Trying to reassure a patient is not always easy

Especially when radiation is involved

“Radiation is not a modern creation of man’s curiosity in tinkering with the atom. Radiation has permeated the universe since time began.”
Oral & Maxillofacial Radiology

Terms & Definitions

- **Exposure**: Quantity of radiation incident upon something.
  - Unit: Roentgen (R) - S.I., Coulombs/kg (1 c/kg = 3870 R)
- **Dose (absorbed)**: energy/unit mass of absorber - rad, S.I. - Gray
  - 1 Gy = 100 rad, 1 cGy = 1 rad, 1 rad = 10 mGy
- **Dose (equivalent)**: biological damage produced by any type of radiation
  - Dose equivalent = absorbed dose X QF
  - Rem, S.I. = Sievert. 1 Sv = 100 rems, 1 mSv = 0.1 rems, 1 rem = 10 mrem

- NCRP - National council for Radiation Protection & measurements
- ICRP - International commission of radiological protection
- BEIR (US National academy of science committee)
- UNSCEAR - UN Scientific committee on the effects of atomic radiation

Dose conversion table

<table>
<thead>
<tr>
<th>µGy/Sv</th>
<th>mGy/mSv</th>
<th>Rad/rem</th>
<th>Gy/Sv</th>
<th>mGy/mGy</th>
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</table>

What type of radiation are we talking about?

- Diagnostic?
- Therapeutic?

Radiation in Diagnostic Imaging

- Medical and Dental Imaging including
  - Plain films/Digital detectors - intraoral and extraoral radiography
  - Tomograms
  - CT
  - IV contrast studies
  - Radionuclide scans
  - Radioimmuno-assays

Radiation in cancer treatment

- Radiotherapy is the treatment of cancer and other diseases with ionizing radiation
- The ionizing radiation deposits energy that injures or destroys cells in the area being treated (target area) by damaging their genetic material.
Radiotherapy contd...

- Radiotherapy may be used to treat localized solid tumors such as cancers of skin, tongue, larynx, brain, breast or uterine cervix.
- It can also be used to treat leukemia and lymphoma.

Types of Radiotherapy

- External beam radiotherapy (linear accelerators/betatrons)
- Gamma ray therapy (radium, uranium, cobalt 60)
- Brachytherapy (interstitial irradiation, internal radiotherapy)
- Intraoperative radiotherapy
- Particle beam radiotherapy (high LET radiation) using neutrons, pions and heavy ions
- Radioimmunotherapy using radiolabeled antibodies

The rationale for RT

- Radiation therapy for malignant lesions in the oral cavity is usually indicated when the lesion is radiosensitive, advanced, or deeply invasive and cannot be approached surgically. Combined surgical and radiotherapeutic treatment often provides optimal treatment. Chemotherapy is being combined with radiation therapy and surgery.
- Fractionation increases the mean oxygen tension in an irradiated tumor, rendering the tumor cells more radiosensitive. The fractionation schedules currently in use have been established empirically. Fractionation of the total x-ray dose into multiple small doses provides greater tumor destruction than is possible with a large single dose.

Goals of Radiation therapy

- To kill the cancer cells with as little risk as possible to the normal cells
- Can be used in combination with chemotherapy, surgery.

How is Radiation therapy given?

- Linear accelerators
  Machines that utilize radioactive substances (like cobalt 60) as the source of high energy rays
- Brachytherapy
  Source of radiation such as radioactive iodine is sealed in a small holder which is called an implant. The implants may be thin wires, plastic tubes or capsules

The process

- Physical exam, medical history
- Treatment is planned in a process called "simulation".
- Patients are kept on examination table in supine position and the therapist uses a special x-ray machine to define the treatment port or field.
- Simulation also involves using CT scans to plan how to direct the radiation
XRT beam confirmation

- Radiographic confirmation of the Line of fire (field of the XRT beam)

Who gives radiation?

- Radiation physicist: makes sure that the equipment is working properly and the machines deliver the right dose of radiation
- Dosimetrist: works with the doctor and the physicist to help carry out the treatment plan by calculating the amount of radiation to be delivered
- Radiation therapist: who positions the patient for treatment and runs the machines
- Radiation nurse: helps coordinate the care

Recent advances in RT

- Hyperfractionation
- Intraoperative radiation
- 3-D conformal RT
- Stereotactic radiosurgery using “gamma knife”
- Cyberknife – for brain tumors. Stereotactic radiosurgery
- Peacock system: computer-generated variation of Cyberknife
- Precision therapy: a method of radiosurgery recently developed in Sweden. High doses of radiation delivered in fewer fractions

More terms........

Sensitivity & Responsiveness

RADIosenitivity:
- The relationship between sensitivity to radiation at the cellular level and dose.

RADIosensitivity:
- The rate a tumor shrinks after irradiation. Not a function of radio-sensitivity but more related to rate of cell removal, i.e. cell loss factor

THE MINIMAL TOLERANCE DOSE:
- TD 5/5: Dose which will produce 5% complication in 5 years.

THE MAXIMAL TOLERANCE DOSE:
- TD 50/5: Dose which will produce 50% complications in 5 years.

Let’s go to the atoms
**Atoms - Radioactivity**
- Atoms found in nature are either stable or unstable. An atom is stable if the forces among the particles that makeup the nucleus are balanced.
- An atom is unstable (radioactive) if these forces are unbalanced — if the nucleus has an excess of internal energy. Instability of an atom's nucleus may result from an excess of either neutrons or protons.
- A radioactive atom will attempt to reach stability by throwing off nucleons (protons or neutrons), as well as other particles, or by releasing energy in other forms.

**Radioactive half-life**
- Radioactive half-life of a radionuclide material, commonly referred to as just half-life
  - "It’s the time required for the disintegration of one-half of the radioactive atoms that are present when measurement starts”

**Radiation and Radioactivity**
- Radiation is the energy or particles that are released during radioactive decay. The radioactivity of a material refers to the rate at which it emits radiation.
- Radioactivity = rate of decay

**Types of radiation**
- **Particulate radiation**
  - Alpha rays
  - Beta rays
  - Cathode rays
- **Electromagnetic radiation**
  - Radio, Television, microwave, radar, infrared, UV, x-rays, gamma rays, cosmic rays

**Alpha particles (symbol α)**
- Alpha particles (symbol α) are a type of ionizing radiation ejected by the nuclei of some unstable atoms. They are large subatomic fragments consisting of 2 protons and 2 neutrons.
- Ernest Rutherford, an English scientist, discovered alpha particles in 1899 while working with uranium.

**Beta particles (β)**
- Beta particles are subatomic particles ejected from the nucleus of some radioactive atoms. They are equivalent to electrons. The difference is that beta particles originate in the nucleus and electrons originate outside the nucleus.
- Henri Becquerel is credited with the discovery of beta particles. In 1900, he showed that beta particles were identical to electrons, which had recently been discovered by Joseph John Thompson.
Gamma Rays (\(\gamma\))

- A gamma ray is a packet of electromagnetic energy \(=\) a photon. Gamma photons are the most energetic photons in the electromagnetic spectrum. Gamma rays (gamma photons) are emitted from the nucleus of some unstable (radioactive) atoms.
- Physicists credit French physicist Henri Becquerel with discovering gamma radiation in 1896.
- Becquerel had found gamma radiation being emitted by radium-226. Radium-226 is part of the uranium decay chain.

Gamma ray emitters

- Uses of Cesium-137:
  - cancer treatment
  - measure and control the flow of liquids in numerous industrial processes
  - investigate subterranean strata in oil wells
  - measure soil density at construction sites
  - ensure the proper fill level for packages of food, drugs and other products.

- Uses of Cobalt-60:
  - sterilize medical equipment in hospitals
  - pasteurize certain foods and spices
  - treat cancer
  - gauge the thickness of metal in steel mills.

Let’s leave the Physics behind

The initial interaction

- The initial interaction between ionizing radiation and matter occurs at the level of the electron within the first \(10^{-13}\) second after exposure.
- These changes result in modification of biologic molecules within the ensuing seconds to hours. In turn, the molecular changes may lead to alterations in cells and organisms that persist for hours, decades, and possibly even generations
- If cells are modified, such changes may lead to cancer or disorders in the descendents of the exposed individual.

Deterministic and Stochastic effects

- Deterministic effects:
  - Effects where in the severity of response is proportional to the dose
  - Dose threshold
- Stochastic effects:
  - Effects where the probability of occurrence of a change rather than severity is dose dependant.
  - All or none response
  - No dose thresholds

Radiation chemistry

- Direct
  - Biologic macromolecules are ionized by the energy of a photon or a secondary electron.
- Indirect
  - Ionization of water molecules occurs first producing free radicals that in turn react with and produce changes in biologic molecules.
**Direct effects of Radiation**

Direct alterations of biologic molecules (RH, where R is the molecule and H is a hydrogen atom) by ionizing radiation begin with absorption of energy by the biologic molecule and formation of unstable free radicals (atoms or molecules having an unpaired electron in the valence shell). The generation of free radicals occurs in less than $10^{-10}$ second after the passage of a photon. They are extremely reactive and have very short lives, quickly reforming into stable configurations by dissociation (breaking apart) or cross-linking (joining of two molecules). Free radicals play a dominant role in producing molecular changes in biologic molecules.

Free radical production:

$$6\text{R} + \text{H}_2\text{O} \rightarrow \text{R} + \text{H}_2\text{O} + \text{H}$$

Dissociation:

$$\text{R} + \text{OH} \rightarrow \text{R} + \text{H}_2\text{O}$$

Cross-linking:

$$\text{R} + \text{R} \rightarrow \text{R}_2$$

Because the altered molecules differ structurally and functionally from the original molecules, the consequence is a biologic change in the irradiated organism. Approximately 1/3 of the biologic effects of x-ray exposure result from direct effects.

**Indirect effects**

The interaction of hydrogen and hydroxyl free radicals with organic molecules can result in the formation of organic free radicals. About 2/3 of radiation-induced biologic damage results from indirect effects. Such reactions may involve the removal of hydrogen:

$$\text{RH} + \text{OH} \rightarrow \text{R} + \text{H}_2\text{O}$$

Organic free radicals are unstable and transform into stable altered molecules. These altered molecules have different chemical and biologic properties from the original molecules. The important role of water radiolysis and the indirect action of radiation may be seen by comparing the radiation dose required to inactivate 37% of dry yeast invertase is 110 kGy but only 60 kGy when the enzyme is irradiated in solution.

**Effects on molecules and cells**

- Proteins/Nucleic acids (DNA/RNA)
- Nucleus/Chromosomes
- Cytoplasm/mitochondria
- Cell kinetics (mitotic delay, cell recovery/death)

**Radiolysis of water**

- **ionizing radiation**
- **excited water**
- **excited ion**
- **hydroxyl radical**
- **superoxide radical**
- **reduced superoxide radical**
- **hydrogen peroxide**
- **radical**
- **ions**
- **excited state**
- **electrons**
- **neutrons**
- **protons**
- **hydrogen**
- **oxygen**
- **water**
- **radiolysis of water**

**Effects on molecules and cells**

- Proteins/Nucleic acids (DNA/RNA)
- Nucleus/Chromosomes
- Cytoplasm/mitochondria
- Cell kinetics (mitotic delay, cell recovery/death)
Nucleic acids

- Breakage of one or both DNA strands
  - The most important types of damage are single- and double-strand breakage. Most single-strand breakage is of little biologic consequence as the broken strand is repaired using the intact second strand as a template. However, misrepair of a strand can result in a mutation and consequent biologic effect.
- Cross-linking of DNA strands within the helix, to other DNA strands, or to proteins
- Change or loss of a base
- Disruption of hydrogen bonds between DNA strands
- Double-strand breakage is believed to be responsible for most cell killing, carcinogenesis as well as mutation.

Proteins

- Disruption or breakage of hydrogen or disulfide bonds leads to denaturation of proteins
- The dose of radiation required to induce significant amounts of protein denaturation (or enzyme inactivation) is much higher than that required to induce gross cellular changes or cell death.

Radiation effects at cellular level

- Changes in cellular organelles occur and manifest many hours after moderate doses of radiation. Cell death may occur eventually.
- The nucleus is more sensitive than cytoplasm (the sensitive site being the DNAs within the chromosomes)

Chromosome aberrations

- A, Irradiation of the cell after DNA synthesis results in a single-arm (chromatid) aberration.
- B, Irradiation before DNA synthesis results in a double-arm (chromosome) aberration.

Other cellular changes

- Cytoplasm:
  - At higher doses of radiation (30 to 50 Gy), mitochondria demonstrate increased permeability, swelling, and disorganization of the internal cristae.
Effects on cell kinetics
- Mitotic delay
- Cell death
- Recovery

Mitotic delay
A low dose of radiation induces mild mitotic delay in the G2 phase. A moderate dose leads to G2 block and some cell death.

Cell injury & repair
- Reproductive death occurs in a dividing cell population after exposure to a moderate dose of radiation, which accounts for the radiosensitivity of tissues. When a population of non-dividing cells is irradiated, much larger doses and longer time intervals are required for induction of interphase death.

Cell survival curves
- Plates of single cells are irradiated before colony growth, and the effect of the irradiation on colony-forming cells is studied. The fraction of surviving cells is compared with the absorbed dose.
- Recovery Cell involves enzymatic repair of single-strand breaks of DNA.

Recovery
- A higher total dose is required to achieve a given degree of cell killing when multiple fractions are used (e.g., in radiation therapy) than when the same total dose is given in a single brief exposure.
- Damage to both strands of DNA at the same site (usually caused by particulate radiation) is usually lethal to the cell.

Radiosensitivity & cell type
- Different cells from various organs of the same individual may respond to irradiation quite differently. This variation was recognized as early as 1906 by the French radiobiologists Bergonie and Tribondeau.
- They observed that the most radiosensitive cells are those that (1) have a high mitotic rate, (2) undergo many future mitoses, and (3) are most primitive in differentiation. These findings are still true except for lymphocytes and oocytes, which are very radiosensitive even though they are highly differentiated and non-dividing.

5 Types of cells (Rubin P. Casarett, 1968)
- Vegetative Intermitotic cells
- Differentiating intermitotic cells
- Multipotential connective tissue cells
- Reverting postmitotic cells
- Fixed post mitotic cells
**Oral & Maxillofacial Radiology**

### CELL TYPE

<table>
<thead>
<tr>
<th>CHARACTERISTICS</th>
<th>EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapidly dividing, undifferentiated</td>
<td>Type A spermatagonia, keratinocytes, Oligi cells of intestines, Blast cells of aplasia</td>
</tr>
</tbody>
</table>

**RADIOPHYSICALLY**

- Rapid cell division
- Early and late divisions

**Differentiating intermitotic (DIM)**

- Actively dividing; more differentiated than VIMs: differentiate between divisions
- Intermediate spermatagonia, Myelocytes

**Multipotential connective tissue (MCT)**

- Irregularly dividing; more differentiated than VIMs or DIMs
- Endothelial cells, Fibroblasts

**Reverting postmitotic (RPM)**

- Do not normally divide but retain capability of division: differentiated
- Parenchymal cells of liver, Lymphocytes*

**Fixed postmitotic (FPM)**

- Do not divide: differentiated
- Reticular cells, Erythrocytes, Spermatozoa

**Relative radiosensitivity of organs**

<table>
<thead>
<tr>
<th>Organ</th>
<th>High</th>
<th>Intermediate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoid organs</td>
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<tr>
<td>Bone marrow</td>
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<td>Testes</td>
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<tr>
<td>Kidney</td>
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<tr>
<td>Liver</td>
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</table>

**Long term effects**

- The relative radiosensitivity of capillaries and connective tissue is intermediate between that of differentiating intermitotic cells and reversion postmitotic cells.
- Irradiation of capillaries causes swelling, degeneration, and necrosis leading to slow progressive fibrosis around the vessels. As a result it leads to premature narrowing and eventual obliteration of vascular lumens impeding the transport of oxygen, nutrients, and waste products and results in death of all cell types. The net result is progressive fibroatrophy of the irradiated tissue.

**Relative radiosensitivity of organs**

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</table>

**Modifying factors**

- **Dose:**
  - Threshold: No effect → Effect in proportion to dose
  - **Dose rate:**
    - Exposure: at a high dose rate kills more cells per unit dose because less time exists for repair of sublethal damage.
    - Oxygen: The Oxygen enhancement ratio:
      - It is the dose required to achieve a given endpoint (e.g., 50% survival of a cell population under anoxic conditions divided by the dose required to produce the same endpoint under fully oxygenated conditions.
      - LET:
        - In general, the dose required to produce a certain biologic effect is reduced as the linear energy transfer(LET) of the radiation is increased.

**Radiation effects on skin**

<table>
<thead>
<tr>
<th>Dose rate &amp; (O_2) enhancement ratio</th>
<th>(D_{10})</th>
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</thead>
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<td>Time (s)</td>
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</tr>
<tr>
<td>Dose rate ((\text{Gy}^{-1}))</td>
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</tbody>
</table>

**Dose rate & \(O_2\) enhancement ratio**

- \(D_{10}\) is the dose required to achieve a given endpoint (e.g., 50% survival of a cell population under anoxic conditions divided by the dose required to produce the same endpoint under fully oxygenated conditions.
- **LET**:
  - In general, the dose required to produce a certain biologic effect is reduced as the linear energy transfer(LET) of the radiation is increased.

**Radiation effects @ tissue and organ level**

- **Short term effects**
  - Cells are lost primarily by mitosis-linked death.
  - The extent of cell loss depends on damage to the stem cell pools and the proliferative rate of the cell population. Tissues composed of cells that rarely or never divide (e.g., muscle) demonstrate little or no radiation-induced hypoplasia over the short term.

**Relative radiosensitivity of organs**

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</tbody>
</table>
Study Links Use of Tanning Lamps to Increased Risk of Skin Cancer

A report published in the *Journal of the National Cancer Institute*, suggests that people who use these devices may have an increased risk of developing skin cancers. Tanning lamp users often get a burn like a sunburn, and sunburns are linked to the risk of all three skin cancers: basal cell, squamous cell carcinoma, and melanoma.1

The findings shouldn’t come as a surprise, according to Dartmouth Medical School epidemiologist Margaret R. Karagas, the lead author of the report. “We know that ultraviolet radiation (UVR) exposure that comes from the sun is a major cause of skin cancer. If that intense, concentrated dose of UVR, we would predict that people who use these devices may get skin cancer,” she explains.1

UV free-Tanning Salons

- **UV free tanning uses DHA, Dihydroxy acetone.** It is a sugar free derivative naturally found in the human body. It only affects the outermost cells of the epidermis and does not damage the skin.

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Effects on Oral tissues

The following sections describe the deterministic effects of a course of radiotherapy on the normal tissue of the oral cavity. This discussion assumes that 2 Gy is delivered daily, bilaterally through 8 × 10 cm fields over the oropharynx, for a weekly exposure of 10 Gy. This continues typically until a total of 50 Gy is administered.

- Cobalt is often the source of gamma radiation; however, on occasion small implants containing radon or iodine-125 are placed directly in a tumor mass. Such implants deliver a high dose of radiation to a relatively small volume of tissue in a short time.

Effects of radiation on oral tissues

- Oral mucous membrane
- Taste buds
- Salivary glands
- Teeth
- Bone

Oral mucous membrane

- Mucositis
- Pseudomembrane formation
- Pain and discomfort
- Candida superinfection
- Healing/atrophy, fibrosis

Radiation mucositis

Teeth
Effects on teeth

- Growth retardation
- Destroys tooth buds if irradiation precedes calcification
- Agenesis of teeth/retarded root development
- Adult teeth resistant to direct effects

Delayed root development

Radiation caries

- Type 1: Widespread superficial caries
- Type 2: Caries of cementum and dentin at cervical region
- Type 3: Dark pigmentation of the entire crown
A combination of the above may exist.

Radiation caries

Taste buds

- Extensive degeneration
- Taste acuity decreases by a factor of 1000-10000
- Aversion and loss of taste may begin with the first 200-400 cGy.
- After three weeks of therapy, it takes 500-8000 times normal concentrations of taste stimulant to elicit a normal taste response.
- Recovery in 60-120 days following completion of therapy, if adequate saliva is available.
Bald tongue

Salivary glands

- Parenchyma more sensitive (parotid > SM, SL)
- Reduced salivary flow (dose dependant)
- Xerostomia
- Complete inhibition of flow at 60 Gy
- Shift to acidogenic microflora
- > of strep. mutans, lactobacillus, candida
- Normal function returns in 6-12 months

Normal

Effects of whole body radiation

- Acute radiation syndrome
- Effects on embryos and fetuses
- Late somatic effects
- Radiation genetics
Irradiation during gestation

A risk estimates study by Mettler & Moseley (1985) revealed that

- 10 mSv exposure: death from childhood leukemias is 1 in 3333
- 10 mSv exposure: death from other childhood cancers in 1 in 3571

- The fetus of a patient exposed to dental radiography receives less than 0.25 µGy from a FMS when a leaded apron is used. The effects of radiation on human embryos and fetuses have been studied in women exposed to diagnostic or therapeutic radiation during pregnancy and in women exposed to radiation from the atomic bombs dropped at Hiroshima and Nagasaki. These embryos received exposures of 0.5 to 3 Gy (well more than one million times the exposure from a dental examination).
- Exposures during the first few days after conception are thought to cause undetectable death of the conceptus. The most sensitive period for inducing developmental abnormalities is during the period of organogenesis, between 18 and 45 days of gestation.
- These effects are deterministic in nature. The most common abnormalities among the Japanese children exposed early in gestation are: microcephaly, mental retardation, small birth size, cataracts, genital and skeletal malformations, and microphthalmia.
- The period of maximal sensitivity of the brain is 8 to 15 weeks postconception. The frequency of severe mental retardation after exposure to 1 Gy during this period is about 43%.

Acute Radiation Syndrome

<table>
<thead>
<tr>
<th>Dose(Gy)</th>
<th>Manifestation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-2</td>
<td>Prodromal</td>
</tr>
<tr>
<td>2-4</td>
<td>Mild hematopoietic</td>
</tr>
<tr>
<td>4-7</td>
<td>Severe. hematopoietic</td>
</tr>
<tr>
<td>7-15</td>
<td>G.I.</td>
</tr>
<tr>
<td>50</td>
<td>CVS and CNS</td>
</tr>
</tbody>
</table>

Prodromal period

- Within the first minutes to hours after exposure to whole-body irradiation of about 1.5 Gy, symptoms characteristic of gastrointestinal tract disturbances may occur. The individual may develop anorexia, nausea, vomiting, diarrhea, weakness, and fatigue. These early symptoms constitute the prodromal period of the acute radiation syndrome.

Latent period

- The extent of the latent period is also dose-related. It extends from hours or days at supralethal exposures (greater than approximately 5 Gy) to a few weeks at sublethal exposures (less than 2 Gy).
- Symptoms follow the latent period when individuals are exposed in the lethal range (approximately 2 to 5 Gy) or supralethal range.

Hematopoietic syndrome

- Whole-body exposures of 2 to 7 Gy cause injury to the hematopoietic stem cells of the bone marrow and spleen. The high mitotic activity of these cells and the presence of many differentiating cells make the bone marrow a highly radiosensitive tissue. As a consequence, doses in this range cause a rapid and profound fall in the numbers of circulating granulocytes, platelets, and finally erythrocytes.
G.I. syndrome
- The level of radiation required to produce the G.I. syndrome (more than 7 Gy) is much greater than that causing sterilization of the blood-forming tissues. However, death occurs before the full effect of the radiation on hematopoietic systems can be evidenced.
- By the end of 24 hours, the number of circulating lymphocytes falls to a very low level. This is followed by decreases in the number of granulocytes and then of platelets.

CVS and CNS syndrome
- Exposures in excess of 50 Gy usually cause death in 1 to 2 days. The few human beings who have been exposed at this level showed collapse of the circulatory system with a precipitous fall in blood pressure in the hours preceding death.
- Autopsy revealed necrosis of cardiac muscle. Victims also may show intermittent stupor, incoordination, disorientation, and convulsions suggestive of extensive damage to the nervous system.

Carcinogenesis
- Radiation causes cancer by modifying the DNA. Although most such damage is repaired, imperfect repair may be transmitted to daughter cells and result in cancer.

Linear dose-response relation
- In the U.S. cancer accounts for nearly 20% of all deaths.
- Accordingly, the estimated number of deaths attributable to low-level radiation exposure is a small fraction of the total number that occur spontaneously.
- Estimates indicate that a single, brief whole-body exposure of 100 mGy (about 30 times the average annual exposure) to 100,000 people would result in about 500 additional cancer deaths over the lifetime of the exposed individuals.
- This would be in addition to the 20,000 that would occur spontaneously. Such a calculation assumes a linear dose-response relationship and no threshold dose below which no risk exists.

Susceptibility of various tissues to radiation induced cancer

<table>
<thead>
<tr>
<th>High</th>
<th>Moderate</th>
<th>Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genads (0.20)</td>
<td>Breast (0.05)</td>
<td>Bladder (0.05)</td>
</tr>
<tr>
<td>Colon (0.12)</td>
<td>Esophagus (0.05)</td>
<td>Liver (0.05)</td>
</tr>
<tr>
<td>Stomach (0.12)</td>
<td></td>
<td>Thyroid (0.05)</td>
</tr>
<tr>
<td>Lung (0.12)</td>
<td></td>
<td>Skin (0.01)</td>
</tr>
<tr>
<td>Bone marrow (red) (0.12)</td>
<td></td>
<td>Bone surface (0.01)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Brain (0.05)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Salivary glands (0.05)</td>
</tr>
</tbody>
</table>

Radiation genetics
- Gene mutation
  - Muller (1927) reported radiation-induced mutations in Drosophila (fruit flies).
  - The husband-and-wife team of Russell and Russell studied radiation-induced mutations in over 7 million mice. Intensive work in this field established a number of basic principles of radiation genetics.
In general, radiation causes increased frequency of spontaneous mutations rather than inducing new mutations.

- The frequency of mutations increases in direct proportion to the dose, even at very low doses, with no evidence of a threshold.
- The vast majority of mutations are deleterious to the organism.
- Dose rate is important in that at low dose rates the frequency of induced mutations is greatly reduced.
- Males are much more radiosensitive than females.
- The rate of mutations is reduced as the time between exposure and conception increases.

Doublet dose: This is the amount of radiation a population requires to produce in the next generation as many additional mutations as arise spontaneously. In human beings the genetic doubling dose for mutations resulting in death is approximately 2 Sv.