A MORTAL FOE

Tuberculosis is one of the world's most lethal infectious diseases. Further progress in consigning it to the past is a massive challenge. By **Tom Paulson**.

GLOBAL BURDEN OF TUBERCULOSIS

In 2011, nearly 9 million people fell ill from TB and 1.4 million died, mostly in poor countries, with 60% of cases in Asia and 24% in Africa.

THE BIGGEST KILLER

Tuberculosis has killed more than any other infectious disease in history. Over a billion lives in the past two hundred years.

THE 100 YEARS BATTLE

Rising living standards in industrialized nations, interrupted by two World wars, and new antibiotics had tuberculosis in decline.

SLOW PROGRESS

Over the past fifteen years, an invigorated anti-TB effort has begun to reduce the global burden of disease worsened by HIV.

8.7M

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1

Transmission

People with active disease develop symptoms such as a cough, which propels bacteria into the air where it can be inhaled by others. Tuberculosis must be diagnosed and treated as soon as possible to render the person non-infectious and prevent the spread of disease (see 'Control issues', page S16).

2

Immune response

The BCG vaccine offers little protection to adolescents and young adults from the form of the disease that causes most deaths. Any effective vaccine will need to harness T cells, but scientists are still looking for correlates of protection (see 'An age-old problem', page S8).

3

Latency

M. tuberculosis can be contained within granulomas for years. It is thought that latency may encompass a spectrum of states, from people who have completely controlled the disease, to those with undetected, subclinical disease (see 'Latency: A sleeping giant', page S14).

4

Activation

If the immune system weakens as a person ages or contracts HIV infection, for example, bacterial replication can overcome the immune system and granuloma breaks down, releasing *M. tuberculosis* into the lungs and advancing disease (see 'A combined effort', page S4).