CHAPTER II

Background
Background | Chapter -II

2.1 HEAVY METAL TOXICITY

Heavy metals are chemical elements, which are commonly present in our environment, without realizing it; we all are exposed to heavy metals on a daily basis. However, the quantities that we inhale, ingest or come into contact with the skin are so small that they are usually harmless. In fact, small amounts of some heavy metals in our diet are essential for good health. These are referred to as trace elements and include iron, copper, manganese, zinc, plus others, which are commonly found naturally in fruits and vegetables.

Heavy metal is a term used for a group of elements that have particular weight characteristics, or we can say that "Heavy metals" are chemical elements with a specific gravity that is at least 5 times the specific gravity of water (specific gravity = 1 at 4°C (39°F)). Some well-known toxic metallic elements with a specific gravity that is 5 or more times that of water are arsenic 5.7, cadmium 8.65, iron 7.9, lead 11.34, and mercury 13.546 (Lide et al, 1992). Some heavy metals such as cobalt, copper, iron, manganese, molybdenum, vanadium, strontium and zinc are essential to health in trace amounts. Others are non-essential and can be harmful to health in excessive amounts. These include cadmium, antimony, chromium, mercury, lead and arsenic, these last three being the most common in cases of heavy metal toxicity.

There are 35 metals that concern us because of occupational or residential exposure; 23 of these are the heavy elements or "heavy metals": antimony, arsenic, bismuth, cadmium, cerium, chromium, cobalt, copper, gallium, gold, iron, lead, manganese, mercury, nickel, platinum, silver, tellurium, thallium, tin, uranium, vanadium, and zinc (Glanz et al, 1996). Interestingly, small amounts of these elements are common in our environment and diet and are necessary for good health, but large amounts of any of them may cause acute or chronic toxicity (poisoning). Heavy metal toxicity can result in damaged or reduced mental and central nervous function, lower energy levels, and damage to blood composition, lungs, kidneys, liver, and other vital organs. Long-term exposure, may result in slowly progressing physical, muscular, and neurological degenerative processes that mimic Alzheimer's disease, Parkinson's disease, muscular dystrophy, and multiple sclerosis. Allergies are not uncommon and repeated long-term contact with some metals or their compounds may even cause cancer (International Occupational Safety and Health Information Centre 1999).
2.1.1 Beneficial Heavy Metals

In small quantities, certain heavy metals are nutritionally essential for a healthy life. Some of these are referred to as the trace elements (e.g., iron, copper, manganese, and zinc). These elements, or some form of them, are commonly found naturally in foodstuffs, in fruits and vegetables, and in commercially available multivitamin products (International Occupational Safety and Health Information Centre 1999). Diagnostic medical applications include direct injection of gallium during radiological procedures, dosing with chromium in parenteral nutrition mixtures, and the use of lead as a radiation shield around x-ray equipment (Roberts et al., 1999). Heavy metals are also common in industrial applications such as in the manufacture of pesticides, batteries, alloys, electroplated metal parts, textile dyes, steel, and so forth. (International Occupational Safety and Health Information Centre 1999). Many of these products are in our homes and add to our quality of life when properly used.

2.1.2 Toxic Heavy Metals

Heavy metals become toxic, when they are not metabolized by the body and accumulate in the soft tissues or ingress is more that outguess leading to increase concentration in tissue. Heavy metals may enter the human body through food, water, air, or absorption through the skin when they come in contact with humans in agriculture and in manufacturing, in pharmaceutical, industrial or residential settings. Industrial exposure accounts for a common route of exposure for adults. Ingestion is the most common route of exposure in children (Roberts et al., 1999). Children may develop toxic levels from the normal hand-to-mouth activity of small children who come in contact with contaminated soil or by actually eating objects that are not food (dirt or paint chips) (Dupler et al., 2001). Less common routes of exposure are during a radiological procedure, from inappropriate dosing or monitoring during intravenous (parenteral) nutrition, from a broken thermometer (Smith et al., 1997), or from a suicide or homicide attempt (Lupton et al., 1985).
### Table 2.1 Diagnosis, metabolism and treatment of heavy metals toxicity

<table>
<thead>
<tr>
<th>Main Sources</th>
<th>Metabolism</th>
<th>Toxicity</th>
<th>Diagnosis</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arsenic</strong></td>
<td>Organic arsenic is ingested in seafood and fish, but is nontoxic; inorganic arsenic is readily absorbed in lungs and GI; sequesters in liver, spleen, kidneys, lungs, and GI tract; residues persist in skin, hair, and nails; biomethylation results in detoxification, but this process saturates.</td>
<td>Acute arsenic poisoning results in necrosis of intestinal mucosa with hemorrhagic gastroenteritis, fluid loss, hypotension, delayed cardiomyopathy, acute tubular necrosis, and hemolysis. Chronic arsenic exposure causes diabetes, vasospasm, peripheral vascular insufficiency and gangrene, peripheral neuropathy, and cancer of skin, lung, liver (angiosarcoma).</td>
<td>Nausea, vomiting, diarrhea, abdominal pain, delirium, coma, seizures; garlicy odor on breath, hyperperistalsis, hyperpigmentation and Mees' lines; sensory and motor polyneuropathy, distal weakness. Radiopaque sign on abdominal x-ray; ECG-QRS broadening, QT prolongation, ST depression, T-wave flattening; 24-h urinary arsenic &gt;67 μmol/d or 50 μg/dL; mineral arsenic in hair or nails.</td>
<td>If acute ingestion, ipecac to induce vomiting, gastric lavage, activated charcoal with a cathartic. Supportive care in ICU. Dimercaptoprotoxyl 3-5 mg/kg IM q4h x 2 days; q6h x 1 day, then q12h x 10 days; alternative: oral succimer.</td>
</tr>
<tr>
<td><strong>Cadmium</strong></td>
<td>Absorbed through ingestion or inhalation; bound by metallothionein; filtered at the glomerulus, but reabsorbed by proximal tubules (poorly excreted). Biologic half-life: 10-30 yr. Binding of cellular thiols (zinc, calcium) for binding sites. Concentrates in liver and kidneys.</td>
<td>Acute cadmium inhalation causes pneumonitis after 4-24 h; acute ingestion causes gastroenteritis. Chronic exposure causes anosmia, yellowing of teeth, emphysema, minor LFT elevations, microcytic hypochromic anemia unresponsive to iron therapy, proteinuria, increased urinary β₂-microglobulin, calciumuria, leading to chronic renal failure, osteomalacia, and fractures.</td>
<td>With inhalation: pleuritic chest pain, dyspnea, cyanosis, fever, tachycardia, nausea; non-cardiogenic pulmonary edema. With ingestion: nausea, vomiting, cramps, diarrhea. Bone pain, fractures with osteomalacia. If recent exposure, serum cadmium &gt;500 nmol/L (5 pg/dL). Urinary cadmium &gt;100 nmol/L (10 g/g creatinine) and/or urinary β₂-microglobulin &gt;750 μg/g creatinine.</td>
<td>There is no effective treatment for cadmium poisoning (chelation not useful; dimercaprol can exacerbate nephrotoxicity). Avoidance of further exposure, supportive therapy, vitamin D for osteomalacia.</td>
</tr>
<tr>
<td>Lead Manufacturing of auto batteries, lead crystal, ceramics, fishing weights, etc.; demolition or sanding of lead-painted houses, bridges; stained glass making, plumbing, soldering; environmental exposure to paint chips, house dust (in home built &lt;1975), firing ranges (from bullet dust), food or water from improperly glazed ceramics, lead pipes; contaminated herbal remedies, candies; exposure to the combustion of leaded fuels.</td>
<td>Absorbed through ingestion or inhalation; organic lead (e.g., tetraethyl lead) absorbed dermally. In blood, 95-99% sequestered in RBCs—thus, must measure lead in whole blood (not serum). Distributed widely in soft tissue, with ½ life ~30 days; 15% of dose sequestered in bone with ½ life of &gt;20 years. Excreted mostly in urine, but also appears in other fluids including breast milk. Interferes with mitochondrial oxidative phosphorylation, ATPases, calcium-dependent messengers; enhances cell apoptosis.</td>
<td>Acute exposure with blood lead levels (BPb) of &gt; 60-80 µg/dL can cause impaired neurotransmission and neuronal cell death (with central and peripheral nervous system effects); impaired hematopoiesis and renal tubular dysfunction. At higher levels of exposure (e.g., BPb&gt; 80-120 µg/dL), acute encephalopathy with convulsions, coma, and death may occur. Subclinical exposures in children (BPb 25-60 µg/dL) are associated with anemia; mental retardation; and deficits in language, motor function, balance, hearing, behavior, and school performance.</td>
<td>Abdominal pain, irritability, lethargy, anemia, azotemia, Fanconi's syndrome, pyramia, anosmia, atraxia, encephalopathy; lead lines on long bone x-rays. Convulsions, coma at BPb&gt; 120 µg/dL. Noticeable neurodevelopmental delays at BPb of 40-80 µg/dL may also see symptoms associated with higher BPb levels. In children as well as adults, acute exposure causes similar symptoms as in children as well as headaches, arthralgias, myalgias, depression, impaired short-term memory, loss of libido. Physical exam may reveal a &quot;lead line&quot; at the gingiva-tooth border, pallor, wrist drop, and cognitive dysfunction; lab tests may reveal a normocytic, normochromic anemia, basophilic stippling, an elevated blood protoporphyrin level, and motor delays on nerve conduction. In the U.S., GSHA requires regular testing of lead-exposed workers with removal if BPb&gt; 40 µg/dL.</td>
<td>Identification and correction of exposure sources is critical. In some U.S. states, screening and reporting to local health boards of children with BPb&gt; 10 µg/dL and workers with BPb&gt; 40 µg/dL is required. In the highly exposed individual with symptoms, chelation is recommended with oral DMSA (succimer); if acutely toxic, hospitalization and IV or IM chelation with edetate calcium disodium (Ca Na₂EDTA) may be required, with the addition of dimeracaprol to prevent worsening of encephalopathy. It is uncertain whether children with asymptomatic lead exposure (e.g., BPb 20-40 µg/dL) benefit from chelation. Correction of dietary deficiencies in iron, calcium, magnesium, and zinc will lower lead absorption and may also improve toxicity. Vitamin C is a weak but natural chelating agent.</td>
</tr>
</tbody>
</table>
Elemental mercury is not well absorbed; however, it will volatilize into highly absorbable vapor. Inorganic mercury is absorbed through the gut and skin. Organic mercury is well absorbed through inhalation and ingestion. Elemental and inorganic mercury cross the blood-brain barrier and placenta. Mercury is excreted in urine and feces and has a ½ life in blood of ~60 days; however, deposits will remain in the kidney and brain for years. Mercury is dispersed by waste incineration.

Environmental bacteria convert inorganic to organic mercury, which then bioaccumulates up the aquatic food chain to contaminate tuna, swordfish, and other pelagic fish. Mercury bioconcentrates up the aquatic food chain to contaminate tuna, swordfish, and other pelagic fish.

Elemental mercury (Hg⁰) is not well absorbed; however, it will volatilize into highly absorbable vapor. Inorganic mercury is absorbed through the gut and skin. Organic mercury is well absorbed through inhalation and ingestion. Elemental and inorganic mercury cross the blood-brain barrier and placenta. Mercury is excreted in urine and feces and has a ½ life in blood of ~60 days; however, deposits will remain in the kidney and brain for years. Mercury is dispersed by waste incineration.

Inorganic mercury is absorbed through the gut and skin. Organic mercury is well absorbed through inhalation and ingestion. Elemental and inorganic mercury cross the blood-brain barrier and placenta. Mercury is excreted in urine and feces and has a ½ life in blood of ~60 days; however, deposits will remain in the kidney and brain for years. Mercury is dispersed by waste incineration.

Environmental bacteria convert inorganic to organic mercury, which then bioaccumulates up the aquatic food chain to contaminate tuna, swordfish, and other pelagic fish. Mercury bioconcentrates up the aquatic food chain to contaminate tuna, swordfish, and other pelagic fish.

Elemental mercury (Hg⁰) is not well absorbed; however, it will volatilize into highly absorbable vapor. Inorganic mercury is absorbed through the gut and skin. Organic mercury is well absorbed through inhalation and ingestion. Elemental and inorganic mercury cross the blood-brain barrier and placenta. Mercury is excreted in urine and feces and has a ½ life in blood of ~60 days; however, deposits will remain in the kidney and brain for years. Mercury is dispersed by waste incineration.

Inorganic mercury is absorbed through the gut and skin. Organic mercury is well absorbed through inhalation and ingestion. Elemental and inorganic mercury cross the blood-brain barrier and placenta. Mercury is excreted in urine and feces and has a ½ life in blood of ~60 days; however, deposits will remain in the kidney and brain for years. Mercury is dispersed by waste incineration.
As a rule, acute poisoning is more likely to result from inhalation or skin contact of dust, fumes or vapors, or materials in the workplace. However, lesser levels of contamination may occur in residential settings, particularly in older homes with lead paint or old plumbing (International Occupational Safety and Health Information Centre 1999). The Agency for Toxic Substances and Disease Registry (ATSDR) is responsible for assessment of waste sites and providing health information concerning hazardous substances, response to emergency release situations, and education and training concerning hazardous substances (ATSDR Mission Statement, November 7, 2001). In cooperation with the U.S. Environmental Protection Agency, the ATSDR has compiled a Priority List for 2001 called the "Top 20 Hazardous Substances." The heavy metals arsenic (1), lead (2), mercury (3), and cadmium (7) appear on this list. Order of toxicity of the metals is generally: Hg\(^{2+}\) > Cd\(^{2+}\) > Cu\(^{2+}\) > Cr\(^{6+}\), Zn\(^{2+}\) > Ni\(^{2+}\) > Pb\(^{2+}\) > As\(^{3+}\) (Donald et al 1984).

Metals are inhaled primarily as dusts and fumes (the latter defined as tiny particles generated by combustion). Metal poisoning can also result from exposure to vapors (e.g., mercury vapor in creating dental amalgams). When metals are ingested in contaminated food or drink or by hand-to-mouth activity (implicated especially in children), their gastrointestinal absorption varies greatly with the specific chemical form of the metal and the nutritional status of the host. Once a metal is absorbed, blood is the main medium for its transport, with the precise kinetics dependent on diffusibility, protein binding, rates of biotransformation, availability of intracellular ligands, and other factors. Most metals are excreted through renal clearance and gastrointestinal excretion; some proportion is also excreted through salivation, perspiration, exhalation, lactation, skin exfoliation, and loss of hair and nails. The intrinsic stability of metals facilitates tracing and measurement in biologic material, although the clinical significance of the levels measured is not always clear.

In addition to the information provided in Table 2.1, several other aspects of exposure, toxicity, or management are worthy of discussion with respect to the four most hazardous toxicants (arsenic, cadmium, lead, and mercury).
Arsenic exposure from natural contamination of shallow tube wells inserted for drinking water is a huge environmental problem for millions of residents in parts of Bangladesh and Western India. Serious cadmium poisoning from the contamination of food and water by mining effluents in Japan contributed to the 1946 outbreak of "itai-itai" ("ouch-ouch") disease, so named because of cadmium-induced bone toxicity that led to painful bone fractures. Advances in our understanding of lead toxicity have recently benefited by the development of K-x-ray fluorescence (KXRF) instruments for making safe in-vivo measurements of lead levels in bone. High bone lead levels measured by KXRF have been linked to increased risk of hypertension in both men and women from an urban population.

The toxicity of low-level organic mercury exposure (as manifested by neurobehavioral performance) is of increasing concern based on studies of the offspring of mothers who ingested mercury-contaminated fish. However, current evidence has not supported the recent contention that ethyl mercury, used as a preservative in multiuse vaccines administered in early childhood, has played a significant role in causing neurodevelopmental problems such as autism.

Aluminum contributes to the encephalopathy in patients with severe renal disease who are undergoing dialysis. High levels of aluminum are found in the neurofibrillary tangles in the cerebral cortex and hippocampus of patients with Alzheimer's disease, as well as in the drinking water and soil of areas with an unusually high incidence of Alzheimer's. Hexavalent chromium is corrosive and sensitizing. Workers in the chromate and chrome pigment production industries have consistently had a greater risk of lung cancer. The introduction of cobalt chloride as a fortifier in beer led to outbreaks of fatal cardiomyopathy among heavy consumers. Occupational exposure (e.g., miners, dry-battery manufacturers, and arc welders) to manganese can cause a Parkinsonian syndrome within 1–2 years, including gait disorders; postural instability; a masked, expressionless face; tremor; and psychiatric symptoms. With the introduction of methylcyclopentadienyl manganese tricarbonyl (MMT) as a gasoline additive, there is concern for the toxic potential of environmental manganese exposure. Nickel exposure induces an allergic response, and inhalation of nickel compounds with low aqueous solubility (e.g., nickel subsulfide and nickel oxide) in occupational settings is associated with an increased risk of lung cancer. Overexposure to selenium may cause local
irritation of the respiratory system and eyes, gastrointestinal irritation, liver inflammation, 
loss of hair, depigmentation, and peripheral nerve damage. Workers exposed to certain 
organic forms of tin (particularly trimethyl and triethyl derivatives) have developed 
psychomotor disturbances, including tremor, convulsions, hallucinations, and psychotic 
behavior. Thallium, which is a component of some insecticides, metal alloys, and fireworks, 
is absorbed through the skin as well as by ingestion and inhalation. Nausea and vomiting, 
abdominal pain, and hematemesis precede confusion, psychosis, organic brain syndrome, and 
coma.

2.1.3. Treatment for Heavy metal toxicity

The principal aim in the therapeutic management of patients with internally deposited heavy 
metal is to prevent the absorption from the site of entry and eliminate heavy metal from the 
blood stream or target organs. Regardless of the therapeutic alternatives planned, it is of 
utmost importance to initiate therapy soon after exposure. Finally, medical intervention in 
heavy metal internal contamination includes the use of chemical agents that bind inorganic 
ions to non-ionized complexes and facilitate their urinary excretion when they are present in 
soluble form. The methods of treatment are based on various aspects that includes

2.1.3.1. Treatment of Patients Contaminated By Ingestion of Heavy Metals

It is important to reduce the GIT absorption of heavy metal to reduce their entry in the 
systemic circulation and its deposition in the target organs. All are applicable to acute 
exposure to a large potential damage dose.

(i) Gastric lavage

The method of gastric lavage is very useful in therapy or early exposure by ingestion. It is 
accomplished by the placement of a nasogastric tube in the stomach and washing it several 
times with water or physiological saline by negative pressure, until the aspirate is declared 
free of the contaminant. These procedures require proper medical skills in order to achieve 
total washout of the gastric contents and prevent aspiration of contaminated fluid into the 
respiratory system.

(ii) Emetics
The most common uses of emetics include subcutaneous administration of apomorphine or oral preparations of ipecac. The most common method is the administration of an emetic after the patient drinks 250ml of water. Apo-morphine primarily acts by stimulating the vomiting center in the area postrema of the medulla oblongata. It is used in a single dose of 5-10 mg subcutaneously, while preparations of ipecac can be used in several doses until vomiting is induced. Both drugs are readily available. Side effects include nausea, weakness, tachypnea, tachycardia, and hypotension.

(iii) Laxatives and purgatives
The use of laxatives is a common therapeutic approach in reducing internal contamination. Purgative agents may be given in different forms, as agents, which act by the release of linoleic acid, stimulating peristalsis in the small intestine. Sustained use of laxatives inhibits absorption of actinides by the formation of insoluble salts. Their hypertonic action causes water extraction in the intestinal mucosa with the cathartic elimination of the intestinal contents. Laxative use is contraindicated in acute abdominal syndrome or non-diagnosed pain in the stomach. Numerous side effects include tachypnea, dyspnea, tachyarrhythmias, intestinal irritation, exanthema, and syncopal attacks, which require professional medical attention.

2.1.3.2. Treatment of patients contaminated by inhalation of heavy metal compounds

(i) Mucolytic agents
The uses of mucolytic substances, which have the effect on mucopolysaccharides and nucleoproteins in the respiratory tree, enable the elimination of actinides by expectoration. However, these substances, such as pancreatic dornase, triton, Tween-90, and F-68 have not been found satisfactory for practical use.

2.1.3.3. Treatment of patients to reduce internal contamination

(i) Complexing agents
Mechanism is based on the ability of a ligand to form non-ionized ring complexes with inorganic ions, which are subsequently eliminated by the kidney. These substances are not useful in binding the actinides, which are deeply incorporated in the cells because of their
hydrophilic properties. Present investigations are focused on the synthesis of lipophilic chelating agents, capable of reaching radionuclides from the cells and facilitating their excretion through the kidneys. Among the numerous complexing agents, which have been tested in clinical trials, only a few appear of practical advantage in heavy metal contamination. Ethylenediaminetetraacetic acid (EDTA) has been used in experiments on animals and in human medicine for the treatment of poisoning with inorganic substances. It was proven useful and effective in the treatment of lead, zinc, copper, chromium, manganese, and nickel poisoning and in contamination with transuranic elements. EDTA is administered intravenously as an infusion in 5% glucose in water or physiological saline. It is essential to evaluate kidney function before the beginning of the treatment because its use is contraindicated in patients with renal disease. Na-EDTA is used in a dose of 50 mg/kg. The total quantity should not exceed 300 mg during 6 days of treatment. It is not administered by oral or intramuscular application. Parenteral use of Na-EDTA may lead to hypocalcaemia. The use of Ca-disodium EDTA in the therapeutic dose of 15-30 mg/kg does not have a hypocalcaemia effect. Diethylene Triaminic penta acetic acid (DTPA) is a chelating agent of polyaminocarboxilate series, which, after parenteral use, binds many polyvalent radionuclides of heavy metals. It forms very stable complexes, which are soluble in water and are excreted by the kidney. The Food and Drug Administration (FDA) approves the use of calcium and zinc salts of DTPA in cases of human contamination with trans-uranium elements.

Ca-DTPA is successful in the treatment of actinide contamination. The therapeutic effectiveness of both Ca-DTPA and Zn-DTPA depends on the chemical form and solubility of transuranic elements. Both agents are useful in the elimination of soluble heavy metal salts, such as nitrates or chlorides, but have a rather low efficiency in poorly soluble compounds such as oxides. Both drugs are used by intravenous injection, intravenous infusion, intramuscular injection, or via inhalation in the form of an aerosol. The mode of administration depends on the given circumstances of heavy metal poisoning, its chemical form, and the pathway of contamination. Ca-DTPA is more efficient than Zn-DTPA if used early after contamination, but they do not differ in efficacy if administered at later time intervals. DTPA therapy has been associated with a loss of trace elements, which is a
reversible process, without reported harmful effect on the organism. The injection of 1 g of Ca-DTPA per week in long-term treatment did not cause toxic effects in patients contaminated with actinides. In contrast, a constant infusion of Ca-DTPA was shown to cause severe toxic effects in experimental animals, leading to death after several days. The toxicity of Zn-DTPA was demonstrated to be 30 times less than Ca-DTPA in fractionated use, not leading to the loss of micro elements and not demonstrating teratogenic effects. In early decontamination therapy of contamination with transuranium elements in humans, Ca-DTPA is the treatment of choice, whereas in the planning of a long-term treatment, Zn-DTPA is preferentially used because of its lesser effect on trace metals. It is also used for patients with renal disease, depressed activity of the bone marrow, and pregnancy, where Ca-DTPA is contraindicated.

(ii) Miscellaneous agents

Other agents used in internal contamination with actinides include desferoxamine (DFOA), which was demonstrated to be effective in oral, intramuscular, and intravenous administration. Its therapeutic effect is enhanced when used together with DTPA, but it has to be used with caution because of the side effects, including exanthema, tachycardia, and hypotension. Bis(carboxy-imethylaminoadiethyl ether (BAETA) is another agent shown to be effective in transuranic contamination, but less than DTPA. From the viewpoint of elimination of most hazardous radionuclides of the transuranic series, DTPA outweighs other agents, including the recently studied sulfonatedtetrameric catecholamines (LICAM-C and LICAM-S), which have been found effective in contamination. However, their use has been limited because of the toxicity.

2.2. RADIATION POISONING / SICKNESS

Man has evolved in the background of natural radiation. The terrestrial and the cosmic radiations which contribute to an average annual dose of about 2.4 mSv, is prevalent everywhere on the earth. Environmental radiation levels could increase due to various technological activities such as use of radioisotopes in industry, research and nuclear medicine institutions, mining and milling operations of uranium and operation of nuclear power plants. In addition, nuclear weapon testing and radiation accidents of various kinds
result in enhancing the environmental radiation levels. A typical breakdown between natural background radiation and artificial sources of radiation is shown in the pie chart on the following page. It shows natural radiation contributes about 82% of the annual dose to the population while medical procedures contribute most of the remaining 18% for a total annual average radiation exposure of 360mrem (3.6mSv). Both natural and artificial radiations affect us in the same way.

2.2.1. Radioactivity

The phenomenon of radioactivity was discovered accidentally by the French scientist, Henri Bacquerel, in 1896. He noted that crystals of potassium uranylsulphate, placed over a wrapped photographic plate even in total darkness, could produce background marks on the plate after its development. Further investigations established that the source of these invisible radiations was the element uranium. Thorium salts also emit similar rays. Following this discovery of radioactivity, Marie and Pierre Curie in 1898 isolated the elements radium and polonium which were found to be much more intensely radioactive than uranium or thorium. Apart from these naturally occurring radioactive elements, there are many man-made elements which are radioactive and are said to exhibit artificial radioactivity. The phenomenon of radioactivity arises from the decay of unstable nuclei. Naturally occurring radioactive elements undergo decay by emitting three types of radiations. Radiations may be particulate or electromagnetic. The principal forms of radiation emitted from radionuclides are alpha particles, beta particles and gamma rays.

2.2.1.1. Alpha Particles

When the nucleus of an atom has too many protons it results in disequilibrium of the nucleus due to excessive repulsion. In order to reduce this repulsion the atom emits an alpha particle. An alpha particle consists of two protons and two neutrons bound together as a stable entity and are designated as \(^{4}\text{He}_2\). The loss of an alpha particle reduces the atomic number by two. They collide with molecules in the air and are stopped by two inches of air. They are unable to penetrate intact human skin or pass through a sheet of paper. Their main danger for humans occurs in case they are inhaled or ingested, thereby becoming quite harmful.
2.2.1.2. Beta Particles

When the neutron to proton ratio in the nucleus is too great a beta particle is emitted. In basic beta decay a neutron is transformed into a proton and an electron. The electron is then emitted as a beta particle, denoted by the symbol $^0e_i$. The path of this light charged particle is very irregular and it travels at nearly the speed of light. It has more speed and less mass than alpha radiation, allowing it to penetrate more. The mass number of the element remains unchanged by the loss of a beta particle. Beta radiation can be stopped by metal sheet but the particles are able to penetrate the human body to approximately an inch.

2.2.1.3. Gamma Radiation

When the nucleus of an atom is at too high an energy, it attempts to reach equilibrium by emitting a high-energy photon known as a gamma particle. Gamma radiation is a form of electromagnetic energy, a ray in the same sense as visible light or X-rays. The photons of gamma rays are physically indistinguishable from X-rays. Gamma radiation behaves differently than radiation consisting of charged particles. Rather than losing energy slowly as it ricochets off molecules in the absorbing material as alpha and beta radiation do, gamma photons lose all their energy at once either by being absorbed or by scattering. Gamma rays have substantially more penetration power than either alpha or beta radiation. Gamma radiation can be stopped by lead or concrete of sufficient thickness or by glass made with lead.

2.2.2. Radiations Disasters

There has been a very sharp increase in the use of radioactivity during past five decades, for both the well-being and destruction of human beings. Radioisotopes like $^{99m}$Te, $^{67}$Ga, $^{111}$In, $^{131}$I, $^{125}$I, $^{57}$Co, $^{51}$Cr, $^{32}$P, $^{59}$Fe, $^{133}$X etc. have been used for therapy and diagnosis of various diseases. All the approved radionuclides are generated at the regulatory bodies approved places under strict controls. In India Bhabha Atomic Research Centre, named Broad of Radiations and isotope Technology generates all the required radioisotopes, and supplies them to BARC approved research centres and hospitals. Even after such strict controls and highly trained staff, accidental contaminations have occurred. Moreover, apart from the
nuclear bomb detonations on Hiroshima and Nagasaki, in 1945, during 2nd world war, several major accidents took place:

- During 1940-1984, approximately 250 radiation accidents were reported: more than 600 individuals were exposed internally/externally. The actual figure is likely to be hundred times as majority of accidents are not reported.

- The Chernobyl accident occurred on April 26, 1986, at the Chernobyl nuclear power plant (originally named after Vladimir Lenin) in Ukraine (then part of the Soviet Union). It was the worst nuclear accident in the history of nuclear power, producing a plume of radioactive iodine debris that drifted over parts of the western Soviet Union, Eastern Europe, Scandinavia, UK, and eastern USA.

<table>
<thead>
<tr>
<th>Date</th>
<th>City</th>
<th>State</th>
<th>Cause</th>
</tr>
</thead>
<tbody>
<tr>
<td>4/05/1987</td>
<td>Kalpakkam</td>
<td>Tamil Naidu</td>
<td>Refueling accident at the Fast breeder test reactor at Kalpakkam ruptures the reactor core</td>
</tr>
<tr>
<td>10/09/1989</td>
<td>Tarapur</td>
<td>Maharashtra</td>
<td>Operators find that reactor leaking radioactive iodine at more than 700 times than normal levels</td>
</tr>
<tr>
<td>13/05/1992</td>
<td>Tarapur</td>
<td>Maharashtra</td>
<td>Tube causes release of 12 Curies of radioactive</td>
</tr>
<tr>
<td>31/03/1993</td>
<td>Bulandshahr</td>
<td>Utter Pradesh</td>
<td>Steam turbine catch fire at Narora Atomic power Station, damaging the heavy water reactor and almost leading to a meltdown</td>
</tr>
<tr>
<td>2/02/1995</td>
<td>Kota</td>
<td>Rajasthan</td>
<td>Radioactive helium and heavy water from the Rajasthan Atomic Power Station leak into the RanaPartapSagar river</td>
</tr>
<tr>
<td>22/10/2002</td>
<td>Kalpakkam</td>
<td>Tamil Naidu</td>
<td>About 100kg of radioactive sodium in a fast breeder reactor leaks into a purification cabin damaging valve and operating systems</td>
</tr>
<tr>
<td>29/11/2009</td>
<td>Kaiga</td>
<td>Karnataka</td>
<td>About 45 employee of Kaiga Atomic Power Station suffer radiation poisoning as radioactive heavy water from the plant contaminates drinking water</td>
</tr>
<tr>
<td>30/11/2009</td>
<td>BARC Lab</td>
<td>Mumbai, Maharashtra</td>
<td>Two young researchers were burnt to death in a mysterious fire in the modular lab of the BARC</td>
</tr>
</tbody>
</table>
Apart from accidental radionuclide contamination, intentional or terrorist activities are a major threat to mankind. The magnitude of destruction due to nuclear detonations does not limit to one generation but it is carried forward to the progenies. Besides a heavy radiation exposure within seconds of a nuclear burst, there is a long-term radiation exposure to the survivors as a consequence of radio nuclide contamination due to the release of nearly 400 different varieties of radioisotopes. Such radio nuclides expose the population to radiation in a large area of the fall out by contaminating the whole atmosphere, including food, water and air. The radionuclides are assimilated in the human body and impart radiation dose until metabolized out. Duration and intensity of the radiation exposure depend on the biological and physical half-lives of the radionuclides and the nature of emission. In the recent past phenomenal growth of the terrorism globally has opened a new source of nuclear threat than the nuclear explosion.

2.2.3. Isotopes of special importance during any nuclear fallout

It includes\textsuperscript{131}I, \textsuperscript{89}Sr, \textsuperscript{90}Sr and \textsuperscript{137}Cs. This is due to both their relative abundance in fallout, and to their special biological affinity. \textsuperscript{131}I is a $\beta$ and $\gamma$ emitter with a half-life of 8.07 d specific activity 124,000 Ci/g. Its decay energy is 606 keV $\beta$, 364 keV $\gamma$. It constitutes some 2\% of fission-produced isotopes -1.6-105Ci/kit. Iodine is readily absorbed by the body and concentrated in one small gland, the thyroid.

\textsuperscript{90}Sr is a $\beta$ emitter (546 keV, no $\gamma$) with a half-life of 28.1 years (specific activity 141 Ci/g), \textsuperscript{89}Sr is a $\beta$ emitter (1.463 MeV, $\gamma$very rarely) with a half-life of 52 d (specific activity 28,200 Ci/g). Each constitutes about 3\% of total fission isotopes: 190 curies of \textsuperscript{90}Sr and 3.8x104curies of \textsuperscript{89}Sr per kiloton. Due to their chemical resemblance to calcium these isotopes are absorbed and stored in bones. \textsuperscript{89}Sr is an important hazard for a year or two after an explosion, but \textsuperscript{90}Sr remains a hazard for centuries. Actually most of the injury from \textsuperscript{90}Sr is due to its daughter isotope \textsuperscript{90}Y which has a half-life of only 64.2 h, so it decays as fast as it is formed, and emits 2.27 MeV $\beta$ particles. \textsuperscript{137}Cs is a $\beta$ and $\gamma$ emitter with a half-life of 30.0 y.
(specific activity 87 Ci/g). Its decay energy is 514 keV $\beta$, 662 keV $\gamma$. It comprises some 3-3.5% of total fission products -200 Ci/kit. It is the primary long-term gamma emitter hazard from fallout, and remains a hazard for centuries.

2.2.4. Radionuclides of Biological Importance

It is difficult to predict which radionuclides are most likely to be used in a nuclear disaster event, but based on accessibility and maximizing terrorist impact; it is not too hard to come up with some educated guesses. Strontium (Sr)-90, yttrium (Y)-90, cesium (Cs)-137, iridium (Ir)-192, cobalt (Co)-60, americium (Am)-241, iodine (I)-125 and 131, uranium (U)-234, 235, and 238, plutonium (Pu)-239, radium (Ra)-226, tritium (hydrogen-3 or H-3), phosphorus (P)-32 and palladium (Pd)-103 are possible candidates. There could always be mixtures of radionuclides, either because the original sealed sources contained a mixture, or because an exploded establishment contained a mixture, or because a terrorist sought to confuse responders and complicate the response situation (Brode 1968).

It is also necessary to set the approximate upper limit of radionuclide contamination that can reasonably be ignored from a radiation safety point of view. These are value judgments that will depend upon the circumstances of the event and the resources available. One very conservative point at which to start would be the upper limit of radionuclide contamination permitted each year for radiation workers (“allowable levels of intake”, or “ALIs”). While radiation workers are permitted fifty times more radiation dose each year than are members of the general public, the radiation doses allowed to workers are not associated with any measurable risk, and so it makes no medical sense to be concerned with lower doses, except perhaps for children (ICRP, 1980).

2.2.5. Modes of Contamination

A radiation disaster leads to both external and internal effects of the radioisotopes.

2.2.5.1. External Contamination

External contamination is associated with the short term effects of radiations. It includes the contamination of skin surface, food stuff, water and gamma radiations from the spread of
radioisotopes in the atmosphere. It can also be explained as external exposure is exposure which occurs when the radioactive source (or other radiation source) is outside (and remains outside) the organism which is exposed.

![Type of radiation exposure](image)

**Figure 2.1: Type of radiation exposure**

### 2.2.5.2. Internal contamination

Internal exposure occurs when the radioactive material enters the organism, and the radioactive atoms become incorporated into the organism. Internal radioactive contamination can arise from accidents involving nuclear reactors, industrial sources, or medical sources. Internal contamination occurs when radioactive material is ingested, inhaled, or absorbed from a contaminated wound. As long as these radioactive contaminants remain in the body, they may pose significant health risks. The risks are largely long term in nature and depend not only on the type and concentration of the radioactive contaminant absorbed, but also on the health status of the exposed individual. The potential for development of cancers of the lung, liver, thyroid, stomach, and bone, among others, are principal long-term health concerns, as are fibrotic changes in tissues such as lung, which may lead to restrictive lung disease and other chronic debilitating conditions. However, early recognition of internal contamination provides the greatest opportunity for radio-contaminant removal (NCRP,
1980). The uptake and retention of a radioactive contaminant is influenced by its portal of entry, chemistry, solubility, metabolism, and particle size (Durakovic 1987; Cerveny 1988).

2.2.6. Route of entry

Internal contamination occurs by three main routes: inhalation, ingestion, and wound contamination. A fourth and infrequent route is percutaneous absorption, which applies almost exclusively to radioactive tritium in association with water.

2.2.6.1. Ingestion

Gastrointestinal absorption of different radionuclides differs from one another. Some of the ingested radioactive isotopes preferentially enter the bloodstream via the intestinal mucosa, whereas other isotopes are not absorbed in any significant amount. Those isotopes whose principal route of entry is gastrointestinal absorption, the most significant are the isotopes of cesium, strontium, cobalt, iodine, phosphorus, mercury, radium and tritium (Glasston & Dolan, 1977; Dunning, 1957). Gastrointestinal absorption is an important route of entry of the osteotropic alkaline earth isotopes such as $^{90}$Sr. Gastrointestinal absorption is particularly important because of the contaminated biosphere and the food contaminated after nuclear accidents. 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. The ingestion of $^{137}$Cs results in its rapid entry into the bloodstream. Numerous cases have been reported of accidental contamination with $^{137}$Cs in humans (Hesp 1964; Miller 1964). The intestinal absorption of radium is an important cause of inducing skeletal malignancies. Over 30% of Ra is absorbed in the intestine after accidental ingestion, and it is almost entirely deposited in the skeleton (Neuman et al., 1955; Lloyd et al., 1961 and Rowland et al., 1963)
2.2.6.2. Inhalation

Of the exposure routes, inhalation poses the greatest threat, especially in a fallout environment (http://www.fda.gov/cder/guidance/6394dft.htm). The size of the radioactive particle influences lung deposition, because particles with an aerodynamic diameter greater than 10 microns tend to be deposited in the upper respiratory tract (Glasston & Dolan, 1977). Insoluble particles (especially plutonium from unspent fuel or industrial accidents) pose a particular threat to the lung because prolonged exposure of the lower respiratory tract to alpha emitters such as plutonium causes an increased incidence of pulmonary malignancy (Muggenburg et al 1977). Depending on the aerodynamic diameter of the particles and other factors, about 25 percent of inhaled radioactive particles may be immediately exhaled, leaving the remaining 75 percent to be deposited along the respiratory tree. 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 blood stream is extremely complex, from the viewpoints of physiology and radiation toxicology (Langham WH, 1972). Inhaled radioactive particles are deposited in the upper bronchial tree on the alveolar surfaces, or, if soluble they are absorbed into systemic circulation (ICRP, 1968). Inhalation of the radioactive particles is the main route of internal contamination with actinides (americium, plutonium, uranium, curium, polonium, radium, and thorium), cobalt, cerium, iodine and tritium (Taylor 1973).

2.2.6.3. Percutaneous absorption

Wounds contaminated by fallout and shrapnel may provide continuous irradiation of surrounding tissues and increase the likelihood of systemic incorporation (Durakovic 1987; Durbin 1973). This hazard remains until the contaminant is removed by irrigation, surgical debridement, or decay. Normal skin is an effective 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. The main pathway of a radioisotope from the skin to the systemic circulation is through hair follicles. A rich network of blood vessels under the hair follicles is the principle site of transcutaneous migration of the radioisotopes from the contaminated 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. Burned, desquamated and necrotic skin loses its integrity and provides an open route 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.

2.2.6.4. Through wounds and injections
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 injury by the blast component of the nuclear weapon explosion usually occurs near the hypocenter. Intradermal or subcutaneous deposition of the fission products has been widely studied because of the therapeutic need to eliminate radioactive isotope from the contamination site without interrupting the integrity of the normal integument. Some isotopes like iodine, strontium, cesium and tritium translocate rapidly from intradermal site whereas some will absorb less avidly from shallow dermal wound (transuranic elements). 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 renal, hepatobiliary and other endogenous systems of elimination. Over 30 % of intravenously injected plutonium will be eliminated, mostly via the gastrointestinal tract by the processes of hepatobiliary and endogenous elimination (Durakovic 1987). 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 slower rate of translocation (e.g. transuranic elements) (Norwood 1962).

2.2.7. Factors affecting radiation hazards of internalized radionuclides
Radiations from the internally deposited radionuclides are of great concern because they not only affect the survivors but also their progenies. Internal deposition of the radionuclide is essentially based on their following typical characteristics: (a) Chemical nature & solubility, (b) Physical half-life, (c) Type of radioactive decay, (d) Distribution & Elimination (a) Chemical Nature & solubility

### 2.2.7.1. Chemical nature & solubility
Absorption, distribution and retention of various radioisotopes are strongly dependent on the chemical form and solubility of the contaminant. Different radioisotopes will be present as different salt forms. As oxides, strontium and barium are about 10% soluble; after entering the blood, they go to bone (Glasston&Dolon, 1977). Iodine is soluble; it readily enters the blood and goes to the thyroid. Different solubility of the radionuclides affects the permeability. For example soluble compound of natural uranium, are easily absorbed in systemic circulation and are potentially nephrotoxic (Nolibe et al 1989).

### 2.2.7.2. Half-lives
Half-life is a very important factor that governs the radiation burden of internalized radioisotopes. Short half-life radionuclides are comparatively easy to handle and they are considered less hazardous. The half-lives of different radioisotopes may vary from few seconds to years like $^{81m}$Kr has $t_{1/2}$ of 13 sec while $^{137}$Cs has a half-life of 30 years (Kowalsky & Perry 1987).

### 2.2.7.3. Type of radioactive decay
Unlike external exposure where gamma radiation emitting radioisotopes are more hazardous, in-vivo particulate emitting radioisotopes (alpha, beta and neutrons) are most toxic because of their high energy deposited per unit path length (LET). Particulate radiations, being completely absorbed by tissue, render a high radiation burden (Saha, 2000). Fission produced radioisotopes show different modes of decay, both particulate and rays. Particulate decay mode is hazardous when the radioisotope is inside the body. However, electromagnetic mode is harmful irrespective of the position of radioisotope as gamma rays can penetrate 100 cm thick aluminum foil.
2.2.7.4. Distribution & Elimination

Organospecificity of certain fission products results in excessive radiation damage to selective tissues; in contrast, other radionuclides that are uniformly distributed in the body fluids will result in the relatively uniform exposure to all organs. Radionuclides when reach their target (Table 1) organs like $^{137}\text{Cs}$ in muscles (Leggett, 1986; Van Der et al 1978), and Sr, Ra, U, Cf in bone, they behavior as normal physiological ion of that part and hence it becomes very difficult to remove them. Incorporation of such radioisotopes in their target organs can result in considerable tissue damage. However, radionuclides that have no specific target organ will be rapidly eliminated by the processes of natural clearance. Most of the fission produced nuclides are rapidly eliminated from the body after initial fallout from a nuclear detonation.

2.2.8. Radiation sickness/symptoms

Radiation poisoning, also called radiation sickness or a creeping dose is a form of damage to organ tissue due to excessive exposure to ionizing radiation. The term is generally used to refer to acute problems caused by a large dosage of radiation in a short period, though this also has occurred with long term exposure. The clinical name for radiation sickness is acute radiation syndrome (ARS) as described by the CDC (Centre for disaster control). A chronic radiation syndrome does exist but is very uncommon; this has been observed among workers in early radium source production sites and in the early days of the Soviet nuclear program. A short exposure can result in acute radiation syndrome; chronic radiation syndrome requires a prolonged high level of exposure. Radiation exposure can also increase the probability of contracting some other diseases, mainly cancer, tumours, and genetic damage.

These are referred to as the stochastic effects of radiation, and are not included in the term radiation sickness. The use of radionuclides in science and industry is strictly regulated in most countries (in the U.S. by the Nuclear Regulatory Commission and in India by Atomic Energy and radiation board (AERB) and Bhaba Atomic Research Center (BARC)). Radiation sickness results when humans (or other animals) are exposed to very large doses of ionizing radiation. Radiation exposure can occur as a single large exposure (acute), or a series of small exposures spread over time (chronic).
Radiation sickness is generally associated with acute exposure and has a characteristic set of symptoms that appear in an orderly fashion. Chronic exposure is usually associated with delayed medical problems such as cancer and premature aging, which may happen over a long period of time. Because it is difficult to determine the amount of radiation exposure from nuclear accidents, the best signs of the severity of the exposure are: the length of time between the exposure and the onset of symptoms, the severity of symptoms, and severity of changes in white blood cells.

Table 2.3: Effect of radiation on radiation exposure

<table>
<thead>
<tr>
<th>Radiation Dose</th>
<th>Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05–0.2Sv</td>
<td>No symptoms. Potential for cancer and mutation of genetic material, according to the LNT model: this is disputed. A few researchers contend that low dose radiation may be beneficial.</td>
</tr>
<tr>
<td>0.2–0.5Sv</td>
<td>No noticeable symptoms. White blood cell count decreases temporarily.</td>
</tr>
<tr>
<td>0.5–1Sv</td>
<td>Mild radiation sickness with headache and increased risk of infection due to disruption of immunity cells. Temporary male sterility is possible.</td>
</tr>
<tr>
<td>1–2Sv</td>
<td>Light radiation poisoning, 10% fatality after 30 days. Typical symptoms include mild to moderate nausea (50% probability at 2 Sv), with occasional vomiting. Temporary male sterility is common.</td>
</tr>
<tr>
<td>2–3Sv</td>
<td>Moderate radiation poisoning, 35% fatality after 30 days (LD 35/30). Nausea is common (100% at 3 Sv), with 50% risk of vomiting at 2.8 Sv. There is a massive loss of leukocytes (white blood cells), greatly increasing the risk of infection. Permanent female sterility is possible.</td>
</tr>
<tr>
<td>3–4Sv</td>
<td>Severe radiation poisoning, 50% fatality after 30 days (LD 50/30). Other symptoms are uncontrollable bleeding in the mouth, under the skin and in the kidneys (50% probability at 4 Sv) after the latent phase.</td>
</tr>
<tr>
<td>4–6Sv</td>
<td>Acute radiation poisoning, 60% fatality after 30 days (LD 60/30). Fatality increases from 60% at 4.5 Sv to 90% at 6 Sv (unless there is intense medical care). Female sterility is common at this point. The primary causes of death are infections and internal bleeding.</td>
</tr>
<tr>
<td>6–10Sv</td>
<td>Acute radiation poisoning, near 100% fatality after 14 days (LD 100/14). Bone marrow is nearly or completely destroyed, so a bone marrow transplant is required. Gastric and intestinal tissues are severely damaged.</td>
</tr>
<tr>
<td>10–50Sv</td>
<td>Acute radiation poisoning, 100% fatality after 7 days (LD 100/7). After powerful fatigue and immediate nausea caused by direct activation of chemical receptors in the brain by the irradiation. After that, cell death in the gastric and intestinal tissue, causing massive diarrhea, intestinal bleeding and loss of water leads to water-electrolyte imbalance.</td>
</tr>
</tbody>
</table>
2.2.9. Management of Internal Radioactive Contamination

A variety of rather simple pharmacologic concepts are exploited in order to rid the body of radioactive contamination (radionuclide decorporation). If radionuclides are in the gastrointestinal tract, speeding up intestinal transit will favor excretion in the stool rather than absorption. A simple laxative thus becomes a radionuclide decorporation drug. Certain drugs will bind radionuclides in the gastrointestinal tract, making the radionuclides unavailable for absorption. Prussian blue, an unabsorbable dye, works this way for cesium and thallium, including radioactive isotopes of these elements (Bhattacharyya et al 1992; NCRP, 1980).

Table 2.4: Time dependent symptom of radiation exposure

<table>
<thead>
<tr>
<th>Phase</th>
<th>Symptom</th>
<th>Exposure (Gray)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-2 Gy</td>
<td>2-6 Gy</td>
</tr>
<tr>
<td>Immediate</td>
<td>Nausea and vomiting</td>
<td>5-50%</td>
</tr>
<tr>
<td></td>
<td>Time of onset</td>
<td>2-6h</td>
</tr>
<tr>
<td></td>
<td>Duration</td>
<td>&lt;24h</td>
</tr>
<tr>
<td></td>
<td>Diarrhea</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Time of onset</td>
<td>-</td>
</tr>
<tr>
<td>Immediate</td>
<td>Headache</td>
<td>Slight</td>
</tr>
<tr>
<td></td>
<td>Time of onset</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>Slight</td>
</tr>
<tr>
<td></td>
<td>Time of onset</td>
<td>-</td>
</tr>
<tr>
<td>Immediate</td>
<td>CNS Function</td>
<td>No Impairment</td>
</tr>
<tr>
<td>Latent Period</td>
<td>28-31 days</td>
<td>7-28 days</td>
</tr>
<tr>
<td>Overt Illness</td>
<td>Mild Leukopenia, Fatigue, Weakness</td>
<td>Leukopenia, Purpura, Hemorrhage, Infection, Epilation</td>
</tr>
<tr>
<td>Mortality w/o medical care</td>
<td>0-5%</td>
<td>5-100%</td>
</tr>
</tbody>
</table>
Flooding the gastrointestinal tract with stable counterparts of the radioactive material will compete with the radioactive material for absorption, and thereby cut down on the absorption of radionuclide. Ingesting calcium salts after strontium (Sr)-90 ingestion is an example of this (calcium is chemically similar to strontium) (Kostial et al 1969). Thus the therapeutic management of internal contamination can be summed up as follows:

1. Prevention of radionuclides absorption from GIT to systemic circulation.
2. Hastening the elimination of absorbed radionuclides from blood stream and Deporortion of radionuclides from their target organs.

2.2.9.1. **Prevention of radionuclides absorption from GIT to systemic circulation.**

After the ingestion of various products of nuclear fission, a high number of these products are rapidly absorbed into the systemic circulation and then deposited in their target organs. Reduction of 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 radioisotopes and facilitating their elimination via the fecal route are gastric containing aluminum salts as well as guluronic and manuronic acid salts of alginates, barium sulfate, and sodium phytate (Sutton 1971).

Gastric lavage is a method of high merit in treating early exposure by ingestion. Emetics may be used to complement gastric lavage, although the two methods are frequently used alone (Groot et al 1985). The most commonly used emetics are opiomorphine for subcutaneous administration and ipecacuana derivatives for oral administration. Apomorphine acts predominately acts by stimulating the vomiting center in the medulla oblongata. It should be administered subcutaneously in a single dose of 5-10mg, whereas ipecacuana derivatives can be used repeatedly (oral administration) until vomiting is induced (Durakovic, 1987). 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...
Background | Chapter-II

Purgatives, which inhibit the absorption of radionuclides by their hypertonicity, which causes extraction of water from the intestinal mucosa. It may also be appropriate to remove or enhance transit of gastrointestinal contents after radioactive contamination if contamination has recently occurred via ingestion (Durakovic, 1987). It is recommended that the current standard of care as it applies to other poisonings and overdoses by the oral route be used unless consciousness is impaired or ingestion of corrosive agents has occurred.

Certain non-absorbed binding resins may have utility in inhibiting the uptake of radioactive contaminants in the gut. For example, Prussian blue, a non-absorbed pigmented resin, has been used since the 1960s as an investigational agent administered orally to enhance the fecal excretion of cesium and thallium by means of ion exchange. After review of the published literature and other available data, FDA concluded in 2003 that Prussian blue, when produced under conditions specified in approved new drug applications (NDAs), is safe and effective for the treatment of internal contamination with radioactive thallium, nonradioactive thallium, or radioactive cesium. There are suggestions in the literature that other nonabsorbed binding resins, such as sodium polystyrene sulfonate, may also have utility in inhibiting the uptake of radioactive contaminants in the gut. Sodium polystyrene sulfonate is approved in the United States under the name Kayexelate but is not approved as a decorporation agent (Nigrović1965). Alginate is a group of ion exchanging therapeutic agents act by binding their active ingredients to radionuclides in the body thereby reducing the absorption through intestinal mucosa. Alginites have been successfully used in decorporation of strontium (Sutton et al, 1971; Kargacin & Kostial 1985). Thus main disadvantage has been high viscosity (Sutton et al, 1971; Kostial et al, 1969). Aluminum-containing antacids are relatively well-tolerated and have been recommended for reducing the absorption of radioactive strontium. There are preliminary data to suggest that either aluminum phosphate gel or aluminum hydroxide, given immediately after exposure, may decrease the absorption of radioactive strontium in the gut.

2.2.9.2. Decorporation of radionuclides from their target organs

2.2.9.2.1. Blocking Agents
For radio-contaminants already in the blood, blocking and diluting agents will reduce uptake at target tissues. Administering a blocking agent such as potassium iodide (KI) allows for saturation of metabolic processes in the thyroid with stable, nonradioactive iodine thereby preventing uptake of radioactive iodine. 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 recommended dose is 130 mg KI for adults daily and 65 mg daily for children.

2.2.9.2.2. Diluting Agents

Dilution is achieved by the administration of large quantities of the stable, nonradioactive isotope so that incorporation of the radioactive contaminant is minimized. For maximum effectiveness, the stable isotopes that are used as the blocking or diluting agents should be at least as rapidly absorbed and metabolized as their radioactive counterparts.

2.2.9.2.3. Mobilizing Agents

Mobilizing agents are compounds that enhance and increase the natural turnover processes of radioactive contaminants and thereby accelerate their release from tissues. Drugs that have been recommended for this purpose include antithyroid drugs, ammonium chloride, diuretics, expectorants and inhalants, parathyroid extract, and corticosteroids.

2.2.9.2.4. Chelating Agents

Chelators are substances that bind with certain metals to form a stable complex that can be more rapidly eliminated from the body via excretion by the kidneys. Diethylenetriaminepentacetate (DTPA), as the calcium or zinc salt, has been used as an investigational agent for many years in this capacity (Breitenstein et al., 1990). DTPA forms stable complexes with transuranium elements, and these complexes are renally excreted, thus decreasing body burden. The calcium and zinc salts of DTPA have both been used investigationally for the treatment of plutonium, americium or curium internal contamination under an IND (investigational new drug) application held by the Radiation Emergency Assistance Center/Training Site (REAC/TS). Ca-DTPA is administered as a
single intravenous injection or inhaled dose as soon as possible after contamination and repeated doses of Zn-DTPA administered intravenously may be given daily as necessary as maintenance therapy (Gray et al. 1995; Stradling et al. 2000). FDA announced the availability of a guidance document, Calcium DTPA and Zinc DTPA Drug Products: Submitting a New Drug Application, to assist manufacturers who plan to submit NDAs for Ca-DTPA and Zn-DTPA. Recently, FDA has approved NDAs submitted by Hameln Pharmaceuticals GmbH for Ca and Zn-DTPA. DTPA’s bind uranium less well and are not expected to be effective for uranium contamination. Uranium contamination has been treated with oral sodium bicarbonate, regulated to maintain an alkaline urine pH, and accompanied by diuretics (Durakovic 1987).

Table 2.5: Radioactive contaminants of immediate medical significance and possible treatments.

<table>
<thead>
<tr>
<th>Radioactive Contaminant</th>
<th>Radiation Type</th>
<th>Target Organ</th>
<th>Contamination Mode</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Americium-241</td>
<td>α, γ</td>
<td>Bone</td>
<td>I/W</td>
<td>CaDTPA, ZnDTPAf</td>
</tr>
<tr>
<td>Californium-252</td>
<td>γ, α, η</td>
<td>Bone</td>
<td>I/W</td>
<td>CaDTPA, ZnDTPA</td>
</tr>
<tr>
<td>Cerium-141, 144</td>
<td>β, γ</td>
<td>GI, lung</td>
<td>I/GI</td>
<td>CaDTPA, ZnDTPA</td>
</tr>
<tr>
<td>Cesium-137</td>
<td>β, γ</td>
<td>Total body</td>
<td>I/S/GI</td>
<td>Prussian blue</td>
</tr>
<tr>
<td>Curium-244</td>
<td>α, γ, η</td>
<td>Bone</td>
<td>I/GI</td>
<td>Ca-DTPA, Zn-DTPA</td>
</tr>
<tr>
<td>Iodine-131,132,134, 135</td>
<td>β, γ</td>
<td>Thyroid</td>
<td>I/GI/S</td>
<td>KI</td>
</tr>
<tr>
<td>Plutonium-239, 238</td>
<td>α, γ</td>
<td>Bone</td>
<td>I/W</td>
<td>CaDTPA, ZnDTPA</td>
</tr>
<tr>
<td>Polonium-210</td>
<td>A</td>
<td>Lung</td>
<td>I</td>
<td>Dimercaprol</td>
</tr>
<tr>
<td>Strontium-89, 90</td>
<td>γ</td>
<td>Bone</td>
<td>I/GI</td>
<td>AlPO4</td>
</tr>
<tr>
<td>Tritium (³H)</td>
<td>B</td>
<td>Total body</td>
<td>I/S/GI</td>
<td>Forced H2O</td>
</tr>
<tr>
<td>Uranium-238, 235, 239</td>
<td>α, β, γ</td>
<td>Bone</td>
<td>I/S/W</td>
<td>NaHCO3</td>
</tr>
</tbody>
</table>

Contamination Mode: I by inhalation; GI by gastrointestinal absorption; S by skin absorption; W by wound absorption
Plan of Work
Chelation Therapy