CHEMICAL MUTAGENES

Chemical mutagens are more harmful than radiations because body is not protected against chemicals.

Source of chemical mutagens are food, air and water.

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Effect of radiation is localized, while chemical mutagens spread in complete body through blood circulation and when they reach in gonads they cause germinal mutation.

Chemicals also cause chromosomal mutations.

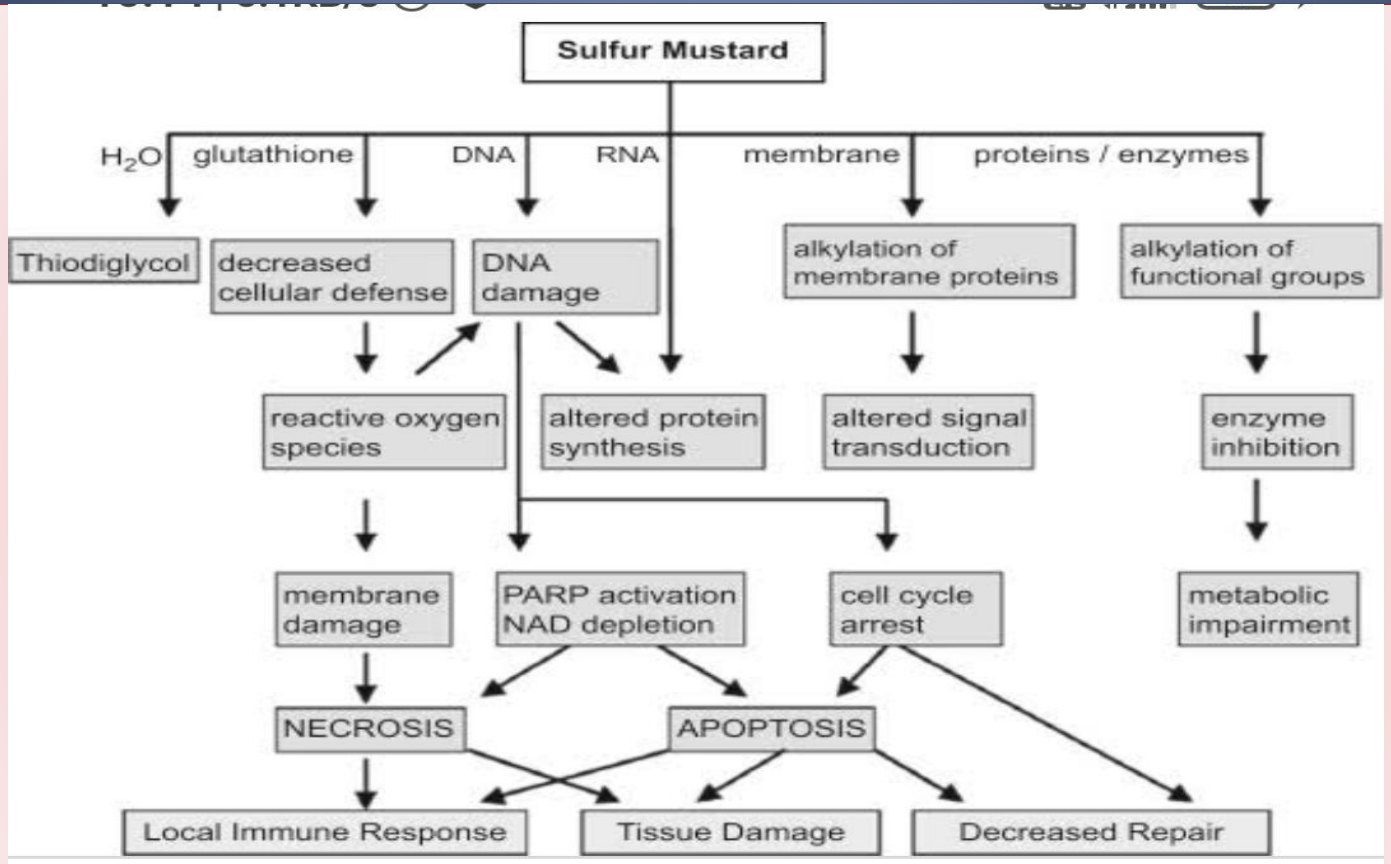
TYPES OF CHEMICAL MUTAGENS

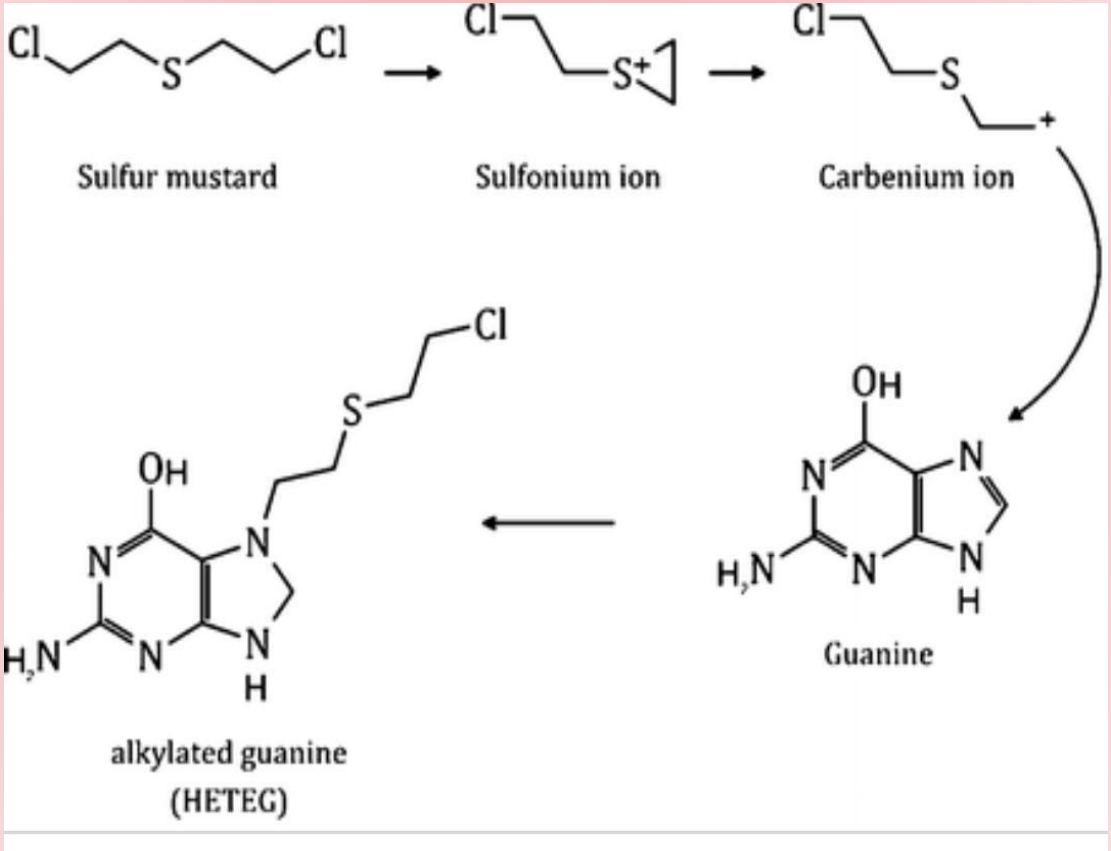
- **Mustard gas**
- **Nitrous acid (HNO_2)**
- **Base Analogues**
- **Alkylating agents**
- **Acredine and proflavin dyes**

Mustard gas

Mustard gas causes genetic damage in all systems in which it was tested.

It caused DNA damage in bacteria and gene mutation in fungi .


Sulfur Mustard
H_2O
glutathione
DNA
RNA
membrane
proteins / enzymes
Thiodiglycol
decreased cellular defense
DNA damage
alkylation of membrane proteins
alkylation of functional groups
reactive oxygen species
altered protein synthesis
altered signal transduction
enzyme inhibition
membrane damage
PARP activation NAD depletion
cell cycle arrest
metabolic impairment
NECROSIS
APOPTOSIS
Local Immune Response
Tissue Damage
Decreased Repair


Cl
S
Cl
Sulfur mustard
Cl
S+
Sulfonium ion
Cl
S
+
Carbenium ion
OH
N
N
H,N
N
N
H
Guanine
Cl
S
OH
N
N
H,N
N
N
H
alkylated guanine
(HETEG)

Adenine ---deamination--→ Hypoxanthine

Guanine ---deamination---→ Xanthine

Cytosine ---deamination---→ Uracil

In first DNA replication, Tautomer of adenine pairs with a normal cytosine and Tautomer of thymine pairs with normal guanine.

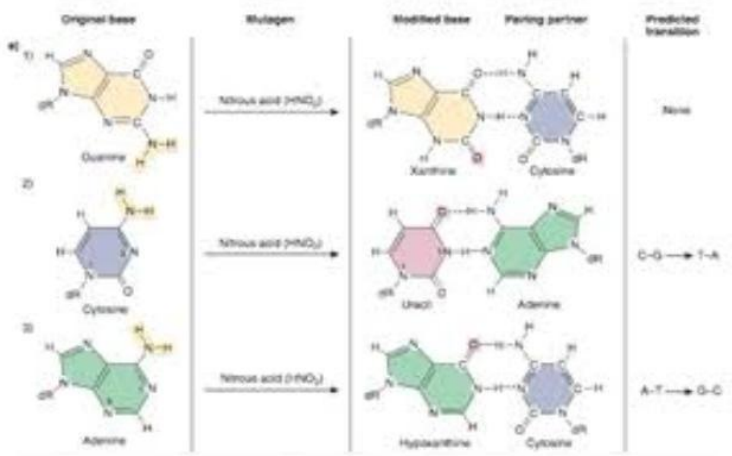
It is unusual pairing which is called as **forbidden pairing** so a wrong type of DNA is formed in cell.

In second DNA replication normal cytosine pairs with normal guanine and normal guanine pairs with normal cytosine.

It is usual pairing so transition completes in two DNA replication (Tautomers always perform forbidden pairing)

Mutations can be induced at any point in the cell cycle

Base-modifying agents: HNO_2



- Nitrous acid (HNO_2) is a **deaminating** agent (removes amino groups - NH_2) from G, C and A bases.
- G to Xanthine (no mutation results).
- C to uracil (C-G to T-A).
- A to hypoxanthine (pairs with C instead of T) --> (A-T to G-C)
- cases 2 and 3 can be reversed by a second treatment of nitrous acid.

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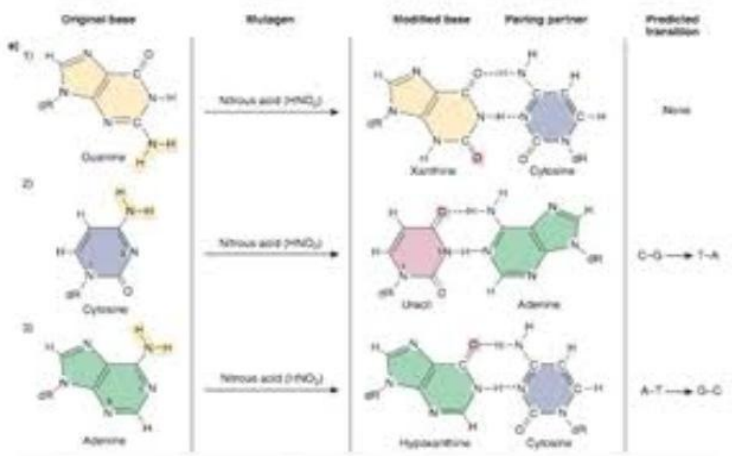

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Base Analogues

Those chemicals which are same as nitrogenous base in function. They are called **base analogues or duplicates of nitrogenous base**.

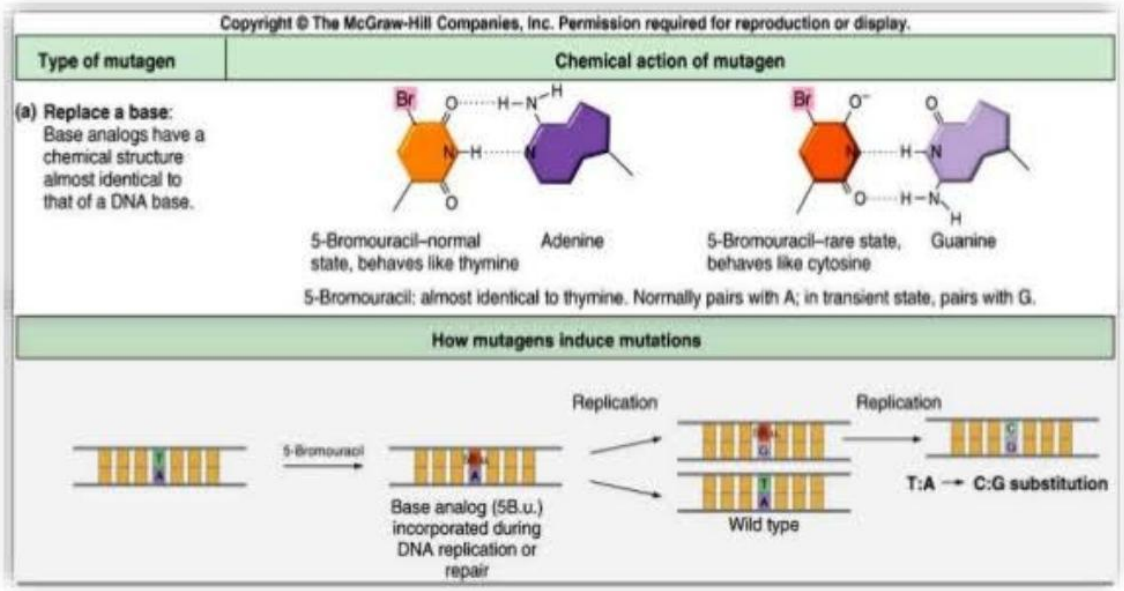
e.g. **Aminopurine** is base analogue to Adenine (purine) **5-Bromo uracil** is base analogue to thymine.

In I DNA replication base analogues get establish in normal structure of DNA.

In II DNA replication they perform forbidden pairing.

In III DNA replication transition is completed.

Chemical Mutagens



Alkylating agents

EMS □ Ethyl methane sulphonate

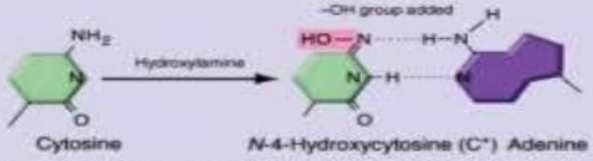
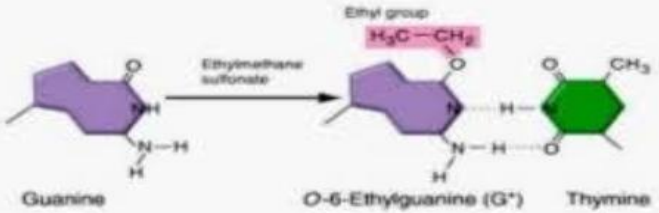
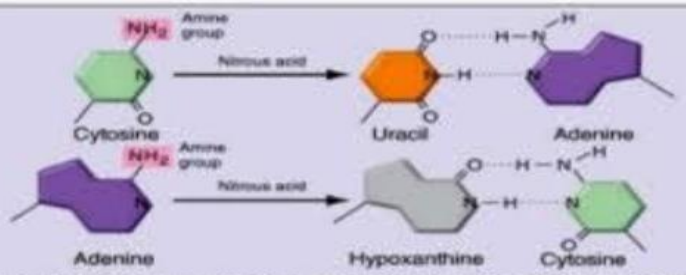
MMS □ Methyl methane sulphonate

These chemicals causes depurination means they remove one purine from structure of DNA. So a gap is formed.

If this gap is filled by another purine then it is called as **transition**.

But if this gap is filled by pyrimidine then it is called as **transversion**.

So EMS and MMS may cause both transition and transversion

Type of mutagen	Chemical action of mutagen
(b) Alter base structure and properties: *Hydroxylating agents*: add a hydroxyl (–OH) group	 Hydroxylamine adds –OH to cytosine; with the –OH, hydroxylated C now pairs with A instead of G.
Alkylating agents: add ethyl ($-CH_2-CH_3$) or methyl ($-CH_3$) groups	 Ethylmethane sulfonate adds an ethyl group to guanine or thymine. Modified G pairs with T above, and modified T pairs with G (not shown).
Deaminating agents: remove amine ($-NH_2$) groups	 Nitrous acid modifies cytosine to uracil, which pairs with A instead of G; modifies adenine to hypoxanthine, a base that pairs with C instead of T.

Acredine and proflavin dyes

They causes loss or addition of one or rarely more than one nitrogenous bases in structure of DNA.
Thus results in frame shift mutation.

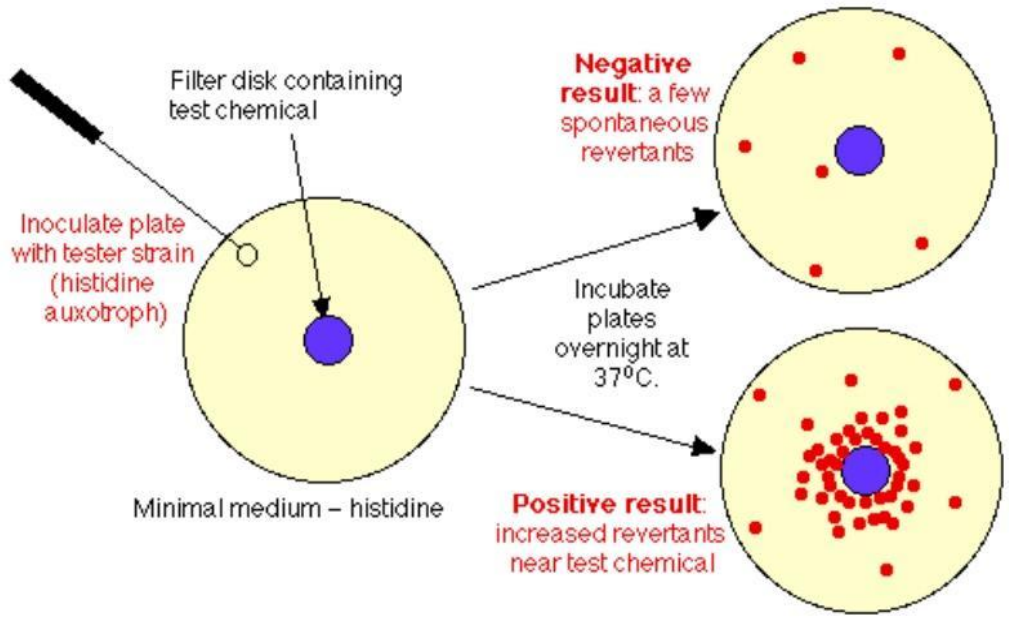
Testing Mutagenesis:
the Ames test

- A quick screening test for potential mutagenic compounds.
- A strain of Salmonella which has a defect in the histidine biosynthetic pathway is plated out, as a lawn, on a medium containing minimal His *(just enough to keep the cells alive but not enough to sustain proliferation)*

Testing Mutagenesis:
the Ames test

- The compound of interest is applied to a disc in the centre of the plate and the plate is incubated overnight.
- Different plates with increasing amounts of the compound are put up.
- Sometimes liver extract is applied also to check for cellular conversions

Ames Test


Filter disk containing test chemical
Inoculate plate with tester strain (histidine auxotroph)
Minimal medium – histidine
Incubate plates overnight at 37°C.
Negative result: a few spontaneous revertants
Positive result: increased revertants near test chemical

Conclusion

Mostly mutations are harmful.
Sometimes they are lethal which leads to death of organisms.
But sometimes they are benificial which are used to obtain good varities of plants and animals .
It is called mutation breeding.
Mostly mutations are recessive and they never eliminate from a population.

THANK YOU

Made by
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