Malaria, Antimalarial drugs and the resistance to drugs

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Manifest pedagogy:

Anti-malarial drug resistance is a global concern. With the misuse of antibiotics and emergence of mutant parasites this resistance is crossing boundaries across the globe. Time has come to devise new methodologies to tackle this drug resistance issue.

In news: In recent years there is increasing evidence for the failure of artemisinin-based combination therapy for treating malaria either alone or with partner drugs.

Placing it in syllabus: Science and technology- Diseases

Static dimensions:

- Malaria: Pathogens and parasites
- Antimalarial Drugs

Current dimensions:

- Antimalarial Drug Resistance (ADR) : Origin and present condition
- Solutions to ADR

Content:

Malaria: Pathogens and parasites

- Malaria is a **tropical disease**.
- Symptoms include: a high temperature of 38C or above, feeling hot and shivery, headaches, vomiting, muscle pains, diarrhoea.
- It is caused by a type of **parasite known as Plasmodium.**

- The Plasmodium parasite is **mainly spread by bites of female Anopheles mosquitoes**, which mainly bite at dusk and at night.
- Malaria can also be spread through blood transfusions and the sharing of needlesMalaria is caused by the Plasmodium parasite.
- The 5 different types of plasmodium parasite that cause malaria in humans are:
- ***Plasmodium falciparum*** – mainly found in Africa, it's the most common type of malaria parasite and is responsible for most malaria deaths worldwide.
- ***Plasmodium vivax*** – mainly found in Asia and South America, this parasite causes milder symptoms than Plasmodium falciparum, but it can stay in the liver for up to 3 year.
- ***Plasmodium ovale*** – fairly uncommon and usually found in West Africa, can remain in the liver for several years without producing symptoms.
- ***Plasmodium malariae*** – this is quite rare and usually only found in Africa.
- ***Plasmodium knowlesi*** – this is very rare and found in parts of southeast Asia.

Antimalarial Drugs

- Antimalarial medications are a **type of antiparasitic chemical agent, often naturally derived, that can be used to treat or to prevent malaria.**
- Specifically, antimalarial drugs may be used to treat malaria in three categories of individuals,

(i) those with suspected or confirmed infection,

(ii) those visiting a malaria-endemic regions who have no immunity, to prevent infection via malaria prophylaxis, and

(iii) or in broader groups of individuals, in routine but intermittent preventive treatment in regions where malaria is

endemic

- **Chloroquine** was, until recently, the most widely used anti-malarial and is also the least expensive, best tested and safest of all available drugs, however emergence of drug-resistant parasitic strains is rapidly decreasing its effectiveness.
- **Hydroxychloroquin**e was derived in the 1950s by adding a hydroxyl group to existing Chloroquine, making it more tolerable than Chloroquine by itself.
- **Pyrimethamine** is used in the treatment of uncomplicated malaria. It is particularly useful in cases of chloroquine-resistant P. falciparum strains when combined with sulfadoxine.
- **Quinine**, extracted from cinchona tree is an alkaloid that acts against Plasmodium vivax and Plasmodium malariae.
- It is still very effective and widely used in the treatment of acute cases of severe P. falciparum and is especially useful in areas where there is known to be a high level of resistance to chloroquine, mefloquine, and pyrimethamine.
- **Artemisinin** is a Chinese herb (qinghaosu) that has been used in the treatment of fevers for over 1,000 years, and has demonstrated the fastest clearance of all antimalarials currently used and acts primarily on the trophozoite phase, thus preventing progression of the disease.
- Practice in treating cases of malaria is most often based on the **concept of combination therapy** (e.g., using agents such as artemether and lumefantrine against chloroquine-resistant Plasmodium falciparum infection).
- This offers advantages including reduced risk of treatment failure, reduced risk of developed resistance, as well as the possibility of reduced side-effects.

Antimalarial Drug Resistance: origin and present condition

- Anti-malarial drug resistance has been defined as: "***the ability of a parasite to survive and/or multiply despite the administration and absorption of a drug given in doses equal to or higher than those usually recommended but within tolerance of the subject***".
- The main drivers of AMR include the misuse and overuse of antimicrobials; lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in health-care facilities and farms; poor access to quality, affordable medicines, vaccines and diagnostics; lack of awareness and knowledge; and lack of enforcement of legislation.
- The **first type of resistance was against chloroquine in Thailand in 1957.**
- It then migrated to India from South-east Asia and then on to Africa with disastrous consequences.
- Similarly, artemisinin resistance developed from the six Southeast Asian countries and migrated to other continents.
- In recent years, there is increasing evidence for the failure of artemisinin-based combination therapy for falciparum malaria either alone or with partner drugs.
- In the past, chloroquine was very effective for all types of malaria treatment in India, but it is no longer used for the treatment of falciparum malaria.
- In India, after the failure of chloroquine to treat P. falciparum malaria successfully, artemisinin-based combination therapy was initially introduced in 117 districts that reported more than 90% falciparum burden in 2008.
- In 2019, a report from Eastern India indicated the presence of two mutations in P. falciparum cases treated with artemisinin that linked to its presence of

resistance.
- Again in early 2021, artemisinin-based combination therapy failure has been reported from Central India.

Solutions to AMR

- **Preventing malaria infections developing** has a substantial effect on the potential rate of development of resistance, by directly reducing the number of cases of malaria thus decreasing the need for anti-malarial therapy.
- **Preventing the transmission of resistant parasites** limits the risk of resistant malarial infections becoming endemic and can be controlled by a variety of non-medical methods including insecticide-treated bed nets, indoor residual spraying, environmental controls (such as swamp draining) and personal protective methods such as using mosquito repellent.
- Molecular Malaria Surveillance has to be carried out to find out the drug-resistant variants so that corrective measures can be undertaken in time to avert any consequences.
- **Artemisinin-based combination therapies (ACTs)** are the recommended first-line treatment for uncomplicated P. falciparum malaria and are used by most malaria endemic countries.
- ACTs are a combination of an artemisinin component and a partner drug.
- Some experts even advocate using **triple artemisinin-based combination therapies** where the partner drug is less effective.

***Global initiatives*–**

- A global action plan on antimicrobial resistance, including antibiotic resistance, was endorsed at the World Health Assembly in May 2015.
- The "**Global action plan on antimicrobial resistance**" has

5 strategic objectives:

- To improve awareness and understanding of antimicrobial resistance.
- To strengthen surveillance and research.
- To reduce the incidence of infection.
- To optimize the use of antimicrobial medicines.
- To ensure sustainable investment in countering antimicrobial resistance.
- The WHO-supported **Global Antimicrobial Resistance Surveillance System (GLASS)** supports a standardized approach to the collection, analysis and sharing of data related to antimicrobial resistance at a global level to inform decision-making, drive local, national and regional action.

Mould your thought–

1. Define Anti-malarial drugs. How has Anti-malarial drug resistance (ADR) emerged in recent years? What needs to be done to tackle it?

Approach to the answer-

- Write briefly about anti-malarial drugs
- Write about origin and present status of ADR
- Brief about the solutions
- Conclude with any one global initiative