

Yellow fever:

I. Introduction.

Yellow fever was one of the first diseases for which an insect vector was confirmed. More soon.

It was also quite important to the history of the United States, and we suffered through numerous yellow fever outbreaks:

- Killed over 3,000 people in Norfolk in 1855.
- Killed over 25,000 people in Memphis and the surroundings in 1878.
- It also did a lot of damage elsewhere, possibly in Europe during the mid 6th century and recurring in Cuba.

II. Cause.

- An arbovirus, a single stranded RNA virus.
- The virus is transmitted by mosquitoes.
 - A Cuban doctor (Carlos Finlay) proposed that mosquitoes transmit yellow fever.
 - although he had some proofs, his work was ignored until Walter Reed picked up on this when he was put in charge of yellow fever for the military.
 - by using human volunteers, he confirmed Finlay's theory (several volunteers died).
 - When an outbreak of yellow fever started in New Orleans in 1905, he (after much resistance) convinced the city to implement anti-mosquito protocols.
 - the death toll was much lower than in similar past outbreaks.

III. Spread and infection & symptoms.

- The virus first replicates near the site where it was injected.
- From there spreads to the rest of the body using the lymphatic system.
- Incubation period is 3 - 6 days, after which symptoms first show up:
 - acute phase: fever, muscle pain, headache, backache, shivers, nausea, vomiting, slow pulse
 - most people get better 3 - 4 days after this.

- but 15% of patients then enter the toxic phase
 - jaundice, abdominal pain, vomiting, bleeding from mouth, nose, stomach, eyes.
 - blood can also appear in bodily secretions.
 - kidneys stop working.
 - about 50% of patients entering this phase die within 14 days. The rest recover without serious lasting damage.

IV. Treatment, prevention & misc..

- The bad news is that (like most viral diseases) there is not much in the way of treatment available.
 - the best that can be done is to try to treat symptoms, such as fluid loss, etc.
- However, some recent research show promise for some antivirals.
- The good news is that there's a vaccine which is relatively effective, though (rarely) it does cause allergic reactions in many people, particularly older folks.
 - More bad news: the reaction can be bad enough to kill.
 - But it is through vaccinations that it disappeared in most of the developed world.
- Other ways of preventing yellow fever include:
 - staying inside in areas with yellow fever
 - also using DEET, long sleeved clothes, etc.
- Yellow fever is most common in South America and Africa
 - vaccinations are sometimes required by the WHO before people can travel to/from areas with yellow fever.
 - there are estimates that there are about 200,000 cases every year, with over 30,000 deaths.
 - The disease is actually on the increase in the last 20 years.
- There is a form of yellow fever (rare) that can be transmitted to/from monkeys.

Typhoid

I. Introduction.

Unfortunately typhoid is still with us, and is surprisingly common:

- World wide, there are between 16 - 33 million cases, with over ½ million deaths.
- Even in the U.S., this was a serious problem until the 20th century, when the death rate hit 174/100,000 people (that's total, not out of infected).
- It also gave us such legacies as “Typhoid Mary” (more a little later).

II. Cause.

Bacteria (*Salmonella enterica*). Gram negative.

(Salmonella, or Salmonellosis is caused by a different strain of the same bacteria - a lot of human diseases are caused by this one!).

Bacteria spreads through the fecal-oral route.

- Remember, this is a lot easier than most people might think:
 - forgetting to wash hands after using bathroom
 - contaminated clothing/bed sheets
 - etc.

Bacteria enters body through the digestive system and then spreads to the rest of the body via the lymphatic system.

III. Spread and infection & symptoms.

The incubation period is between 8 and 14 days, and depends on how many bacteria are ingested.

- symptoms include high fever (104), sweating, gastroenteritis (inflammation of the gut), diarrhea, slow heart rate & dehydration.
 - occasionally a rash may show up as well.
 - as disease progresses, delirium (occasionally coma) may occur.
 - fever and general illness can last over 4 weeks.
- mortality rate without treatment is about 12%. With treatment (prompt) < 1%.

- after recovery, many (10 - 20%) patients may experience a relapse (strangely, antibiotics make a relapse more likely, though they'll stop a relapse just as well the second time around.

Bacteria can be found in blood, stool & urine, though presence may vary over the course of the illness.

IV. Treatment, prevention & misc..

Antibiotics work!

- ampicillin, ciprofloxacin, chloramphenicol, others.
- if these are used right away, mortality rate is less than 1%
- Bad news is that antibiotic resistance (even to cipro, though not so much in the U.S.) is growing, and we have MDR typhoid (multiple drug resistant)
 - ceftriaxone still works

Otherwise it's the usual, treat symptoms and hope for the best.

Vaccines are also available that are between 50 and 80% effective (a first vaccine was available in 1897).

- generally, vaccines are only recommended for people living or traveling to endemic areas.

Chlorine in drinking water also substantially reduced typhoid, as this kills the bacteria.

One problem is that some people remain completely asymptomatic:

- They are essentially healthy, yet have typhoid and can spread it.
- “Typhoid Mary” was the best example:
 - Mary Mallon: in brief, she worked a number of different jobs, and spread typhoid to many of the people she was working with.
 - On one occasion, she helped care for some of the sick, which only made things worse.
 - When she took a job as a cook, she began to be noticed. A number of patrons at the place she worked became ill, several died.
 - She was placed in quarantine (she denied she had typhoid), where it was confirmed she was the carrier.
 - After three years in isolation she was released on the condition

that she not work as a cook.

- She changed her name, and started working as a cook again.

- she infected 25 people, 2 of whom died.

- This time she was placed in quarantine for life.

- She died in 1938 of pneumonia (an autopsy found live typhoid bacteria in her body, particularly the gall bladder).

Typhoid may have been responsible for several historic plagues, including one in Athens in about 430 - 426 B.C. (though that may have been something else).

Miscellaneous comment:

- some recent research suggests that being heterozygous for cystic fibrosis just might confer an advantage in fighting typhoid. This might make this similar to sickle cell anemia. However, this is ongoing research.

(Cystic fibrosis is lethal in early childhood unless treated, and even with treatment kills people by their 30's.)

Tetanus

I. Introduction

We've all heard about this one - "have you had your tetanus shot" after stepping on a rusty nail, scratching yourself on something rusty, etc.

It's been with us for a long time (descriptions come from the 5th century B.C.), though it's not one of the big "killers" since it doesn't spread like many other disease.

Still, it has an untreated mortality rate of about 50% worldwide, causing about 300,000 to 500,000 deaths.

II. Cause

Cause is a bacterium: *Clostridium tetani*, gram-positive, anaerobic (obligative), rod shaped.

Often it is introduced through some kind of wound, cut, sore, etc.

Bacteria are found in soil (it's ubiquitous) , intestines & feces of animals. Some humans may also have the bacteria in their guts.

- Bacteria can also form endospores.

III. Spread and infection & symptoms.

Once the bacteria has entered the body, it spreads using the lymphatic system.

It releases several toxins, one of which is a very potent neurotoxin (one of the most toxic substances known - 175 nanograms (= $6.17294334 \times 10^{-9}$ ounces) will kill a 150 pound human)

- It is this neurotoxin that causes the classic tetanus symptoms.

Incubation period is from 3 to 21 days (some sources say up to 50 days), usually about 8.

Tetanus has several different manifestations, but most commonly, symptoms include:

- lockjaw, stiff neck, difficulty swallowing, rigid abdominal muscles (in that order)
- other symptoms include: fever, sweating, high blood pressure, sporadic high heart rate.
- Spasms can occur frequently, and continue for 3 - 4 weeks
- Other, rarer symptoms include spasms of the vocal cord and/or chest muscles.
 - Spasms can also cause bone fractures.

Complete recovery can take months.

There's an interesting diagnostic test called the "spatula" test:

- Back of the throat is touched with a wooden spatula.
 - In normal folks, this would cause a gag reflex.
 - In people with tetanus, this causes the patient to bite down on the spatula.

IV. Treatment, prevention & misc..

Well, as should be obvious, there's a vaccine.

- fairly effective, but should be renewed every 10 years.
- Most kids get this as a combined DPT vaccine (diphtheria, pertussis & tetanus).

Treatment is difficult:

- Antibiotics do reduce the number of bacteria, but have no effect on the toxin already in the body.
- Human tetanus immunoglobulin is used to try and reduce effects of toxin.
- Other treatments are supportive:
 - center on preventing muscles from seizing:

- magnesium, valium, other muscle relaxants.
- in severe cases the patient is paralyzed with something like curare to prevent spasms.
- airway is maintained, nutrition is given, etc.

Comment

- Rusty nails (etc.) provide an ideal spot/habitat for the bacteria, which is why tetanus is so often associated with rust.

Botulism

I. Introduction

This disease is closely related to tetanus. If anything, the toxin produced by the bacteria is even deadlier than that produced by the tetanus bacterium.

Usually we associate this with food, but there are other ways to get this disease.

Strangely, adults can eat the bacteria without ill effect, BUT, eating the toxin is another story.

II. Cause

Cause is a bacterium: *Clostridium botulinum*, gram-positive, anaerobic (obligative), rod shaped.

- obviously closely related to tetanus.

Also found in soil.

- however, it usually enters the body through the mouth (there is “wound botulism”, though)

III. Spread and infection & symptoms.

Although it doesn't really spread human to human, it can infect a large number of people if they eat contaminated food.

- Notice that all that is needed here is for the toxin to be in the food (the bacteria don't necessarily have to be there).
- In fact, acid conditions can stop the bacteria from growing (one reason infants are more susceptible as their digestive systems are not yet acidic enough).

1 - food borne botulism - in this case the bacteria may grow in food and release the toxin into the food. Humans eat the toxin and get sick.

symptoms start suddenly, about 18 - 36 hours after eating contaminated food.

- include nausea, vomiting, abdominal cramps, diarrhea
- followed by weakness & paralysis as nervous system is affected.
 - sensory system isn't affected that much
 - the toxin interferes with acetylcholine, a neurotransmitter that causes muscle contractions.

2 - wound botulism - bacteria gets into infected tissue, grows, and makes toxin. This form is fortunately quite rare.

Symptoms are similar to food borne botulism, but without the gut involvement.

3 - infant botulism - infant consumes bacteria, which then “thrives” in the gut.

Symptoms start with constipation, then proceed to nervous system involvement.

(5% of children who die due to SIDS may be attributed to this)

IV. Treatment, prevention & misc..

Although untreated it has a fatality rate of about 60%, supportive care can reduce this to less than 10% (depending on whom you ask).

- Even activated charcoal can be helpful if it is known someone swallowed the toxin.
 - (Activated charcoal absorbs many toxins).
- Otherwise, things like breathing assistance, intense nursing care, etc. help quite a bit.
 - respiratory failure seems to be the most worrisome complication.
 - breathing machines can help here
 - fatigue and shortness of breath may be symptoms of survivors for years.

There is antitoxin available which is effective (actually, there are several).

- Does not take care of toxin that has already bound to synapses, but does slow or stop more toxin from attacking synapses.
- Due to the high toxicity of the toxin (about 2 ½ times as toxic as the tetanus toxin) the government is quite worried about its use in bioterrorism.
 - 500 grams could kill everyone on the planet (= 17.6 ounces).

- As such, the government is stockpiling antitoxin, although only 200,000 doses are being stockpiled.

Prevention:

- sometimes difficult to prevent

- due to that endospore, food must be cooked at 121 degrees C (250 F) for at least 3 minutes to destroy the endospores.

- commercial canneries do do this, but home canning doesn't always do this (it's difficult without a good pressure cooker).

- high acid foods are generally okay since the acid prevents the bacteria from growing.

- boiling the food for 10 minutes before eating can destroy the toxin.

- otherwise, following proper food handling techniques work.

- obviously spoiled/swollen cans should be tossed

- (HOWEVER: food infected with botulism may not show any obvious symptoms).

- don't feed honey to infants, as honey may have spores in it (it doesn't affect adults due to the acid stomach).

Finally, a word on Botox:

- yes, it's toxin derived from the bacteria.

- it causes muscle paralysis, and since it's used in minuscule dosages, it usually doesn't affect the person (except where one is trying to remove wrinkles)

- also, it's usually injected directly into a muscle, so it doesn't spread much.

- cases of botulism have been reported from botox injections (accidental injection and/or overdose).

- it can also be used to treat various conditions, such as excessive sweating, uncontrollable muscle movements, etc.