

Drugs against TB: Are They Really Necessary?

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In the Twentieth Century, several outstanding breakthroughs towards cure and control of tuberculosis were finally found, saving millions of human lives. Due to these achievements in the 1960s, 1970s and 1980s, the scientific community believed that the disease would finally be eradicated. However, in 1981, a new disease, known as AIDS (Acquired Immune Deficiency Syndrome) was identified, turning into one of the major causes of the resurgence of TB. Nowadays there are different factors that also contributed for the resurgence of TB, especially multi-drug-resistant tuberculosis (MDR-TB), which is defined as resistance to, at the minimum, rifampicin and isoniazid. Recently, another important factor in TB treatment worldwide is the advent of XDR-TB (Extensive Drug Resistant or Extreme Drug Resistance TB), which is commonly defined as strains resistant to all the current first-line drugs, as well as any of fluoroquinolone and, at least, to 1 of 3 injectable second-line drugs (capreomycin, kanamycin or amikacin). Like MDR-TB, XDR-TB can be transmitted from an infected patient to other people. The WHO Global Task Force agreed to this definition of XDR-TB on XDR-TB in October 2006. In spite of the high impact caused by tuberculosis worldwide nowadays, nearly 45 years have passed without a novel drug being introduced into the market, except for rifapentine in 1998, which is a very close analogue of rifampin. Due to the increase of MDR and XDR-TB in the world, we need new strategies and drugs to face this new problem or no treatment will be available again. Alternatively, we just go back into the past, when people died of tuberculosis in sanatoriums, without any treatment at all.

There are basic factors involved in the development of new anti-TB drugs, such as more effective treatment of latent tuberculosis infection, prevention and treatment of the MDR-TB and potential sterilizing activity, which is defined as the ability of a drug, such as pyrazinamide and rifampin to destroy the bacteria, known as persisters. Other important factors can be mentioned, for instance, cost, new mechanisms of action, good pharmacokinetic distribution and permeation into cells and lung tissue, potent bactericidal and selective activity against the *Mycobacterial* species. An other problem to be solved is the combined treatment TB/HIV, which has several problems, such as a large number of pills, patient adherence, prolonged treatment regimens, immune reconstitution inflammatory syndrome, drug resistance in both etiological agents and drug-drug interactions. Despite of the complexity of the development of new anti-TB drugs, some compounds are in advanced clinical trials, such as the fluoroquinolones Gati and Moxifloxacin, the diarylquinoline TMC207, the nitroimidazoles OPC 67683 and PA-824, and the diamine SQ-109. However, in spite of several activities undertaken in the last twelve years by different organizations, such as academic institutions, government research laboratories, non-governmental organizations, pharmaceutical industry and contract research houses, new TB drugs and strategies are desperately necessary to face the new challenges of this disease.

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