Biological Effects

INTRODUCTION

In this module you will learn about the potential health effects of ionizing radiation, chronic and acute radiation exposure, and ways that acute radiation doses can affect the body. You will learn that the potential for you to receive significant or damaging amounts of radiation while providing emergency care is extremely low.

PURPOSE

The purpose of this module is to increase your understanding of how ionizing radiation affects the human body. This knowledge will help you recognize the biological effects of ionizing radiation and function with confidence during incidents involving radioactive material.

MODULE OBJECTIVES

Upon completion of this module, you will be able to:

1. Identify the potential health effects of radiation exposure.
2. Define chronic and acute radiation doses.
3. Identify the stages and phases of the Acute Radiation Syndrome.

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RADIATION: Dose and Dose Rate

Radiation dose is the amount of radiation energy deposited in the body. Radiation dose rate is a measure of the rate at which radiation energy is deposited in the body. Radiation dose rate is often measured in terms of exposure per unit time (e.g., millirem/hour). Dose and dose rate can be compared to the odometer and speedometer in your car. The speedometer measures your rate of speed—like dose rate. And, the odometer measures the total distance traveled—like total dose received.

BIOLOGICAL EFFECTS OF IONIZING RADIATION

Scientists began to collect and analyze information about the biological effects of ionizing radiation shortly after its discovery. We now know more about the biological effects of ionizing radiation than we do about many other environmental hazards.

Information on the biological effects of ionizing radiation generally comes from four groups of people who have been exposed to significant levels of radiation:

- Early radiation workers who received large doses of radiation before scientists recognized that there were biological effects and consequences. Exposure standards have since been established to protect workers and the public.
- 100,000+ survivors of the atomic blasts in Hiroshima and Nagasaki.
- People who have been involved in radiation accidents at nuclear facilities. There have been incidents involving radiological material, equipment, and processes throughout the world. The Chernobyl nuclear reactor accident is one example.
- Cancer patients. This group is the largest. Patients in this group undergo exposure to high levels of ionizing radiation to treat their disease.

Information obtained from years of radiation-related research has helped us better understand how ionizing radiation can damage the human body, and what levels of exposure cause what kinds of damage.

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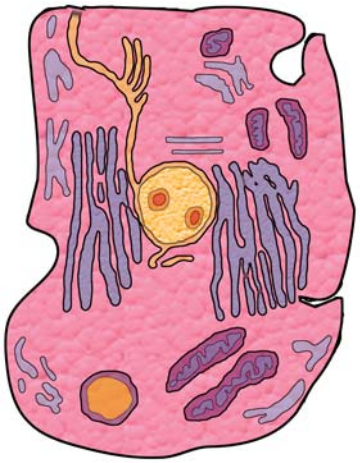
How Ionizing Radiation Affects the Body

Scientists have determined that the effects of ionizing radiation occur at the cellular level. The human body is made up of many organs, and each organ of the body is made up of specialized cells. Ionizing radiation can affect the normal operation of these cells.



The way radiation causes damage to any material is by ionizing the atoms in that material—changing the atomic structure of the material. When atoms are ionized, the chemical properties of those atoms are altered. This is how radiation can damage a cell; it ionizes the atoms and changes the resulting chemical behavior of the atoms and/or molecules in the cell. If a person receives a sufficiently high dose of radiation and many cells are damaged, there may be observable health effects.

Some human cells are more sensitive to environmental factors than others. These environmental factors include viruses, toxins, and ionizing radiation. The extent of radiation damage to cells depends on how sensitive the cells are to ionizing radiation.

Generally speaking, the most sensitive cells are those that divide rapidly or those that are in the process of dividing. These cells are most vulnerable because it is difficult or impossible for them to repair any damage that may occur during cell division. Examples of highly vulnerable cells include blood-forming cells, the cells that line our intestinal tract, hair follicle cells, and the cells in an embryo or fetus. Cells that divide more slowly and cells that are more specialized (brain and muscle cells) are not as easily damaged by ionizing radiation.

The biological effects of ionizing radiation depend on how much and how fast a radiation dose is received. There are two categories of radiation doses: chronic radiation doses and acute radiation doses.

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Chronic Doses

A chronic dose of radiation is a small amount of radiation received over a long period of time. The body is better equipped to handle a chronic dose of radiation than it is an acute dose of radiation. The body can repair the damage from chronic doses, because a smaller percentage of cells will need repair at any given time. The body has enough time to replace dead or non-functioning cells with healthy ones.

Chronic doses do not result in the detectable health effects seen with acute doses. Because of cellular repair, even a sophisticated blood analysis will not reveal any biological effects. Examples of chronic radiation doses include everyday doses we receive from natural background radiation and the doses received by workers in nuclear and medical facilities.

Acute Doses

Exposure to a large dose of radiation received in a short period of time is called an acute dose. The body can not always repair or replace cells fast enough after a large acute dose of radiation, so physical effects may be seen. Some possible health effects from acute doses of radiation include reduced blood count, hair loss, nausea, and fatigue. The physical reaction to an acute dose of radiation is the result of extensive cell damage over a short period of time.

Radiation therapy patients (e.g., patients undergoing cancer treatment) receive high doses of radiation over a short period of time, generally applied to a small portion of the body. Ionizing radiation is used to treat cancer because cancer cells divide rapidly and are sensitive to ionizing radiation.

It takes a large acute dose of radiation before people experience any observable physical effects. Physical effects may take days to manifest themselves and may include nausea, vomiting, and diarrhea. Other than radiation therapy patients, acute doses have only been received by survivors exposed at Hiroshima and Nagasaki and by people at a few radiation incidents at nuclear facilities.

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Radiation dose can be delivered to the whole body homogeneously or locally. For example, a person may enter a radiation field such as would be seen around an operating sterilizer that uses a radioactive source or an exposed industrial radiography source, etc. Conversely, the dose can also be delivered to only a portion of the body. For example, a person may place his or her hand into the path of an x-ray beam, or pick up a radioactive source and place it in a pocket. The dose may also occur in combination. For example, in one case, a janitor placed an industrial radiography source in his back pocket and sustained severe local injury to his buttock; he also received a whole body dose sufficient to cause acute radiation syndrome. Dose effects from acute whole body doses are summarized in the table below:

Summary of Radiation Acute Dose-Response. Effects in Humans (whole body doses)

Acute Dose	Clinical Effects	Survival without Treatment
<100 rem	Possibly anorexia and nausea, vomiting unlikely, onset usually within four to six hours	Virtually 100%
100 - 200 rem	Anorexia, nausea, possibly vomiting, usually within four to six hours	Probable
200 - 400 rem	Anorexia, nausea, vomiting; diarrhea unlikely, usually within one to two hours	Possible
450 rem	LD 50-60 (50% of people will be expected to die within 60 days)	50%
500 - 700 rem	Nausea, vomiting, dizziness, disorientation, possibly diarrhea; onset usually within one hour	Highly unlikely
>700 rem	Rapid onset of vomiting, dizziness, disorientation, possibly diarrhea, coma, seizures, hypotension at higher doses.	Esentially impossible

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It is important to note that the dose effects shown on page 5 represent what are referred to as "whole body" doses. The doses and effects listed are generalizations only and a great deal of variability exists among people. Doses delivered to only a portion of the body or to an extremity will not produce the same effect as the same dose delivered to the whole body.

Local Irradiation

If a large acute dose is received to only a portion of the body, the effects shown in the table below are applicable.

Summary of Radiation Acute Dose-Response. Effects in Humans (local injuries)	
Acute Dose	**Clinical Effects**
300 rad	Epilation (loss of hair)
600 rad	Erythema (redness of skin)
1,200 rad	Dry desquamation
1,500 rad	Blistering or wet desquamation
2,500 rad	Radionecrosis

Risks in Perspective

Most radioactive material shipments contain small quantities of radioactivity. Federal packaging regulations require that the level of radiation (measured on the external surface of shipping packages) be low enough that those who handle packages, or those who are potentially exposed to the package, will not experience any adverse health effects. When highly radioactive material is shipped, special packages are used that have been designed to withstand severe accident conditions without breaching or releasing their radioactive contents.

The probability that you, as an emergency care provider, will receive an acute dose of radiation while treating a radiologically contaminated patient is extremely low.

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ACUTE RADIATION SYNDROME

Acute radiation syndrome (ARS) is a disease that occurs in stages over hours to months as tissue and organ damage is expressed. The clinical syndrome is divided into several distinct stages and phases based on time and organ systems affected.

The stages based on **time** are:

- Prodrome Stage
- Latent Stage
- Manifest Illness Stage
- Recovery or Death

The phases based on the **clinical picture** are:

- Hematopoietic Syndrome
- Gastrointestinal Syndrome
- Central Nervous System/Cardiovascular Syndrome

This discussion assumes that exposure takes place acutely, i.e., over minutes or hours.

Prodrome Stage

The onset of the prodrome stage can occur within minutes to several hours after the exposure. The symptoms are nonspecific and consist of nausea, vomiting, diarrhea, anorexia, and malaise. Depending on the magnitude of the exposure, the symptoms range from mild nausea to violent vomiting with hematemesis and bloody diarrhea with circulatory collapse. In general, the higher the radiation dose, the greater in magnitude the patient's symptoms will be, and the more rapid their onset.

It is during this stage that you will usually see personnel in the emergency department, as the other stages take days to weeks to develop. Most patients will remain asymptomatic during the emergency department phase of their care; therefore, the absence of symptoms during this phase does not mean that a patient has not been exposed. The symptoms of the prodrome stage can easily be attributed to other causes such as a head injury, abdominal injury, or even fright. For this reason, it is important to keep ARS in mind if the patient history warrants, but also not to over diagnose it.

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It is possible that a patient will arrive in the emergency department with symptoms of the later stages. This occurs if the patient is not aware of exposure to ionizing radiation, as in the case of the person who picked up an object that he did not know was radioactive. Many cases such as this exist in literature. Emergency department personnel must be familiar with the later stages to avoid misdiagnosis.

Latent Stage

During the latent stage, symptoms subside except for possibly some mild fatigue, and the patient appears to clinically recover for hours to several weeks. This is the period in which cellular damage becomes clinically apparent.

Manifest Illness Stage

During this stage, the actual biological damage becomes apparent, with the clinical picture dependent on the tissues/organs damaged. For example, if bone marrow were damaged, there would be evidence of pancytopenia. Or, if the brain or heart were damaged, the patient might experience seizures, coma or shock. The clinical manifestations of acute radiation syndrome will be discussed in detail below.

Recovery or Death Stage

The final stage is when the patient either recovers to some degree or dies as a result of the exposure. Death can occur directly from the exposure or from a complication caused by the radiation exposure, such as infection.

CLINICAL MANIFESTATIONS OF ARS

The clinical manifestations of ARS fall into one or more of the following syndromes: hematopoietic, gastrointestinal, and central nervous system/cardiovascular.

Hematopoietic Syndrome

Exposure to 100 to 700 rem of ionizing radiation can lead to the hematopoietic syndrome. In this syndrome, the clinical picture can be attributed to damage to the bone marrow.

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The stem cells from which the blood cells arise are the most radiosensitive of the marrow cells, with sensitivity decreasing as the cell lines mature. The mature circulating blood cells are, for the most part, quite radioresistant. The one notable exception is the mature lymphocyte, which is among the most radiosensitive cell types. These differences in sensitivity help to explain the timing of the changes seen in peripheral blood counts and the clinical picture observed in patients with the hematopoietic syndrome.

The clinical picture of the hematopoietic syndrome is related to progressively decreasing numbers of cellular components of circulating blood, including anemia (red blood count – RBC), immune depression (white blood count – WBC), and clotting dysfunction (platelet). The timing of the appearance of symptoms can be attributed to differences in sensitivities of the precursor cells vs. the mature cells. The stem cell populations in the marrow are depleted rapidly following relatively low doses of radiation. Based on transplantation data, less than 50 percent of the erythrocytic stem cells will be expected to survive a dose of 150 rem, while less than 1 percent will be expected to survive a dose of 500 rem.

Surviving cells will also exhibit a dose-dependent inhibition of mitosis. Thus, following a dose of radiation, the mature populations of blood cells will be relatively unharmed and will continue to function. The stem cells from which they are formed will, however, be severely depleted. As the mature cells age and die, inadequate numbers of new cells will be produced and circulating populations will decrease.

The prodrome for the hematopoietic syndrome may take several hours to develop and consists mainly of gastrointestinal symptoms such as nausea, vomiting, and anorexia with weakness and fatigue lasting for a few days. The latent period may last about three weeks and will consist of possibly just mild weakness. During this period, the mature, circulating cell lines will become depleted, as the damaged bone marrow is unable to supply sufficient blood cells to keep up with demands. The manifest illness stage is entered when circulating blood cell numbers become depleted enough to become clinically apparent.

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Clinical symptoms relate to the depletion of circulating blood cells. Depletion of the red cell line will lead to anemia, often complicated by excessive bleeding due to thrombocytopenia. Depletion of the white cell line will lead to infections that may be difficult to control, possibly caused by opportunistic organisms. Depletion of the platelets will lead to prolonged, spontaneous bleeding. Doses over about 500 rem are rarely survivable without marrow transplantation or stimulation.

Effects on Blood Cells (hematopoietic syndrome)

Lymphocytes—As mature lymphocytes are extremely radiosensitive, they will begin to decrease almost immediately, with nadir reached in 10 to 15 days. The absolute lymphocyte count at two days post exposure can be used as an indicator of the dose received, as well as the lethality of the exposure.

Granulocyte line (neutrophils, etc.)—Initially, there will be a rise attributed to a stress demargination, followed by a steady decline. At eight to ten days, there may be another slight rise termed an abortive rise, with the onset of gradual decline and nadir reached by 30 days post-exposure. At doses above 300 to 500 rem, spontaneous recovery of the bone marrow is unlikely. Infection becomes a problem when levels decline below about 1,000/mm^3.

Platelets—Following radiation exposure, platelet counts will fall steadily, with the rate of decline somewhat dependent on the dose. At lower doses, the nadir may take 30 days, while at higher doses it may be reached within eight to ten days. Bleeding is usually a problem when levels decline below about 50,000/mm^3.

Erythrocytes—Hemoglobin and hematocrit values show a steady decline in the absence of bleeding and/or transfusions, with a nadir usually reached by five to six weeks.

Increases in blood cell counts are apparent in about five to seven weeks post-exposure if the dose is at a level at which the spontaneous recovery of bone marrow is possible (below 500 rem).

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Treatment of the hematopoietic syndrome consists of antibiotics to treat infection and transfusion of blood and platelets. If the bone marrow does not recover spontaneously, it can be stimulated with growth stimulation factors or transplantation may be required.

Gastrointestinal Syndrome

Exposure to radiation in the 700 to 3,000 rem range can cause damage to the gastrointestinal tract, leading to the gastrointestinal syndrome. The hematopoietic syndrome occurs concurrently, as the doses are well above those required to produce severe bone marrow depletion.

The small intestine is the most radiosensitive area of the digestive tract. The mucosal epithelial cells have a rapid turnover rate, and the immature cells in the bases of the crypts of Lieberkuhn are more sensitive than the underlying muscle, vascular tissue, etc. that comprise the remainder of the wall of the intestine. Changes caused by radiation are therefore attributable to the destruction of the lining of the intestine. Radiation in the higher ranges causes sloughing of the epithelium and atrophy of the villi. At lower dose rates, regeneration of the epithelium begins in about seven days. The "ends" of the gastrointestinal tract are relatively more resistant to radiation, with the oropharynx, esophagus, and colon being less sensitive and showing less damage than the small intestine. Prior abdominal surgery with the formation of adhesions appears to make the bowel more susceptible to radiation damage.

The loss of the epithelial lining of the intestine causes the patient to experience nausea, vomiting, diarrhea, crampy abdominal pain, and malabsorption. Breakdown of the barrier between the vascular system and the gut lumen leads to invasion of bacteria normally found within the gut, leading to sepsis. Bleeding will also occur across the denuded areas of the intestine. Bleeding and infection are further complicated by the inhibition of the immune system, clotting disorders, and anemia that are a result of the concurrent development of the hematopoietic syndrome.

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The prodrome for the gastrointestinal syndrome will usually develop within an hour, but may be delayed. Symptoms include anorexia, nausea, vomiting, and probably diarrhea with weakness and fatigue. A latent period of one to four days with some weakness and fatigue will be followed by the manifest illness stage. As the mucosal lining is sloughed, the patient develops abdominal pain, nausea, vomiting, and diarrhea leading to dehydration and electrolyte derangements.

Denuding of the mucosal barrier leads to breakdown of the natural barrier preventing intestinal bacteria from gaining access to the remainder of the body. The sepsis that results will be further complicated by the breakdown in the immune system also caused by the radiation. Bleeding is likely to result, leading to bloody diarrhea. This will be more difficult to control due to platelet loss caused by the radiation and will lead to worsening of the anemia also caused by bone marrow suppression. Depending on the dose and availability of treatment, death usually occurs in three to 14 days post-exposure from either infection, blood loss, or fluid/electrolyte abnormalities.

The mouth, stomach, esophagus, and colon will be affected by radiation but are more resistant than the small intestine. The effects in the mouth include redness, inflammation (mucositis) and ulceration of the mucous membranes. Involvement of the salivary glands leads to a dry mouth, and there may be alteration of taste. The esophagus reacts similarly to the mouth with the development of esophagitis and dysphagia. Irradiation of the stomach causes decreased acid production (thus the prior use of stomach irradiation to treat peptic ulcer disease) as well as gastric ulceration. The colon reacts similarly to the small intestine with the loss of epithelial cells and absorptive capacity as well as bleeding and a breakdown of the bacterial barrier. The colon, however, is able to tolerate higher doses than the small intestine due, in part, to the longer turnover time of the epithelial cells.

Treatment of the gastrointestinal syndrome can be extensive and intensive. Treatment consists of replacing fluid and electrolyte losses, antibiotics for infection, as well as the treatment required for the severe hematopoietic syndrome that is certain to occur. Despite intensive treatment, patients are likely to die.

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Central Nervous System (CNS)/Cardiovascular (CV) Syndrome
Doses above 3,000 rem will lead to damage to the relatively radioresistant central nervous and cardiovascular systems. Most of the damage is to radiosensitive vascular components supplying blood to the nervous system. The heart and great vessels are more radioresistant than the capillaries.

The onset of the prodrome for the CNS/CV syndrome is rapid, usually occurring within the first hour. Symptoms include severe nausea and vomiting, confusion, ataxia, and prostration. The prodrome is followed by a short latent period lasting, at most, a few hours. The manifest illness stage then begins with the return of severe nausea, vomiting, and watery diarrhea. Confusion, combativeness, seizures, loss of consciousness, respiratory distress, hypotension and death will follow within a few hours to days. Doses sufficient to cause the CNS/CV syndrome are essentially fatal despite treatment.

TREATMENT PRIORITIES

Serious medical problems always have priority over concerns about radiation, such as radiation monitoring, contamination control, and decontamination. Triage and treatment of medical concerns, especially life-threatening cases, take precedence over radiological injuries and other radiological concerns beyond scene safety.

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Radiation injury rarely causes unconsciousness or immediately visible signs of injury and is rarely immediately life threatening. Therefore, other causes of injury or illness must be considered. Upon arrival at the hospital, non-contaminated patients are admitted to the usual treatment area, while contaminated patients must be admitted to a specially prepared area. Non-contaminated patients can be cared for like any other patient. Following attention to medical needs, question the patient to determine the possibility of radiation exposure from an external source. Remember, the victim of exposure without contamination poses no radiological hazard.

After you thoroughly examine the patient and identify injuries, you can do a radiological survey of the body. In reality, these will occur concurrently, but the medical exam and concerns take priority. In addition, some radioactive materials have a significant coexistent chemical or toxic hazard that will be of concern.

You will have to use good judgment when assessing treatment priorities. Some radioactive materials are corrosive or toxic because of their chemical properties; therefore, you may have to direct your attention first to a non-radiological problem. In the extremely unlikely event that a victim has been exposed to an acute life-threatening dose, the effect my be untreatable. The Department of Energy's Radiation Emergency Assistance Center and Training Site (REAC/TS) is available to assist hospitals with treatment and care of acutely exposed patients. REAC/TS can be reached by calling (865) 576-1005 and asking for REAC/TS. REAC/TS is available 24-hours a day to provide over-the-phone consultation, and will come to your location if the case warrants. There is no charge for this service.

Check Your Understanding

1. The way radiation causes damage to any material is by _____ the atoms in that material—changing the atomic structure of the material.

2. If a sufficiently high dose of radiation is received, and a large number of cells are damaged, observable _____ may be seen.

3. A(n) _____ dose is a small dose received in a continuous, repeated, or long-term exposure.

4. A(n) _____ dose is a large dose received in a short period of time.

5. The stages of the Acute Radiation Syndrome, which are based on time, include:
   1) _____
   2) _____
   3) _____
   4) _____

6. A patient arrives in the emergency department within one hour of receiving an acute dose of radiation at a medical equipment sterilization facility. The patient is experiencing severe nausea, vomiting, confusion, ataxia, and prostration. Based upon this information, within what dose range would you suspect the patient has been exposed?
   a. 50 to 100 rem
   b. 300 to 700 rem
   c. 700 to 3,000 rem
   d. Greater than 3,000 rem

Idaho Transportation Emergency Preparedness Program




ANSWERS

1. ionizing
2. effects
3. chronic
4. acute
5. prodrome
   latent
   manifest illness
   recovery/death
6. d