



Combination Therapy for TB

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Why in News

Researchers from Bengaluru have made an important discovery of the mechanism used by Tuberculosis (TB) bacteria to tolerate TB drugs.

What is the Mechanism?

- **Macrophages** (a type of white blood cell), when infected with **pathogens** (such as bacteria or virus), as a first-line of defence, **reduce the pH range in the body**, i.e. making pH acidic.
- The researchers found that instead of controlling the TB bacteria, **the mildly acidic pH was actually facilitating a fraction of the bacteria to continue multiplying** and develop drug tolerance.
 - Anti-TB drugs induce oxidative stress to kill bacteria inside macrophages.
 - However, the drug tolerant bacteria have a remarkable ability **to counter oxidative stress**.
 - The bacteria uses the acidic pH of macrophages as a cue to specifically increase its capacity to deal with oxidative stress.
 - The bacteria also induce efflux pumps (to expel antibiotics) as an additional mechanism to reduce antibiotic efficacy.
- This is against the common notion that only the non-replicating or slowly metabolising TB bacteria become tolerant to anti-TB drugs.
- The mechanism was found responsible for longer TB treatment of six-nine months.
- The drug-tolerant bacteria were found in macrophages that were more acidic (pH 5.8) while the drug-sensitive bacteria were seen in macrophages that were less acidic (pH 6.6).

Researchers' Solution

- The researchers used already approved **anti-malaria drug chloroquine in combination with a TB drug isoniazid** in mice and guinea pigs.
- The **chloroquine** drug **neutralised the pH** within the macrophages. This prevented the bacteria from inducing the mechanism to protect themselves from oxidative stress. So no drug-tolerant TB bacteria emerged.
- Once the pH was neutralised, the **isoniazid drug** was able to **eradicate TB from animals**.
- The two-month treatment was able to completely sterilise mouse lungs and a near-complete eradication was observed from the lungs of guinea pigs.
- In addition, it was found that the drug combination also reduces the chances of TB relapse.

Tuberculosis

- TB is caused by **bacteria (Mycobacterium tuberculosis)** that most often affect the **lungs**.
- **Transmission:** TB is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air.
- **Symptoms:** Cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats.
- **Treatment:** TB is **treatable and curable disease**. It is treated with a standard 6 month course of 4 antimicrobial drugs that are provided with information, supervision and support to the patient by a health worker or trained volunteer.
- Anti-TB medicines have been used for decades and strains that are resistant to 1 or more of the medicines have been documented in every country surveyed.
 - **Multidrug-resistant tuberculosis (MDR-TB)** is a form of TB caused by bacteria that do not respond to isoniazid and rifampicin, the 2 most powerful, first-line anti-TB drugs. MDR-TB is treatable and curable by using second-line drugs.
 - **Extensively drug-resistant TB (XDR-TB)** is a more serious form of MDR-TB caused by bacteria that do not respond to the most effective second-line anti-TB drugs, often leaving patients without any further treatment options.

Source: TH