PRIMEVIEW

TUBERCULOSIS

nature REVIEWS DISEASE PRIMERS

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Tuberculosis (TB) is an airborne, predominantly pulmonary disease caused by *Mycobacterium tuberculosis*. It is clinically classified as latent TB infection (LTBI) — an asymptomatic, contained, non-transmissible state — or active TB disease, which is symptomatic and potentially transmissible.

EPIDEMIOLOGY

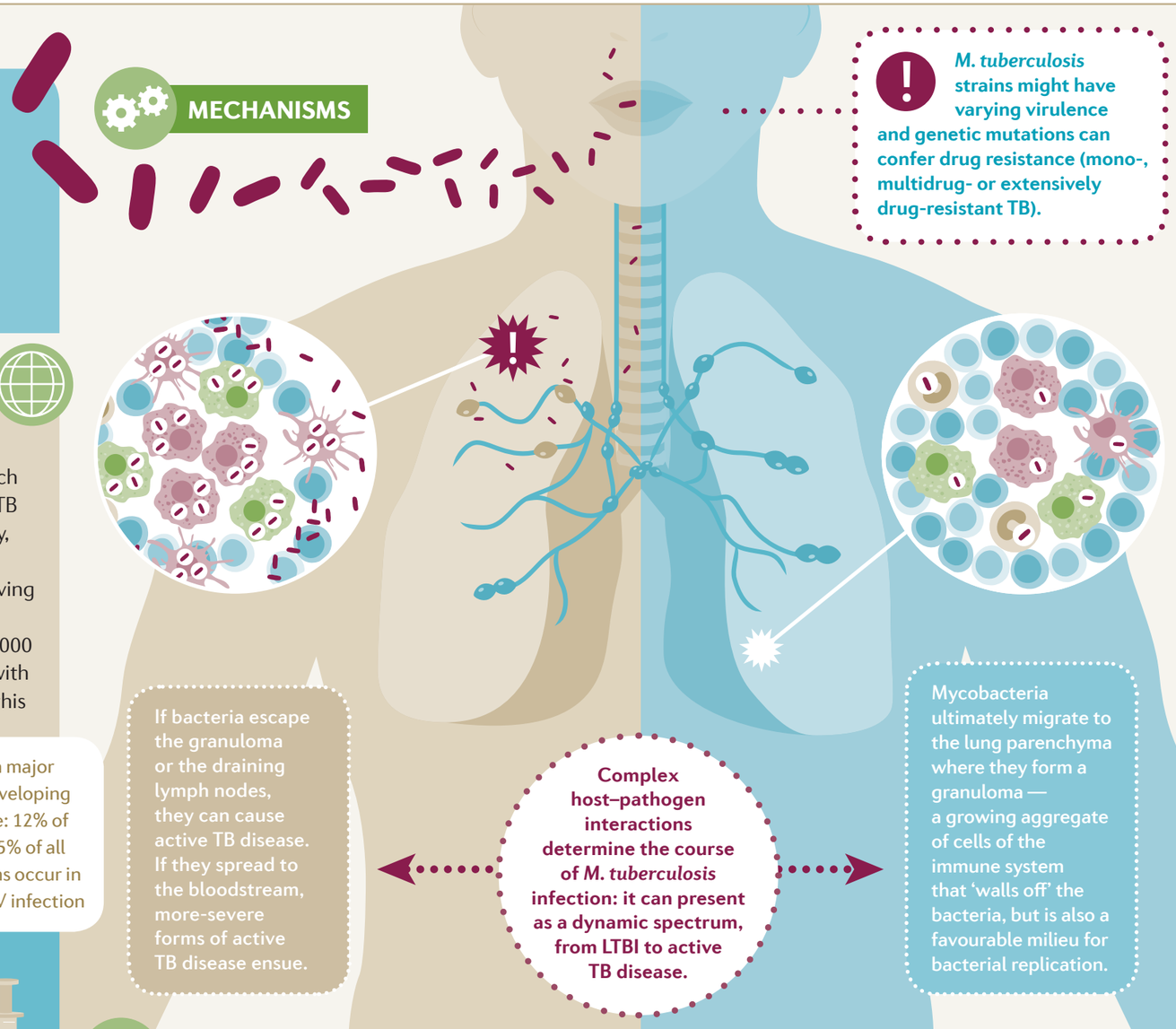
Approximately 9.6 million new cases of active TB disease were estimated in 2014 — 10% of which occurred in children and >1.5 million were fatal. TB incidence is heterogeneously distributed globally, with low-income regions, such as South Africa (>800 cases per 100,000 population per year), having a higher burden than higher-income regions (for example, the United States, with 3 cases per 100,000 population per year). Only 5–15% of individuals with LTBI will progress to active TB disease. However, this large pool of people who are infected with *M. tuberculosis* is an important hurdle for achieving epidemic control.

HIV infection is a major risk factor for developing active TB disease: 12% of new cases and 25% of all TB-related deaths occur in patients with HIV infection

PREVENTION

The only available vaccine is the Bacillus Calmette–Guérin (BCG), which was introduced in the 1920s. Worldwide, >90% of infants are vaccinated with BCG every year, but the vaccine efficacy in adolescents and adults — the age groups that are most likely to spread *M. tuberculosis* infection — is limited. New vaccines are under development, which are being designed to prevent the development of active TB disease or prevent the establishment of LTBI altogether upon exposure.

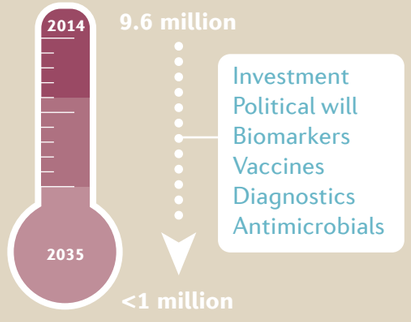
MECHANISMS



OUTLOOK

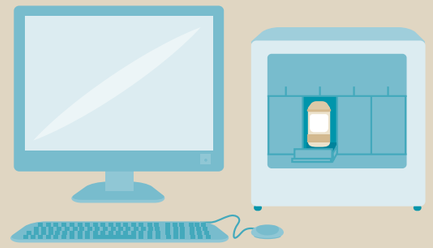
The goal of the WHO End TB Strategy is to decrease the worldwide TB incidence to <10 per 100,000 people by 2035. Eliminating TB will require investments in research, to develop new diagnostics, vaccines and drugs.

The emergence of drug resistance also needs to be tackled. Finally, it will be vital to improve TB control programmes in high-burden settings through global, political and financial efforts.



DIAGNOSIS

Diagnosis of active TB disease requires sputum smear microscopy (to identify the bacteria) and culture-based and molecular tests, such as GeneXpert technology. GeneXpert detects the presence of *M. tuberculosis* and can also detect rifampicin-resistant strains. However, implementing this molecular assay is often not feasible in low-income settings. Accordingly, new biomarkers are being sought to develop simpler, non-sputum-based, point-of-care diagnostics. New molecular tests for universal rapid drug susceptibility testing are also required to ensure maximal efficacy of current and emerging drug regimens.



MANAGEMENT

Individuals with LTBI who are at increased risk of developing active TB disease should receive preventive therapy (typically, isoniazid for 6–9 months). Drug-sensitive active TB disease responds well (~85% cure rate) to antibiotics (typically, a 6-month regimen with isoniazid, rifampicin, pyrazinamide and ethambutol), but drug-resistant (particularly multidrug-resistant and extensively drug-resistant) TB needs longer treatment and is associated with poorer outcomes. The long duration of treatment can cause toxicity and undermine patient adherence. Antiretroviral therapy in HIV-positive patients can reduce the risk of concomitant TB, although drug–drug interactions between antiretroviral and anti-TB agents might cause severe adverse effects.

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