commission on Radiation Protection in 1955 (19). This model was later revised (20), with emphasis on the significance of different variables that determine the metabolic fate of inhaled radioactive particles.

According to that model, about 75% of inhaled radioactive particles are deposited in the respiratory tree, and 25% are immediately exhaled. About 50% of the inhaled particles are deposited in the upper bronchial tree; then they are moved by the ciliary epithelium to the nasopharynx. From there they are swallowed and handled according to the mechanisms of their gastrointestinal kinetics.

This is an important factor in contamination with actinides. Their intestinal absorption is negligible, but their deposition in the lung is a major radiotoxicologic hazard. To move them from the respiratory system to the gastrointestinal system is one of the aims of therapeutic management of accidentally inhaled actinides. About 25% of these inhaled particles are deposited on the alveolar surfaces; at this site, the metabolic behavior of the particles largely depends on their solubility. In general, about 10% of particles reaching alveolar surfaces are transferred into the systemic circulation. The remaining 15% ascend the bronchial tree and are ultimately eliminated by expectoration or by transport to the gastrointestinal tract.

Inhalation of radioactive particles is the main route of internal contamination with actinides (thorium), of the kinetic toxicity of the target organ, depends on the distribution of particle size.

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with actinides (Americium, Plutonium, Uranium, Curium, Polonium, Radium, Thorium), Cobalt, Cerium, Iodine, and Tritium. Quantitative differences exist in the kinetics of different radioisotopes that gain access to the body via the respiratory tract, but their ultimate distribution after reaching the systemic circulation depends on their metabolic pathways and organospecificity. Differences in distribution occur as a consequence of the radionuclide's portal of entry, solubility, particle size, and chemical form.

The transport of americium to extrapulmonary tissues after inhalation will be greater if the isotope is in a citrate form. Less body burden and accumulation in the target organ (liver and bone) occur if the radionuclide is present in the form of a nitrate. If americium-241 ($^{241}\text{Am}$) is inhaled as an oxide, the target organs will be the tracheobronchial lymph nodes, liver, lung, bone, and thyroid, in descending order of importance. When humans were accidentally contaminated by inhalation of an undetermined chemical form of $^{241}\text{Am}$, the main target organs were bone and liver (21). Americium is eliminated from lung tissue by its absorption in the blood, by endobronchial ciliary mechanisms, and by expectoration or ingestion after reaching the nasopharynx (22). $^{241}\text{Am}$ that gains access to the systemic circulation from the lung is distributed equally in bone (45%) and liver (45%) for all of its compounds.

Internal contamination with plutonium ($^{239}\text{Pu}$) via the respiratory tract is the major route of accidental contamination. It accounts for over 75% of all industrial exposures to plutonium (23). Absorption from the respiratory tract depends on the compound’s solubility. Soluble compounds (nitrate, citrate, and fluoride) are absorbed into the systemic circulation and deposited in the liver and bone within a few weeks. Retention of plutonium compounds (oxides) in the lung is much longer, with slow translocation into the pulmonary and tracheobronchial lymph nodes, followed by liver uptake many years after the inhalation exposure (24).

Uranium isotopes are a considerable hazard for accidental exposure through inhalation. The absorption and retention of a uranium isotope depend on its chemical form and particle size. Its biological half-life in the lung is estimated to be 120 days, with considerably longer half-life (1470 days) in the case of inhalation of uranium oxides. Soluble uranium salts are primarily absorbed by the respiratory route. Fatal cases have been reported of accidental inhalation in humans, which caused nephrotoxic changes including glomerular and tubular damage, azotemia, albuminuria, and tubular necrosis. These changes may be reversible; tolerance has been reported after subsequent exposure to soluble uranium compounds. Renal damage is caused by chemical rather than radiation injury. The less soluble uranium compounds are less readily absorbed in the lung (25).

Accidental internal contamination with the isotopes of iodine occurs mostly with $^{131}\text{I}$, although about ten radioactive isotopes of iodine are produced in nuclear fission. Inhalation is not a major route of entry for iodine, but iodine is a significant radiation hazard because of its volatility. Inhaled iodine reaches equi-
librium with body fluids in less than 1 hr, and it selectively accumulates in the thyroid gland. A thyroid bioassay should be performed in each case of suspected internal contamination with $^{131}$I. As in other routes of internal contamination with $^{131}$I, follow-up studies should be performed for many years. Some patients have developed hypothyroidism as late as 17 years after exposure (7).

Tritium presents a radiation hazard when inhaled. But the radiation–toxicology consequences for inhalation are less significant than for ingestion of elemental tritium as tritiated water.

Internal contamination with medically significant radioisotopes via inhalation has been described in humans, related to exposures from nuclear weapons and from industrial accidents. But a need exists for analyzing the various parameters of metabolic behavior and the consequences of internal contamination by various radionuclides via the respiratory route of exposure. To date, compartmental analysis, kinetics, and autopsy data have not been sufficiently well defined for human exposure. Further insight into the metabolic fate of inhaled radioisotopes is being gained from animal experiments and from excretion data in humans after pulmonary exposure.

C. Percutaneous Absorption

Normal skin is an effective mechanical barrier to internal contamination from most radionuclides. This route of entry is the least important in the transfer of radioisotopes from the contaminated biosphere to the internal environment of the human body, but still is of potential concern for internal contamination.

Studies on the percutaneous absorption of transuranic elements have been described in laboratory animals, with the absorption of 2% of plutonium through intact skin (26). Transcutaneous absorption in these exposure studies was facilitated by the high acidity and by complexing the plutonium with tributylphosphate. The amount of radionuclide absorbed also depended on the quantity of applied radionuclide and on the anatomic site of the skin to which applied.

The main pathway of a radioisotope from the skin to the systemic circulation is through hair follicles. The hair bulbs below their keratogenous zone are supplied by a highly vascularized connective tissue, part of a normal hair papilla. This rich network of blood vessels is the principal site of transcutaneous migration of the radioisotope from the contaminted skin into the systemic circulation.

The surface epithelium (epidermis), with its primary function of protecting the internal environment of the body, is less important as a route of entry for radioisotopes into the body. This is mainly because of its thick structure of many layers and because the keratinized stratified squamous epithelium of the outermost layer provides an effective mechanical barrier to the insults of the external environment.

However, it is not possible to consider the events in a nuclear accident as separate physical or biological events. A nuclear weapon explosion is a physical event that produces a blast wave, fire, and radioactive contamination. The blast wave can cause injuries, and the radioactive contamination can be ingested or inhaled, leading to internal contamination.
13. INTERNAL CONTAMINATION WITH RADIONUCLIDES

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...h tributylphosph- the quantity of ich applied. eculation is me are supplied ir papilla. This us migration of eculation. of protecting the te of entry for nure of many m of the outer...of the external ear accident as...separate phenomena, because the possibility of combined injury produced by a nuclear weapon results in multiple and complex effects on the human body. It is possible that the protective capacity of the skin will be deranged in both primary and secondary thermal injury, which results in significant alterations of the skin and permits easier entry of the externally deposited contaminants into the body. Burned, desquamated, and necrotic skin loses its integrity and provides an open route of entry for radioactive and infectious insults to reach the internal organs. The main concern in preventing internal contamination through this route is to maintain the integrity of the skin.

II. INTERNAL CONTAMINATION THROUGH WOUNDS AND INJECTION INTO THE SYSTEMIC CIRCULATION

Radionuclides may have direct access to the internal environment of the body as a result of thermal or traumatic injury after atomic bomb exposure, industrial or laboratory accidents, or misadministration of radiopharmaceuticals in the diagnostic and therapeutic use of radioisotopes in hospitals.

Primary injuries by the blast component of the nuclear weapon explosion usually occur near the hypocenter. These take the form of vascular and visceral damage, without apparent damage to the skin. This type of primary traumatic injury is of no consequence for internal contamination. However, secondary blast injuries are a considerable concern for internal contamination through bruised, lacerated, or cut wounds; open fractures of bones; or multiple wounds caused by fragments of building material, glass splinters, wood, or any other contaminated projectile. These lesions pose a complex problem because of the complications of infection and internal contamination.

Intradermal or subcutaneous deposition of the fission products has been widely studied because of the therapeutic need to eliminate radioactive isotopes from the contamination site without interrupting the integrity of the normal integument. The quantity of absorbed contaminant will largely depend on the depth of the deposition, anatomic site of the skin, and size of the contaminated area. Some isotopes will translocate relatively rapidly from the intradermal or subdermal site of deposition (iodine, strontium, cesium, tritium), whereas others will absorb less avidly from the shallow dermal wounds (transuranic elements).

The fate of the isotopes at the site of superficial deposition will largely depend on the healing processes or the complications of the superficial lesions (e.g., eschar, fibrous tissue, infection, draining ulcers). Translocation from the intradermal sites of contamination is mainly via the lymphatic system. The ultimate deposition will depend on the physical and chemical natures of the isotope, solubility, particle size, and organotropism. Management of the contaminated intradermal and subdermal wounds is still an area in which further investigation...
is needed, preferably by professionals with experience in the medical and surgical management of contaminated wounds (24).

The intramuscular deposition of radioactive isotopes has been widely studied and documented in animal experiments and in accidental exposures of humans. Some radionuclides are completely and rapidly absorbed into the systemic circulation (e.g., strontium, iodine, and tritium), while others have a slower rate of translocation (e.g., transuranic elements).

Retention of radionuclides in the various organic systems can be affected by the site of initial deposition. That is, intramuscular deposition of the actinides will result mainly in final incorporation in the skeleton, with relatively low deposition in the liver, compared with intravenous injection. The other radioisotopes, such as iodine or osteotropic alkaline earths (calcium and strontium), will be much less affected by the site of primary incorporation, and will be ultimately deposited in the organs of their biologically specific avidity (thorax and bone).

Radioisotopes that are normally widely distributed in the body fluids (cesium and tritium) will be largely unaffected by the site of their initial incorporation. The only effect on their intramuscular administration (versus intravenous) will be on the kinetics in the various compartments of the body.

The intravenous route of internal contamination results in the rapid incorporation of different radioisotopes in their respective target organs, as well as in their rapid removal through the renal, hepatobiliary, and other endogenous systems of elimination. Similar to that observed for absorption, the retention and elimination of various radionuclides depend on their chemical form in plasma. For example, strontium ions are present in plasma in the protein-bound, complexed, and free (hydrated) forms; strontium’s elimination and reabsorption in the renal tubules will be determined by its chemical form. The osteotropic alkaline earth ions will be eliminated faster if they are in the ionized form.

Other radioisotopes such as actinides, which are preferentially incorporated in the liver and bone, will be largely affected in their deposition and elimination after intravenous administration (versus other parenteral routes). Actinides injected intravenously will be deposited in the liver in higher quantities than when injected intramuscularly, with a smaller percentage depositing in bone.

Over 30% of intravenously injected plutonium will be rapidly eliminated, mostly via the gastrointestinal tract by the processes of hepatobiliary and endogenous elimination. After intravenous injection, the rate and amount of deposition of transuranic elements in the liver and bone will depend on the elements’ polymerized forms, acidity, the presence of complexing agents, and their valence.

The intraperitoneal route of contamination occurs in radiation accidents of nuclear weapon origin or industrial origin, as well as in the misadministration of isotopes used in colloidal form to treat metastatic deposits in the peritoneal cavity ($^{32}$P).
III. PHYSICAL AND METABOLIC CHARACTERISTICS OF RADIOISOTOPES COMMON IN INTERNAL CONTAMINATION

Radioisotopes of medical concern can be classified according to their physical or chemical properties, their metabolic behavior, and the pathogenesis induced in the target organs of their final incorporation. Classification is extremely complex because of the many factors governing the metabolic pathways of each radioisotope. Significant differences may exist in the metabolic behavior of similar radioisotopes, and metabolic similarities may exist for radioisotopes that have dissimilar physical or chemical characteristics. Furthermore, radioactive isotopes of the same element can differ greatly in their behaviors in the living organism. So classifying radioisotopes is a complex and as-yet-unsolved problem. The problem can be addressed by considering each radioactive isotope as a separate entity with a variety of parameters and by individually considering each parameter.

Internal contamination by the fission products released in the explosion of nuclear weapons or after accidents in nuclear industry frequently occurs as simultaneous contamination by multiple isotopes and their products of radioactive decay. These mixed-fission products will make the diagnostic assessment of a contaminated patient a challenging task. Assessment requires diagnostically identifying the principal radioisotopes involved in the internal contamination so that proper therapeutic management can begin.

A. AMERICIUM

Two isotopes of americium are important in internal contamination: $^{241}\text{Am}$ and $^{243}\text{Am}$. $^{241}\text{Am}$ ($t_{1/2} \text{ Ph} = 458 \text{ years, } t_{1/2} \text{ Eff} = 140 \text{ years}$) is a daughter product of plutonium, which decays to neptunium ($^{237}\text{Np}$) by the emission of high-energy alpha particles. It also decays by a low-energy photon emission (60 keV). $^{243}\text{Am}$ ($t_{1/2} \text{ Ph} = 7950 \text{ years, } t_{1/2} \text{ Eff} = 195 \text{ years}$) decays by emission of alpha particles. Both isotopes most commonly occur in the trivalent state, but they may be present in oxidation states from II to VII.

Internal contamination with americium most commonly occurs by the respiratory route or through contaminated wounds. Gastrointestinal absorption is negligible, but is higher in the young organism (27). Absorption through the skin is low, but increases if the isotopes are present in a solution of high acidity. The intramuscular route of contamination results in 10–60% absorption from the site of incorporation, depending on the chemical form of americium.

Target organs of americium are liver and bone (50–70% versus 20–30% of the retained dose, respectively) after parenteral administration. The skeleton is the primary target organ, followed by the liver. Reports exist of a high incidence of
malignant changes in hematopoietic tissue, bone, and gonads after the intraperitoneal injection of americium in experimental animals (28).

Inhaled americium results in preferential deposition in the lung, tracheobronchial lymph nodes, liver, bone, and thyroid, with resulting tissue degeneration, fibrotic changes, and malignant changes. Human data on the metabolic fate of americium indicate that all americium compounds result in similar distribution in the liver (45%) and skeleton (45%), with the remainder (10%) distributed in other tissues and excreta.

B. CALIFORNIUM

Among 13 isotopes of californium, only one is a potential hazard of internal contamination, $^{252}\text{Cf}$. It is an alpha emitter, with a $t_{1/2}$ of 2.6 years and a photon emission of 43, 100, and 160 keV. This isotope is used in radiation oncology as a neutron source for intracavitary use (28).

$^{252}\text{Cf}$ is a serious hazard of external and internal radiation, with metabolic properties similar to other transuranic elements. It is absorbed into the systemic circulation mainly through the respiratory tract or contaminated wounds. Inhaled $^{252}\text{Cf}$ is retained mainly in the liver and bone, with other significant retention in the pulmonary and tracheobronchial lymph nodes. Intravenous or intramuscular administration of $^{252}\text{Cf}$ results in 60% deposition in the skeleton and about 15% in the liver.

Over 90% of $^{252}\text{Cf}$ initially deposits in the liver; it is then eliminated by hepatobiliary secretion into the small intestine. Human exposure to $^{252}\text{Cf}$ has been reported after the inhalation of $^{252}\text{Cf}$ particles (29). The main data on biodistribution, internal dosimetry, pathology, and treatment are derived from the work on experimental animals.

C. CERIUM

Two radioactive isotopes of cerium, $^{141}\text{Ce}$ and $^{144}\text{Ce}$, are of potential significance as a hazard of internal contamination. $^{141}\text{Ce}$ ($t_{1/2} = 32$ days) decays by beta and gamma emission, and is produced by neutron irradiation of stable cerium ($^{144}\text{Ce}$). $^{144}\text{Ce}$ ($t_{1/2} = 284$ days) is a fission product of uranium, and it decays by beta and gamma emission.

The route of internal exposure is mainly by inhalation. Gastrointestinal absorption is negligible in humans and in experimental animals (30). The critical organ for $^{141}\text{Ce}$ is the liver, and $^{141}\text{Ce}$ is preferentially deposited in the skeleton. Inhaled cerium is preferentially deposited in the lung, whereas the critical organ for ingested cerium isotopes is the descending colon and rectosigmoid.
D. Cesium

Among 21 radioisotopes of cesium, only 2 are medically significant for potential risk of internal contamination: $^{137}$Cs and $^{134}$Cs. $^{137}$Cs ($t_{1/2} = 30$ years) decays by beta emission, and its daughter-product emission of photons ($E = 662$ keV) accompanies its spectrum of radioactive decay. $^{134}$Cs ($t_{1/2} = 2.1$ years) decays by both beta and gamma emissions, with multiple energy levels for each mode of decay.

$^{137}$Cs is a product of nuclear fission, and it has been studied extensively as a significant component of radioactive fallout. As a metabolic homolog of potassium, it is uniformly distributed in the body and is eliminated by the renal system. Cesium enters the systemic circulation through either the respiratory or the gastrointestinal system. Its average biological half-life in humans is 110 days in males, 80 days in females, and 60 days in children (31). Accidental contamination with $^{137}$Cs has been declining, because of its decreasing levels in the biosphere due to reduced atmospheric testing of nuclear weapons.

E. Curium

Among 13 curium isotopes, the $^{242}$Cm ($t_{1/2} = 152$ days), $^{244}$Cm ($t_{1/2} = 16.7$ years), and $^{245}$Cm ($t_{1/2} = 9300$ years) are medically significant. The main route of entry into the body is by the respiratory system. Fifteen to forty-five percent of inhaled curium is absorbed into the circulation, and 10% is retained in the skeleton.

Initial excretion of curium is by the urine. Delayed excretion is equal between the urinary and intestinal routes, because the initial deposition in the liver is slowly eliminated via the hepatobiliary mechanisms.

Bone retention of curium isotopes predominantly occurs on the mucopolysaccharides of endosteal surfaces rather than in the bone minerals. The retention is affected by the active growth of bone and is particularly high in the areas of enchondral ossification (32).

F. Iodine

Ten radioactive isotopes of iodine are produced in the explosion of a nuclear weapon. Of all the fission products of medical interest, the radioisotope of iodine ($^{131}$I) is one of the most frequent concerns for internal contamination. Other isotopes of iodine ($^{132}$I, $^{133}$I, $^{134}$I, and $^{135}$I) are important in early exposure to the products of nuclear fission.

$^{131}$I ($t_{1/2} = 8$ days) is a principal cause of internal contamination in any...
nuclear incident and in early exposure to the radioactive fallout. $^{131}\text{I}$ decays by beta and gamma radiations. In reactor accidents, iodine is a major cause of concern for internal hazard because of its volatility and ability to enter the body via inhalation (33). In nuclear weapon testing, it is estimated that over 30,000 Ci of $^{131}\text{I}$ are released for each kiloton (kt) of fission energy (34). In reactor accidents, it has been estimated that over 20,000 Ci of $^{131}\text{I}$ were released into the atmosphere (35).

Other routes of internal contamination are by gastrointestinal absorption and by the cutaneous route of entry (intact skin, abrasions, and wounds). Contaminated grasslands after atmospheric tests of nuclear weapons are the major hazard of internal contamination because they result in contaminated dairy products. In the Marshall Islands experience, the ingestion of radioiodine was the main hazard from the standpoint of internal contamination (36).

In any case of suspected contamination with radioiodine, it is essential to determine the amount of thyroid incorporation by using the thyroid bioassay for both gamma and beta radiations. In cases of significant external contamination, the early estimate of thyroid uptake has to be interpreted with caution, because contaminated skin contributes to the findings of the thyroid assay. Bioassay of the $^{131}\text{I}$ body burden includes whole-body counting and studies of urinary excretion. Continuous follow-up monitoring of the thyroid should be performed routinely on all patients who are internally contaminated with radioiodine.

**G. Plutonium**

First in the chain of transuranic elements, plutonium is a very toxic substance. Among 15 radioactive isotopes of plutonium, 2 have been important as a potential hazard of internal contamination.

$^{239}\text{Pu} (t_{1/2} = 24,400 \text{ years})$ is an alpha emitter with infrequent gamma decay. A plutonium mass of 16 g contains 1 Ci of radioactivity. $^{239}\text{Pu}$ produces a fission after exposure to slow neutrons (fuel for nuclear weapons and reactors). $^{238}\text{Pu} (t_{1/2} = 86 \text{ years})$ is an alpha emitter whose mass of 57 mg contains 1 Ci of radioactivity. Both isotopes are retained in the bone, liver, and all other tissues in the ratio of 45:45:10% of the absorbed quantity (37).

Factors that determine the distribution and retention of plutonium include the portal of entry, the valence state, polymeric particulate or soluble compounds, and chemical form. The main route of entry is inhalation. Intestinal absorption is negligible, but plutonium does gain access to the systemic circulation through intact skin (38). Entry through contaminated wounds results in a localized deposit of plutonium at the site of entry, with the formation of reactive fibrous tissue (38) and the potential induction of malignant changes.

Most of the cases of accidental contamination are through the respiratory
system (75%); from there, absorption into the circulation largely depends on the solubility of the plutonium compounds. Soluble compounds are absorbed from the alveolar site to the circulation, and are ultimately deposited in the critical organs: liver and bone. Less soluble plutonium compounds are retained in the lung tissue, with slow migration to the pulmonary or tracheobronchial lymph nodes. Lung deposits of insoluble plutonium particles can be reduced by bronchopulmonary lavage.

H. Strontium

One of the most hazardous radioisotopes for internal contamination is $^{90}$Sr, which is produced with five other strontium radioisotopes in the process of nuclear fission of uranium. $^{90}$Sr ($t_{1/2} = 28$ years) decays by beta emission to $^{90}$Y, which is also a beta-emitting radionuclide. $^{89}$Sr ($t_{1/2} = 51$ days) and $^{85}$Sr ($t_{1/2} = 65$ days) are medically important, but their implications have been of less concern in radiation toxicology than the effects of $^{90}$Sr. $^{85}$Sr has been used in tracer and nuclear medicine diagnostic studies of skeletal metabolism and bone scintigraphy.

The metabolism of radiostrontium has been widely studied in animals and humans, as a consequence of a contaminated biosphere from radioactive fallout after nuclear weapons testing. The routes of entry for strontium are predominantly ingestion and inhalation, but strontium's access to the body fluids and target organs is rapid after being absorbed through skin lesions.

After its entry into the systemic circulation, strontium is rapidly deposited in the bone: first in its exchangeable fraction and then followed by its deep incorporation into the nonexchangeable bone mineral structures, through the process of exchange with the stable calcium ions and physicochemical absorption in the crystals of hydroxyapatite. The amount of $^{90}$Sr in the trabecular bone can be reduced by therapeutic management to facilitate the exchange of mineral salts between bone and plasma. However, once $^{90}$Sr has been incorporated into the nonexchangeable structures of the bone minerals, its therapeutic removal is impractical, if not impossible. The consequences of its retention in bone, its beta radiation, and its long half-life include genetic changes, leukemia, and osteogenic sarcoma (39, 40).

Strontium in the body behaves similarly to its metabolic homolog calcium, but some quantitative differences exist in their kinetics and the ultimate quantities retained. Biological membranes (intestinal mucosa, renal tubular epithelium, placenta, and mammary gland) possess the ability to discriminate against strontium, and favor the transfer of calcium ions. It is still controversial whether such discriminating processes affect the transfer of strontium across the basal membrane in the bone tissue. Physiological factors (such as the growth, nutritional,
hormonal, and reproductive processes) that affect the metabolism and homeostatic function of bone are important in determining the ultimate fate of this greatly hazardous product of nuclear fission.

I. TRITIUM

Tritium (³H) is the only isotope of hydrogen that decays to ³He by beta emission. Tritium (t₁/₂ = 12.3 years) is a normal constituent of the atmosphere and biosphere, produced by the fission of radioactive elements in the earth’s crust, as well as by cosmic ray irradiation of stable nitrogen in the atmosphere. The testing of nuclear weapons has resulted in an increased concentration of tritium in the atmosphere.

The routes of entry of ³H into an organism include inhalation, ingestion, and penetration through the skin. Ingestion of tritium, in the form of tritiated water, results in rapid and complete absorption in the body fluids, with diffuse distribution throughout the body. The body burden is monitored by using the urinary bioassay and by using liquid scintillation counting to detect its weak beta emission (Eₘₐₓ = 18 MeV).

Accidental contamination with tritium has been reported in humans (41). A multicurie dose of tritium exposure led to clinical symptoms of nausea and exhaustion, which led to death due to pancytopenia. Analysis of tissue samples from casualties contaminated internally by tritium has shown the presence of tritium in the endocellular structural elements and in the body fluids (42).

J. URANIUM

Three isotopes of uranium are important in medicine as potential hazards of internal contamination. ²³⁸U (t₁/₂ = 4.5 × 10⁹ years), ²³⁵U (t₁/₂ = 7.1 × 10⁸), and ²³⁴U (t₁/₂ = 2.5 × 10⁵ years) are alpha, beta, and gamma emitters, with spontaneous fission below the level of criticality. Decay products of uranium isotopes include the alpha-emitting isotope of radon (²²²Rn), which presents a hazard of internal contamination when radioactive particles are inhaled in uranium mines.

Uranium ore (U₃O₈) is obtained from mines and then concentrated and processed to ammonium diuranate (yellow cake), which is fluorinated and enriched for use as fuel for nuclear reactors or nuclear weapons. Uranium recycling is the process of obtaining uranium from the fuel dissolved in nitric acid, resulting in the removal of fission products and transuranic elements. The handling of uranium presents a hazard because of the possibility of a chemical explosion in the process of uranium oxidation.

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Uranium isotopes have different metabolic behaviors in the body, depending on their physical forms. The ingestion of uranium isotopes results in relatively low absorption (1–5%). This absorbed dose is rapidly excreted through the kidneys. Other routes of internal contamination include inhalation or direct entry into the body fluids through the skin and contaminated wounds.

The critical organ for uranyl salts (U-VI) is the bone, while uranium salts (U-IV) are retained in the skeleton in a much smaller quantity. Soluble uranium (238U) is rapidly eliminated through renal excretion. Less soluble compounds of uranium, particularly when enriched with 234U and 235U, are primarily retained in the bone or in the lung if inhaled. Soluble uranium compounds cause mainly chemical damage to the proximal convoluted tubules of the kidneys (43), with resulting albuminuria, hematuria, hyaline and granular casts, azotemia, and tubular necrosis.

Renal recovery even after exposure to high levels of uranium is quite common, and additional exposures seem to cause less damage to the kidney after its initial recovery. Urine bioassay should be routinely performed in any case of exposure to uranium compounds.

IV. THERAPEUTIC MANAGEMENT OF INTERNAL CONTAMINATION

The principal goals in reducing a radiation dose and the pathologic effects of internally deposited radionuclides are (1) to prevent the absorption of contamination from the treatment site(s) and (2) to eliminate absorbed radionuclides already in the bloodstream or in their respective target organs. It is of utmost importance to initiate therapy of the contaminated patient very early after exposure. Therapy includes the use of diluting and blocking agents to prevent and reduce gastrointestinal absorption, use of agents to decouple radionuclides from the sites of internal deposition and mobilize them into the bloodstream, and measures to facilitate excretion through the urinary, gastrointestinal, or respiratory system.

Finally, the medical management of internal contamination includes administering chemical agents to facilitate the elimination of radioisotopes from the body by binding inorganic ions to nonionized complexes, which then can be eliminated through the kidney when present in soluble forms.

V. PREVENTION OF GASTROINTESTINAL ABSORPTION

After the ingestion of various products of nuclear fission, a high number of these products are rapidly absorbed into the systemic circulation and then depos-
ited in their target organs. Reduction of the intestinal absorption of alkaline earth ions (calcium and strontium), cesium, cobalt, iodine, iron, gold, tritium, uranium, and radium is of special importance in this therapeutic approach. The most important methods for reducing the intestinal absorption of medically significant radioisotopes and facilitating their elimination via the fecal route are gastric lavage and the administration of emetics, ion-exchange agents, and antacids containing aluminum salts as well as guluronic and manuronic acid salts of alginates, barium sulfate, and sodium phyate.

Gastric lavage is a method of high merit in treating early exposure by ingestion. It is performed by inserting a nasogastric or orogastric tube into the stomach and repeatedly washing the stomach (by introducing water or physiological saline into the gastric lumen and then removing it by aspiration) until the aspirate is free of contaminating substance. All necessary precautions should be applied, including proper positioning of the patient during the procedure, so that the gastric lavage will be complete and will prevent the aspiration of contaminated gastric contents into the respiratory system.

Emetics may be used to complement gastric lavage, although the two methods are frequently used alone. An emetic should be used only after careful diagnosis of the contaminated patient, because it is contraindicated for a patient in shock, in altered consciousness, or after ingestion of petroleum or corrosive substances. The most commonly used emetics are apomorphine for subcutaneous administration and ippecacuan derivatives for oral administration. Sound clinical knowledge of the management of direct effects and side effects of the emetic drugs is required in each case of their use. Application is best immediately after drinking 250 ml water. Emetics act directly on the gastric mucosa and by stimulating the vomiting center in the medulla oblongata. Apomorphine acts predominantly by stimulating the vomiting center. It should be administered subcutaneously in a single dose of 5–10 mg, whereas ippecacuan derivatives can be used repeatedly (oral administration) until vomiting is induced. Both agents are readily available. The potential side effects (nausea, weakness, tachypnea, tachycardia, and hypotension) can be treated by symptomatic therapy, but frequently do not require specific treatment.

The use of laxatives has been a common therapeutic approach in reducing internal contamination. Laxatives are administered in various forms, such as (1) the rhinoleic acid-releasing drugs, which stimulate contractions of the small intestine (castor oil and cascara), and (2) saline purgatives, which inhibit the absorption of radionuclides by forming insoluble salts, by cathartic elimination from the intestine, and by their hypertonicity, which causes extraction of water from the intestinal mucosa. Detailed clinical diagnostic management is required before using laxative therapy because it is contraindicated in any case of undiagnosed abdominal pain or in an acute surgical abdominal syndrome. The use of laxatives is associated with multiple side effects (including heart dysrhythmia,
tachypnea, dyspnea, intestinal irritation, exanthema, electrolyte imbalance, and syncope), which must be addressed by appropriate symptomatic therapy.

A. Alginites

In this group of ion-exchange therapeutic agents are the extracts of brown seaweeds (Phaeophyceae). These compounds act by the binding of their active ingredients [alginate acids (guluronic and manuronic)] to radionuclides in the intestinal lumen. Radionuclides chelated in this way are not as well absorbed through the intestinal mucosa (44). The action of alginites has been most intensively studied in the comparative absorption of strontium and calcium through the intestinal mucosa. These cations are metabolic homologs that selectively incorporate in the skeleton. However, their metabolism is affected by the processes that control their transfer across the biological membranes, resulting in the favorable retention and transfer of calcium and also discrimination against strontium.

Alginites possess the ability to preferentially bind the strontium ion in the intestine, without much effect on the absorption of calcium. This phenomenon has been used in the therapeutic management of internal contamination by ingested strontium (45), and has resulted in significant decrease of its retention in the skeleton. Alginites are administered orally. Their main disadvantage has been high viscosity, although low-viscosity preparations (such as manucol SSLD) are available (46, 47).

Ion-exchange drugs reduce the intestinal absorption of ingested radioisotopes. These drugs include activated charcoal, sodium polystyrene sulfonate, biorex-40, and ferric ferrocyanide. They should be used with caution because of their side effects, including gastritis, anorexia, vomiting, and diarrhea. Ion-exchange resins can also interfere with the absorption of essential inorganic and organic nutrients by binding them and eliminating them from the intestinal lumen.

One of the forms of ferrocyanide used to decrease the intestinal absorption of ingested radioisotopes is Berlin blue (Prussian blue), which is particularly useful in binding and removal. This compound is commercially available in Europe. Its use in the United States is restricted to emergency situations in which FDA investigational-drug approval is required.

Aluminum-containing antacids have been effectively used to therapeutically remove strontium, with a highly significant decrease of ⁸⁸Sr absorption by the intestine. Aluminum phosphate administered orally reduces the absorption of strontium by over 80%. Aluminum hydroxide reduces the uptake of strontium by 50%. No side effects are associated with their therapeutic use.

Other drugs to eliminate ingested radionuclides from the digestive tract in-
clude barium sulfate, which is highly effective in reducing absorption of strontium and radium, and phytates, which reduce the absorption of calcium, iron, magnesium, and zinc ions.

B. ISOTOPIC DILUTION, BLOCKING AGENTS, AND DISPLACEMENT THERAPY

The use of water to reduce tritium in the body fluids is a common therapeutic method, applied by the oral or the intravenous route of administration. Clinical assessment of each patient is essential to avoid possible side effects from fluid overload in patients with cardiovascular or renal disease.

In therapy using blocking agents, the uptake of radioactive iodine is inhibited by the immediate administration of stable iodide after an accidental exposure (KI and NaI). This therapy should be continued for 2 weeks to allow the elimination of the radioactive iodine and to prevent its reuptake. The FDA-recommended dose is 130 mg KI for adults daily and 65 mg daily for children.

The uptake of radioactive strontium can be reduced by administering stable strontium compounds (lactate and gluconate). The intestinal absorption of radiostontium can be significantly reduced by oral administration of phosphates, which reduce over 60% of the strontium absorption. This effect is sometimes counterbalanced by increased tubular reabsorption of strontium, if the phosphate content is elevated in the extracellular fluid.

Tubular reabsorption of strontium will increase after the intravenous administration of phosphate. This factor reduces the net effect of diminished skeletal retention of strontium by the high phosphate content in the digestive system (48). Parenteral administration of phosphate can be used to treat internal contamination (soluble radioactive phosphorus, $^{32}$P).

Calcium salts have been used to reduce the intestinal absorption of radioactive strontium (Ca-lactate and Ca-gluconate). Other stable cations (potassium and zinc) are rarely used as potential agents in managing internal contamination by $^{65}$Zn or $^{32}$K.

Therapeutic agents for decarboxylating and mobilizing the organotropics radioisotopes include hormonal preparations (PTH, corticosteroids, and calcitonin), propylthiouracil (PTU), methimazole (MMI), diuretics, expectorants, perchlorate, and ammonium chloride. Parathormone has been used in different species of experimental animals to enhance bone resorption, with the subsequent release of incorporated osteotropic radionuclides (calcium, strontium, phosphorus, and radium).

It has been demonstrated that physiological processes that result in increased catabolic processes in the skeleton produce significant reduction in the amount of incorporated bone-seeking radioisotopes. These effects have been observed in lactating animals, whose skeletal uptake of calcium and strontium was reduced by over 50% after catabolic processes of the skeleton were induced by lactation.
This reduction of bone mass and the demineralization of both the exchangeable and nonexchangeable fractions of the skeleton were observed, regardless of hyperphagia in the lactating animals.

The influence of corticosteroid hormones (prednisone, cortisone, dexamethasone, and methylprednisolone) has been studied in various experimental models in an attempt to evaluate their use in mobilizing the incorporated bone-seeking radioisotopes. No significant effect of corticosteroids was seen in the metabolic behavior of transuranium or alkaline earth isotopes in the bone, regardless of the catabolic processes induced in the skeleton by the long-term use of corticosteroids.

Propylthiouracil and methimazole decrease the synthesis of thyroid hormones (T3 and T4) by their inhibitory effect on the iodide oxidation. These antithyroid drugs are not widely accepted for use in antagonizing radioiodine uptake by the thyroid, because of their complex metabolic effects on the radioiodine in the kidney and liver, as well as numerous toxic side effects. Other antithyroid drugs (e.g., thiocyanate) are not of practical use for radioiodine elimination because of questionable effects and toxic reactions. Of all the compounds used to inhibit thyroid uptake of radioactive iodine, stable iodide is the drug of choice for the competitive inhibition of ¹²³I incorporation.

For mobilizing radiostrontium from the body, ammonium chloride was found to be of certain benefit in reducing the body burden of ⁹⁰Sr. However, the toxic effects (gastritis and hepatitis) of ammonium chloride make it less than an ideal drug for strontium decarboxylation.

Diuretic therapy with various conventional agents has been used in various studies on the excretion of internally deposited radioisotopes. Because of the complex metabolic effects of diuretic drugs, with the need for meticulous monitoring of the electrolyte and ECF metabolism, diuretic therapy of internal contamination is still an unexplored area. Ethacrinic acid is the only diuretic agent now recommended for excretion of the alkaline earth isotopes.

Treatment of patients exposed to radioactive particles via the respiratory route of contamination includes administering (1) drugs that reduce the viscosity of endobronchial mucus and (2) various mucolytic drugs that act on mucopolysaccharides and nucleoproteins in the respiratory tree, thus mobilizing its contents by expectoration. The results of testing these agents (pancreatic dornase, triton, Tween-80, ⁶⁸F, etc.) have been unsatisfactory in reducing the uptake of inhaled radioisotopes from the lung.

C. Treatment of Internal Contamination with Chelating Agents

Complexing agents have been used to treat internal contamination in experimental animals and in accidentally exposed humans, with more success than other therapeutic modalities. The elimination of radioactive isotopes by chelation
therapy is based on the ligand’s ability to form nonionized ring complexes with inorganic ions, which are then excreted by the kidney.

Treatment with chelating agents should be instituted as soon as possible after internal contamination, before the radionuclides are retained in their target organs. The hydrophilic nature of these agents makes them ineffective in reaching the isotopes that are incorporated in the endocellular environment. Therefore, many studies are concentrating on the synthesis and production of lipophilic chelating agents, for their potential use in mobilizing radionuclides from the cells for excretion by the kidney.

The effect of chelation therapy with various complexing agents has been an area of extensive experimental and clinical research. Among many chelating agents tested in the experimental and clinical trials, only a few are of practical use at the present time.

Ethylenediamine tetraacetic acid (EDTA) has been used in animal experiments and to treat poisoning in humans from various inorganic compounds. EDTA has been beneficial in the treatment of lead poisoning and in the treatment of internal contamination with zinc, copper, cadmium, chromium, manganese, nickel, and transuranic elements (41).

The parenteral administration of EDTA results in its binding of stable calcium, resulting in hypocalcemia (tetany) and toxic side effects. Among them, nephrotoxicity is the primary complication, with a potentially fatal outcome. EDTA can be used as Ca-EDTA or Na-EDTA. The intravenous administration dose for Na-EDTA is 75 mg/kg bid, not exceeding a total dose of 550 mg/kg in the entire therapeutic regimen.

Intramuscular administration (75 mg/kg tid) of EDTA should be used with a local anesthetic because of tissue irritation and pain at the injection site. The intravenous route is the preferred method of administration, by infusion in physiological saline or 5% glucose in water.

Renal function tests and urinalysis should be performed before treatment, because EDTA therapy is contraindicated in patients with renal disease. Na-EDTA is used in a lower dose (50 mg/kg) as physiological saline or 5% glucose, not exceeding 300 mg/6-day treatment period. Oral or intramuscular administration is not used, being contraindicated in renal and hepatic impairment.

Diethyleneetriamine pentaacetic acid (DTPA) is more effective than EDTA in the therapeutic removal of radioisotopes that are common in internal contamination. DTPA is used as Ca-DTPA or Zn-DTPA. Ca-DTPA is administered as intravenous infusion (1000 mg in 250 ml of physiological saline or 5% glucose) for a maximum of 5 consecutive days. DTPA can be obtained in the United States as an investigational new drug from the United States Department of Energy, Office of Health and Environmental Research, Human Health and Assessment Division, Washington, D.C., or the Radiation Emergency Assistance Center/Training Site, Oak Ridge Associated Universities, Oak Ridge, Tennessee.
Administration of DTPA is contraindicated in leukopenia or thrombocytopenia, renal disease, hypertension, or pulmonary disease (if used as inhalation therapy). Zn-DTPA can be used in the same dose as Ca-DTPA by the intravenous or inhalation routes, and it is less toxic than Ca-DTPA. Na-DTPA is not used because it chelates calcium, with resulting hypocalcemia and tetany.

DTPA is now the most effective agent in treating internal contamination with transuranic elements, particularly plutonium and americium. DTPA does not produce toxic symptoms if used in recommended doses administered either intravenously or by inhalation.

The treatment of internal contamination is currently limited to a few therapeutic agents, and considerable problems are associated with their use. The present therapeutic modalities are still unsatisfactory, particularly in the removal of radionuclides that are already incorporated in their respective critical organs.

In removing the most hazardous radionuclides of the transuranium series, DTPA is clearly superior to other chelating agents. However, its use is limited because it is not commercially available, its administration must be performed by qualified personnel, it is effective only in early treatment, and its strong hydrophilicity prevents it from reaching the intracellular environment. It is not practical in treating mass casualties of internal contamination, although it has distinct benefits in treating cases of sporadic contamination in a medical facility.

These factors have contributed to the continuous investigational efforts to produce new chelating agents. Derivatives of paraaminocarboxylic acid (PACA) have been studied in an attempt to synthesize adequate lipophilic agents (chelons) for the intracellular binding and removal of incorporated radioisotopes. These agents, when administered orally, rectally, or by depot, have potential use in treating mass casualties of endemic or epidemic proportions.

Other agents being studied for the potential treatment of internal contamination include synthetic polyanine catecholamines (49), various phospholipid compounds (liposomes) for encapsulation of the radiotoxic substances (50), and natural chelates isolated from the cultures of various microorganisms (51). Their place in the medical management of internal contamination is yet to be determined by experimental and clinical trials.

When live-saving measures have been instituted and the patient stabilized, diagnostic monitoring of contaminated wounds should be performed to establish the nature and quantity of possible contamination with the organotropic radionuclides. Mechanical removal is instituted by cleansing, chemical therapy, and surgical procedures. Tissue samples from the contaminated wounds, obtained in the process of debriement, are placed in a counting vial and analyzed by radioimmunoassay methods. Monitoring of the body surface, wound assessment, and tissue counts of radiation from the surgical debridement should be compared, and procedures of internal decontamination should be instituted if it has been determined that a radionuclide is present in the internal environment of the body.
Therapeutic decisions in the radionuclide decontamination of combined-injury patients are assisted considerably by available human data on the early assessment of radionuclide excretion from contaminated wounds. These data provide significant clinical aid in the determination of an optimal dosage of chelating agents that are used in internal decontamination therapy (52). Early therapeutic decisions in combined injury are of the utmost importance because the effectiveness of chelating agents is significantly reduced by delay in treatment. This is particularly important in the case of open wounds, where therapy with complexing agents is clearly indicated for all soluble compounds. Follow-up diagnostic procedures by bioassay methods should be part of the routine management for patients with combined injury, because these patients have the potential for a larger fraction of organotropic radionuclides in the extracellular fluid and parenchymal organs than patients without wounds.

It can be expected that internal contamination with organotropic radionuclides will be of particular concern in combined injury because of additional diagnostic and therapeutic requirements in monitoring the radiation type and quantity in a contaminated wound. A patient population subjected to traumatic, thermal, and infectious complications in addition to internal contamination will require particular clinical skills for the maintenance of homeostasis and the determination of clinical priorities.

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