Learning Objectives:

1. Describe the main components of health systems
2. Identify risk factors for developing drug resistance
3. Evaluate designs of health systems in the setting of poverty
Introduction

Tuberculosis is a disease that has affected humans since prehistoric times. Evidence of tuberculosis infections have been found in the remains of humans who lived 6,000 years ago. Cases have been described by physicians such as Hippocrates in Ancient Greece and Galen of the Roman Empire.¹ However, during the nineteenth century new developments increased both the incidence of tuberculosis and our understanding of it.

The organism, *mycobacterium tuberculosis*, causes the infection and spreads through the air via droplets. As industrialization spread throughout Europe and the United States people began to move to city centers, living close together and in poor conditions, the ideal environment for the bacteria to spread. At the same time, scientific advancement led to the identification of the causative bacteria by physician Robert Koch, and the means to contain it through the new field of public health.² Then, in the 1950s, two new antibiotics, Streptomycin and Rifampin, came into use as a means of curing tuberculosis infections, and many thought that it was only a matter of time before the disease could be eradicated.³ Unfortunately, that was not the case and tuberculosis continues to affect millions of people throughout the world.

*Tuberculosis: Infection and Disease*⁴

The illness caused by the tuberculosis bacterium can be complicated and highly variable. At every stage tuberculosis is reacting to conditions inside the body and the larger environment.

**Etiology:** *Mycobacterium tuberculosis* come from the family of mycobacteria, rod shape organisms which grow in oxygen rich environments and cause a number of diseases in humans, including tuberculosis and leprosy.

**Transmission:** The bacteria spread when a person with active pulmonary tuberculosis expels small amounts of the bacteria into the air while coughing, talking, sneezing or singing. Due to the exceptionally small size of the bacteria (0.4x3 micrometers) it can remain in the air for minutes to hours. An individual is exposed by inhaling the droplets into their lungs. It is important to note that not all persons exposed to the bacteria will go on to develop an infection.

**Infection** (Latent tuberculosis): Infection occurs when the bacteria invade the lung tissue. The bacteria replicate and form a *granuloma*, walling itself off from the host’s immune system. At this point, the infected person is without symptoms and cannot spread the bacteria. The individual’s immune system keeps the bacteria segregated, in its latent form.
**Disease:** Should the host’s immune system falter, the bacteria that have been living inside the granulomas can begin to spread and cause symptoms. Transition to active disease is influence by a number of factors, including: age (children under 5 years old and elderly adults), immune suppression (due to HIV, cancer, chemotherapy, etc.), and malnutrition. However, the transition to active disease only happens in a fraction of patients. A young person with a new infection has only a 10% lifetime risk of developing active disease.

**Tuberculosis can have many different manifestations:**

- **Pulmonary:** This is the most common form of tuberculosis and accounts for 80% of cases in HIV-negative patients. Possible symptoms include: persistent coughing (>2 weeks), cough productive of phlegm and/or blood, shortness of breath, chest pain, fevers, night sweats and weight loss.

- **Lymphatic:** The traditional term for this type of tuberculosis is “scrofula”. The bacteria invade and spread through the individual’s lymph nodes causing them to enlarge. The enlarged lymph nodes appear as rubber, painless masses below the skin. It is a form more common in women and children.

- **Extra-pulmonary:** Tuberculosis can affect any organ system in the body including the brain, bones and kidneys.

**Diagnosis:** Due to the wide variety of presentations in tuberculosis, diagnosis of infection and disease can be complicated.

- **Clinical:** Healthcare providers identify individuals with symptoms (persistent cough, fevers, night sweats, weight loss) and/or radiographic signs (typical findings on chest x-ray); this combined with response to treatment constitutes a clinical diagnosis.
- **TB Skin Test**: this test identifies individuals who have been exposed and developed an immune response to tuberculosis. A small amount of tuberculin protein is injected into the skin and in 48-72 hours a raised bump will identify those with an immune response.
  - This test does not differentiate between those who have infection, disease or previously treated tuberculosis

- **Sputum Sample**: this is the current standard for identifying tuberculosis disease. The sputum coughed up by a symptomatic individual is stained and examined under a microscope for evidence of mycobacterium tuberculosis
  - Can only be utilized in individuals with productive cough
  - High level of false negatives – individuals with active TB that have negative sputum samples (diagnosed by symptoms, x-rays and response to treatment)

- **Nucleic Acid Amplification**: a newer technology that also uses sputum samples to look for tuberculosis by identifying components of the bacteria
  - Technology is more expensive than sputum samples but can detect lower levels of bacteria in a given sample

**Treatment**: The current standard of treatment was developed by the Centers for Disease Control and adopted for general use by the WHO in the 1990s and is termed Directly Observed Treatment, Short-course (DOTS). It involves a system within a country to identify symptomatic patients and confirm diagnosis through sputum samples and/or clinical diagnosis. The patients are enrolled in a program to supply 6 months of daily treatment with 2-3 drugs (primarily the antibiotics Isoniazid and Rifampin). Healthcare workers observe patients taking their medications each day and monitor symptoms and side-effects.

**Resistance**: One feature of tuberculosis that makes it difficult to treat is the bacteria’s ability to develop resistance to antibiotics. As the individual is treated with antibiotics, the bacteria continue to replicate, and some strains may adapt mechanisms to counteract the antibiotics. Risk factors for developing resistance include the use of a single drug, inadequate length of therapy and interrupted therapy. Strains resistant to the standard therapy (isoniazid and rifampin) are termed Multi-Drug Resistant Tuberculosis (MDRTB) and stains resistant to standard and second line therapy are termed Extremely Drug Resistant Tuberculosis (XDRTB).

**Tuberculosis Today**

As effective treatments for tuberculosis came about, rates of infection and disease fell drastically over the 20th century, but the hoped for eradication of the disease did not materialize. In 2013, the WHO estimated that 11 million people were living with tuberculosis in the world and 1.1 million had died from tuberculosis. Though the mortality rate has decreased 45% from
1990 to 2013, tuberculosis continues to be the second leading infectious disease cause of death and disability, preceded only by HIV.\textsuperscript{v}

Of the estimated 9 million new cases of tuberculosis diagnosed in 2013, 25\% were in the WHO’s African Region and 56\% in the South East Asia and Western Pacific Regions.\textsuperscript{vi} The distribution of tuberculosis and mortality from tuberculosis is closely related to poverty with 95\% of tuberculosis disease and 98\% of deaths from tuberculosis occurring in developing countries.\textsuperscript{vii} The conditions of poverty (overcrowding, malnutrition and limited access to healthcare) make it much more likely for both the transmission of tuberculosis and the development of active disease. Though tuberculosis rate are higher in low-income countries (LICs), high-income countries (HICs) continue to have outbreaks of tuberculosis in areas of poverty. Furthermore, the surveillance and treatment of tuberculosis requires dedicated healthcare workers, laboratory facilities and consistent supply of drugs that can be difficult to maintain in a resource poor setting.

Despite these barriers, great strides have been made to address tuberculosis in the developing world. National Tuberculosis Programs (NTPs) are found in most countries, which allows for surveillance of latent tuberculosis and treatment with DOTS. As a result the overall incidence of tuberculosis fell by an average of 1.5\% per year between 2000 and 2013, reflecting a decrease in transmission. The overall prevalence of TB fell 41\% between 1990 and 2013, marking a significant improvement in treatment.\textsuperscript{viii} Much of the improvements are due to expanded health services that utilize community health workers, nurses and doctors to provide the daily care needed for tuberculosis treatment.\textsuperscript{ix}
Healthcare Systems

Healthcare systems are the method by which healthcare is financed, organized and delivered to a population. Across the world there are many variations of health systems as each is particular to the culture and history of the population they serve. However, there are some common features to health systems and many of the variations can be attributed to a ratio of public to private control in the areas of finance, organization and delivery.

Organization: Health systems can be divided into three broad categories of care. Variation between systems is due to varying amounts of facilities, funding and geographic placement of each category of care.

Public Health: This includes the healthcare provided by the government or government agencies to address population health. Public health includes infection disease control, water safety, and reporting of births, deaths, injuries, and accidents. In some countries a robust public health can include departments for food and drug safety, workplace safety, vaccination programs and other measures to ensure population health.

Primary Care: Primary care refers to the routine care of an individual including vaccinations for children, care before and during childbirth and care for chronic illnesses. Delivery tends to be within communities by anyone from physicians to nurses to laypersons with training in healthcare. In the developing world tradition healers can be an important part of primary care.

Secondary/Tertiary Care: Care that is beyond the purview of primary care falls into this category, including surgery and other services that require hospitalization. Delivery tends to be by physicians and other medical personnel with specialized training. Care tends to take place in a more formal setting of clinics and/or hospitals.

While public health facilities are owned and operated by governments, primary and secondary care facilities can be either privately or publicly owned. The matter of ownership is important because it can factor into the location of primary and secondary care centers. For example, a public hospital may be built to serve the health needs of a specific community, while privately owned hospitals are located based on demand for services.

Delivery: A primary goal of healthcare systems is to deliver care to individuals, often in a combination of materials, personnel and facilities.

Materials: Medicines, machines, protective equipment and other medical resources make up the materials needed to deliver care.

Personnel: This includes lay-persons trained as community health workers, physicians, nurses, physical therapists, all the way up to public health and government administrators. In general, the term “personnel” includes those with special training necessary to delivery healthcare.
Facilities: Healthcare facilities include structures such as offices, clinics, nursing homes and hospitals where people receive care. In addition, places such as diagnostic laboratories, blood banks and schools for health professionals are also important components to healthcare delivery in many countries.

Financing: How healthcare services are paid for is an important part of every health system. Methods of payment can affect both the organization of the system and how individuals access care. Most health care systems incorporate a number of different methods of financing in order to pay for health services.

Taxation/Revenue: This is the method of collecting payment for components of the health system that is under public control.

External Resources: A method of financing in low-income countries, this refers to external aid for the provision of health services.

Health Insurance: This is a method for pooling health risks by paying into an organization that then reimburses providers and facilities for health services.

Social Insurance – in this model the market for insurance is regulated by the government which requires all (or most) to purchase insurance and also uses public funds to subsidize the poor.

Private Insurance – in this model, insurance is offered in the marketplace and generally purchased by individuals or employers on behalf of their workers. There is not requirement for individuals to purchase in this model.

Direct Payment: This refers to payment from individuals directly to providers and facilities for health services, also known as “out-of-pocket” payments

Cost-effectiveness and the Controversy of MDRTB

One of the new challenges in the fight to control tuberculosis is the development of Multi-Drug Resistant Tuberculosis (MDRTB). Resistant strains can develop within previously treated individuals or be spread as new cases of tuberculosis. The number of cases of MDRTB has tripled between 2009 and 2013 and in 2013; an estimated 3.5% of new cases and 20.5% of previously treated cases were MDRTB strains. Ultimately drug resistance can happen spontaneously, but is much more likely to develop if an individual has incomplete or inadequate initial therapy. There are many factors which can contribute to the development of MDRTB, including:

- Barriers in Therapy: A complete treatment for a new case of tuberculosis takes 6 months of taking antibiotics every day. Patients as part of observed therapy may be required to travel to a clinic daily or have a worker come to their house. The drugs can cause
unpleasant side effects, such as nausea. Furthermore, there can be a social stigma to living with tuberculosis that can prevent people from completing treatment.

- **Drug Supply:** For many patients in developing countries, therapy comes as part of a National Tuberculosis Program (NTP) which provides drugs at low or no cost. However, as a result of depending on government budgets and/or international aid, disruptions such as civil conflict or decreased funds can limit the purchase of appropriate drugs.

- **Drug Quality:** Even if drug supply is secure, antibiotics may be of low quality. This is especially a concern in countries such as India where much of the treatment of tuberculosis happens in the private sector with patients purchasing drugs directly from pharmacies.

In order to diagnose MDRTB, symptomatic individuals who have failed treatment or new cases must have their sputum samples cultured and tested against the available antibiotics to confirm resistance and reveal possible drug choices. Once an individual contracts or develops MDRTB, they can no longer be cured by the standard treatment. Instead they must be treated with second-line antibiotics, which usually have more side effects, for a longer period of time (18-24 months). In addition, the cost of treating one person with MDRTB is currently US$ 4,000, ten times the cost of treating drug-sensitive tuberculosis. Due to the difficulties in diagnosing and treating MDRTB, it is estimated that less than 20% of cases receive the appropriate treatment.

In response to MDRTB, many countries are adopting additional programs to address the identification and treatment of these cases. Furthermore, the WHO and other international aid organizations are trying to lower the cost of treatment for MDRTB through the lowering of existing drug prices, the development of new second line drugs and trials of shorter courses of
However, many countries still face difficult decisions in how to allocate resources for tuberculosis treatment.

**Questions to Consider:**

The delivery of tuberculosis treatment requires taking daily medications observed by a health worker each day. This demonstrates how vital adequate health systems are in providing effective health care. However, the structure of health systems varies widely between countries with some systems being under the control of the government, while others allow for mostly private healthcare.

Recently, the WHO has focused on a new issue, providing universal healthcare in all countries. Part of this work is determining the basic level of healthcare for individuals, without undue financial hardship. Consider the structure of health systems outlined above:

What should be the levels of care included in basic healthcare? Public health? Plus primary care? Plus secondary/tertiary care? What would be some services not included?

Consider health care for an impoverished individual that is unable to pay? What type of healthcare should they receive? Who should pay for it?

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2. Ibid.
5. Global Tuberculosis Report 2014
xiv Shin et al., “Community-Based Treatment of Multidrug-Resistant Tuberculosis in Lima, Peru: 7 Years of Experience.”
xvi Global TB 2010
xviii WHO Factsheet