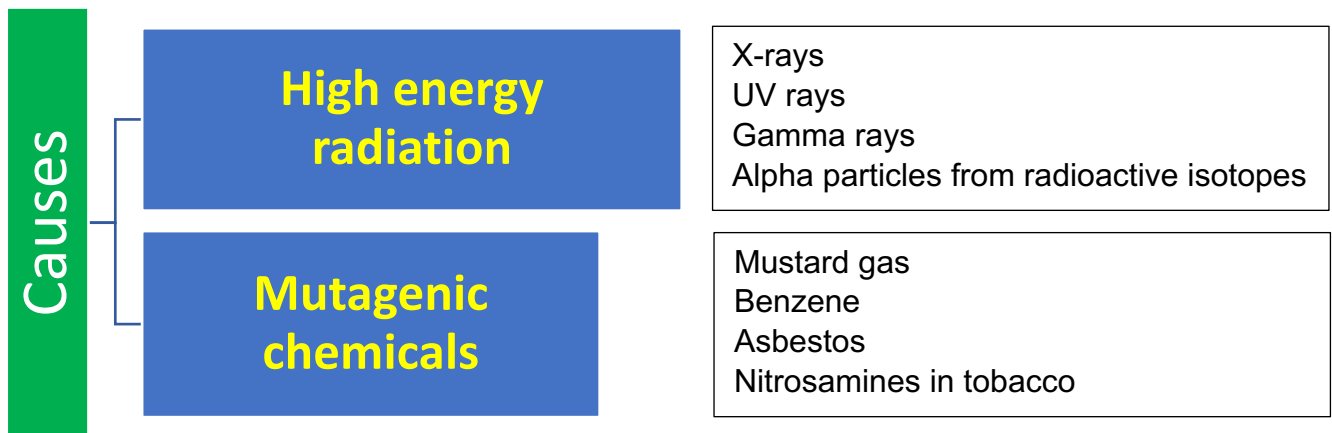


A. MUTATION

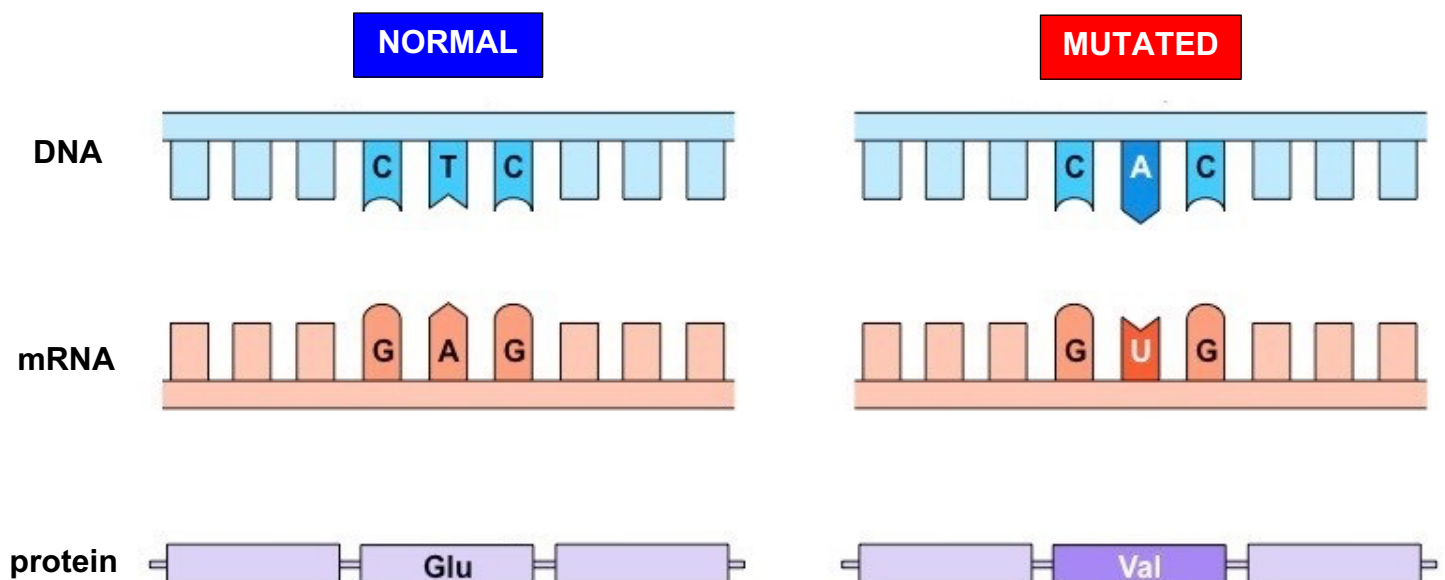
- A **change** in the **DNA base sequence**.
- A **base substitution** is when **one base** in the **DNA sequence** is **replaced** by **another base**.



B. SICKLE-CELL ANAEMIA

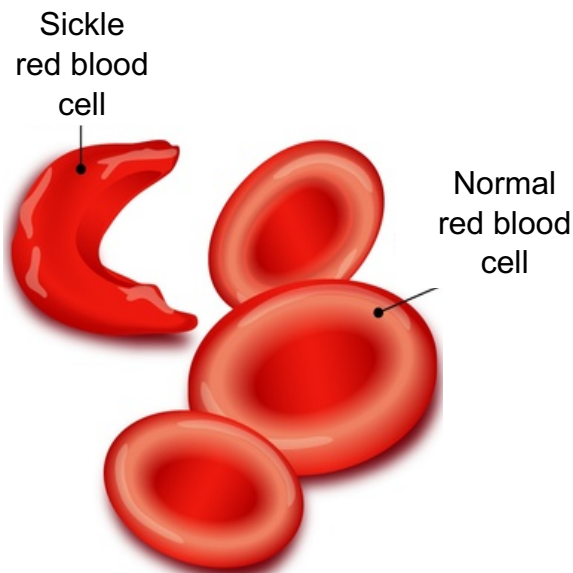
How it is caused

- Caused by a **base substitution mutation** in the **haemoglobin beta (HBB) gene**.



- **DNA** base sequence changes from **CTC** → **CAC**.
- **mRNA** codon changes from **GAG** → **GUG**.
- **Protein** amino acid sequence changes.
- **Glu** (6th amino acid) is **replaced** by **Val**.
- Protein **folds differently**.
- Protein has a **different tertiary structure**.
- **(So) haemoglobin molecules** stick together/form long strands
- **(Causing) red blood cells** to become sickle-shaped

Symptoms of sickle-cell anaemia



Sickle-shaped red blood cells have a **reduced SA:VOL**

(So) **slower/less diffusion of oxygen**

(Also) they can get **stuck in capillaries**

(So) **blood clots / blockages** occur

(So) **cells/tissues** receive **less oxygen**

(So) slower/less (aerobic) **respiration**

(So) less **energy released/ATP produced**

(So feel) **weak and tired**

- Sickle cells are also **destroyed** more **rapidly** than **normal** cells, leading to a **low red blood cell count (anaemia)**.

Sickle-cell anaemia and malaria

- There are two alleles involved in sickle-cell anaemia: **Hb^A** (normal) and **Hb^S** (sickle-cell).

Genotype	Phenotype
Hb^A Hb^A	Healthy
Hb^A Hb^S	Sickle-cell trait (but fine)
Hb^S Hb^S	Sickle-cell anaemia

The **Hb^S** allele that causes sickle-cell anaemia has become **quite common** in parts of the world affected by **malaria**

The **Hb^S** allele provides **some resistance** to **malaria**.

Genotype	Selection
Hb^A Hb^A	Greater risk of dying from malaria
Hb^A Hb^S	Gives a selective advantage as oxygen carriage is okay and has some resistance to malaria
Hb^S Hb^S	Greater risk of dying from sickle-cell anaemia

- **Hb^A Hb^S** individuals (heterozygotes) have a **selective advantage** and are **more likely to survive, reproduce and pass on their alleles**.
- This is why the **Hb^S** allele is at a **higher frequency than expected** in some parts of **Africa**.