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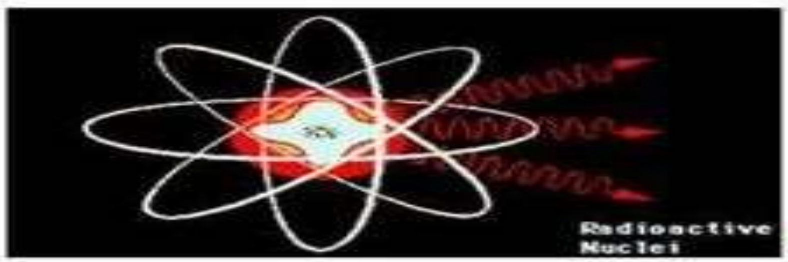


RADIOPHARMACEUTICALS

1. **Write a short note on radiopharmaceuticals/What are radiopharmaceuticals? Enumerate units of radioactivity.**
2. **Properties of alpha, beta and gamma rays/Note on behavioural properties of different radiations.**
3. **Define half life, radioisotopes.**
4. **Give an account of clinical applications of radiopharmaceuticals/Applications of radiopharmaceuticals in medicine. Give a brief account on the therapeutic and diagnostic applications of inorganic radiopharmaceuticals.**
5. **Give an account of precautions to be taken while handling and storage of radiopharmaceuticals or note on handling and storage of radioactive materials.**
6. **Discuss about measurement of radioactivity or S.N on GM counter. Explain working of GM counter or Note on scintillation counter. Write a note on GM counter. Give preparation, properties and uses of Barium sulphate.**
7. **Give uses of Sodium iodide [131], Iron [59 Fe], Cyanocobalamine [57 Co]/study of sodium iodide as radioisotope.**

WHAT ARE RADIOACTIVE SUBSTANCES???? (GTU imp)

- ✓ Radioactive substances have a property of emitting rays or particles which affect the photographic plate. Forty radioactive elements are known which are arranged as Uranium series, Thorium series and Actinium series.

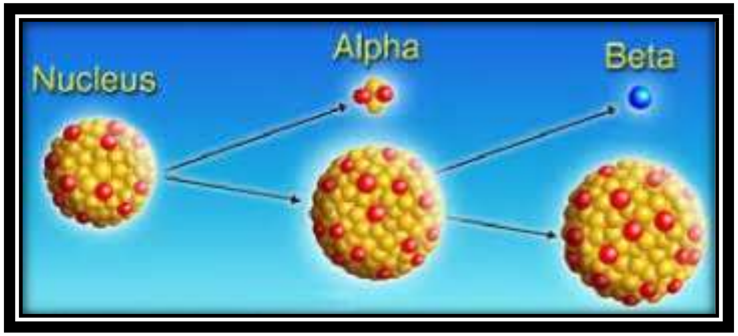
- ✓ The elements are known as radioactive because they are unstable and undergo decomposition along with emission of radiations or rays.

- ✓ The radiations or rays which are emitted are following:

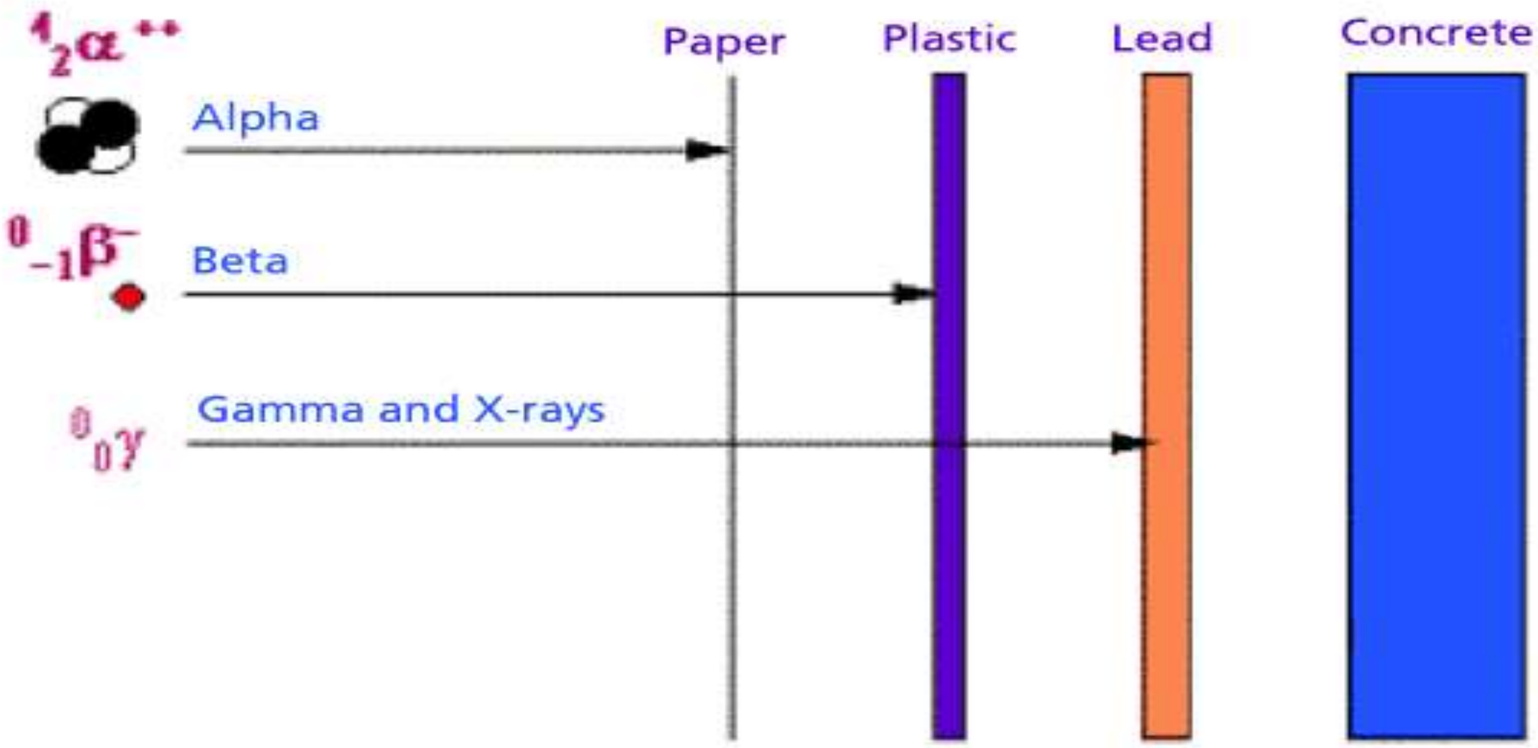
- ❑ Alpha rays
- ❑ Beta rays
- ❑ Gamma rays

- ✓ **Any nucleotide which is not radioactive in nature is regarded as stable. To be stable, a nuclide may possess appropriate energy.**

- ✓ **Those nuclides which undergo spontaneous nuclear change so as to attain stability by emitting radiations are called as radionuclides or radioisotopes.**



Penetrating Distances



Alpha rays

- These rays or particles have low penetrating power.
- They have positive charge and can be detected by a strong magnetic field.
- They carry **two positive charge**.
- They have a mass of **4 amu** (atomic mass unit)
- Heavy metals have capacity to emit such type of rays.
- All alpha particles are having the same energy.
- The penetrating power of alpha rays is less as compared to other emissions.

- **Because of low penetrating power of alpha particles, elements which emit alpha rays do not find use in biological applications because they cannot penetrate tissue.**

- $^{226}_{88}Ra$ --------------------------→ $^{222}_{86}Rn + ^{4}_{2}He$

Beta Rays:

- These have 2 types:

1. Electrically positively charged particles which are called 'positrons'
2. Electrically negatively charged particles which are called 'Negatrons'

- They have greater penetrating power than that of alpha rays.
- Beta particles have negligible mass.
- These particles are usually accompanied by gamma radiation. Beta particles have less ionizing power than alpha particles.

Gamma rays:

- These have been more penetrating than alpha and beta rays.
- They are having the same character as that of very short electromagnetic waves called X-rays.
- **They have no mass or charge.**
- Gamma rays are produced during disintegration of radioactive substances along with **beta radiation** and during nuclear fission.
- They are uncharged and have poor ionizing power.

Type of radiation emitted & symbol	Nature of the radiation formation, structure, relative mass, electric charge	Penetrating power (and speed), and what will block it (more dense material, more radiation is absorbed BUT smaller mass or charge of particle, more penetrating)	Ionising power - the ability to remove electrons from atoms to form positive ions, the process is called ionisation
Alpha particle radiation	**a helium nucleus of 2 protons and 2 neutrons, mass = 4, charge = +2, is expelled at high speed from the nucleus**	**Low penetration**, slowest speed ,biggest mass and charge, stopped by a few cm of air or thin sheet of paper	**Very high ionising power**, the biggest mass and charge of the three radiation's, the biggest 'punch' in ripping off electrons from molecules, other ions are formed
Beta particle	**high kinetic energy electrons**	**Moderate penetration**	**Moderate ionizing power**
Gamma	**Very high frequency electromagnetic radiation mass = 0, charge = 0, gamma emission often accompanies beta decay**	**Very highly penetrating**	**The lowest ionising power**

What are isotopes??

Types of Radionucleotides

1) Natural radionucleotides:

They include about 40 high atomic weight elements such as Uranium 238, Radium 226, which may be alpha, beta, or gamma emitters and also some moderate weight elements such as Potassium 40, Rubidium 87.

2) Artificial Radionucleotides

What are radiopharmaceuticals? Enumerate units of radioactivity.

❖ **Units of radioactivity**

1. **Curie (c) : Defined as quantity of any radioactive substance which undergoes the same number of disintegrations in unit time as of 1 g of radium and is equal to 3.7×10^{10} disintegrations per second.**

2. **Roentgen: it is the unit of exposure $1R = 2.58 \times 10^{-4}$ coulomb kg^{-1}**

3. **RAD: it is the unit of absorbed dose. Pharmaceutical dosage forms are described in RAD units.**

4. **REM: I t is unit of dose equivalent.**

5. **Exposure rate constant**

6. **RBE (Relative biological effectiveness): shows effect of radiation, alpha, beta and gamma on the biological system.**

Production of Radioisotopes:

They are produced as:

1)Reactor irradiation: Reactor is having an arrangement of fissionable material in a moderator, which slows down the fast neutrons to thermal energies. The fissionable material like uranium is taken in the form of rods which are arranged in a lattice pattern and hence the neutron flux is maximum in the centre where there is most uranium. A heavy water moderated reactor using enriched uranium is having a maximum flux of 10^{14} neutrons cm^{-2} s^{-1}

2)Cyclotron irradiation: While the reactors are able to produce a flux of neutrons and gamma rays, accelerating mechanisms can use many other types of bombarding particles which have been charged particles. They can be accelerated to high velocities so as to overcome the repulsive forces of the nucleus. The beam of energetic particles has been small and targets for irradiation have to be put in this beam. The number of samples that can be irradiated at a time has been limited and the yields has been low. But on the other hand many isotopes which otherwise cannot be produced in a reactor could be produced in a cyclotron.

Q: Note on handling and storage of radiopharmaceuticals (GTU Imp.)

- Great care needs to be taken in handling and storage of radioactive materials for protecting people and personnel who handle it, from the harmful radiation they emit.
- Certain precautions have to be taken while working with detectors, tracer equipment, radio assay manufacturing or handling of radioactive materials.

- In order to have protection from hazards of radiation, radioactive materials must be stored in an area not frequently visited by people.
- **Shielding** may be required.
- Thick glass or Perspex containers provide sufficient shielding.
- To protect from gamma rays (high penetration power), **lead shielding** has to be used.
- The storage area must be regularly checked for radioactivity.

RADIOACTIVE LIQUIDS.

- Working area should not get contaminated with radioactive material.

- If radioactive liquid is to be handled, it must be carried in **trays with absorbent tissue paper**, so that any spillage will get absorbed by the paper.

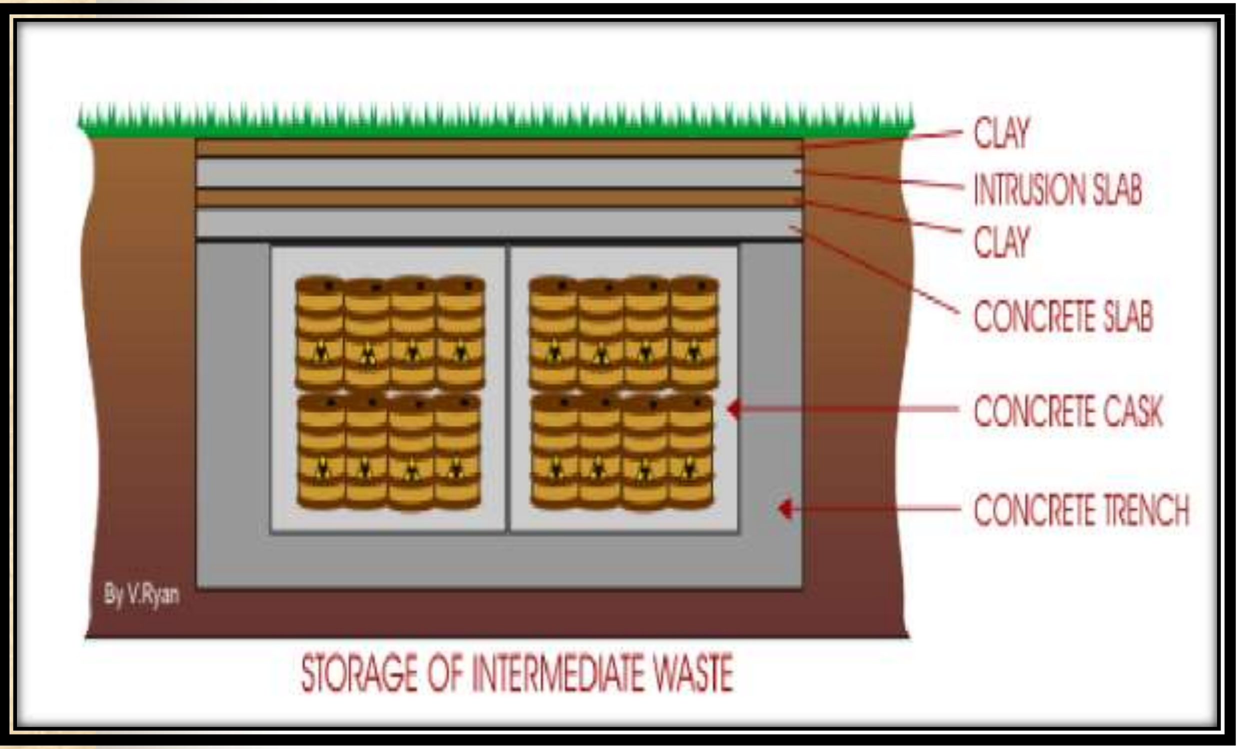
- **Rubber gloves** have to be used when working with radioactive liquids.
- **Pipettes** operated by mouth should never be used.
- Waste of radioactive material has to be stored till its activity becomes low and then only it should be disposed.

PRECAUTIONS While handling and storage of radioactive substances:

1. One should not touch the radioactive emitter with hand but it should be handled by means of **forceps.**
2. **Smoking, eating and drinking activities** should not be handled in laboratory where radioactive material is handled.
3. Sufficient protective clothing and shielding have to be used while handling of materials.
4. Radioactive materials have to be stored in suitable labelled containers, covered (shielded by lead bricks) and preferably in a remote corner.
5. Areas where radioactive materials are stored should be monitored and tested for radioactivity regularly.
6. **Disposal of radioactive materials should be carried out with great care.**

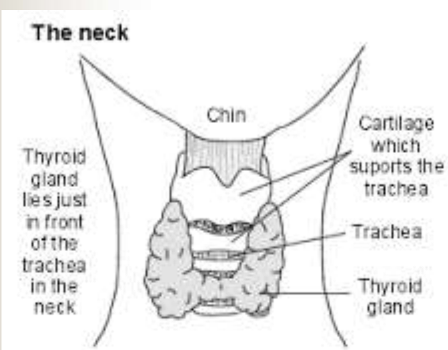
Strict requirements are prescribed by the department of Atomic energy (DAE) for the establishment of a radioactive facility in the hospital or pharmacy.

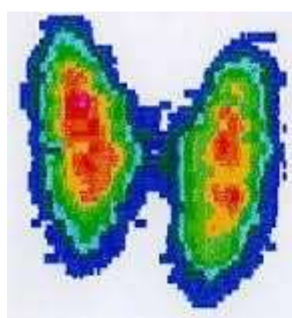
These include specifications for premises, storage space, working area, disposal protocol, training of personnel, periodic check on contamination or leakage.

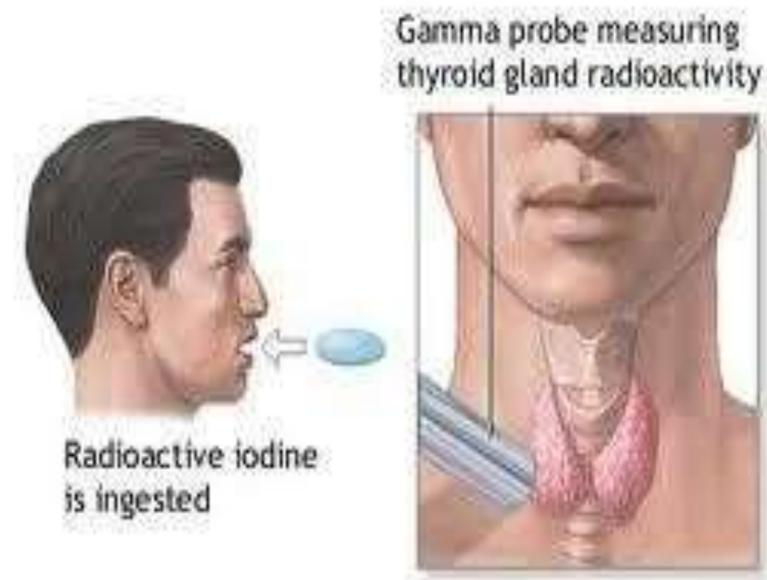


Give uses of Sodium iodide I-131

- Used as a **diagnostic aid** for studying the functioning of the thyroid gland.
- Used in scanning the thyroid for determining the **size, position and possible tumour location.**
- **Used in the treatment of severe cardiac disease (Sodium iodide I-131), which reduces work load on heart.**
- **Radioactive iodine in thyroid carcinoma (cancer): The isotope is used most frequently after the surgical removal of cancer to treat any residual tumour tissues.**







ADAM

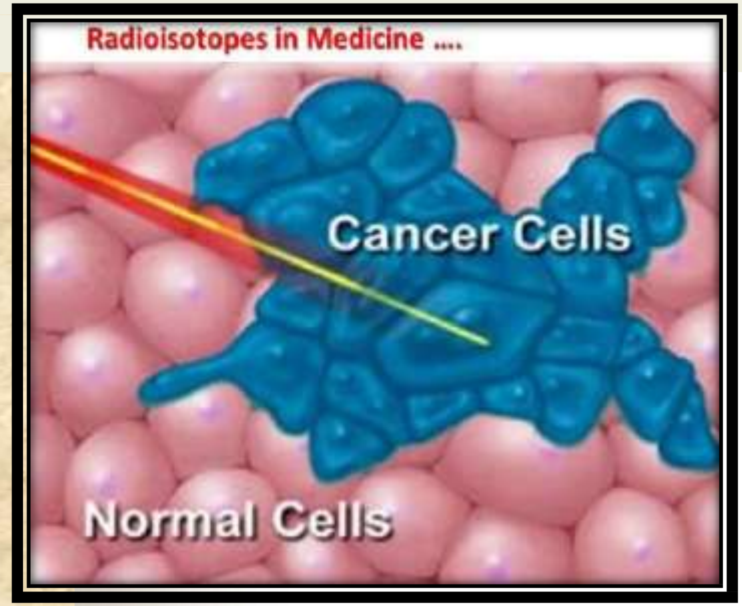
Iron 59:

- ✓ Iron 59 is a beta and gamma emitting isotope.
- ✓ Used in diagnosis to study the iron metabolism and to study the red blood cell formation.
- ✓ The preparation is administered orally for studying the absorption of iron from GIT.
- ✓ Administered I.V to study incorporation of iron in formation of red blood cells.
- ✓ Used to study the formation and destruction of spleen, liver etc. from outside the body.

Applications of Radioisotopes :(GTU imp)

They find use in medicine in 4 different ways:

1. **Radioisotopes in Therapy (Emitted radiations used to destroy cells in condition like cancer)**
2. **Radioisotopes in Diagnosis (Radioactive tracers)**
3. **Research (Biological and medicinal studies by use of radioactive isotopes as tracers)**
4. **Sterilization (For sterilization of pharmaceuticals and surgical instruments)**



Applications:

Diagnostic applications: Radiopharmaceuticals are developed based on the ADME (absorption, distribution, metabolism, excretion) properties of the body. By administering a radiopharmaceutical to a patient, images of the targeted site can be produced by a gamma camera. The images can then be analyzed by the nuclear medicine doctor to detect any medical problems. Radiopharmaceuticals are most widely used to detect various forms of cancer. Depending on the site for diagnosis there is a specified route of administration.

Therapeutic use of Radiopharmaceuticals: Radioactivity can be used in medicine and pharmacy in different areas, the first being radiology, in which an external source of radioactivity passes through a patient and radiation is absorbed by more dense tissues and not by less dense tissues and an image is ultimately formed. The second is radiation therapy, which treats for tumors using an external source of radiation to try and ablate a tumor. This requires lots of radiation in very high doses. Nuclear medicine uses an internal source of radiation to be detected externally, unlike the two previously mentioned. A patient is injected with a radiopharmaceutical, which has a radioactive component that decays and a pharmaceutical component which takes it a desired organ.

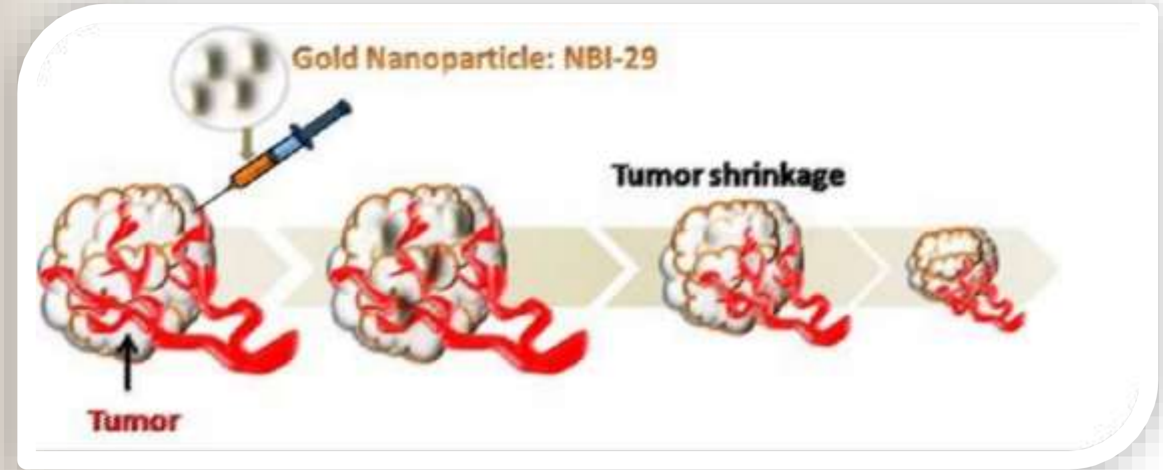
Radiopharmaceuticals can be used to destroy malfunctioning cells. This method of therapy is called radiotherapy. It can be used for both benign and malignant cancers. In order to destroy the diseased tissue, a radionuclide has to emit beta, alpha, or low energy conversion electron emitters. Beta radiation is effective for large tumors and alpha radiation is effective for smaller tumors.

I) In therapeutics:

- The therapeutically used radioisotopes have been found to depend mainly on their ability to **ionize atoms**.
- The energy measurement involved in radiation and resulting in ionization may be expressed in millions of electron volts called MeV.
- **The strength of alpha, beta and gamma rays in expressed in MeV.**
- All radiations bring about ionization of atoms in their paths.
- The radiation of short wavelength (gamma rays) is having high penetrating power than long wavelength (beta rays).
- **The greater the MeV of the rays, the more destructive it becomes to the surrounding tissues.**
- **RADIOPHARMACEUTICALS CAN DESTROY MALFUNCTIONING CELLS.**
- This method of therapy is called **radiotherapy**. It can be used for both benign and malignant cancers.

Examples:

- Gold (^{198}Au) is used in treatment of abdominal and pleural effusions associated with malignant tumours. It is given in the form of colloidal gold suspension.
- Gold (^{198}Au) also used in treatment of carcinoma of uterus and urinary bladder.
- Cobalt labelled cyanocobalamine (vitamin B12) is used in diagnosis of pernicious anaemia.
- **Sodium iodide** preparation finds use in treatment of **thyroid disorders**.
- **Calcium** is used to study bone structure and in **carcinoma of bone**.
- Strontium 90 is used in diagnosis of superficial carcinomas.



- ✓ Radioisotopes may be used internally or externally.
- ✓ If the radioisotope are used externally or used as implants in sealed capsule in a tissue, the dose could be terminated by removal or sources.
- ✓ If they are given internally, as unsealed sources, the dose cannot be stopped by the 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 the radiation emitted.

In diagnosis:

- **Radioactive tracers find use in medicine for diagnostic purposes.**

1. Labelled cyanocobalamine finds use for measuring the **glomerular filtration rate**.
2. **Ferric citrate injection** finds use for the diagnosis of **haematological disorders.**
3. Colloidal gold injection is used diagnostically to study blood circulation in liver.
4. **Sodium iodide injection** finds use in diagnosis of **proper functioning of thyroid gland**.
5. **Sodium iodohippurate** injection finds use in the study of **renal function**.
6. Sodium rose Bengal injection finds use as diagnostic agent to test liver function.

III) In research:

Excellent biological and medicinal studies have been carried out with radioactive isotopes as tracers.

IV) Sterilization:

- Excellent use is being made of the radiation constantly available from some strong radiation source for sterilizing **pharmaceuticals in their final packed containers** and **surgical instruments in hospitals**.
- No heat or chemical gets involved.
- Thermolabile substances like vitamins, hormones antibiotics can be safely sterilized.
- Finds use in sterilization of pharmaceuticals.

Calcium (Ca-44 and Ca-45)	**The radioactive calcium has been used to study bone structure and in treatment of carcinoma of bone.**
Strontium -90	**Used in the radiotherapy of superficial carcinomas.**
Cyanocobalamine (Co-57)	Used in the diagnosis of pernicious anaemia.
Calcium -47	It is having half life of 4.7 days. It is used in calcium absorption studies.
Cyanocobalamine (Co-60 Solution USP)	Used to study absorption and deposition of vitamin B12 in normal individuals.
Gold (Au-198) solution	Finds use in estimation of reticuloendothelial activity.
Iron (Fe-59)	Finds use in research studies about utilization and absorption of Iron salts.

Measurement of Radioactivity

To measure the radiations of alpha, beta and gamma particles, many techniques involving detection and counting of individual particles or photons are used.

The method selected for the measurement of radioactivity depends upon the extent of energy dissipation and penetrability of radiation.

Gas ionization devices:

1) **Ionization chambers**
2) **Proportional counters**
3) **Geiger Muller counters**
4) **Scintillation Counters**
5) **Autoradiography**
6) **Solid state detectors**

1) Ionisation Chambers:

- They are available in various shapes and sizes.
- An ionization chamber consists of a chambers filled with gas and fitted with two electrodes kept at different electrical potentials and a measuring device to indicate the flow of electric current
- Radiation brings about ionization of gas molecules or ions which cause emission of electrons which in turn reveals the changes in electrical potential.

2) Proportional counters:

- **They are modified ionization chambers in which an applied potential ionization of primary electrons causes production of more free electrons which gets carried to the anode.**
- **For each primary electron liberated, much more additional electrons get liberated, the current pulse through electrical circuit is greatly amplified.**
- **The voltage range over which the gas amplification (ionization) occurs is called the proportional region, and the counters working in this region are called Proportional counters.**

3) Geiger-Muller Counter

- These are most popular **radiation detectors**.
- They do not need the use of high gain amplifier.
- **They can detect alpha, beta and gamma radiations.**

- **Geiger-Muller counter is having ionizing gas and is also having a quenching vapour whose functions are:**

1. To prevent the spurious pulses that may get produced due to the positive ions (cations) reaching the cathode (- electrode).
2. To absorb the photons emitted by excited atoms and molecules returning to their ground state.

- **Chlorine and bromine** are generally used as quenching agent.
- **Ethyl alcohol and ethyl formate** are used as organic quenching agents.
- The filling gas pressure has been much below the atmospheric pressure to avoid use of high operating voltages.

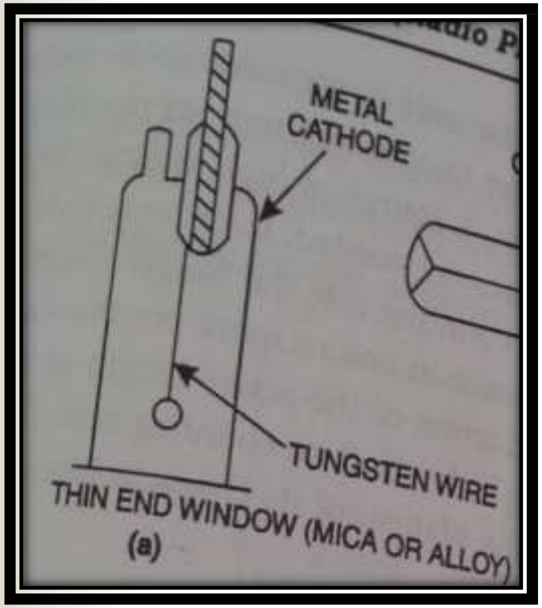
Construction:

- A GM Counter possesses a cylindrical cathode (- electrode) , which is usually 1-2 cm in diameter, along the centre of which is a **wire anode** (+ electrode) .
- The space is filled with a special gas mixture which gets readily ionized together, with a small proportion of quenching vapour.

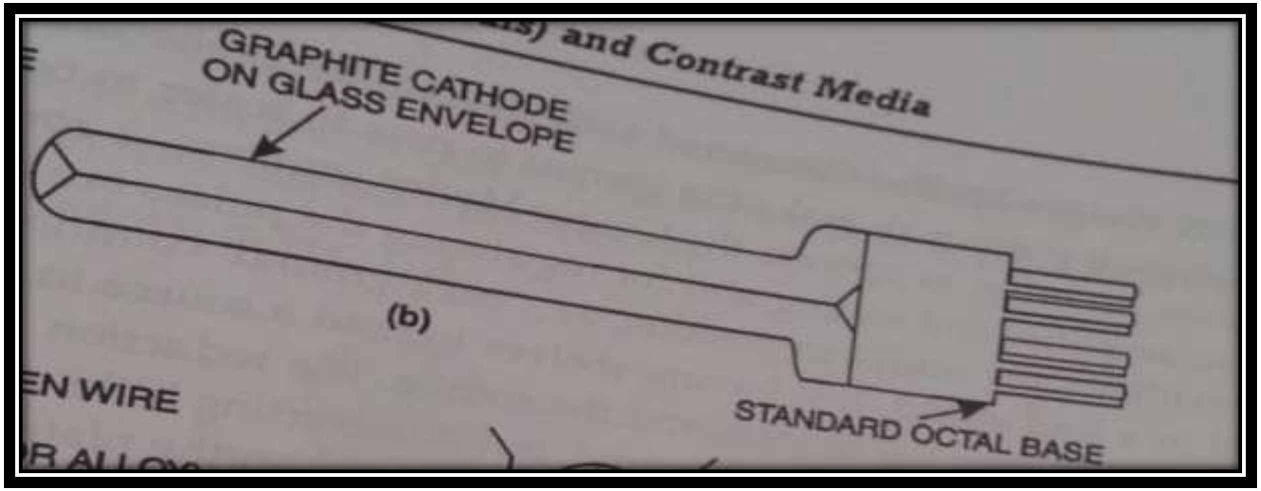
- **For solid radioactive sources**:

✓ For solid radioactive sources, the end window type GM counter has been the most popular.

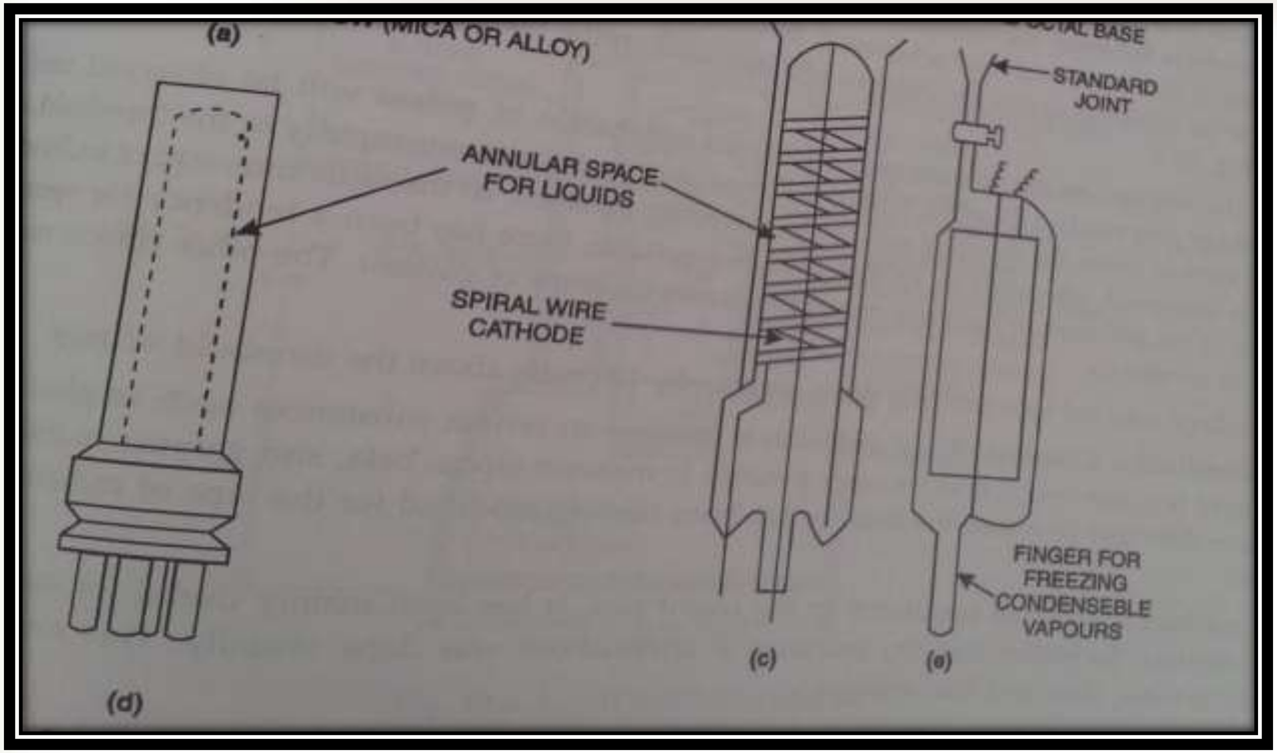
✓ The window has been made of an **aluminium alloy, mica or a thin glass bubble**.



- In order to count the medium and high energy beta particles and for gamma counting, thin glass walled counters may be used.
- They are normally 1 cm in diameter and having a glass wall of 20 – 40 mg cm^{-2} thickness.
- The tube is coated on the inside to form the cathode.



For radioactive liquid sources:



It is having a capacity of 10 cm^3 in annular space. In such a counter 10 cm^3 of 3 % solution of Uranium salt gives nearly 10,000 counts per minute.

Operation:

- When ionizing radiation such as alpha, beta or gamma particle enters the tube, it can ionize some of the gas molecules in the tube.
- From these ionized atoms, an electron is knocked out of the atom and so the remaining atom is positively charged.
- The high voltage in the tube produces an electric field inside the tube.
- The electrons that were knocked out of the atom are attracted to the positive electrode (anode) and the positively charged ions are attracted to the negative electrode (cathode)
- This produces a pulse of current in the wires connecting the electrodes an this pulse is counted.
- After the pulse is counted, the charged ions become neutralized and the Geiger counter is ready to record another pulse.
- In order for the Geiger tube to restore itself quickly to its original state after radiation has entered, a gas is added to the tube.

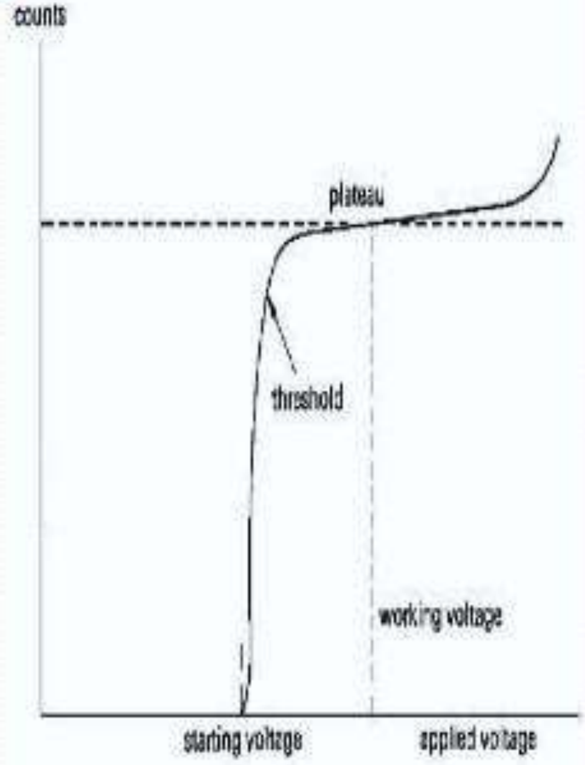
- For proper use of the Geiger counter, one must have appropriate voltage across the electrodes.
- If the voltage is too low, the electric field in the tube is too weak to cause a current pulse. If the voltage is too high, the tube will undergo continuous discharge and it will be damaged.
- For low voltages, no counts are recorded. This is because the electric field is too weak for even one pulse to be recorded. As the voltage is increased, one obtains a counting rate.
- The voltage at which the GM tube just begins to count is called the stating potential. The counting rate quickly rises as the voltage is increased.
- The rise is so fast that the graph looks like a step potential.
- After the quick rise, the counting rate levels 0.This range of voltages is termed as pleateau region.
- Eventually the voltage becomes too high and we have continuous discharge.
- The threshold voltage is the voltage where the plateau region begins. Proper operation is when the voltage is in the plateau region of the curve.
- For best operation, voltage should be selected fairly close to the threshold voltage.

Characteristics of gm counter

- The rate of counting is recorded as function of voltage . A graph between voltage and rate of counting is called ***characteristic curve of counter***

- *When voltage is low counter operates in **ionization chamber** region where there is no gas amplification. The voltage pulse will be small and no counts will be recorded*
- *unless the voltage exceeds v_s the **threshold voltage** .*

- *As voltage increases over v_s counting rate increases as gas amplification sets in and output pulse size increases. This is region of **proportional counter** where more and more low energetic particles are counted until point C is reached . From this point onwards counting rate become constant. The flat region CD is called **plateau of counter**.*



Scintillation counters: (For gamma counting)

- ✓ When radiation is incident on certain substances such as phosphor, a flash of light is given out. It thus becomes possible to measure alpha, beta and gamma radiations by scintillation detectors provided the detector has been suitably modified for the type of radiation to be measured.
- ✓ The scintillation counter consists of a cell, a photomultiplier tube which is coupled with phosphor or fluorescent material to convert scintillation into electrical pulses, amplifier and scaler

Radio-opaque contrast media

- ❖ Radio-opaque substances are those compounds (both inorganic and organic) which are having the property of casting a shadow on X-ray films.
- ❖ These compounds have the ability to stop the passage of X-rays and appear opaque on X-ray examination.

❖ BARIUM SULPHATE

Formula: $BaSO_4$

Preparation:

1. For pharmaceutical purposes, Barium sulphate is prepared by treating an aqueous solution containing Barium ions with a solution containing sulphate ions.

$Ba(OH)_2 + H_2SO_4$ ----------------→ $BaSO_4 + 2H_2O$

$BaCl_2 + H_2SO_4$ ----------------→ $BaSO_4 + 2HCl$

The precipitated salt is washed, dried and screened.

2.It is also prepared by the action of dilute H_2SO_4 on BaS

$BaS + H_2SO_4$ -----------------→ $BaSO_4 + H_2S$

Properties:

- Heavy
- Fine white bulky powder
- Odourless
- Tasteless
- Free from grittiness
- Insoluble in water
- It may be solubilized by fusing with alkali carbonates.

- **Uses:**

- It is used as a diagnostic drug which is used medicinally in X ray examination.
- It is administered by enema before X ray examination in the form of Barium meal to make intestinal tract opaque to X rays, so that it can be photographed.