GENE THERAPY FOE HAEMOPHILIA: SCIENCE & TECHNOLOGY

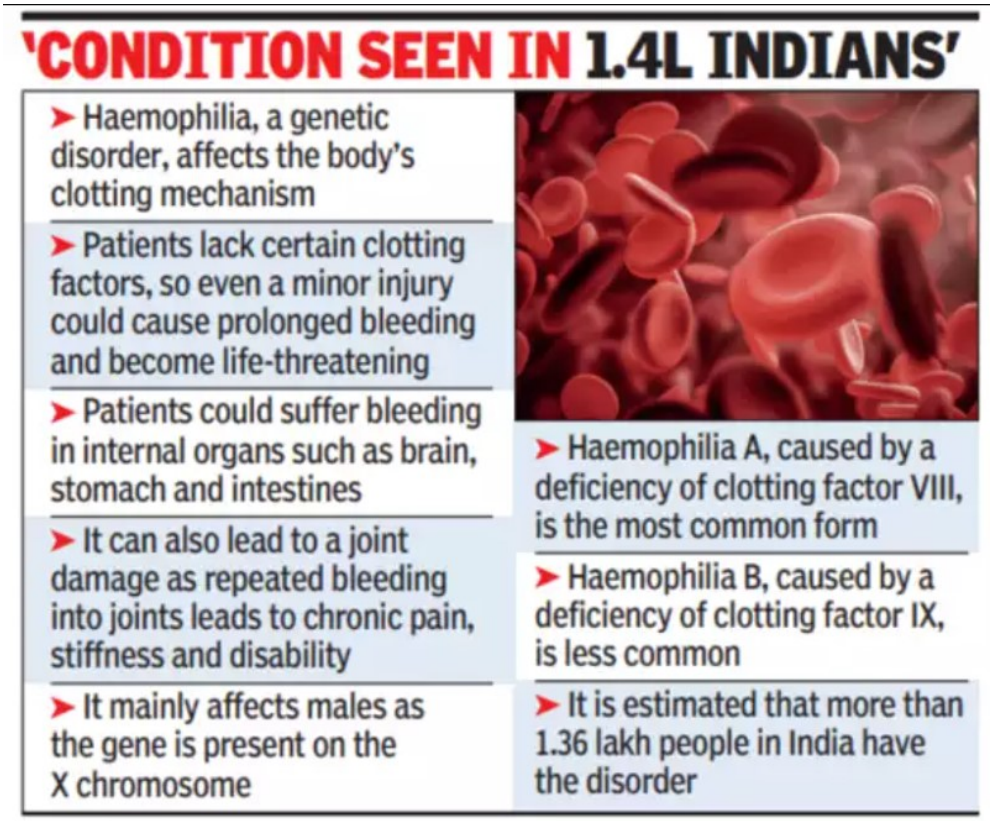
NEWS:

WHAT'S IN THE NEWS?

India conducted its first human gene therapy trial for severe hemophilia A, using genetically modified hematopoietic stem cells to enable long-term production of clotting Factor VIII. This breakthrough offers hope to reduce dependence on repeated clotting factor infusions and represents a major step forward in gene-based therapies.

Context

- India's first human gene therapy trial for haemophilia marks a major scientific achievement and was conducted through the collaboration of the Biotechnology Research and Innovation Council's Institute for Stem Cell Science and Regenerative Medicine (BRIC-inStem) and Christian Medical College (CMC) Vellore.
- This breakthrough trial focuses on developing a long-term curative approach for severe hemophilia A patients through gene modification techniques.



What is Hemophilia?

- Hemophilia is a rare genetic bleeding disorder where the body's natural ability to form blood clots is impaired, leading to prolonged or spontaneous bleeding episodes.
- Even minor injuries can cause extended bleeding, and internal bleeding episodes without any trauma are common in severe cases.
- The disorder stems from mutations in the genes responsible for producing clotting factor proteins essential for blood clot formation.
- These specific genes are located on the X chromosome, making hemophilia far more common in males (XY) than in females (XX), as males lack a second X chromosome to compensate for the faulty gene.

Consequences of Hemophilia

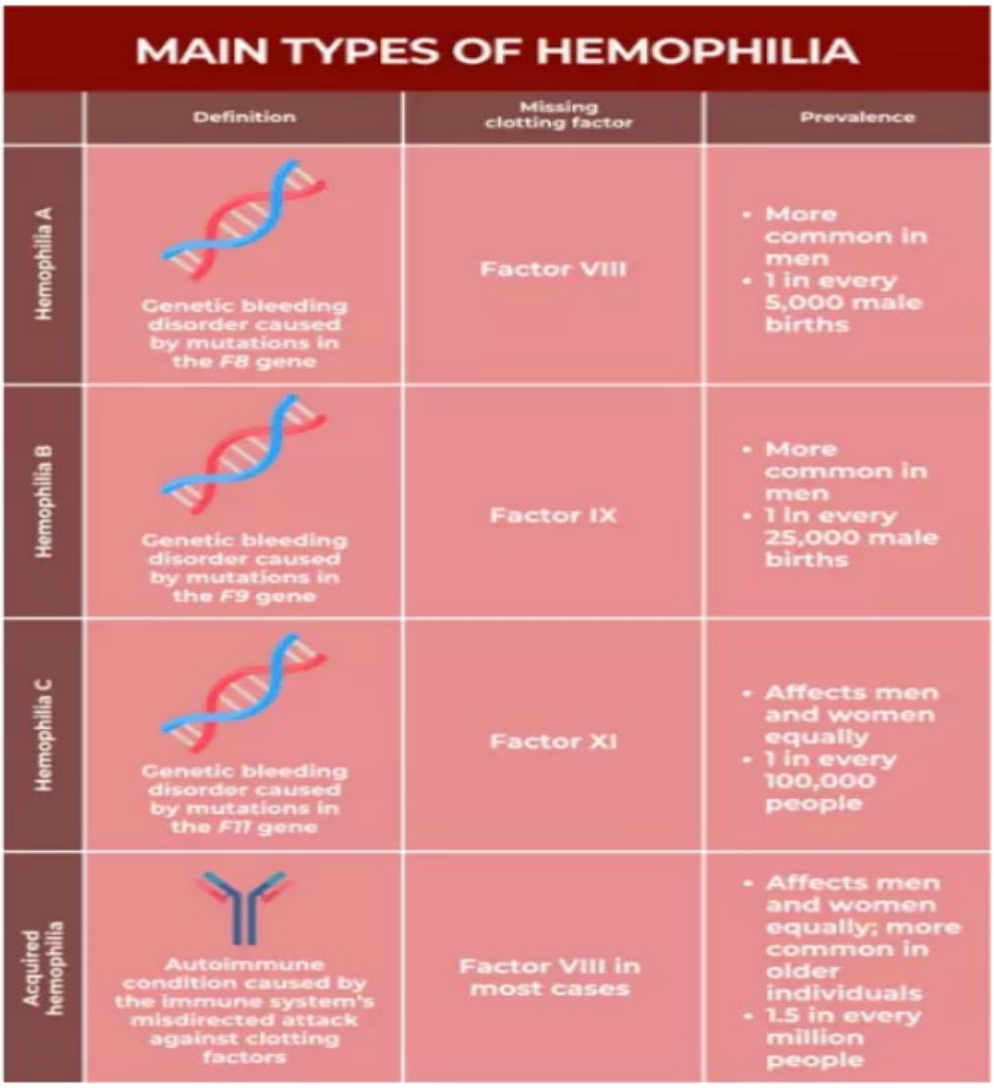
- Hemophilia can lead to internal bleeding in joints (hemarthrosis), resulting in chronic joint damage, restricted movement, and persistent pain.
- In severe cases, bleeding can occur inside vital organs such as the brain, leading to neurological complications like seizures, paralysis, or even death if not treated promptly.
- Uncontrolled bleeding incidents, even from minor injuries, pose significant health risks for individuals living with hemophilia.

Types of Hemophilia

- Hemophilia A (Classic Hemophilia) results from a deficiency or absence of clotting factor VIII, making it the more common form of the disorder.
- Hemophilia B (Christmas Disease) is caused by a deficiency or absence of clotting factor IX, named after the first patient formally diagnosed with this type.

Treatment Approaches for Hemophilia

- **Preventative Treatment (Prophylaxis):** Patients receive regular infusions of clotting factors to prevent bleeding episodes before they occur, aiming to maintain clotting factor levels above the threshold needed to prevent spontaneous bleeds.
- **On-Demand Treatment:** This approach involves administering clotting factor infusions only when a bleeding episode occurs, used more commonly in settings where continuous access to treatment is challenging.



Gene Therapy to Cure Hemophilia (India's Trial)

- The Indian trial specifically targeted severe hemophilia A cases, aiming to offer a long-lasting solution to the dependency on clotting factor infusions.
- Participants' own hematopoietic stem cells (HSCs) were harvested, genetically engineered using lentiviral vectors to insert a functional copy of the gene responsible for producing clotting Factor VIII.
- The genetically modified HSCs were then infused back into the participants, with the goal of achieving sustained production of Factor VIII within their blood cells.
- If successful on a larger scale, this gene therapy could substantially reduce or even eliminate the need for repeated intravenous clotting factor treatments.

What is Gene Therapy?

- Gene therapy is an advanced biomedical technique that aims to treat, cure, or prevent diseases by directly modifying or manipulating genes at the molecular level.
- Gene therapy can work by:
    - Replacing defective or missing genes with healthy versions.
    - Deactivating malfunctioning or harmful genes causing disease.
    - Introducing entirely new genes into the body to help fight a disease or restore healthy function.

Methods of Gene Therapy

- **Somatic Cell Gene Therapy:**
    - Therapeutic genes are inserted into somatic (non-reproductive) cells, meaning changes affect only the treated individual and are not inherited by offspring.
    - This method is currently used in treating conditions like hemophilia, certain cancers, and rare inherited diseases.
- **Germline Gene Therapy:**
    - Therapeutic genetic modifications are made in reproductive cells (sperm, eggs, or embryos), causing changes that are heritable and passed on to future generations.
    - Due to major ethical, legal, and safety concerns, germline gene therapy is banned or heavily restricted in most countries, including India, to prevent unforeseen consequences in human genetics.

Source: https://www.pib.gov.in/PressReleasePage.aspx?PRID=2124073