

Tuberculosis:

I. Introduction.

In the early part of the 20th century, a suburb of Cairo (Helwan) was renowned for its good climate, healthy springs, etc.

- Although it was partly a resort, eventually a hospital for tuberculosis patients was built.
- One thing thought to help tuberculosis patients (back then) was clean air, and Helwan had lots of it.
 - It gained international notice for its “healthy” air.
- If you go to Helwan today, the air is so bad it's been compared to smoking two packs of cigarettes a day.
 - Air pollution has not been kind to Helwan (or Cairo, for that matter).
 - There are days when it's hard to see across the street.

Tuberculosis has been around for an awfully long time, and is known from both the New and Old worlds.

- we have evidence of tuberculosis in South America from about 2000 years ago.
- In the Old World, we go as far back as 18,000 years in animals, and 4,000 B.C. for humans.
 - Several Egyptian mummies have evidence of tuberculosis.
- The Ancient Romans knew about the disease, and Pliny the Elder prescribed:

"wolf's liver taken in thin wine, the lard of a sow that has been fed upon grass, or the flesh of a she-ass taken in broth"

 - did it work????
- More serious study can probably be traced back to Ibn Sina (Avicenna) in the 1020's.
 - While science was seriously stagnating in Europe, it was flourishing in the middle East.
 - Although Avicenna did a lot of different things, he's probably best remembered for his work in medicine.
 - he wrote over 40 treatises (that survive) on medicine, and is often considered the father of modern medicine.
 - some of the things Avicenna did:

- introduced systematic experimentation.
- discovered the contagious nature of infectious disease
- introduced quarantines, clinical trials, efficacy tests, randomized trials, and a bunch more.

- of course, many of these have changed considerably since his day.

- he also made contributions to physics, theology, natural history, chemistry and astronomy.

- he was born in 980 (370 AH) and died in 1037 (428 AH) and lived in central Asia and Persia.

- Anyway, Avicenna was the first to recognize tuberculosis as an infectious disease, and also suggested that it could spread through soil and water.

- He also devised specific types of quarantine to limit the spread of tuberculosis.

- Incidentally, one could argue that the first true hospitals came from the Islamic world, since up until then “hospitals” were mostly concerned with isolating the sick from society.

- Islamic hospitals welcomed the sick, cared for them, and generally tried to make them better.

- Hospitals in Baghdad between 800 and 1200 had staff physicians, separate wards for different conditions. Others had waiting rooms, and even female nurses.

Now that we've been thoroughly side tracked, let's get back to tuberculosis.

II. Cause.

A bacterium, *Mycobacterium tuberculosis*. It's aerobic, rod shaped, and gram positive (though it stains very weakly).

- the bacterium grows very slowly compared to other kinds of bacteria.

- there are three closely related bacteria, two of which can occasionally cause problems in humans, but this is rare.

III. Transmission.

Tuberculosis is transmitted usually as an aerosol:

- people sneezing, coughing, speaking, kissing, spitting, etc.

- inhaling just one bacterium is enough to cause infection.
- but generally, it's people who have more intense, prolonged contact that are most susceptible - these folks have an infection rate of close to 22%.
- if someone has active tuberculosis, he or she can infect between 10 and 15 people per year.
 - one needs to have active TB for transmission to occur.
- although it takes a while to cure TB, a person can become non-infectious within a few weeks of starting treatment (more later).

IV. Progression.

Generally, a TB infection starts when the bacteria reach the alveoli of the lungs (the microscopic sacks at the end of the bronchioles where gas exchange takes place)

- The bacteria (or bacterium) invade macrophages, and start to replicate.
- From there, they can spread to the lymph nodes and eventually the rest of the body via the blood stream.
- At this point, the immune system often manages to neutralize the bacteria.
 - numerous different lymphocytes and macrophages form a “granule” surrounding the infected macrophages.
 - the immune system can destroy the bacteria (or at least some of them).
 - but often the bacteria only become dormant, and a “latent” infection develops.
 - this is perfectly all right, in the sense that the health of the person isn't affected.
 - it's estimated that 1.6 billion people have a latent infection.
 - a latent infection usually remains that way unless something happens to weaken the immune system.
- On rare occasions, TB bacteria can break out of one of these nodes and cause massive damage very quickly (miliary tuberculosis).
- Normally, to progress to active TB requires that the bacteria overcome the immune system of the host.
 - in 1 - 5 % of cases this happens almost immediately

- in 2 - 23% of latent infections this happens years after infection, and increases if there is some kind of damage to the immune system.

- people infected with both TB and HIV have a 10% chance of having TB become active every year.

- some drugs can also increase the risk of getting the active form.

- Some of the damage is often caused by immune responses.

V. Symptoms.

If active TB develops, 75% of cases progress to pulmonary TB (TB infects the lungs). Other forms are possible.

- chest pain, coughing up blood

- prolonged cough for more than three weeks

- fever, chills, night sweats, appetite loss, weight loss, fatigue

- in those instance where lungs are not the primary target, symptoms can involve the:

- pleura, CNS (meningitis), urogenital system, bones, joints, spine.

Untreated, mortality is around 50% (though this number seems to vary)

VI. Diagnosis.

It's difficult to diagnose TB due to the rather vague symptoms (which could be almost anything).

A few things work, though. Most people have probably had a TB skin test.

- it detects any kind of infection, including a latent infection (and those immunized).

- more precise diagnosis needs a full medical work up, including x-rays.

- it's difficult to grow TB because it grows so slowly.

- more accurate and cheaper tests are being worked on.

VII. Treatment & Prevention.

The good news is that TB can be treated.

Antibiotics work (mostly).

- however, the regime can be difficult and long, often requiring patients to take

antibiotics for six months to a year (or more).

- mostly because the bacteria grows so slowly, and many antibiotics interfere with growth.

The bad news is that TB is becoming increasingly resistant to antibiotics.

- One source mentioned the problem:

- Usually antibiotics kill off just about all the bacteria in the body; any that are left can be finished by the immune system.

- With tuberculosis, it only needs a few bacteria to survive for the disease to start up again.

- so with tuberculosis in particular, multiple antibiotics are recommended.

- There are two main forms of drug resistant TB:

- MDR TB (multiple drug resistant TB): resistant to two or more of the most useful TB antibiotics (e.g. isoniazid and rifampin).

- XDR TB (extensively drug resistant TB): resistant to just about all known antibiotics (a few still seem to work).

- this form can still be treated in some cases, though much depends on the condition of the person and the extent of drug resistance

- it appears (not sure) to involve use of all six second line drugs.

- In the U.S., drug resistant TB isn't quite so much of a problem yet, and even the old standby (streptomycin) seems to work reasonably well (though it should be combined with at least one other antibiotic).

- Vaccinations:

- There is a vaccine (BCG) that has been available for many years and is used in many parts of the world (it's estimated that 80% of children are vaccinated).

- it's not terribly effective, and doesn't prevent TB

- it does seem to prevent non-pulmonary TB in children

- there seem to be conflicting figures about just how effective this vaccine is. It's generally not available in the U.S., except in special instances.

- Recently a new vaccine has entered trials:

- it works together with the BCG vaccine, but stimulates T-cells to make a

stronger response to TB.

- early results are promising.

- Another recent vaccine has been developed in the U.S.; clinical trials should start in about 1 -2 years.

- There's hope that in a few years we may have a much more effective vaccine/vaccine regimen for TB.

- Other means of prevention:

- being careful with sneezes and stuff.

- a diet high in protein (Pliny the Elder??) seems to help prevent the active form from developing.

- isolating patients (quarantining patients)

- everyone has probably heard of the case of Andrew Speaker. He made headlines about a year ago.

- flew from Atlanta to Paris, then returned via a flight from Prague to Montreal, from where he crossed back into the U.S.

- it was believed that he suffered from XDR-TB.

- after he returned to the U.S. he was placed in involuntary quarantine.

- what really happened?

- he was diagnosed with TB in early March

- in late march MDR-TB was suspected

- he was told (in May) that he was not contagious, but advised not to travel.

- he flew from Atlanta to Paris, to Athens, to Santorini, to Rome (honeymoon).

- at this point the CDC informed him that he may have XDR-TB.

- the CDC had no way of getting him home and told him to arrange for private transportation.

- he flew to Prague and then Montreal.

- he claimed that had he been offered private transport, he

would have accepted it (he also claimed that the CDC had told him that he was to be quarantined in Italy for up to two years).

- during a congressional hearing Speaker played audio recordings from the CDC and other health officials that indicated that he was not a danger to others.

- he even asked several times, and also informed the CDC that he was planning to go abroad.

- the CDC later admitted that they knew about this.

- currently there is a civil suit by several people who were on the same flight as Speaker.

- finally, it turns out that Speaker has MDR-TB, not XDR-TB.

- (oh, yes, in a coincidence, his father in law is a physician that had done research on TB, but not MDR or XDR TB).

- Unfortunately early hopes that the disease could be completely eliminated evaporated due to the emergence of multiple drug resistant TB.

VII. Final comments.

Currently, TB is one of the leading causes of death (from infectious disease) world wide.

In 2004, 1.6 million people are thought to have died from tuberculosis.

- another 8.9 million new cases, and 14.6 chronic active TB cases.

More recent figures seem to indicate 2 million people dying each year from TB.

As usual, most of these are in the less developed world, particularly in Africa.

- HIV is obviously an important contributing factor.

- other factors that increase the incidence of TB are smoking (increases risk 2 - 4 times) and diabetes.

Although not so much a problem in the industrialized world, it used be endemic:

- in England, ¼ deaths was of consumption in 1815.

- As late as 1918, 1/6 of all deaths in France were caused by TB

- It's estimated that in the 20th century, TB killed 100 million people.

Finally, because TB has been around for so long, it's had an impact on art:

- La Bohème (Puccini), La Traviata (Verdi) are operas where the heroine dies of consumption.

- Dostoevsky, Victor Hugo, Thomas Mann, and many others have novels in which tuberculosis plays an important part.

- Even a film by Peter Jackson (Lord of the Rings) features a major character with TB (though the film is really about a lot of other things).