TUBERCULOSIS

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HISTORY/ETIOLOGIC AGENT

- **Ancient Times**: Tuberculosis (TB) has been found in relics from ancient Egypt, India, and China. Archeologists have found in Egyptian mummies a form of spinal tuberculosis known as Pott’s disease.

- **Middle Ages**: Indications of tuberculosis of the cervical lymph nodes, called scrofula, was apparent in the Middle ages. Coined as, “the king’s evil”, it was largely believed that the kings of England and France could cure scrofula simply by touching sufferers of the disease.

- **18th Century**: TB reached its peak prevalence in Western Europe—with as many as 900 deaths per 100,000. A host of poor living conditions and sanitation, among malnutrition and others lead to this rise. TB was renamed “The White plague” around this time.
Investigation of TB: The tubercle bacilli or the causative organism of tuberculosis was demonstrated by Robert Koch in 1882. He showed that the organism’s unique protein coat made it difficult to visualize earlier until a specific stain called the Zeihl Neelson stain was discovered.

The bacteria was called Koch’s bacillus and since it took up the red acidic dye, it was called AFB or acid fast bacilli. Koch was awarded the Nobel Prize in 1905. In 1895 Wilhelm Roentgen developed X rays which further advanced diagnostics of tuberculosis. This allowed early diagnosis and isolation of infected individuals.
12/18/10 34 year old male, Hispanic, diagnosed with pulmonary TB. Positive for M. TB

Children under investigation. 11 month old, 4 year old showed asymptomatic. TST was 0mm. 15 year old complained of pain. TST 13mm all test negative.

15 year old contact showed right upper lobe abnormalities. Culture obtained and patient is under treatment regimen for active pulmonary TB, rifampin, isoniazid, pyrazinamide and ethambutal.

Further test showed negative for the 4 year old. Infant was diagnosed with military pulmonary TB and hilar lymphadenopathy. Underwent lumbar puncture and CSF. No indication of TB manigitis.
Infant was started on isoniazid, rifampin, ethambtol, and pyrazinamide.

2/24/2011: 4 year old contact tested again positive 10mm reaction to TST. Diagnosed with latent TB Infection (LTBI). Treatment extended to 9 months completed treatment in Sept. 2011.

Infant completed 6 months of short course therapy in May 2011.

Children improved clinically and radiograpgically, course treatment uneventful.

FUN FACT: I was diagnosed similar to the 4 year old, showing beginning stages of TB at the same age. I underwent a 9 month treatment and was cleared.
WHAT IS TB?

TB is a slow-growing obligate aerobe and a facultative intracellular parasite. They grow in parallel groups called cords. It retains many stains after decoloration with acid-alcohol, which is the basis of the acid-fast stains used for pathologic identification.

Mycobacteria, such as M. tuberculosis, are aerobic, non-spore-forming, nonmotile, facultative, curved intracellular rods measuring 0.2-0.5 μm by 2-4 μm. Their cell walls contain mycolic, acid-rich, long-chain glycolipids and phospholipoglycans that protect mycobacteria from cell lysosomal attack and also retain red basic fuchsin dye after acid rinsing (acid-fast stain).
Tuberculosis infection can take 1 of a variety of paths, which don’t have to lead to actual TB. The infection may be cleared by the host immune system or suppressed into an inactive form called latent tuberculosis infection, with resistant hosts controlling mycobacterial growth before the development of active disease. Patients with LTBI cannot spread TB. The lungs are the most common site for the development of TB; 85% of patients with TB have pulmonary complaints. Extra-pulmonary TB can occur as part of a primary or late, generalized infection. An extra-pulmonary location may also serve as a reactivation site; extra-pulmonary reactivation may coexist with pulmonary reactivation.
The most common sites of extra-pulmonary: Mediastinal, retroperitoneal, and cervical (scrofula) lymph nodes -The most common site of tuberculous lymphadenitis (scrofula) is in the neck, along the sternocleidomastoid muscle; it is usually unilateral and causes little or no pain.

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The typical TB lesion is an epithelioid granuloma with central caseation necrosis. The most common site of the primary lesion is within alveolar macrophages in sub pleural regions of the lung. Bacilli proliferate locally and spread through the lymphatics to a hilar node, forming the Ghon complex.

Initial lesions may heal and the infection become latent before symptomatic disease occurs. Smaller tubercles may resolve completely. Fibrosis occurs when hydrolytic enzymes dissolve tubercles and larger lesions are surrounded by a fibrous capsule. Fibrocaseous nodules usually contain viable mycobacteria and are potential lifelong foci for reactivation or cavitation. Some nodules calcify or ossify and are seen easily on chest radiographs.

Tissues within areas of caseation necrosis have high levels of fatty acids, low pH, and low oxygen tension, all of which inhibit growth of the tubercle bacillus.
If the host is unable to defend against the initial infection, the patient develops progressive, primary TB with tuberculous pneumonia in the lower and middle lobes of the lung. Purulent exudates with large numbers of acid-fast bacilli can be found in sputum and tissue. Subserosal granulomas may rupture into the pleural or pericardial spaces and create serous inflammation and effusions.

With the onset of the host immune response, lesions that develop around mycobacterial foci can be either proliferative or exudative. Both types of lesions develop in the same host, since infective dose and local immunity vary from site to site.

Proliferative lesions develop where the bacillary load is small and host cellular immune responses dominate. These tubercles are compact, with activated macrophages admixed, and are surrounded by proliferating lymphocytes, plasma cells, and an outer rim of fibrosis. Intracellular killing of mycobacteria is effective, and the bacillary load remains low.

Exudative lesions predominate when large numbers of bacilli are present and host defenses are weak. These loose aggregates of immature macrophages, neutrophils, fibrin, and caseation necrosis are sites of mycobacterial growth. Without treatment, these lesions progress and infection spreads.
Tuberculosis is transmitted from an infected person to a susceptible person in airborne particles, called droplet nuclei. These are tiny water droplets with the bacteria that are released when infected persons cough, sneeze, laugh, and shout, among others. The droplet nuclei remain suspended in the air for up to several hours. Tuberculosis bacteria, (*Mycobacterium tuberculosis*) however are transmitted through the air. They can only be spread if they are breathed in.

Transmission occurs when a person inhales droplet nuclei containing tuberculosis bacteria. These droplet nuclei travels via mouth or nasal passages and move into the upper respiratory tract. Thereafter they reach the bronchi and ultimately to the lungs and the alveoli.
Pulmonary tuberculosis

In this type of tuberculosis the lesions are in the lungs. A Chest X ray shows the lesion within the lungs. There may be scarred appearance of the lungs. Primary tuberculosis generally appears in the central upper portion of the lungs with a pleural effusion. In severe disease there may be a picture like millet seeds over the X ray plate of the lungs. This is called miliary tuberculosis.

The phlegm or mucus is collected from the patient. It is placed onto a glass slide and stained with a special dye called the Ziehl-Neelsonstain and then viewed under the microscope. The tubercle bacilli show up as tiny red thread like organisms.

At least 3 spontaneous sputum samples need to be examined for culture and microscopy. Due to the time necessary for culture results, treatment with anti tubercular drugs may be started on the basis of microscopy if there are symptoms are present. Sputum is cultured on a medium called the Löwenstein-Jensen slope which takes 4-8 weeks due to slow bacterial growth.
In tuberculosis suspected outside the lungs several tests are suggested:

A CT scan or a MRI scan of the part of the body affected or of the whole body to look for other routes of the disease.

An ultrasound scan of the abdomen and other hollow parts of the body that may be affected.

Series of routine and special blood tests to detect tuberculosis.

Urine tests for the bacteria if the urinary tract is affected.

Biopsy of the affected tissues and parts of the body and microscopic examination of the sample.

Those with suspected tuberculosis of the nervous system or of the brain and meninges need a lumbar puncture. This involves taking a small sample of CSF from the base of the spine. The fluid is checked under the microscope of using biochemical tests to detect tuberculosis.
Tuberculosis vaccine: Bacillus Calmette-Guérin (BCG) The BCG vaccine is given to all infants in countries where the disease is prevalent. In low risk countries, it is given to those who are at risk. This is not recommended for people who have latent TB. To test for latent TB in persons of high risk, the person is given a Mantoux skin test to check for latent tuberculosis.

If suspected of Pulmonary TB, a Chest X-ray is performed to confirm whether the infection is active or frank tuberculosis.

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Antibiotics -First line drugs:
Isoniazid is one of the most effective agents. It has the capability to penetrate the tubercular lesions. Rifampicin has good tissue penetration. Both Isoniazid and Rifampicin may cause liver damage. Pyrazimamide acts on slow growing and semi-dormant bacilli that lie within the cells. Ethambutol also slowly inhibits mycobacterial growth.

Antibiotics -Second-line drugs:
Second line drugs come into play in the instance of resistance to and inefficacy of the first line agents. Drugs include amikacin, capreomycin, cycloserine, azithromycin, clarithromycin, moxifloxacin, levofloxacin etc. Streptomycin is now rarely used in the UK.
Number of cases in the U.S. each year:
A total of 9,945 TB cases (a rate of 3.2 cases per 100,000 persons) were reported in the United States in 2012.

There were 569 deaths from TB in 2010, the most recent year for which these data are available. Compared to 2000 data, when 776 deaths from TB occurred, this represents a 27% decrease in TB deaths over a decade.

Number of cases in Salem each year:
In 2012, 61 cases of TB were verified in Oregon, for a rate of 1.6 cases per 100,000 residents.
Why is TB important to study?

- It is important to know about it because it can be easily spread and symptoms in the long run could be fatal.
- Though it is not eradicated it is very much preventable. The herd immunity in the U.S. is so strong, we no longer require a vaccination for it.
- TB could easily be a disease of the past, allowing many populations relief and a chance at recovery.
- Because it can be prevented it is important to raise awareness for people in the medical to bring the attention for vaccines in their countries.


UThealth Northeast: Case studies, Pediatric TB http://www.heartlandntbc.org/casestudies.asp