# ***UNIT-5***

# ***RADIOPHARMACEUTICALS***

## What is ionizing radiation?

Ionizing radiation is radiation that has enough energy to remove electrons from atoms or molecules (groups of atoms) when it passes through or collides with some material. The loss of an electron with its negative charge causes the atom (or molecule) to become positively charged. The loss (or gain) of an electron is called ionization and a charged atom (or molecule) is called an ion.

## What are some examples of ionizing radiation?

Forms of ionizing radiation include:

- Gamma rays
- X rays
- Alpha particles
- Beta particles
- Neutrons.

X rays refer to a kind of electromagnetic radiation generated when a strong electron beam bombards metal inside a glass tube. The frequency of this radiation is very high - 0.3 to 30 Ehz (exahertz or million gigahertz). By comparison FM radio stations transmit at frequencies around 100 MHz (megahertz) or 0.1 Ghz (gigahertz).

Some compounds like uranium are radioactive and give off radiation when the nucleus breaks down or disintegrates. The three kinds of radiation generated by radioactive materials or sources are alpha particle, beta particles and gamma-rays.

## What properties are considered when ionizing radiation is measured?

Ionizing radiation is measured in terms of:

- the strength or radioactivity of the radiation source,
- the energy of the radiation,
- the level of radiation in the environment, and
- the radiation dose or the amount of radiation energy absorbed by the human body.

From the point of view of the occupational exposure, the radiation dose is the most important measure. Occupational exposure limits like the ACGIH TLVs are given in terms of the permitted maximum dose. The risk of radiation-induced diseases depends on the total radiation dose that a person receives over time.

## What units are used for measuring radioactivity?

Radioactivity or the strength of radioactive source is measured in units of becquerel (Bq).
1 Bq = 1 event of radiation emission per second.
One becquerel is an extremely small amount of radioactivity. Commonly used multiples of the Bq unit are kBq (kilobecquerel), MBq (megabecquerel), and GBq (gigabecquerel).
1 kBq = 1000 Bq, 1 MBq = 1000 kBq, 1 GBq = 1000 MBq.
An old and still popular unit of measuring radioactivity is the curie (Ci).
1 Ci = 37 GBq = 37000 MBq.
One curie is a large amount of radioactivity. Commonly used subunits are mCi (millicurie), μCi (microcurie), nCi (nanocurie), and pCi (picocurie).
1 Ci = 1000 mCi; 1 mCi = 1000 μCi; 1 μCi = 1000 nCi; 1 nCi = 1000 pCi.
Another useful conversion formula is:
1 Bq = 27 pCi.
Becquerel (Bq) or Curie (Ci) is a measure of the rate (not energy) of radiation emission from a source.

## What does half-life mean when people talk about radioactivity?

Radiation intensity from a radioactive source diminishes with time as more and more radioactive atoms decay and become stable atoms. Half-life is the time after which the radiation intensity is reduced by half. This happens because half of the radioactive atoms will have decayed in one half-life period. For example a 50 Bq radioactive source will become a 25 Bq radioactive source after one half-life.

**Table 1**
**Radioactive Decay**

| Number of half-lives elapsed | Percent radioactivity remaining |
|---|---|
| 0 | 100 |
| 1 | 50 |
| 2 | 25 |
| 3 | 12.55 |
| 4 | 6.25 |
| 5 | 3.125 |

Half-lives widely differ from one radioactive material to another and range from a fraction of a second to millions of years.

## What units are used for measuring radiation energy?

The energy of ionizing radiation is measured in electronvolts (eV). One electronvolt is an extremely small amount of energy. Commonly used multiple units are kiloelectron (keV) and megaelectronvolt (MeV).
6,200 billion MeV = 1 joule

1 joule per second = 1 watt
1 keV = 1000 eV, 1 MeV = 1000 keV
Watt is a unit of power, which is the equivalent of energy (or work) per unit time (e.g., minute, hour).

## What units are used for measuring radiation exposure?

X-ray and gamma-ray exposure is often expressed in units of roentgen (R). The roentgen (R) unit refers to the amount of ionization present in the air. One roentgen of gamma- or x-ray exposure produces approximately 1 rad (0.01 gray) tissue dose (see next section for definitions of gray (Gy) and rad units of dose).

Another unit of measuring gamma ray intensity in the air is "air dose or absorbed dose rate in the air" in grays per hour (Gy/h) units. This unit is used to express gamma ray intensity in the air from radioactive materials in the earth and in the atmosphere.

## What effects do different doses of radiation have on people?

One sievert is a large dose. The recommended TLV is average annual dose of 0.05 Sv (50 mSv). The effects of being exposed to large doses of radiation at one time (acute exposure) vary with the dose. Here are some examples:
10 Sv - Risk of death within days or weeks
1 Sv - Risk of cancer later in life (5 in 100)
100 mSv - Risk of cancer later in life (5 in 1000)
50 mSv - TLV for annual dose for radiation workers in any one year
20 mSv - TLV for annual average dose, averaged over five years

## What is the relationship between SI units and non-SI units?

Table 3 shows SI units (International System of Units or Systéme Internationale d'unités), the corresponding non-SI units, their symbols, and the conversion factors.

**Table 3**
**Units of Radioactivity and Radiation Dose**

| Quantity | SI unit and symbol | Non-SI unit | Conversion factor |
|---|---|---|---|
| Radioactivity | becquerel, Bq | curie, Ci | 1 Ci = 3.7 x $10^{10}$ Bq<br>= 37 Gigabecquerels (GBq)<br>1 Bq = 27 picocurie (pCi) |
| Absorbed dose | gray, Gy | rad | 1 rad = 0.01 Gy |
| "Dose"<br>(Equivalent dose) | sievert, Sv | rem | 1 rem = 0.01 Sv<br>1 rem = 10 mSv |

# Measuring Radiation

There are four different but interrelated units for measuring radioactivity, exposure, absorbed dose, and dose equivalent. These can be remembered by the mnemonic **R-E-A-D**, as follows, with both common (British, e.g., Ci) and international (metric, e.g., Bq) units in use:

- **R**adioactivity refers to the amount of ionizing radiation released by a material. Whether it emits alpha or beta particles, gamma rays, x-rays, or neutrons, a quantity of radioactive material is expressed in terms of its radioactivity (or simply its activity), which represents how many atoms in the material decay in a given time period. The units of measure for radioactivity are the curie (Ci) and becquerel (Bq).

- **E**xposure describes the amount of radiation traveling through the air. Many radiation monitors measure exposure. The units for exposure are the roentgen (R) and coulomb/kilogram (C/kg).

- **A**bsorbed dose describes the amount of radiation absorbed by an object or person (that is, the amount of energy that radioactive sources deposit in materials through which they pass). The units for absorbed dose are the radiation absorbed dose (rad) and gray (Gy).

- **D**ose equivalent (or effective dose) combines the amount of radiation absorbed and the medical effects of that type of radiation. For beta and gamma radiation, the dose equivalent is the same as the absorbed dose. By contrast, the dose equivalent is larger than the absorbed dose for alpha and neutron radiation, because these types of radiation are more damaging to the human body. Units fordose equivalent are the roentgen equivalent man (rem) and sievert (Sv), and biological dose equivalents are commonly measured in 1/1000th of a rem (known as a millirem or mrem).

## ***Geiger Müller counter***

**Geiger–Müller counter**

A "two-piece" bench type Geiger–Müller counter with end-window detector.

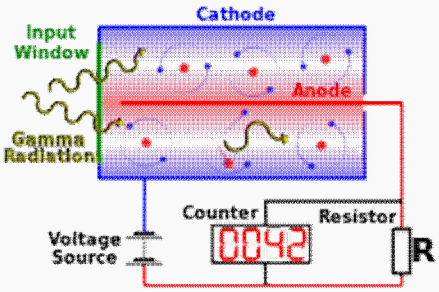
| | |
|---|---|
| **Other names** | Geiger counter |
| **Uses** | Particle detector |
| **Inventor** | Hans Geiger<br>Walther Muller |
| **Related items** | Geiger–Müller tube |

The **Geiger–Müller counter**, also called a **Geiger counter**, is an instrument used for measuring ionizing radiation.

It detects radiation such as alpha particles, beta particles and gamma rays using the ionization produced in a Geiger–Müller tube, which gives its name to the instrument. [1] In wide and prominent use as a hand-held radiation survey instrument, it is perhaps one of the world's best-known radiation instruments.

The original detection principle was discovered in 1908, but it was not until the development of the Geiger-Müller tube in 1928 that the Geiger-Müller counter became a popular instrument for use in such as radiation dosimetry, radiological protection, experimental physics and the nuclear industry. This was mainly due to its robust sensing element and relatively low cost, however there are limitations in measuring high radiation rates and in measuring the energy of incident radiation.[2]

## Principle of operation




Schematic of a Geiger counter using an "end window" tube for low penetration radiation.

*Main article: Geiger-Müller tube*

The Geiger counter consists of two main elements; the Geiger-Müller tube which detects the radiation, and the processing and display electronics. The Geiger-Müller tube is filled with an inert gas such as helium, neon, or argon at low pressure, which briefly conducts electrical charge when a particle or photon of incident radiation makes the gas conductive by ionization. The ionization current is greatly amplified within the tube by the Townsend avalanche effect to produce an easily measured detection pulse. This makes the G-M counter relatively cheap to manufacture, as the subsequent electronic processing is greatly simplified.[2]

The article on the Geiger-Muller tube has a more detailed description of the fundamental ionisation mechanism.

**Readout**

There are fundamentally two types of radiation readout; counts or radiation dose. The counts display is the simplest and is the number of ionizing events displayed either as a count rate, commonly "counts per second", or as a total over a set time period (an integrated total). The counts readout is normally used when alpha or beta particles are being detected. More complex to achieve is a display of radiation dose rate, displayed in a unit such as the sievertwhich is normally used for measuring gamma or X-ray dose rates. However a G-M tube can detect the presence of radiation, but not its energy which also influences the radiation's ionising effect. Consequently, dose rate measurement requires the use of an energy compensated G-M tube, so that the dose displayed relates to the counts detected.[2] The electronics will apply known factors to make this conversion, which is specific to each instrument and is determined by design and calibration.

The readout can be analog or digital, and increasingly, modern instruments are offering serial communications with a host computer or network.

There is usually an option to produce audible clicks representing the number of ionization events detected. This is the distinctive sound normally associated with hand held or portable Geiger counters. The purpose of this is to allow the user to concentrate on manipulation of the instrument whilst retaining auditory feedback on the radiation rate.

The electronics also generates the relatively high voltage, typically 400–600 volts, that has to be applied to the Geiger-Müller tube to enable its operation.

**Limitations**

There are two main limitations of the Geiger counter. Because the output pulse from a Geiger-Müller tube is always the same magnitude regardless of the energy of the incident radiation, the tube cannot differentiate between radiation types.[2] A further limitation is the inability to measure high radiation rates due to the "dead time" of the tube. This is an insensitive period after each ionization of the gas during which any further incident radiation will not result in a count, and the indicated rate is therefore lower than actual. Typically the dead time will reduce indicated count rates above about $10^4$ to $10^5$ counts per second depending on the characteristic of the tube being used.[2] Whilst some counters have circuitry which can compensate for this, for accurate measurements ion chamber instruments are preferred for high radiation rates.

Types and applications

G-M counter with pancake type probe

Laboratory use of a G-M counter with end window probe to measure beta radiation from a radioactive source

The application and use of a Geiger counter is dictated entirely by the design of the tube, of which there are a great many, but they can be generally categorised as "end-window", or windowless "thin-walled" or "thick-walled", and sometimes hybrids of these types.

**Particle detection**

The first historical uses of the Geiger principle were for the detection of alpha and beta particles, and the instrument is still used for this purpose today. For alpha particles and low energy beta particles the "end-window" type of G-M tube has to be used as these particles have a limited range even in free air, and are easily stopped by a solid material. Therefore the tube requires a window which is thin enough to allow as many as possible of these particles through to the fill gas. The window is usually made of mica with a density of about 1.5 - 2.0 mg/cm$^2$. [1]

Alpha particles have the shortest range, and to detect these the window should ideally be within 10mm of the radiation source due to alpha particle attenuation in free air.[1] However, the G-M tube produces a pulse output which is the same magnitude for all detected radiation, so a Geiger counter with an end window tube cannot distinguish between alpha and beta particles.[2] A skilled operator can use distance to differentiate alpha and high energy beta, but with the detector in close contact with the radiation source the types are indistinguishable. The "pancake" Geiger-Muller detector is a variant of the end window probe, but designed with a larger detection area to make checking quicker. However the pressure of the

atmosphere against the low pressure of the fill gas limits the window size due to the limited strength of the window membrane.

High energy beta particles are can also be detected by a thin-walled "windowless" G-M tube, which has no end window. Although the tube walls have a greater stopping power than a thin end window, they still allow these more energetic particles to reach the fill gas.[1]

End-window G-M detectors are still used as a general purpose portable Radioactive contamination measurement and detection instrument, owing to their relatively low cost, robustness and their relatively high detection efficiency; particularly with high energy beta particles.[2]However for discrimination between alpha and beta particles or provision of particle energy information, scintillation counters or proportional counters should be used.[3] Those instrument types are manufactured with much larger detector areas, which means that checking for surface contamination is quicker than with a G-M instrument.

**Gamma and X-ray detection**

Geiger counters are widely used to detect gamma radiation, and for this the windowless tube is used. However, efficiency is generally low due to the poor interaction of gamma rays compared with alpha and beta particles. For instance, a chrome steel G-M tube is only about 1% efficient over a wide range of energies.[1]

## Precautions to be Taken in Handling of Radiopharmaceuticals

Great care has to be taken in handling storage of radioactive material for protecting people and personnel who handle it:
i) The working areas should not get contaminated with radioactive material.
ii) If the radioactive liquid has to be handled, it must be carried in trays having absorbent tissue paper so that any spillage will get absorbed by paper.
iii) Rubber gloves have to be used when working with radioactive liquids.
iv) Pipettes operated by mouth should never be employed. Before making use of glass apparatus, it must be ensured that they have been inactive. The waste radioactive materials have to be stored till the activity becomes low before its disposal.
v) Smoking, eating, drinking activities are prohibited in the area of radioactive work.
vi) The radioactive emitter should be handled with forceps and never by hand.
vii) Sufficient shielding device should be used.
viii) Radioactive materials have to be stored in suitable labeled containers, shielding by bricks and preferably in a remote corner.
ix) Great care has to be applied for disposal of radioactive materials.
x) A regular monitoring of radioactivity be done in area where radioactive material is stored.

**TABLE** Approximate Radiation Dose Rates at 1 Meter from Nuclear Medicine PatientsAdapted from sources and magnitude of occupational and public exposures from nuclear medicine procedures: Report no. 124. Bethesda, Md.: National Council on Radiation Protection and Measurements; 1996.

| STUDY | RADIOPHARMACEUTICAL | ADMINISTERED ACTIVITY, mCi (mBq) | TIME AFTER ADMINISTRATION (hr) | DOSE RATE, mrad/hr (µGy/hr) |
|---|---|---|---|---|
| Bone | $^{99m}$Tc-MDP | 20 (740) | 0 | 0.9 (9) |
| | | 20 (740) | 3 | 0.35 (3.5) |
| Blood pool | $^{99m}$Tc red blood cells | 20 (740) | 0 | 1.4 (14) |
| Heart | $^{201}$Tl-chloride | 20 (740) | 0 | 2 (20) |
| | $^{99m}$Tc-sestamibi | 20 (740) | 0 | 0.9 (9) |
| Liver | $^{99m}$Tc sulfur-colloid | 4 (148) | 0 | 0.2 (2) |
| Tumor/infection | $^{67}$Ga citrate | 3 (111) | 0 | 0.35 (3.5) |
| Tumor | $^{18}$F-FDG | 10 (370) | 0 | 30 (300) |
| | $^{18}$F-FDG | 10 (370) | 0-1 | 10 (100) |
| | $^{18}$F-FDG | 10 (370) | 1 | 5 (50) |
| Thyroid cancer therapy | $^{131}$I-sodium-iodide$^{131}$I-sodium-iodide$^{131}$I-sodium-iodide$^{131}$I-sodium-iodide | 100 (3700)100 (3700)100 (3700)100 (3700) | 0122472 | 22 (220)12 (120)11 (110)1.8 (18) |

*DTPA,* Diethylenetriamine pentaacetic acid; $^{18}$*F-FDG,* fluorine-18 fluorodeoxyglucose; *67Ga,* gallium-67;*111In,* indium-111; *MDP,* methylene diphosphonate; *99mTc,* technetium-99m; *201Tl,* thallium-201.

## Uses of Radiopharmaceuticals

Radioisotopes are extensively used in medicine for diagnosis, either *in vivo*or *in vitro*, for therapeutics and also for investigation purposes. Nuclear medicine (NM) studies *in vivo* are used to detect minimal amounts of radiopharmaceuticals in organs (the morphology) and their course over time (the function), resulting from physico-chemical interactions of the tracers within the body, in the sequence of specific physiological processes.*In vitro* applications of radioisotopes have become a most important tool in biochemical analysis. Therapeutic uses of radioisotopes cover from external gamma-ray sources in teleradiotherapy to direct cell irradiation in metabolic therapy.[3]
As described above radioisotopes find use in medicine in four different ways. They are:

1. Radioactive tracers for diagnostic purposes

2. Radiation source in therapy

3. Research and

4. Sterilization

The radioisotope therapy has been available to those disease conditions in which extensive cellular malfunction exists. [4]
**Diagnostic radiopharmaceuticals** are used to derive detailed description of the morphology and dynamic functioning of the various internal organs of the body. The radiopharmaceutical accumulated in an organ of interest emit gamma radiation which are used for imaging of the organs with the help of an external imaging device called gamma
camera
. A typical example is the imaging of a neuro-endocrine-tumour using $^{131}$I-meta-iodobenzyl guanidine (mIBG).
The following are examples of radiopharmaceuticals, which are in practice worldwide for various diagnostic purposes[5]-

- Abscess and infection—Gallium Citrate Ga 67, Indium In 111 Oxyquinoline
- Appendicitis—Technetium (99m Tc) Fanolesomab
- Biliary tract blockage—Technetium Tc 99m Disofenin, Technetium Tc 99m Lidofenin, Technetium Tc 99m Mebrofenin
- Blood volume studies—Radioiodinated Albumin, Sodium Chromate Cr 51
- Blood vessel diseases—Sodium Pertechnetate Tc 99m
- Blood vessel diseases of the brain—Ammonia N 13, Iofetamine I 123, Technetium Tc 99m Bicisate, Technetium Tc 99m Exametazime, Xenon Xe 133
- Bone diseases—Sodium Fluoride F 18, Technetium Tc 99m Medronate, Technetium Tc 99m Oxidronate, Technetium Tc 99m Pyrophosphate, Technetium Tc 99m (Pyro- and trimeta-) Phosphates
- Bone marrow diseases—Sodium Chromate Cr 51, Technetium Tc 99m Albumin Colloid, Technetium Tc 99m Sulfur Colloid
- Brain diseases and tumors—Fludeoxyglucose F 18, Indium In 111 Pentetreotide, Iofetamine I 123, Sodium Pertechnetate Tc 99m, Technetium Tc 99m Exametazime, Technetium Tc 99m Gluceptate, Technetium Tc 99m Pentetate
- Cancer; tumors—Fludeoxyglucose F 18, Gallium Citrate Ga 67, Indium In 111 Pentetreotide, Indium In 111 Satumomab Pendetide, Methionine C 11, Radioiodinated Iobenguane, Sodium Fluoride F 18, Technetium Tc 99m Arcitumomab, Technetium Tc 99m Nofetumomab Merpentan
- Colorectal disease—Technetium Tc 99m Arcitumomab
- Disorders of iron metabolism and absorption—Ferrous Citrate Fe 59
- Heart disease—Ammonia N 13, Fludeoxyglucose F 18, Rubidium Rb 82, Sodium Pertechnetate Tc 99m, Technetium Tc 99m Albumin, Technetium Tc 99m Sestamibi, Technetium Tc 99m Teboroxime, Technetium Tc 99m Tetrofosmin, Thallous Chloride Tl 201
- Heart muscle damage (infarct)—Ammonia N 13, Fludeoxyglucose F 18, Rubidium Rb 82, Technetium Tc 99m Pyrophosphate, Technetium Tc 99m (Pyro- and trimeta-) Phosphates, Technetium Tc 99m Sestamibi, Technetium Tc 99m Teboroxime, Technetium Tc 99m Tetrofosmin, Thallous Chloride Tl 201
- Impaired flow of cerebrospinal fluid in brain—Indium In 111 Pentetate

- Kidney diseases—Iodohippurate Sodium I 123, Iodohippurate Sodium I 131, Iothalamate Sodium I 125, Technetium Tc 99m Gluceptate, Technetium Tc 99m Mertiatide, Technetium Tc 99m Pentetate, Technetium Tc 99m Succimer
- Liver diseases—Ammonia N 13, Fludeoxyglucose F 18, Technetium Tc 99m Albumin Colloid, Technetium Tc 99m Disofenin, Technetium Tc 99m Lidofenin, Technetium Tc 99m Mebrofenin, Technetium Tc 99m Sulfur Colloid
- Lung diseases—Krypton Kr 81m, Technetium Tc 99m Albumin Aggregated, Technetium Tc 99m Pentetate, Xenon Xe 127, Xenon Xe 133
- Parathyroid diseases; parathyroid cancer—Technetium Tc 99m Sestamibi, Thallous Chloride Tl 201
- Pernicious anemia; improper absorption of vitamin $B_{12}$ from intestines—Cyanocobalamin Co 57
- Red blood cell diseases—Sodium Chromate Cr 51
- Salivary gland diseases—Sodium Pertechnetate Tc 99m
- Spleen diseases—Sodium Chromate Cr 51, Technetium Tc 99m Albumin Colloid, Technetium Tc 99m Sulfur Colloid
- Stomach and intestinal bleeding—Sodium Chromate Cr 51, Sodium Pertechnetate Tc 99m, Technetium Tc 99m (Pyro- and trimeta-) Phosphates, Technetium Tc 99m Sulfur Colloid
- Stomach problems—Technetium Tc 99m Sulfur Colloid
- Tear duct blockage—Sodium Pertechnetate Tc 99m
- Thyroid diseases; thyroid cancer—Fludeoxyglucose F 18, Indium In 111 Pentetreotide, Radioiodinated Iobenguane, Sodium Iodide I 123, Sodium Iodide I 131, Sodium Pertechnetate Tc 99m, Technetium Tc 99m Sestamibi
- Urinary bladder diseases—Sodium Pertechnetate Tc 99m

**Therapeutic Radiopharmaceuticals** are radiolabeled molecules designed to deliver therapeutic doses of ionizing radiation to specific diseased sites. Therapeutic applications of radiopharmaceuticals have emerged from the concept that certain radionuclides possessing particulate emission such as alpha and beta radiations or low-energy low-range electrons (Auger electrons) possess the ability to destroy diseased tissues.
The dual facets of these agents constitute either curative or palliative measures in treatment modalities. Table 2 lists the usual routes of administration of radiopharmaceuticals.

Contrary to the usual requirement that intravenous injections be true solutions, some radiopharmaceuticals are deliberately particulate to achieve site-specific localization of radioactivity in the body. These specialized dosage forms permit imaging of, for example, the principal organs of the reticuloendothelial system (liver, spleen, and bone marrow) with radiolabeled colloidal particles, the cardiac blood pool with radiolabeled red blood cells, and lung perfusion with albumin aggregates.

Radioisotopes may be used internally or externally. If the radioisotopes are used externally or as implants in sealed capsules in a tissue, the dose could be terminated by removal of the sources. If they are given internally as unsealed source, the dose cannot be stopped by removal of the source. The total dose in therapeutic applications may be calculated on the basis of effective half- life of the isotope, concentration of the isotope and the type and energy of radiation emitted.

Research – Excellent biological and medicinal studies have been carried out with radioactive isotopes as tracers. Modern knowledge of many biochemical processes has been the cause of such elaborate studies $^{14}_{6}$ C and $^{3}_{1}$H are most commonly used radionuclides for this purpose.
Sterilization – Excellent use is being made of the radiation constantly available from some strong radiation sources for sterilizing pharmaceuticals in their final packed containers and surgical instruments in hospitals. The radiation does not destroy or harm most pharmaceuticals. No heat or chemicals get involve.

Thermolabile substance such as vitamins, hormones, antibiotics etc can be safely sterilized $^{60}_{27}$Co or Cesium-37 may be used for sterilizing surgical instruments. It also finds use for sterilizing pharmaceuticals.[7]

## HAZARDS OF RADIOACTIVE MATERIALS

### BIOLOGICAL EFFECTS

Interaction of X-rays or gamma rays with matter causes ionization, resulting in the production of negatively charged electrons and positively charged ions. Electrons will travel short distances, and can produce further ionization.

Positive ions can bring about chemical changes, which are the prime cause of radiation injury.

The most significant effect of the interaction of radiation with tissues is radiolysis of water. Initially, absorption of energy by water molecules leads to the ejection of electrons. The resulting positively charged ion dissociates to produce a hydrogen ion and a hydroxide free radical. Electrons react with further water molecules to produce hydroxide ions and hydrogen free radicals. It is the production of these highly reactive free radicals, either electron-acceptors or electron donors, which induces subsequent damage.

At the molecular level, free radicals can initiate strand breakage in DNA, or disruption in the structure of protein molecules. An outward manifestation of this molecular damage can occur at different times after the event, depending on the extent of the initial exposure and the nature of the molecular damage. For instance, if double-strand breakage in a DNA molecule occurs, there is little chance of repair. Cell death may occur, or cell abnormality and mutation may be transmitted to daughter cells, leading to possible malignancy. Abnormality in germinal cells may lead to offspring inheriting abnormal characteristics.

### RADIATION RISKS

All clinical procedures involving the exposure of subjects to ionizing radiations involve risk. It is part of the philosophy of current regulations and guidance that the risk is minimized and also justified.[8] In other words, an assessment of the associated risks and benefits of any procedure should be made before that procedure is performed.

Therapeutic procedures will naturally carry a much greater intrinsic risk than diagnostic ones, simply because the administered doses are so much higher, sometimes by several orders of magnitude.
The potential benefits are, however, also very high, because in many instances treatment of medical conditions with ionizing radiation is performed in cases of life-threatening disease.

Risk/benefit analysis during diagnosis is often more difficult to perform. It is true that the radiation doses are lower than those used during therapeutic procedures, but at the same time, there is no direct benefit in terms of a tangible therapeutic effect. Benefits accrue later if the diagnostic procedure leads to an outcome, which has a direct bearing on the way the patient is subsequently managed, either by suggesting a particular therapeutic regime, or sometimes by suggesting that a particular course of action should not be adopted. This situation is well illustrated by the procedure adopted for assessment of the presence of pulmonary embolism by lung scanning. The outcome may be a negative result, which means that anticoagulant therapy is not indicated. In the case of patients presenting shortly after major surgery, this is of significant benefit, and the small risk associated with the radiation exposure is well justified.

The risks associated with all nuclear medicine procedures have been quantified and have associated with them a factor known as the "effective dose", expressed in units of milliSieverts.

This is defined as the sum of equivalent doses in all tissues and organs, weighted using tissue weighting factors specified by the International Commission on Radiological Protection. Adherence to these levels of exposure is assured through a system of prior authorizations on the part of doctors performing the procedures. The system sets out reference levels for the doses of radioactive substance, which should not normally be exceeded during the performance of any diagnostic procedure.[9]
Direct influences relate to the potential alteration in biodistribution, which can lead to the delivery of unnecessary radiation doses to organs or areas of the body.

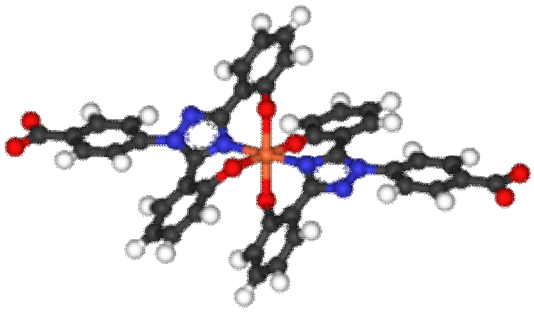
Indirect influences also arise from changes in biodistribution, but relate to interpretation of the images produced by these altered biodistributions. Pathological conditions may be masked, leading to misinterpretation and incomplete or inaccurate reporting. This, in turn can result in the adoption of inappropriate patient management regimes, or may require investigations to be repeated, resulting in additional radiation exposure. In order to understand the significance of inappropriate product quality, it is necessary to know some biological effects of radiation.

# Chelation therapy

**Chelation therapy** is a medical procedure that involves the administration of chelating agents to remove heavy metals from the body. Chelation therapy has a long history of use in clinical toxicology [1] and remains in use for some very specific medical treatments, although it is administered under very careful medical supervision due to various inherent risks.[2]

Chelation therapy must be administered with care as it has a number of possible side effects, including death.[3] In response to increasing use of chelation therapy as alternative medicine and in circumstances in which the therapy should not be used in conventional medicine, various health organizations have confirmed that medical evidence does not support the effectiveness of chelation therapy for any purpose other than the treatment of heavy metal poisoning.[3] Over-the-counter chelation products are not approved for sale in the United States.[4]

**Medical uses**



Two molecules of deferasirox, an orally administered chelator, binding iron. Deferasirox is used in the treatment oftransfusional iron overload in people withthalassemia.

Chelation therapy is used as a treatment for metal poisoning, including acute mercury, iron (including in cases of thalassemia),[5] arsenic, lead, uranium, plutonium and other forms of toxic metal poisoning. The chelating agent may be administered intravenously, intramuscularly, or orally, depending on the agent and the type of poisoning.[6]

Any urine testing for metals should be done before, and not after, the administration of any chelation therapy.[7] Healthy individuals have normal amounts of metal in their bodies which would be removed by chelation therapy, and urine testing after chelation therapy cannot reliably diagnose metal poisoning.[7] Urine testing done after chelation therapy has been associated with harm, including further testing or treatment based on those unreliable results.[7]

**Common chelating agents**

Common chelating agents follow. Each of these will have their own physical characteristics and biological mechanism of action. Several chelating agents are available, having different affinities for different metals. For the most common forms of heavy metal intoxication – lead, arsenic, or mercury – a number of chelating agents are available. Dimercaptosuccinic acid (DMSA) has been recommended for the treatment of lead poisoning in children by Poison Centers around the world.[8] Other chelating agents, such as 2,3-dimercapto-1-propanesulfonic acid (DMPS) and alpha lipoic acid (ALA), are used inconventional and alternative medicine. Some common chelating agents are EDTA (ethylenediaminetetraacetic acid), DMPS (2,3-dimercaptopropanesulfonic acid), TTFD (thiamine tetrahydrofurfuryl disulfide), and DMSA (2,3-dimercaptosuccinic acid). Calcium-disodium EDTA and DMSA are only approved for the removal of lead by the Food and Drug Administration while DMPS and TTFD are not approved by the FDA. These drugs bind to heavy metals in the body and prevent them from binding to other agents. They are then excreted from the body. The chelating process also removes vital nutrients such as vitamins C and E, therefore these must be supplemented.[9]

The German Environmental Agency (Umweltbundesamt) listed DMSA and DMPS as the two most useful and safe chelating agents available.[10]

| Chelator | Used in |
|---|---|
| Dimercaprol (British anti-Lewisite; BAL) | • acute arsenic poisoning[11]<br>• acute mercury poisoning[11] |

| | |
|---|---|
| | • lead poisoning (in addition to EDTA)[11]<br>• Lewisite poisoning (for which it was developed as an antidote) |
| Dimercaptosuccinic acid (DMSA) | • lead poisoning[11]<br>• arsenic poisoning[11]<br>• mercury poisoning [11] |
| Dimercapto-propane sulfonate (DMPS) | • severe acute arsenic poisoning[11]<br>• severe acute mercury poisoning[11] |
| Penicillamine | *Mainly in:*<br>• copper toxicity[11]<br>*Occasionally adjunctive therapy in:*<br>• gold toxicity[11]<br>• arsenic poisoning[11]<br>• lead poisoning[11]<br>• rheumatoid arthritis[11] |
| Ethylenediamine tetraacetic acid (calcium disodium versante) ($CaNa_2$-EDTA) | • lead poisoning[11] |
| Deferoxamine and Deferasirox | • acute iron poisoning[11]<br>• iron overload[11] |

**Side effects and safety concerns**

When used properly in response to a diagnosis of harm from metal toxicity, side effects of chelation therapy include dehydration, hypocalcemia, harm to kidneys, increased enzymes as would be detected inliver function tests, allergic reactions, and lowered levels of dietary elements.[12] When administered inappropriately, chelation therapy brings risk of cancer, neurodevelopmental disorder from toxicity, and death.[12]

## Antidote

An **antidote** is a substance which can counteract a form of poisoning.[1] The term ultimately derives from the Greek αντιδιδοναι *antididonai*, "given against".

The antidotes for some particular toxins are manufactured by injecting the toxin into an animal in small doses and extracting the resulting antibodies from the host animals' blood. This results in

an antivenom that can be used to counteract poison produced by certain species of snakes, spiders, and other venomous animals. A number of venoms lack a viable antivenom, and a bite or sting from an animal producing such a toxin often results in death.[citation needed] Some animal venoms, especially those produced by arthropods(e.g. certain spiders, scorpions, bees, etc.) are only potentially lethal when they provoke allergic reactions and induce anaphylactic shock; as such, there is no "antidote" for these venoms because it is not a form of poisoning and anaphylactic shock can be treated (e.g., by the use of epinephrine).

Some other toxins have no known antidote. For example, the poison aconitine – a highly poisonous alkaloid derived from various aconite species – has no antidote, and as a result is often fatal if it enters the human body in sufficient quantities.

### List of antidotes

| Agent | Indication |
|---|---|
| Activated charcoal with sorbitol | used for many oral toxins |
| Theophylline | adenosine poisoning |
| Atropine | organophosphate and carbamate insecticides, nerve agents, somemushrooms |
| Beta blocker | theophylline |
| Calcium chloride | calcium channel blockers, black widow spider bites |
| Calcium gluconate | hydrofluoric acid |
| Chelators such as EDTA, dimercaprol (BAL), penicillamine, and 2,3-dimercaptosuccinic acid (DMSA, succimer) | heavy metal poisoning |
| Cyanide antidote (amyl nitrite, sodium nitrite, or thiosulfate) | cyanide poisoning |
| Cyproheptadine | serotonin syndrome |
| Deferoxamine mesylate | Iron poisoning |
| Digoxin Immune Fab antibody (Digibind and Digifab) | digoxin poisoning |
| Diphenhydramine hydrochloride and benztropine mesylate | Extrapyramidal reactions associated with antipsychotic |
| Ethanol or fomepizole | ethylene glycol poisoning and methanol poisoning |
| Flumazenil | benzodiazepine poisoning |
| Glucagon | beta blocker poisoning and calcium channel blocker poisoning |

## SODIUM THIOSULFATE

**Sodium thiosulfate** ($Na_2S_2O_3$), also spelled **sodium thiosulphate**, is a colorless crystalline compound that is more familiar as thepentahydrate, $Na_2S_2O_3 \cdot 5H_2O$, an efflorescent, monoclinic crystalline substance also called sodium hyposulfite or “hypo”.

The thiosulfate anion is tetrahedral in shape and is notionally derived by replacing one of the oxygen atoms by a sulfur atom in asulfate anion. The S-S distance indicates a single bond, implying that the sulfur bears significant negative charge and the S-O interactions have more double-bond character. The first protonation of thiosulfate occurs at sulfur.

### Industrial production and laboratory synthesis

On an industrial scale, sodium thiosulfate is produced chiefly from liquid waste products of sodium sulfide or sulfur dyemanufacture.[2]

In the laboratory, this salt can be prepared by heating an aqueous solution of sodium sulfite with sulfur or by boiling aqueous sodium hydroxide and sulfur according to this equation:[3]

$$6\ NaOH + 4\ S \rightarrow 2\ Na_2S + Na_2S_2O_3 + 3\ H_2O$$

Upon cooling, sodium thiosulfate crystallizes out of solution.

| Properties | |
|---|---|
| Molecular formula | $Na_2S_2O_3$ |
| Molar mass | 158.11 g/mol (anhydrous)<br>248.18 g/mol (pentahydrate) |
| Appearance | White crystals |
| Odor | Odorless |
| Density | 1.667 g/cm$^3$ |
| Melting point | 48.3 °C (pentahydrate) |
| Boiling point | 100 °C (pentahydrate, - $5H_2O$ decomposition) |
| Solubility inwater | 70.1 g/100 mL (20 °C)[1]<br>231 g/100 mL (100 °C) |
| Solubility | negligible in alcohol |

### Medical Uses

- It has been used as treatment of calciphylaxis in hemodialysis patients with end-stage renal disease.
- It is used as an antidote to cyanide poisoning.[7][8] Thiosulfate serves as a sulfur donor for the conversion of cyanide tothiocyanate (which can then be safely excreted in the urine), catalyzed by the enzyme rhodanase.
- as a topical antifungal agent
- In measuring the volume of extracellular body fluid and the renal glomerular filtration rate.

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