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Gene Drives and CRISPR — The Science Behind Malaria's Potential Defeat

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CURATED & WRITTEN BY

Bharat Choudhary

UPSC Educator & Content Creator

linkedin.com/in/epicbharat

Gene Drives and CRISPR — The Science Behind Malaria's Potential Defeat

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WHY IN NEWS

Studies in **Tanzania** using **CRISPR-Cas9 gene drive** mosquitoes have achieved **"transmission zero"** — a milestone in which malaria parasite transmission was eliminated in controlled real-world test conditions. The technology uses genetic engineering to ensure **~90% of offspring inherit a modified trait**, either suppressing mosquito populations entirely or making them incapable of transmitting the parasite. No gene-drive mosquitoes have yet been released into wild ecosystems; regulatory and ethical review is ongoing.

THE MALARIA PROBLEM

Malaria remains one of the world's deadliest infectious diseases:

STATISTIC	VALUE
Global cases (2024 WHO report)	~263 million
Global deaths (2024)	~597,000
Africa share of deaths	~95%
India cases (2023)	~5.3 million (declining)
India deaths (2023)	~7,000 (declining)
Causative agent	*Plasmodium* parasites (P. falciparum, P. vivax)
Primary vector	Female *Anopheles* mosquito

Despite decades of interventions — insecticide-treated nets, indoor residual spraying, artemisinin combination therapies (ACT), the **RTS,S/AS01 vaccine (Mosquirix)** and **R21/Matrix-M vaccine** — malaria persists, partly because mosquitoes have developed resistance to pesticides and the parasite shows drug resistance.

WHAT IS A GENE DRIVE?

A **gene drive** is a genetic technology that **biases inheritance** in favour of a specific gene — overriding the normal 50/50 inheritance ratio (Mendelian inheritance). In nature, each parent passes one copy of each gene to offspring; gene drives cause **~90% of offspring to inherit the modified gene**, ensuring rapid spread through a population over generations.

The Mechanism

STAGE	PROCESS
1	Modified gene containing CRISPR-Cas9 machinery is inserted into a mosquito
2	In offspring, CRISPR-Cas9 "edits" the corresponding gene on the unmodified chromosome
3	The wild-type gene is replaced with the drive gene on both chromosomes
4	~90% of offspring carry the drive gene (instead of normal 50%)
5	Drive spreads exponentially through the population

CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats — CRISPR Associated protein 9) is the molecular "scissors" used to cut DNA at precise locations. It was awarded the **Nobel Prize in Chemistry (2020)** to Jennifer Doudna and Emmanuelle Charpentier.

TWO GENE DRIVE STRATEGIES FOR MALARIA

Strategy 1 — Population Suppression

Goal: Drive mosquito population to extinction (or near-extinction) in a target area.

Mechanism: Gene drives that spread a trait causing **female infertility** (females are the malaria vectors; males don't bite). As the infertility gene spreads, fewer females reproduce, and the population collapses.

Tanzania breakthrough: Studies demonstrated that a suppression drive could reduce *Anopheles gambiae* populations to near-zero in caged trial settings — achieving "transmission zero" (no malaria parasite transmission).

Strategy 2 — Population Modification (Replacement)

Goal: Replace the mosquito population with mosquitoes that **cannot transmit malaria** (rather than eliminating mosquitoes entirely).

Mechanism: Gene drives that spread **anti-parasite genes** — mosquitoes produce proteins that block *Plasmodium* development in the mosquito gut, preventing onward transmission.

Advantage: Preserves the mosquito's ecological role (mosquito larvae are a food source for fish and other insects); only eliminates malaria transmission, not the mosquito.

CURRENT STATUS AND CHALLENGES

Where We Are

- **No gene-drive mosquitoes have been released into wild ecosystems** anywhere in the world
- Caged trial success in Tanzania (population suppression) is the most advanced real-world evidence
- **Target Malaria** (Gates Foundation-funded consortium) is the leading research programme in sub-Saharan Africa
- India's **ICMR (Indian Council of Medical Research)** and **DBT (Department of Biotechnology)** are monitoring developments but have no active gene drive programme

Challenges

CHALLENGE	NATURE
Ecological risk	Mosquito extinction could disrupt food chains (fish, birds, bats that feed on larvae and adults)
Evolutionary resistance	Wild mosquitoes may evolve resistance to drive mechanisms
Geographic spread	Gene drives cannot be contained to one country — mosquitoes cross borders
Regulatory vacuum	No international framework for approving gene drive releases
Community consent	Local communities must consent; "informed consent" for entire ecosystems is ethically complex
Reversibility	Once released, gene drives may be impossible to recall from wild populations

INDIA'S MALARIA CONTEXT

India is the **only non-African country** among the top 5 malaria-burden nations. Key features of India's malaria:

FEATURE	DETAIL
Dominant species	*P. vivax* (most common, causes relapsing malaria) and *P. falciparum* (most dangerous)
High-burden states	Odisha, Jharkhand, Chhattisgarh, MP, West Bengal, NE states
National Vector Borne Disease Control Programme (NVBDCP)	Nodal programme for malaria control
National Framework for Malaria Elimination	Target: eliminate malaria by 2030
Achievements	Cases fell from 88 million (1976 peak) to ~5.3 million (2023)

A gene drive specific to *Anopheles stephensi* — an invasive mosquito species spreading malaria in South Asian and African cities — could be of direct relevance to India's urban malaria problem.

REGULATORY AND ETHICAL FRAMEWORK

Gene drives would require clearance under:

- **Environment Protection Act, 1986** (India)
- **Biological Diversity Act, 2002**
- **Rules for Manufacture, Use, Import, Export and Storage of Hazardous Micro-organisms (1989)** — under EPA
- International: **Convention on Biological Diversity (CBD)** — the **Cartagena Protocol on Biosafety** governs transboundary movements of LMOs (Living Modified Organisms)

No international treaty specifically regulates gene drives — a governance gap that the WHO and CBD Secretariat are working to address.

UPSC RELEVANCE

PAPER	ANGLE
GS3 — Science & Tech	CRISPR-Cas9, gene drives, biotechnology, Nobel 2020
GS2 — Health	Malaria burden, NVBDCP, malaria elimination 2030
GS3 — Environment	Ecological risk, biodiversity, Cartagena Protocol
GS2 — Governance	Regulatory framework for GMOs, biosafety
Mains Keywords	Gene drive, CRISPR-Cas9, Anopheles gambiae, population suppression, Cartagena Protocol, NVBDCP, malaria elimination 2030, Target Malaria

FACTS CORNER

- **Gene drive inheritance rate:** ~90% (vs. normal 50% Mendelian inheritance)
- **CRISPR-Cas9 Nobel Prize:** Chemistry 2020 — Jennifer Doudna and Emmanuelle Charpentier
- **“Transmission zero”:** Milestone achieved in Tanzania caged trials — no malaria parasite transmission
- **Global malaria deaths (2024):** ~597,000; 95% in Africa
- **India malaria burden (2023):** ~5.3 million cases, ~7,000 deaths
- **India’s malaria elimination target:** 2030
- **Dominant vectors in India:** Anopheles culicifacies (rural), Anopheles stephensi (urban)
- **Invasive concern:** An. stephensi expanding into African cities — gene drives against it are a priority
- **RTS,S/AS01 (Mosquirix):** First approved malaria vaccine (WHO recommendation 2021); ~30-40% efficacy
- **R21/Matrix-M:** Second malaria vaccine (WHO recommendation 2023); ~75% efficacy in trials
- **Target Malaria:** Gates Foundation-funded gene drive research consortium active in Burkina Faso, Mali, Uganda

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