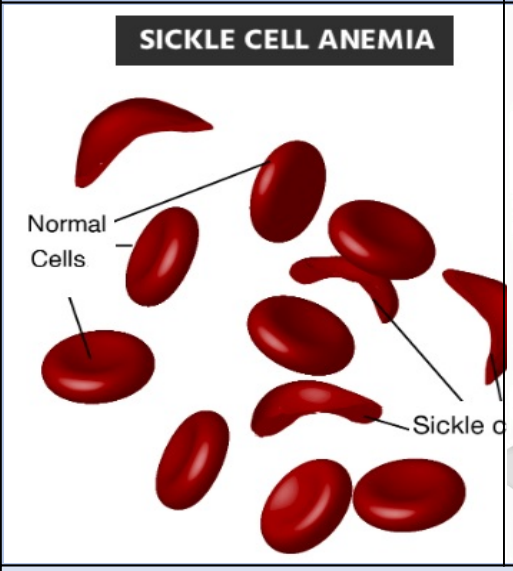
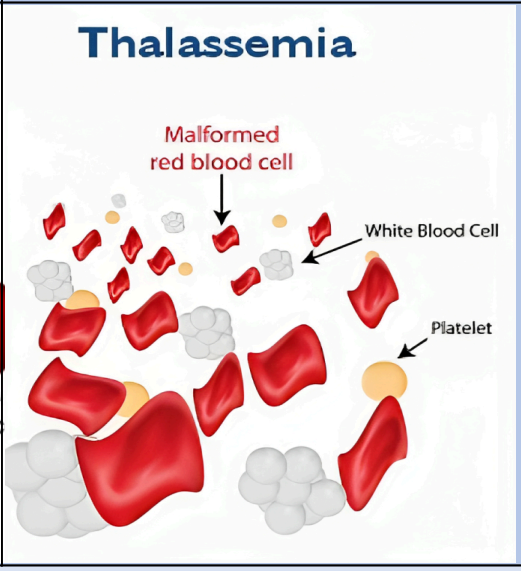
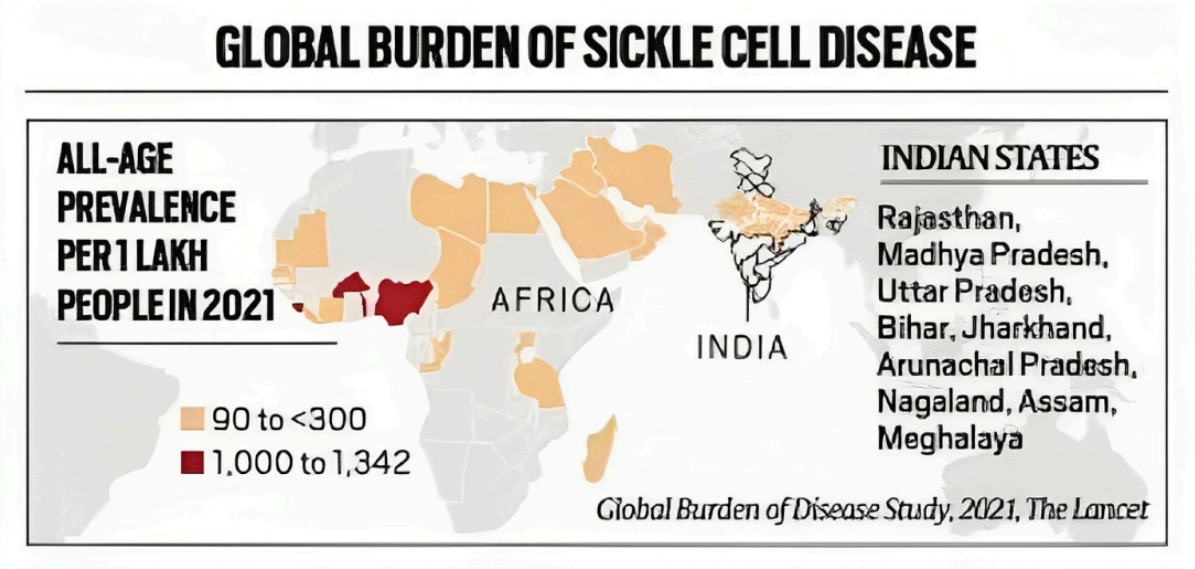
Gene Therapy for Sickle Cell Anaemia

Why in news?

The first therapy based on gene editing technology Crispr-Cas9 for sickle cell disease and thalassaemia has been approved in UK.

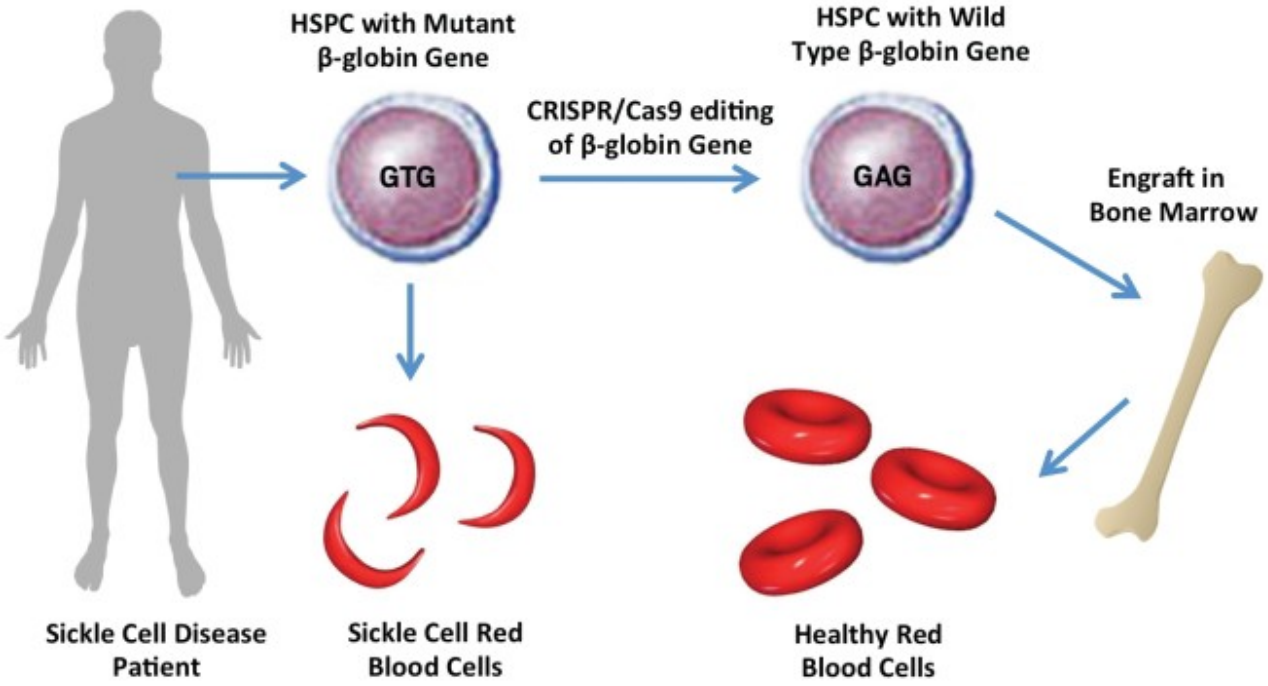
What is sickle cell anaemia and thalassemia?

About	Sickle Cell Anaemia	Thalassemia
Disease	An inherited blood disorder where people who inherit a pair of genes from both parents experience symptoms like severe anaemia.	
Effect on haemoglobin chain	Caused by a mutation in the haemoglobin-β gene found on ***Chromosome 11*** affecting *only the beta chain*	Production of *either the alpha or beta chains* is reduced resulting in either alpha-thalassemia or beta-thalassemia
Haemoglobin production	Mutation in haemoglobin chains makes them into a *crescent shape* under low oxygen level	Caused by reduced production of haemoglobin chains
Effects	Pain, fever, infection, stroke and organ damage	Fatigue, shortness of breath, irregular heartbeats and need blood transfusions throughout their life
Status in India	An estimated 30,000-40,000 children in India are born with the disorder every year.	India has the largest number of children with thalassaemia (about 1-1.5 lakh).
		
Treatment	Treated by blood transfusions, iron supplements, or stem cell transplants.	



What is Casgevy?

- Casgevy is the 1st licensed therapy in the world based on the gene editing technology *Crispr-Cas9.*
- **Apheresis** - It is a *one-time treatment* for which the doctor has to first collect blood stem cells from the bone marrow using a process called ***apheresis*** (filtering out the blood for different components).
- The cells are then sent to the manufacturing site where it takes about 6 months for them to be edited and tested.
- **Gene editing** - The therapy uses the patient's own blood stem cells, which are precisely edited using ***Crispr-Cas9.***
    - So far, the only permanent treatment has been a bone marrow transplant, for which a closely matched donor is needed.
- A gene called ***BCL11A***, which is crucial for switching from foetal to adult haemoglobin, is targeted by the therapy.
    - Foetal haemoglobin (naturally present in everyone at birth), does not carry the same abnormalities as adult haemoglobin.
- The therapy uses the body's own mechanisms to start producing more of foetal haemoglobin, alleviating the symptoms of the two conditions.
- **Side effects**- They are similar to those associated with autologous stem cell transplants, including nausea, fatigue, fever and increased risk of infection.



What are the pros and cons of this treatment?

Significance	Challenges
Efficacy- It restores haemoglobin production and alleviates symptoms in most patients.	**Limited authorization**- It is currently approved in the UK only and is being reviewed by other regulatory bodies.
Pain reliever- It reduces the need for blood transfusions and pain crises in the patients.	**Health inequity**- It is expensive, thereby limiting the accessibility in poor countries.
Reliable- No serious safety concerns were reported, but long-term effects are still being monitored.	**Inaccuracy**- There are concerns with potential off targets effects of CRISPR editing, which could cause unwanted changes in other parts of the genome.

References

1. Indian Express- Sickle cell breakthrough
2. Live Science- World's first CRISPR therapy has been approved