

TUBERCULOSIS

WHY DO WE CARE AND WHAT CAN WE DO?

Actions for Life
TOWARDS A WORLD FREE OF TUBERCULOSIS

Reach

Commit

Treat

Act

Achieve

Advocate

Invest

Hope

Innovate

Collaborate

Make an "Action for Life" on World TB Day 2006

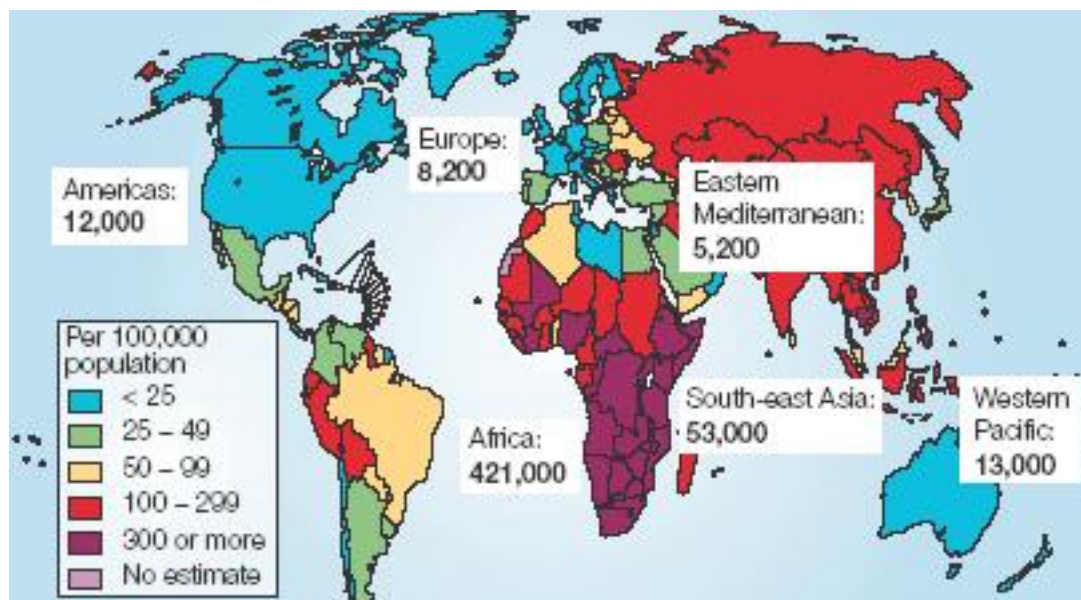
These 10 actions are at the heart of the Global Plan to Stop TB 2006-2015 and are key to achievement of the Partnership's 2015 targets.

World Health Organization

Stop TB Partnership

www.stoptb.org

While tuberculosis is mostly a memory in the Western countries it remains a grim reality for the majority of the worlds population



•Every year 8-10 million people catch the disease and 2 million will die from it.

•About a third of the world's population carry the TB bacteria but most never develop the active disease.

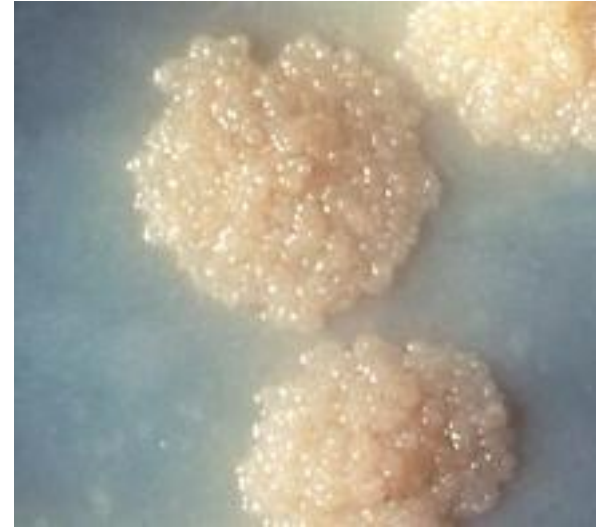
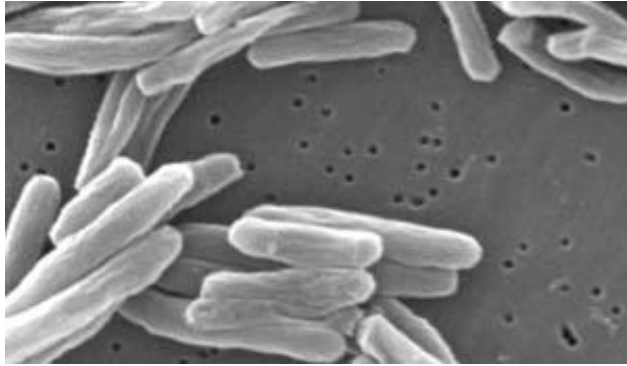
•Around 10% of people infected with TB actually develop the disease in their lifetimes, but this proportion is increasing in the face of the HIV epidemic.

•TB infection is currently spreading at the rate of one person per second.

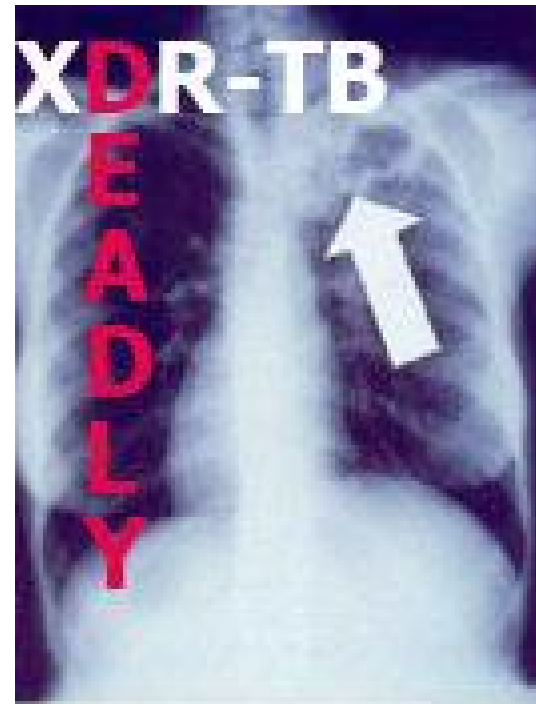
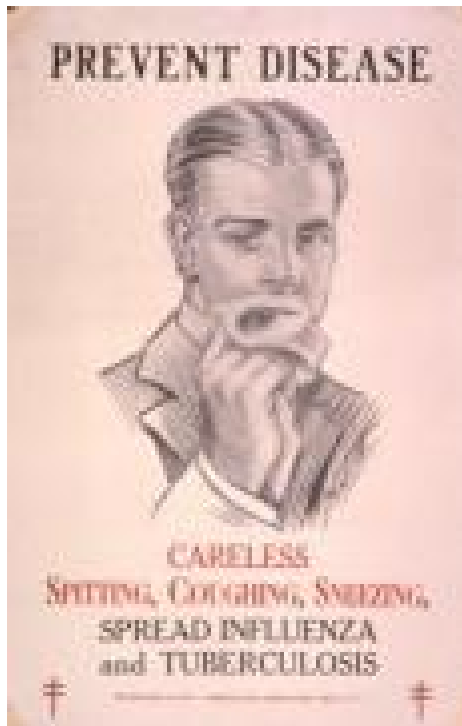
•It kills more young people and adults than any other infectious disease

•It is the infectious disease that kills more women than any other.

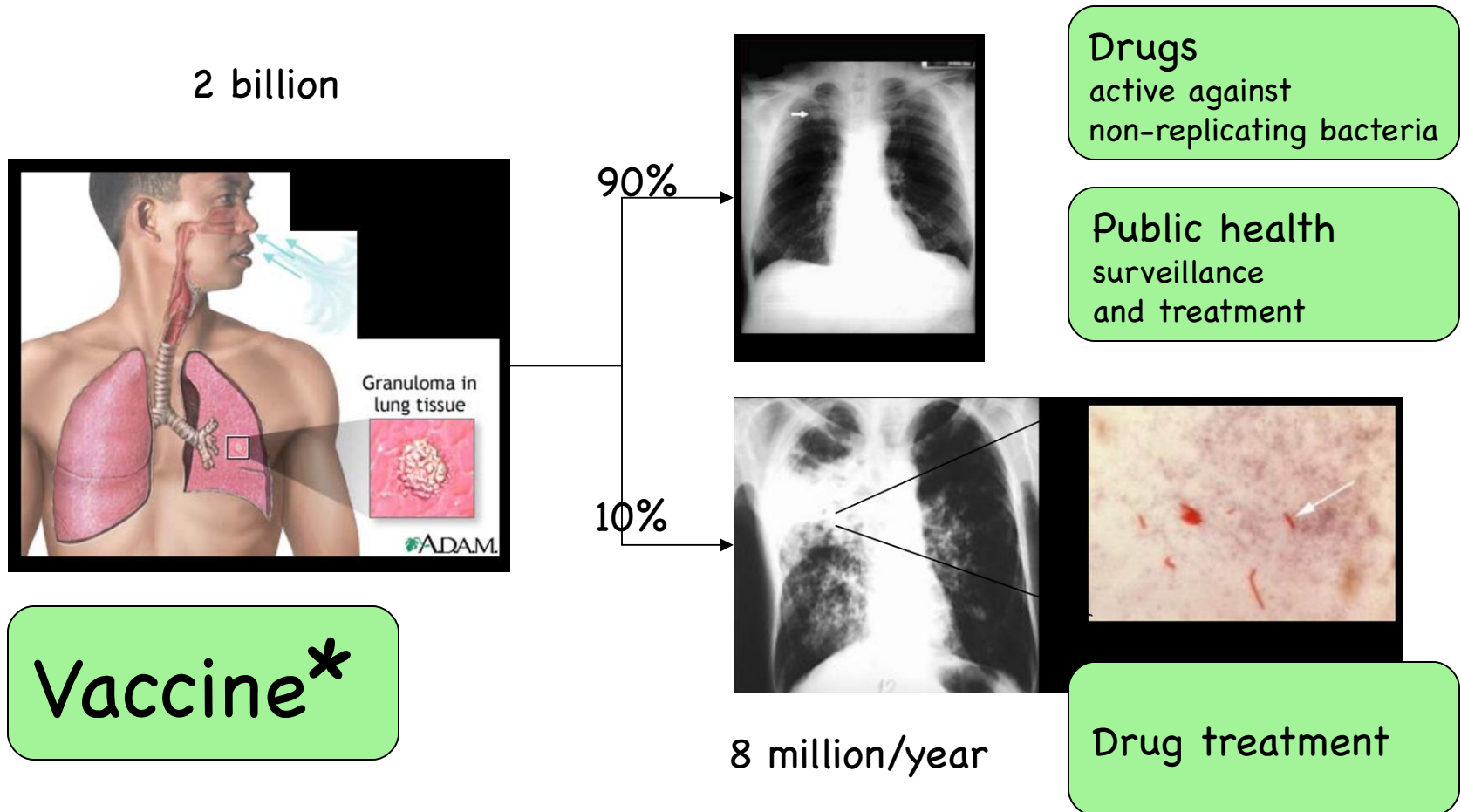
Tuberculosis: under control?



Tuberculosis is always with us



What makes tuberculosis so pervasive?

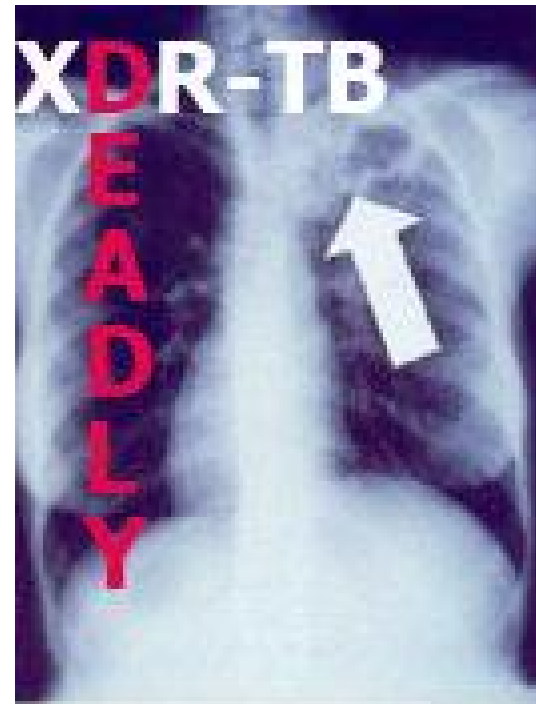
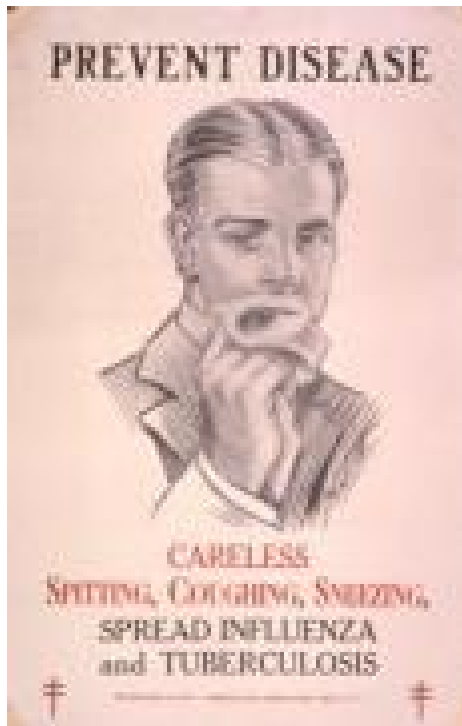


Understanding of bacterial physiology

* Understanding of what constitutes a protective immune response

Understanding of factors that affect transmission

Tuberculosis is always with us





MMWR™

Morbidity and Mortality Weekly Report

Weekly

March 24, 2006 / Vol. 55 / No. 11

World TB Day — March 24, 2006

World TB Day is March 24. This annual event commemorates the date in 1882 when Robert Koch announced his discovery of *Mycobacterium tuberculosis*, the bacterium that causes tuberculosis (TB). Worldwide, TB remains one of the leading causes of death from infectious disease. An estimated 2 billion persons (i.e., one third of the world's population) are infected with *M. tuberculosis*. Each year, approximately 9 million persons become ill from TB, and approximately 2 million die as a result. World TB Day provides an opportunity for TB programs, nongovernmental organizations, and other partners to describe TB-related problems and solutions and to support TB control worldwide.

During 1985–1992, after more than 30 years of decline, the number of TB cases reported in the United States increased by 20%. This resurgence generated a renewed emphasis on TB control and prevention during the 1990s, which reversed the trend. Although the 2005 TB rate was the lowest recorded in the United States since national reporting began in 1953, the average annual decline has slowed during the past 3 years, multidrug-resistant TB remains a threat, and disparate rates of TB persist among certain racial, ethnic, and foreign-born populations.

Many states are offering educational programs organized by local TB coalitions in recognition of World TB Day. For example, the Georgia Department of Human Resources, Division of Public Health, Tuberculosis Program is hosting an observance recognizing the activities of a coalition working to reduce disparities in TB among blacks in the Atlanta area. Additional information about World TB Day and CDC TB-elimination activities is available at <http://www.cdc.gov/nchstp/tb/worldtbday/2006/activities.htm>.

Emergence of *Mycobacterium tuberculosis* with Extensive Resistance to Second-Line Drugs — Worldwide, 2000–2004

During the 1990s, multidrug-resistant (MDR) tuberculosis (TB), defined as resistance to at least isoniazid and rifampin, emerged as a threat to TB control, both in the United States (1) and worldwide (2). MDR TB treatment requires the use of second-line drugs (SLDs) that are less effective, more toxic, and costlier than first-line isoniazid- and rifampin-based regimens (3). In 2000, the Stop TB Partnership's Green Light Committee was created to increase access to SLDs worldwide while ensuring their proper use to prevent increased drug resistance. While assisting MDR TB treatment programs worldwide, the committee encountered reports of multiple cases of TB with resistance to virtually all SLDs. To assess the frequency and distribution of extensively drug-resistant (XDR) TB cases,* CDC and the World Health Organization (WHO) surveyed an international network of TB laboratories. This report summarizes the results of that survey, which determined that, during 2000–2004, of 17,690 TB isolates, 20% were MDR and 2% were XDR. In addition, population-based data

* Defined as cases in persons with TB whose isolates were resistant to isoniazid and rifampin and at least three of the six main classes of SLDs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and para-aminosalicylic acid).

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
CENTERS FOR DISEASE CONTROL AND PREVENTION

XDR = Multidrug-resistant TB (MDR-TB) plus resistance to (i) any *fluoroquinolone*, and (ii) at least 1 of 3 injectable second-line drugs *capreomycin*, *kanamycin*, *amikacin* (new definition agreed October 2006)

MDR-TB = resistance to at least *isoniazid* and *rifampicin*, the two most powerful first-line anti-TB drugs

Of 17,690 isolates from 49 countries during 2000–2004, 20% were MDR-TB and 2% were XDR-TB

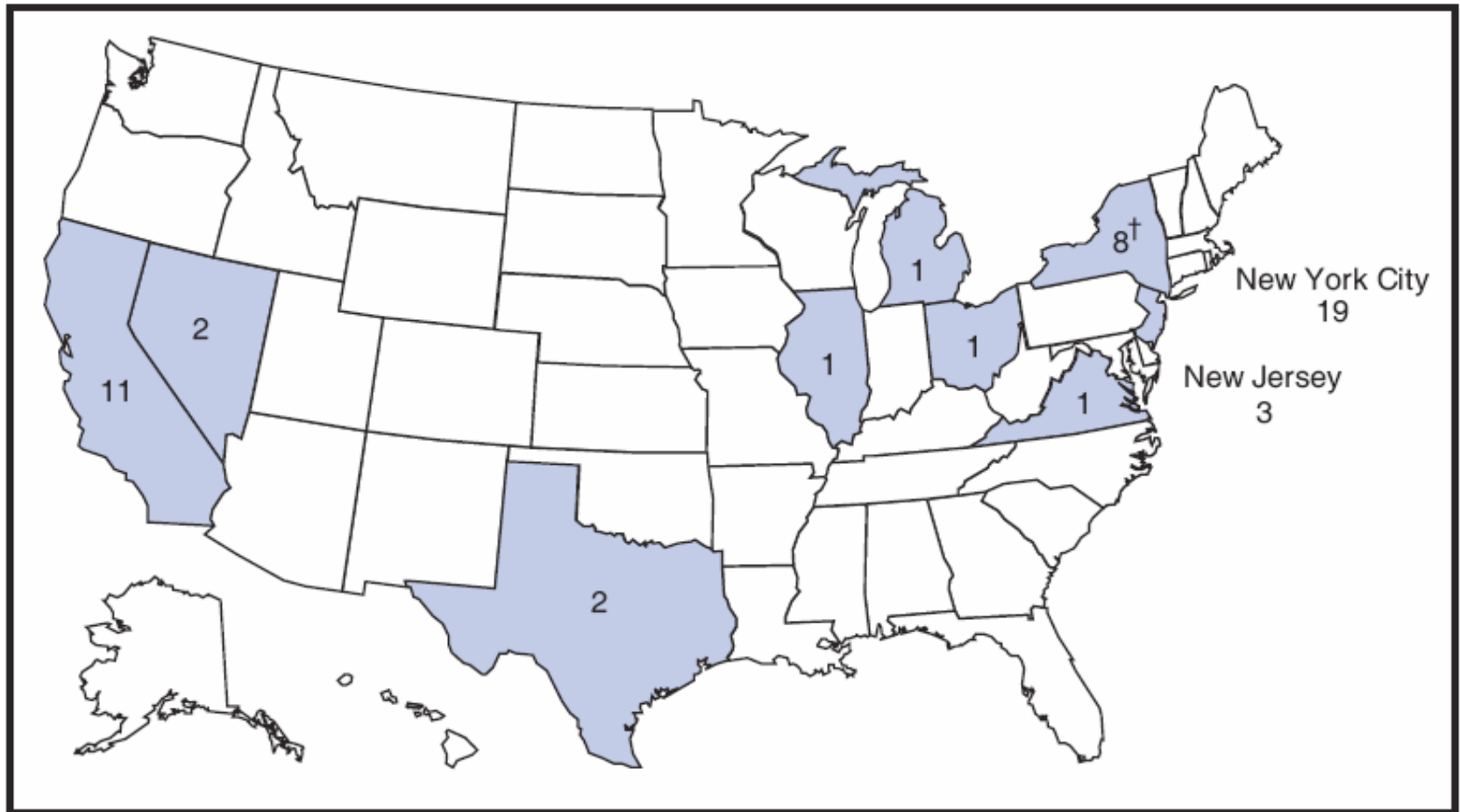
XDR-TB found in:
USA: 4% of MDR-TB
Latvia: 19% of MDR-TB
S Korea: 15% of MDR-TB





Figure 2 Countries with confirmed XDR-TB cases thus far (pink). From the World Health Organization, http://www.who.int/tb/xdr/xdr_jan.pdf (accessed 22 January 2007).

FIGURE. Number of reported cases of extensively drug-resistant tuberculosis (XDR TB)* — United States, 1993–2006



* XDR TB defined as resistance to at least isoniazid, rifampin, any fluoroquinolone, and at least one second-line injectable drug (kanamycin, amikacin, or capreomycin).

† Excludes New York City.

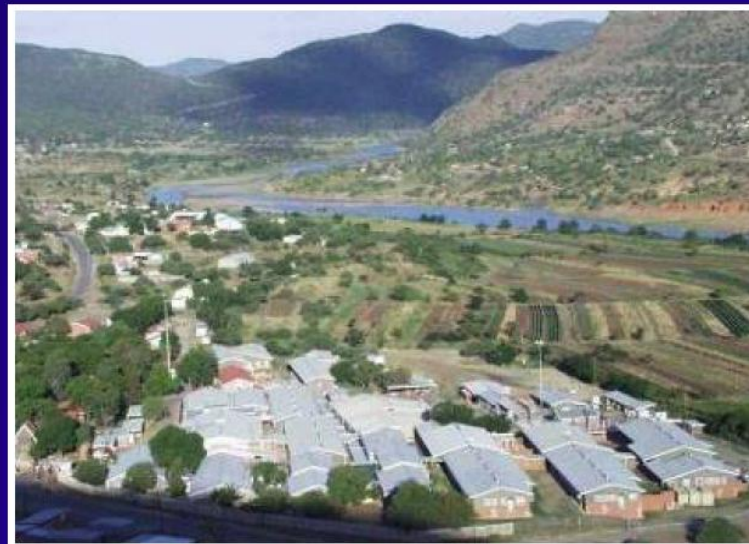
XDR-TB in Southern Africa

August 2006



Church of Scotland Hospital, Tugela Ferry, KwaZulu-Natal Province, South Africa

- 53 of 544 patients defined as XDR-TB cases
- 52 of the 53 patients died on average within 25 days, including those on antiretroviral therapy
- Further investigations being carried out
- XDR-TB likely in bordering African countries



Given the underlying HIV epidemic in Africa,
drug-resistant TB could have a major impact on mortality
and requires urgent action on care and prevention

The fresh air cure 2010

What is it about good food, resting outdoors and no longer
being shunned by that makes you feel better when you
have TB

Vitamin D

Vitamin A

Stress hormones

How do we work out how to vaccinate?

Have a hypothesis as to what is

protective

Test the hypothesis in an experimental

model

Interpret results and determine what the outcome

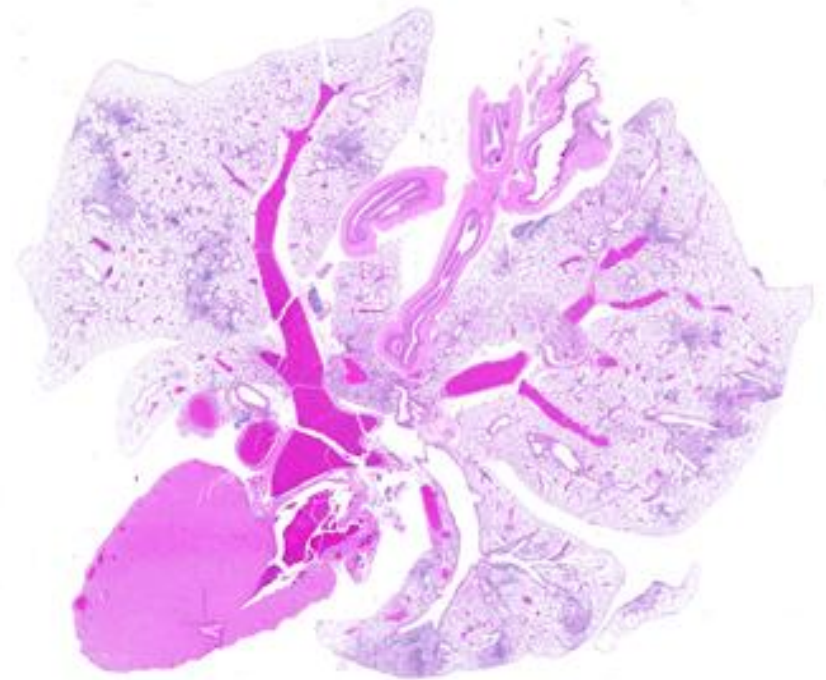
is

Publish results allowing investigators who study
human disease to integrate the information into their
data sets

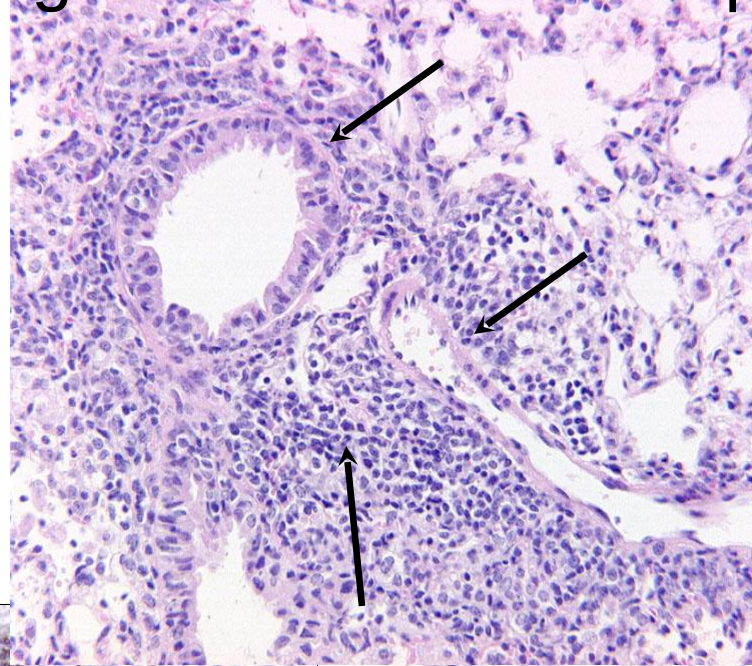
Mice can be infected with a cloud of droplets similar to those released by cough or sneeze. The cellular and pathological response can be analyzed and definitive results obtained



What does this mean for the mouse?

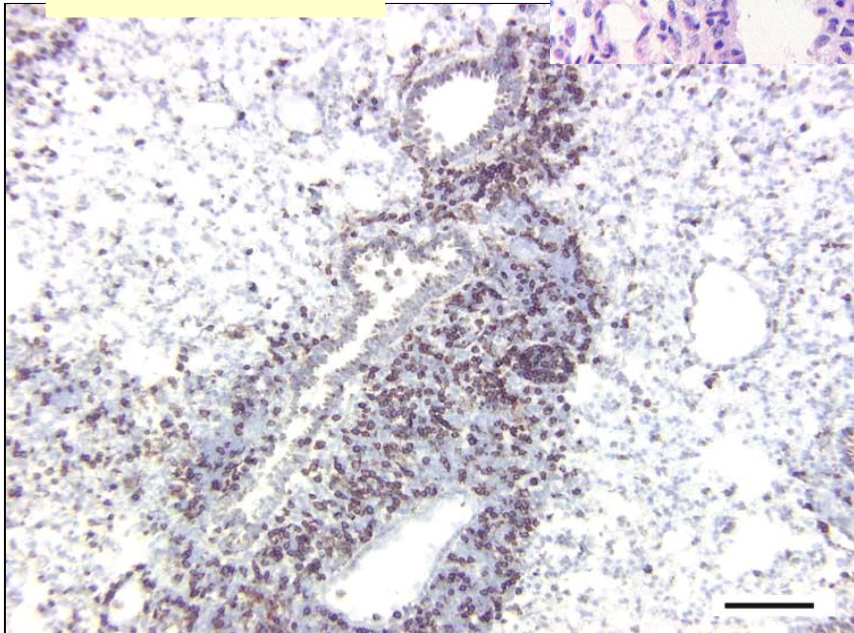


We can investigate the function of specific cell types

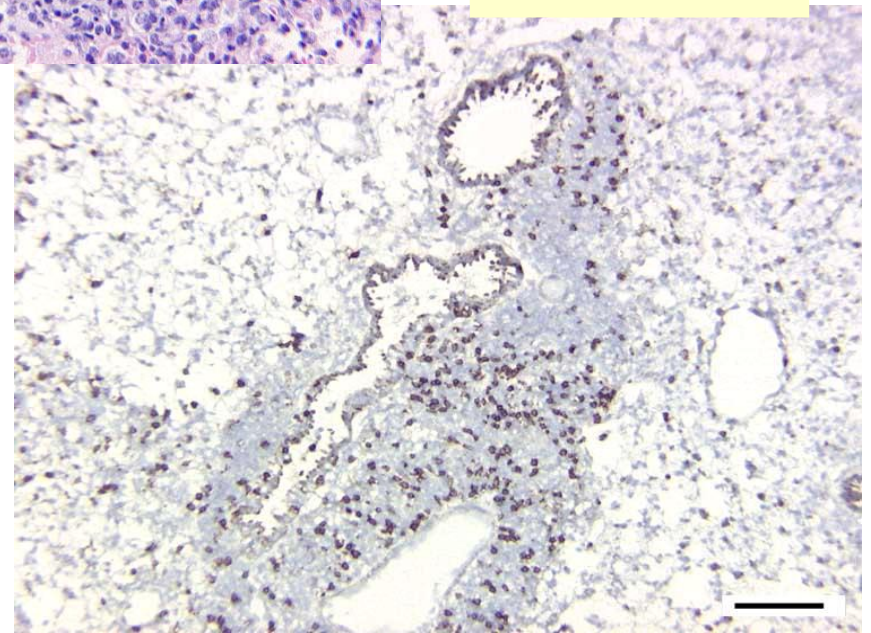


H&E

IHC CD4 cells



IHC CD8 cells



We can determine what specific cells do

Proliferation

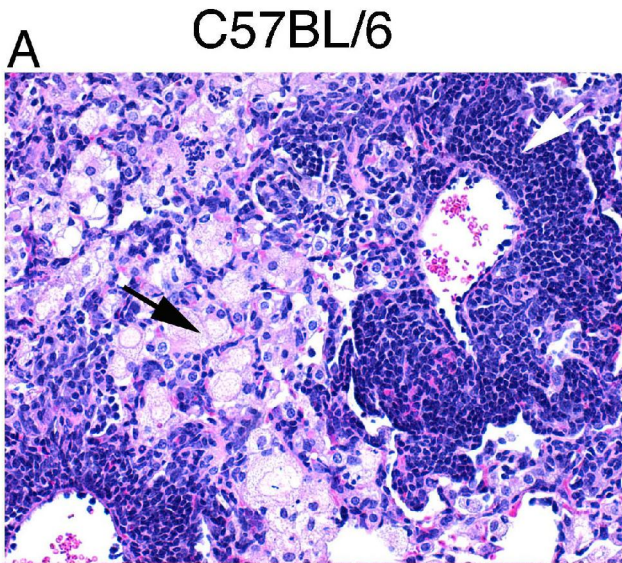
CD4 T cells divide

Cytokine production

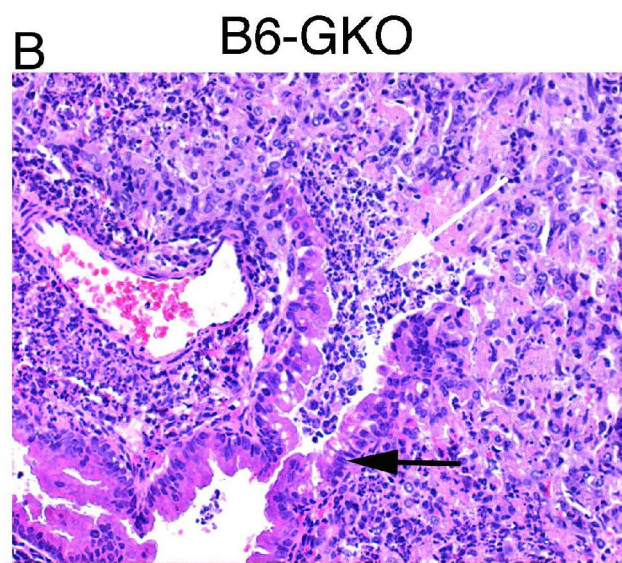
CD4 T cells produce molecules to activate macrophages

Expression of CD44, a marker of T cell activation

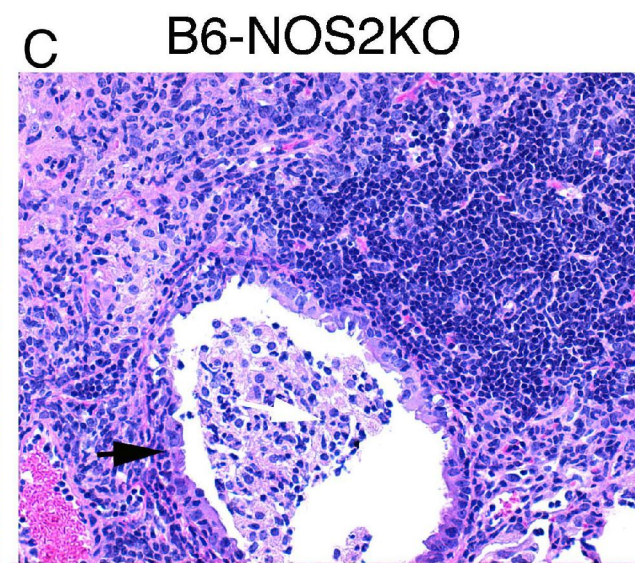
White blood cells accumulate in the lung.
The inflammation is controlled by
feedback mechanisms



Intact

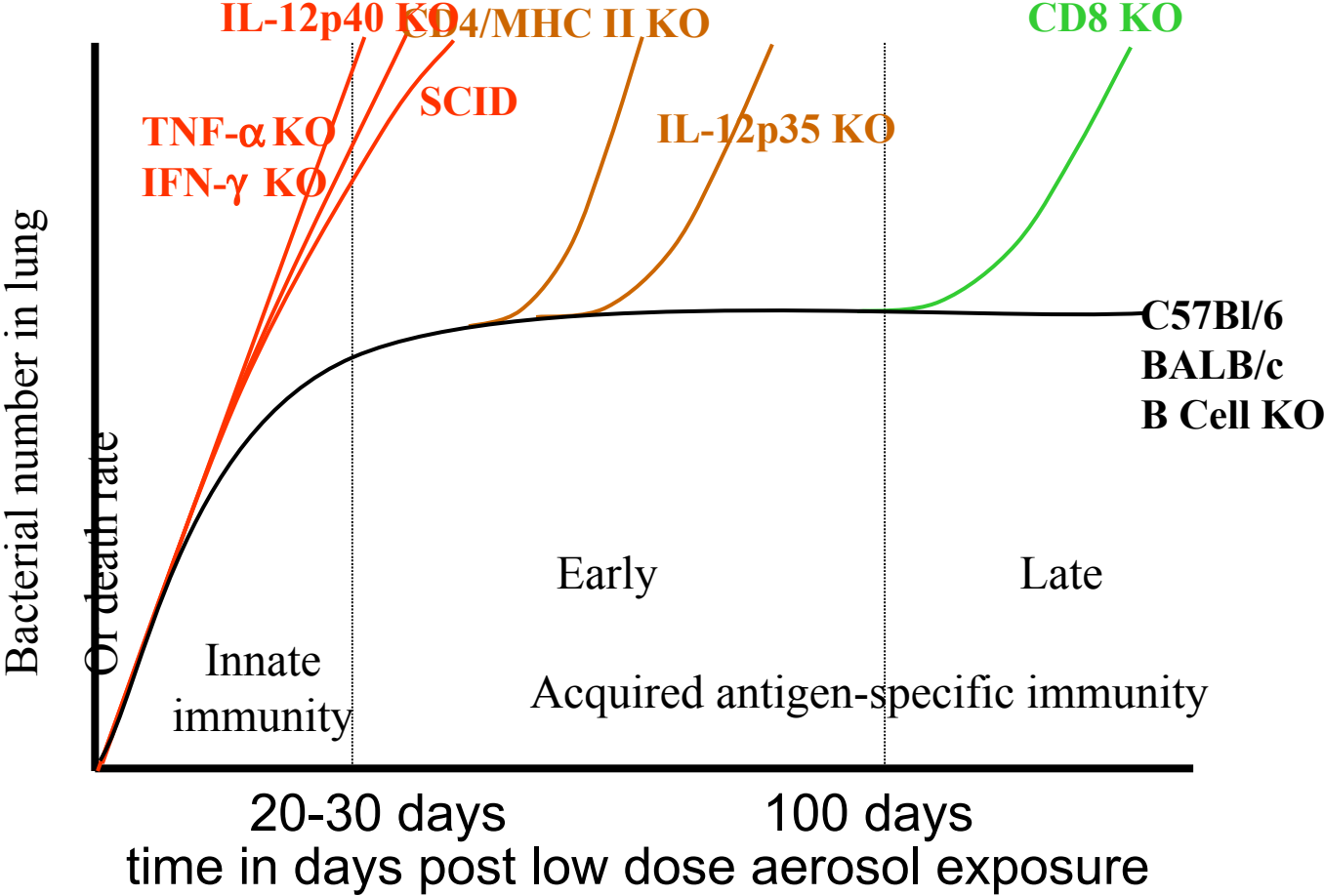


Deficient

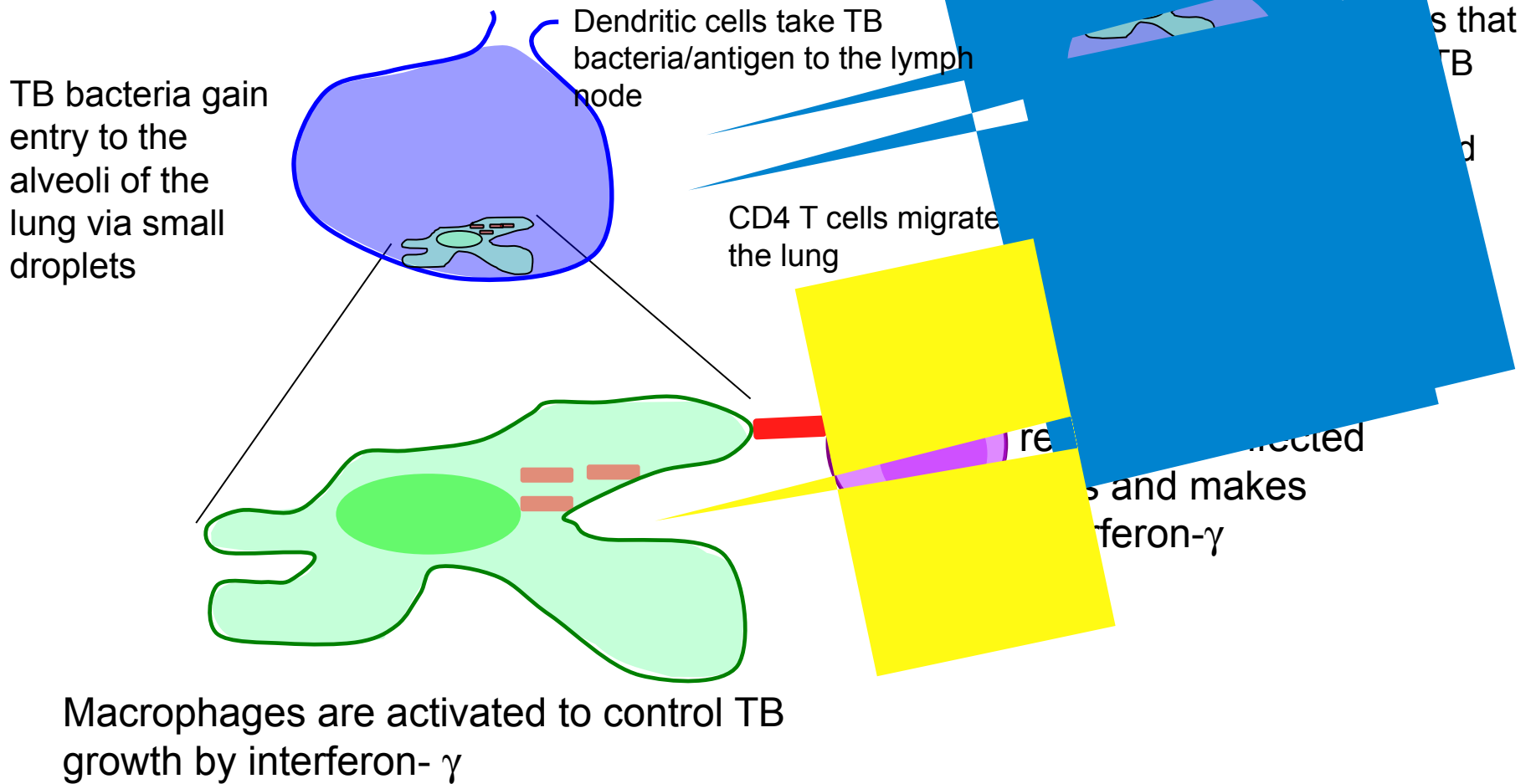


Deficient

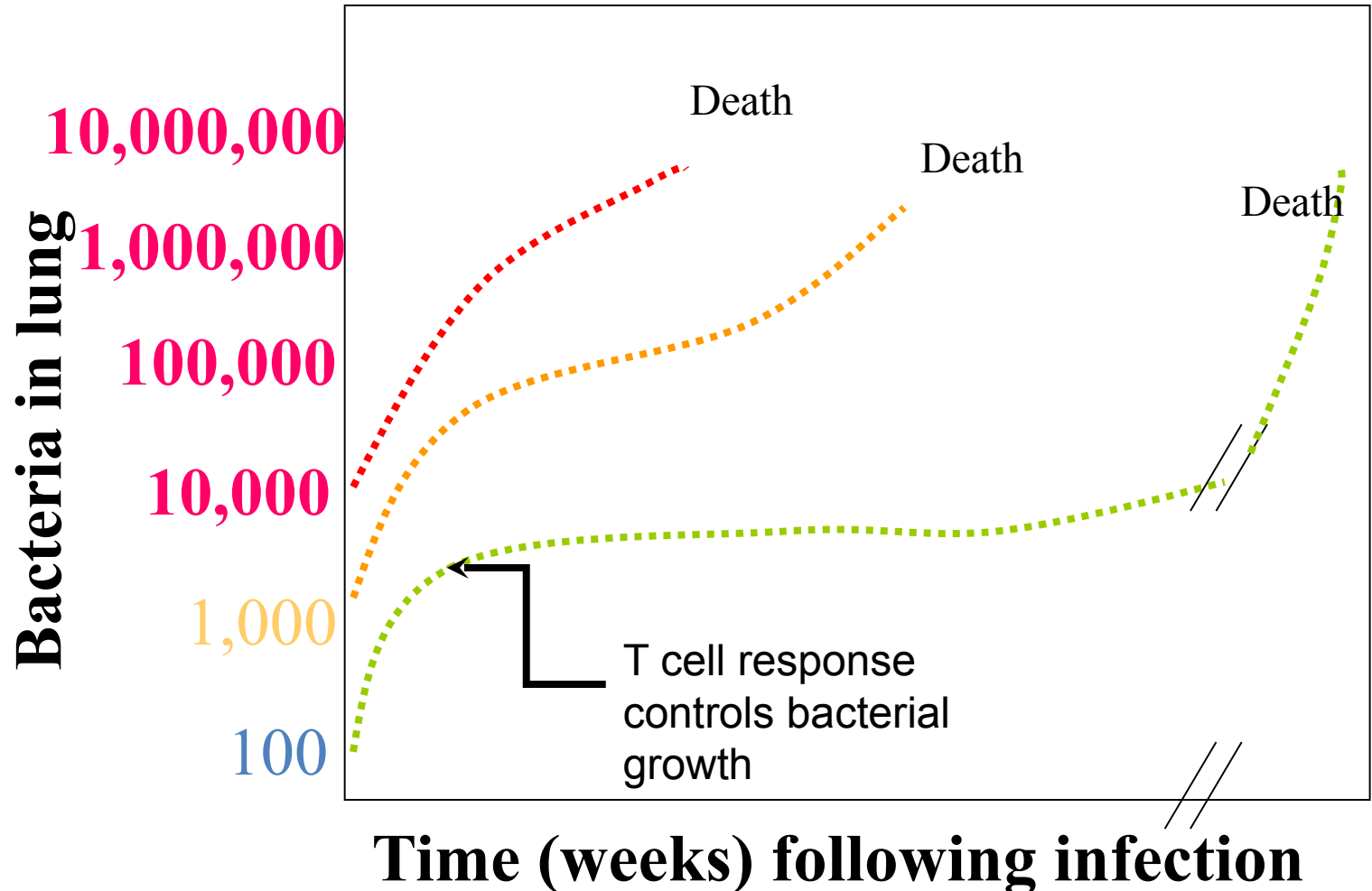
Animal experiments have allowed us to identify what parts of the immune response control tuberculosis



Using animal models at T... developed this working model



Animal experiments allow us to understand important aspects of disease development



How can we improve this?

