Acute Radiation Syndrome
Fact Sheet for Physicians

Acute Radiation Syndrome (ARS) (sometimes known as radiation toxicity or radiation sickness) is an acute illness caused by irradiation of the entire body (or most of the body) by a high dose of penetrating radiation in a very short period of time (usually a matter of minutes). The major cause of this syndrome is depletion of immature parenchymal stem cells in specific tissues. Examples of persons who suffered from ARS are the survivors of the Hiroshima and Nagasaki atomic bombs, the firefighters that first responded after the Chernobyl Nuclear Power Plant 1986 event, and some unintentional exposures to sterilization irradiators.

The required conditions for Acute Radiation Syndrome (ARS) are:

- **The radiation dose must be large:**
  greater than 0.7 Gray (Gy)[1, 2] or 70 rads. (Mild symptoms may be observed as low as 0.3 Gy or 30 rads.)
- **The dose usually must be external**
  (i.e., the source of radiation was outside of the patient's body).
  - Radioactive materials deposited inside the body have produced some ARS effects only in extremely rare cases.
- **The radiation must be penetrating**
  (i.e., able to reach the internal organs).
  - High energy X-rays, gamma rays and neutrons are penetrating radiations.
- **The entire body** (or a significant portion of it) **must have received the dose**[3].
  - Most radiation injuries are local, frequently involving the hands, and these local injuries seldom cause classical signs of ARS.
- **The dose must have been delivered in a short time** (usually a matter of minutes).
  - Fractionated doses are often used in radiation therapy. These are large total doses delivered in small daily amounts over a period of time. Fractionated doses are less effective at inducing ARS than a single dose of the same magnitude.

The three classic ARS Syndromes are:

- **Bone marrow syndrome:**
  the full syndrome will usually occur with a dose between 0.7 and 10 Gy (70 – 1000 rads) though mild symptoms may occur as low as 0.3 Gy or 30 rads[4].
  - The survival rate of patients with this syndrome decreases with increasing dose. The primary cause of death is the destruction of the bone marrow, resulting in infection and hemorrhage.
- **Gastrointestinal (GI) syndrome:**
  the full syndrome will usually occur with a dose between 10 and 100 Gy (1000 – 10,000 rads) though some symptoms may occur as low as 6 Gy or 600 rads.
  - Survival is extremely unlikely with this syndrome. Destructive and irreparable changes in the GI tract and bone marrow usually cause infection, dehydration and electrolyte imbalance. Death usually occurs within 2 weeks.
- **Cardiovascular (CV)/ Central Nervous System (CNS) syndrome:**
  the full syndrome will usually occur with a dose greater than 50 Gy (5000 rads) though some symptoms may occur as low as 20 Gy or 2000 rads.
  - Death occurs within 3 days. Death is likely due to collapse of the circulatory system as well as increased pressure in the confining cranial vault as the result of increased fluid content caused by edema, vasculitis and meningitis.

The four stages of ARS are:

- **Prodromal stage (N-V-D stage):**
  The classic symptoms for this stage are nausea, vomiting and diarrhea that occur from minutes to days following exposure. The symptoms may last (episodically) for minutes up to several days.
- **Latent stage:**
  In this stage the patient looks and feels generally healthy for a few hours or even up to a few weeks.
- **Manifest illness stage:**
  In this stage the symptoms depend on the specific syndrome (see Appendix) and last from hours up to several months.
- **Recovery or death:**
  Most patients who do not recover will die within several months of exposure. The recovery process lasts from several weeks up to two years.

Cutaneous Radiation Syndrome (CRS)

The concept of cutaneous radiation syndrome (CRS) was introduced in recent years to describe the complex pathological syndrome resulting from acute radiation exposure to the skin.

Acute Radiation Syndrome will usually be accompanied by some skin damage. It is also possible to receive a damaging dose to the skin without symptoms of ARS, especially with acute exposures to beta radiation or x-rays. Sometimes this occurs when radioactive materials contaminate a patient's skin or clothes.

When the basal cell layer of the skin is damaged by radiation, inflammation, erythema, and dry or moist desquamation can occur. Also, hair follicles may be damaged causing epilation. Within a few hours after irradiation a transient and inconsistent erythema (associated with itching) can occur. Then, there may be a latent phase that lasts from a few days up to several weeks, when intense reddening, blistering and ulceration of the irradiated site is visible.

In most cases healing occurs by regenerative means; however, very large skin doses can cause permanent hair loss, damaged sebaceous and sweat glands, atrophy, fibrosis, decreased or increased skin pigmentation, and ulceration or necrosis of the exposed tissue.

Patient Management

- **Triage:** If radiation exposure is suspected:
  - Secure ABCs (airway, breathing, circulation) and physiologic monitoring (blood pressure, blood gases, electrolyte and urine output) as appropriate.
  - Treat major trauma, burns and respiratory injury if evident.
  - In addition to the blood samples required to address the trauma, obtain blood samples for CBC (complete blood count), with attention to lymphocyte count, and HLA (human leukocyte antigen) typing prior to any initial transfusion and at periodic intervals following transfusion.
  - Treat contamination as needed.
  - If exposure occurred within 8 to 12 hours, repeat CBC, with attention to lymphocyte count, 2 or 3 more times (approximately every 2 to 3 hours) to assess lymphocyte depletion.

Diagnosis

The diagnosis of ARS can be difficult to make because it causes no unique disease. Also; depending on dose, the prodromal stage may not occur for hours or days after exposure, or, the patient may already be in the latent stage by the time they receive treatment, in which case the patient may appear and feel fine when first assessed.

If a patient received more than 0.05 Gy (5 rads) and 3 or 4 CBCs are taken within 8 to 12 hours of the exposure,

a quick estimate of the dose can be made (see Ricks, et. al. for details). If these initial blood counts are not taken, the dose can still be estimated using CBC results over the first few days. However, chromosome-aberration cytogenetic bioassay is the "gold standard" for dose assessment following acute exposures and should be used to confirm the initial dose estimate. It would be best to have radiation dosimetrists conduct the dose assessment, if possible.

If a patient is known or suspected of having been exposed to a large radiation dose, draw blood for CBC analysis, with special attention to the lymphocyte count, every 2 to 3 hours for the first 8 hours following exposure (and every 4 to 6 hours for the following 2 days). Observe the patient during this time for symptoms and consult with radiation experts before ruling out ARS.

If no radiation exposure is initially suspected you may consider acute radiation syndrome in the differential diagnosis if there is a history of nausea and vomiting that is unexplained by other causes. Other indications are bleeding or epilation or WBC (white blood count) and platelet counts abnormally low a few days or weeks following unexplained nausea and vomiting. Again, consider CBC and chromosome analysis and consultation with radiation experts to confirm diagnosis.

Initial Treatment and Diagnostic Evaluation

Treat vomiting[5]. Repeat CBC analysis, with special attention to the lymphocyte count, every 2 to 3 hours for the first 8 to 12 hours following exposure (and every 4 to 6 hours for the following 2 or 3 days). Precisely record all clinical symptoms, particularly nausea, vomiting, diarrhea, and itching, reddening or blistering of the skin. (Be sure to include time of onset.)

Draw blood for chromosome breakage analysis and note and record areas of erythema. If possible, take color photographs of suspected radiation skin damage. Consider tissue, blood typing and initiating viral prophylaxis. Promptly consult with radiation and hematology experts in regards to dosimetry and prognosis, use of colony stimulating factors, stem cell transfusion and other treatment options. Call the Radiation Emergency Assistance Center/Training Site (REAC/TS) at (865) 576-3131 (M-F, 8 am to 4:30 am EST) or (865) 576-1005 (after hours) to record the incident in the Radiation Accident Registry System.

Then, begin the following (as indicated):

- supportive care in a clean environment[6]
- prevention and treatment of infections
- stimulation of hematopoiesis by use of growth factors
- stem cell transfusions or platelet transfusions (if platelet count is too low)
- psychological support
- observe carefully for erythema (document locations), hair loss, skin injury, mucositis, parotitis, weight loss and or fever
- consult with experts in radiation accident management

For More Help

Technical assistance can be obtained from the Radiation Emergency Assistance Center/Training Site (REAC/TS) at **(865) 576-3131** (M-F, 8 am to 4:30 pm EST) or **(865) 576-1005** (after hours), or on their internet site at **http://www.orau.gov/reacts/**, and the Medical Radiobiology Advisory Team (MRAT) at **(301) 295-0316**.

Also, more information can be obtained from the CDC Health Alert Network at **http://www.bt.cdc.gov** or by calling **1-800-311-3435**.

References

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Jarrett, D. G., 1999, Medical Management of Radiological Casualties Handbook, First Edition, AFRRI (Armed Forces Radiobiology Research Institute), Bethesda, Maryland.

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Prasad, K. N., 1995, Handbook of Radiobiology, Second Edition, CRC Press, Inc., New York, New York.

Ricks, R.C., et. al., Eds. ,2002, The Medical Basis for Radiation Accident Preparedness: The Clinical Care of Victims, Parthenon Publishing, New York.

Appendix: Acute Radiation Syndromes

Syndrome	Dose[7]	Prodromal Stage	Latent Stage	Manifest Illness Stage	Recovery
Bone Marrow	• 0.7 – 10 Gy (70 –1000 rads) • mild symptoms may occur as low as 0.3 Gy or 30 rads	• anorexia, nausea and vomiting • occurs 1 hour to 2 days after exposure • lasts for minutes to days	• stem cells in bone marrow are dying, though patient may appear and feel well • lasts 1 to 6 weeks	• drop in all blood cell counts for several weeks • anorexia, fever, malaise • primary cause of death is infection and hemorrhage • survival decreases with increasing dose • most deaths occur within a few months after exposure	• in most cases, bone marrow cells will begin to repopulate the marrow • there should be full recovery for a large percentage of individuals from a few weeks up to two years after exposure • death may occur in some individuals at 1.2 Gy (120 rads) • the $LD_{50/60}$[8] is about 2.5 to 5 Gy (250 to 500 rads)
Gastrointestinal (GI)	• 10 – 100 Gy (1000 – 10,000 rads) • some symptoms may occur as low as 6 Gy or 600 rads	• anorexia, severe nausea, vomiting, cramps and diarrhea • occurs within a few hours after exposure • lasts about 2 days	• stem cells in bone marrow and cells lining GI tract are dying, though patient may appear and feel well • lasts less than 1 week	• malaise, anorexia, severe diarrhea, fever, dehydration, electrolyte imbalance • death is due to infection, dehydration and electrolyte imbalance • death occurs within 2 weeks of exposure	• the LD_{100}[9] is about 10 Gy (1000 rads)
Cardiovascular (CV) ***Central Nervous System (CNS)***	• > 50 Gy (5000 rads) • some symptoms may occur as low as 20 Gy or 2000 rads	• extreme nervousness; confusion; severe nausea, vomiting, and watery diarrhea; loss of consciousness; burning sensations of the skin • occurs within minutes of exposure • lasts for minutes to hours	• patient may return to partial functionality • may last for hours but often is less	• return of watery diarrhea, convulsions, coma • begins 5 to 6 hours after exposure • death within 3 days of exposure	• no recovery

(Footnotes)

[1] The Gray (Gy) is a unit of absorbed dose and reflects an amount of energy deposited into a mass of tissue (1 Gy = 100 rads). In this document, the absorbed dose we are referring to is that dose inside the patient's body (i.e., the dose which is normally measured with personnel dosimeters).

[2] The referenced absorbed dose levels in this document are assumed to be from beta, gamma or x-ray radiation. Neutron or proton radiation produce many of the health effects described herein at lower absorbed dose levels.

[3] The dose may not be uniform, but a large portion of the body must have received more than 0.7 Gy (70 rads).

[4] Note that though the dose ranges provided in this document apply to most healthy adult members of the public, there is a great deal of variability of radiosensitivity among individuals, depending in large part on the age and condition of health of the individual at the time of exposure. Children and infants are especially sensitive.

[5] Collect vomitus in the first few days for later analysis.

[6] Use of a burn unit (if available) may be quite effective.

[7] The absorbed doses quoted here are "gamma equivalent" values. Neutrons or protons generally produce the same effects as gamma, beta or X-rays, but at lower doses. If the patient has been exposed to neutrons or protons, consult radiation experts on how to interpret the dose.

[8] The $LD_{50/60}$ is the dose necessary to kill 50% of the exposed population in 60 days.

[9] The LD_{100} is the dose necessary to kill 100% of the exposed population.