RADIOISOTOPES

BY: KAMLESH YADAV
(MSC.MEDICAL BIOCHEMISTRY)

INTRODUCTION

An Atom is composed of a positively charged nucleus that is surrounded by a cloud of negatively charged electrons.

The number of orbital electrons is equal to the number of protons present in the nucleus , this number is known as atomic number (Z) .

The sum of protons & neutrons in a given nucleus is the mass number.

$$A = Z + N$$

(N is the number of neutrons)

DEFINITION

ISOTOPES

These are elements with the *same atomic number* but *different mass numbers.*

RADIOISOTOPES

Radioactive isotopes of an element.

RADIOACTIVITY

- Isotopes may be stable or unstable.
- Isotopes containing unstable combination regain stability by shedding radiation or particles.
- Thus, this spontaneous degradation of nucleus and transmutation of one isotope to another with consequent emission of rays or particles is known as ***radioactivity.***

EXAMPLES OF SOME IMPORTANT RADIOISOTOPES

ELEMENT	ISOTOPE	IMPORTANT APPLICATION
Carbon	^{14}C	Research in metabolism
Hydrogen	^{3}H	Research in cell biology
Iodine	^{125}I	Radio immunoassay
Iodine	^{131}I	Treating hyperthyroidism and thyroid cancer
Phosphorus	^{32}P	Nucleic acid research
Radium	^{226}Ra	Treatment of cancer

APPLICATIONS

Radioisotopes are used for the following :

A. Research

B. Diagnostic

C. Therapeutic

RESEARCH

Radioisotopes are used for the study of pathways and there intermediate metabolites.

DIAGNOSTIC APPLICATIONS OF RADIOISOTOPES

- The branch of medicine that deals with the diagnostic applications of radioisotope is referred to as ***nuclear medicine.***
- Diagnostic techniques in nuclear medicine ***use radioactive tracers which emit gamma rays from within the body***.
- These tracers are generally short-lived isotopes ***linked to chemical compounds which permit specific physiological processes to be scrutinized.*** They can be given by injection, inhalation or orally.

Here there are some important application of radioisotopes :

1. **RBC's** can be tagged with ^{51}**Cr**. These cells when injected back will remain in circulation till the RBC is lysed. Therefore life span of RBC and intravascular hemolysis , if any may be detected.
2. **Thyroid** uptake studies by ^{131}**I** are used to detect functional derangement of thyroid gland. In hyperthyroidism there will be increased uptake and in hypothyroidism shows the reverse effect.
3. *Thyroid scanning*. 24 hour after administering the dose of ^{131}I intravenously, the patient is placed under the scanner, which detects the radioactive emissions from the neck region. In hyperthyroidism increased radioactivity uptake is shown as heavily shaded areas. Sometimes the uptake of iodine is seen defective in certain circumscribed region of the gland, such a 'silent nodule' is suggestive of cancer thyroid.

4. ***Bone scanning.*** ^{90}Sr is employed. Osteoblastoma could be detected very early by this method.

5. ***Kidney scanning.*** Done by injecting ^{131}I- labelled hippuran or ^{131}I-labelled diodrast. Both are excreted by kidney within a few minutes after injection. Anatomical and physiological defects in the renal excretion could be easily identified.

6. ***Technetium for blood flow studies.*** Blood flow of heart could be analysed by ^{99m}Tc. The method is sometime called 'nuclear stethoscope'.

7. ***Positron emission tomography scan.*** In this technique2-[^{18}F]fluoro-2-deoxy-glucose(FDG) is used as a molecular probe which is taken up by all cells and gets phosphorylated to FDG-6-Phosphate by hexokinase. Cells accumulate FDG as per the rate of glycolysis. Tumour cells accumulate more FDG since they have higher rate of glycolysis and detected by PET Scan.

8. ***Radioimmuno assay (RIA):*** Assays using ^{125}I labelled antigens are used to quantitate hormones, tumor markers and other biological substances present in blood in very small quantities.

RADIOIMMUNO ASSAY (RIA)

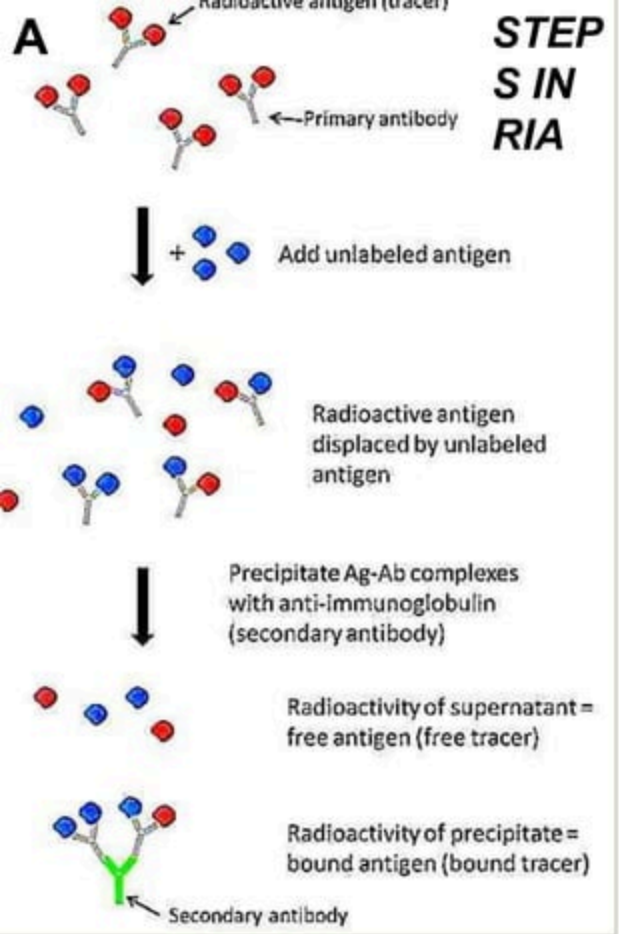
INTRODUCTION

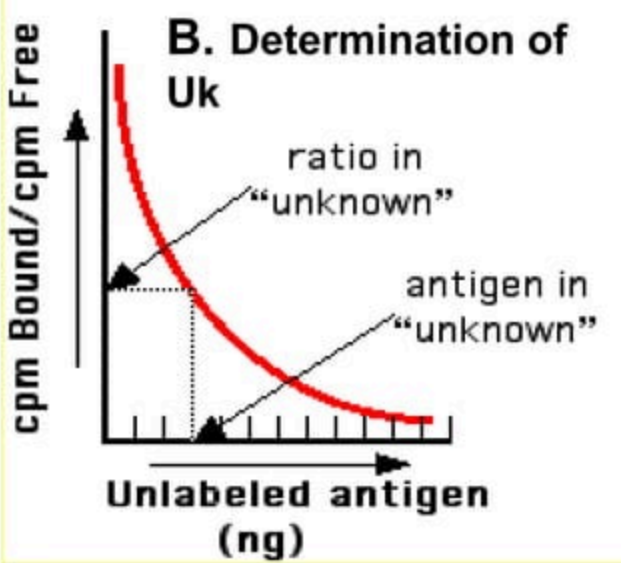
- Developed by Solomon, Benson and Rosalyn in 1959.
- A revolutionary technique to estimate some compounds found in exceedingly low concentration in biological fluids.
- Highly sensitive and specific analytical tool.

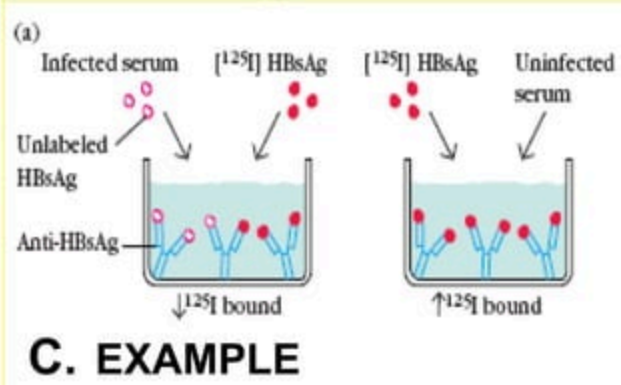
PRINCIPLE

- RIA combines the principles of radioactivity of isotopes and immunological reactions of antigen and antibody.
- The principles of RIA is primarily based on the competition between the labelled and unlabelled antigens to bind with antibody to form antigen-antibody complexes(either labelled or unlabelled).
- The unlabelled antigen is the substance (say insulin) to be determined.
- The antibody to it binds is produced by injecting the antigen to a goat or a rabbit.
- The specific antibody is then subjected to react with unlabelled antigen in the presence of excess amounts of isotopically labelled (^{131}I) antigen with known radioactivity.

- As the concentration of unlabelled antigen increases amount of labelled antigen-antibody complex decreases.
- Thus the concentration of Ag-Ab is inversely related to the concentration of unlabelled Ag i.e. the substance to be determined.
- This relation is almost linear.
- A standard curve can be drawn by using different concentrations of unlabelled antigen and the same quantities of antibody and labelled antigen.


A
STEP S IN RIA
Radioactive antigen (tracer)
Primary antibody
Add unlabeled antigen
Radioactive antigen displaced by unlabeled antigen
Precipitate Ag-Ab complexes with anti-immunoglobulin (secondary antibody)
Radioactivity of supernatant = free antigen (free tracer)
Radioactivity of precipitate = bound antigen (bound tracer)
Secondary antibody


B. Determination of Uk
cpm Bound/cpm Free
ratio in "unknown"
antigen in "unknown"
Unlabeled antigen (ng)


(a)
Infected serum
[125I] HBsAg
[125I] HBsAg
Uninfected serum
Unlabeled HBsAg
Anti-HBsAg
↓125I bound
↑125I bound
C. EXAMPLE

APPLICATIONS OF RIA

Analysis of hormones, vitamins, metabolites, diagnostic markers

- Eg. ACTH, FSH, T3, T4, Glucagon, Insulin, Testosterone, vitamin B12, prostaglandins, glucocorticoids,

Therapeutic drug monitoring:

- Barbiturates, morphine, digoxin,

Diagnostic procedures for detecting infection

- HIV, Hepatitis A, B etc

RADIOIMMUNOASSAY: PROS AND CONS

PROS:

1. Versatility : using the same principle, almost any biomolecules can be assayed.
2. Fast
3. Sensitive (comparable to the most sensitive bioassays, that is < ng/ml)
4. Large capacity : thousands of samples/day specific (antibody-dependent)

CONS

- Use of radioactivity: hazardous
- Expensive equipment
- Requires specially trained persons
- Labs require special license to handle radioactive material
- Requires special arrangements for
  - Requisition, storage of radioactive material
  - radioactive waste disposal.

THERAPEUTIC APPLICATIONS

- Radioisotopes have role in management of malignancies.
- Tumors tissues are attacked by beam of radiation .
- Radioactive material is impregnated into body in form of beads or needles or either as surface applicants .
- ^{131}I is used for treatment of thyroid cancer.
- ^{60}Co or radium rods are used in treatment of cervical cancer .

- **Yttrium^{90} synovectomy is useful in management of arthrites in hemophelics .**

- **^{48}Au (gold) is used for treatment of malignant pleural & peritoneal effusions.**

- **Boron 10 neutron irradiation has been recently used in the treatment of the inoperable & rapidly fatal brain tumour like glioblastoma multiforme.**

RADIATION HAZARDS

- Biological effects of radiation may be divided into two groups:

1. Somatic effect

- It includes immediate effect and delayed effect.
- Immediate effects of radiation leads to acute radiation syndrome characterized by severe nausea, vomiting and prostration due to necrosis and ulceration of the GIT.
- Delayed effects can rise due to chronic exposure to low level of radiation characterized by i) aging effects such as graying of hair, epilation, lenticular cataracts etc. and ii)induction of neoplasm (cancer) such as carcinoma of the skin following radiation, lung cancer following inhalation of radon in uranium mine workers.

2. Genetic effect

Genetic effects result from injury to chromosomes that lead to chromosome mutations, and point mutations that affects gene.

RADIATION SAFETY AND PROTECTION

1. Prevention of External exposure

Methods that help to reduce exposure from external sources are:

- ❑ **Reduce time**
- ❑ **Increase distance**
- ❑ **Use shielding**

2. Prevention of Internal exposure

- ❑ **Limiting inhalation**
- ❑ **Limiting ingestion**
- ❑ **Limiting absorption through skin**
- ❑ **Proper storage**
- ❑ **Proper disposal**


THANK YOU