

The flu

I. Introduction:

In 1914, on June 28, Serb nationals assassinated the heir to the Austro-Hungarian throne, Archduke Franz Ferdinand.

- the immediate result was that the Austrians retaliated against Serbia.
- Russia (allied with Serbia) mobilized against Austria
- Germany then declared war on Russia, and then France two days later.
- The British joined the war on the side of the French.
- Eventually Italy joined (w/ France & Britain), followed the Ottoman Empire (w/ Germany & Austria).
- The U.S. joined in 1917, and is widely credited with helping stop the stalemate that existed in the trenches.

This led to World War I. Fighting occurred mostly in Europe, Africa & the Middle East, though engagements were held in many other areas as well.

- some of the effects are still with us (the carving up of the Middle East, Serbia, etc.)
- over 40 million people died.

What does this have to do with the flu??

In March of 1918, the first of three waves of one of the most lethal epidemics (pandemics) to hit humans got started (some say it killed more people than the black death (plague), though that's debatable - even if, the % killed was much higher during the plague).

The Spanish flu killed between 40 and 100 million people world wide.

- Even in some isolated areas like the Arctic and pacific islands were hit.
- Some people even credit it with bringing an earlier end to World War I (though most would probably disagree).
- Still, several major offensives were halted by sick soldiers, and it is thought that conditions in the trenches proved ideal to help the flu spread quicker than it would have otherwise.

The flu is no "lightweight" disease, though often we seem to think that it's not that serious.

- It kills people every year, even when outbreaks are "fairly mild".

- A new strain of the flu (H5N1) has the potential to become a major cause of human mortality, though thankfully it has remained mostly a disease of birds so far.

So, what is this “flu”?

II. Causes

The flu is caused by a group of RNA viruses belonging to the Orthomyxoviridae.

There are three strains:

Influenzavirus A: probably the most dangerous. It can infect numerous other species and is often found in birds. There are many different strains of this virus:

H1N1 - Spanish flu
H2N2 - Asian flue
H5N1 - Bird flu
etc.

The H and N stand for different enzyme strains found on the surface of the virus:

H - Hemagglutinin

N- Neuraminidase (also found in human cells)

These surface enzymes can also act as antigens, and as these mutate, it makes it more difficult for our immune system to react to new strains.

Influenzavirus B: found only in humans, and (strangely) seals. Does not mutate as quickly as type A, and is generally not as dangerous. Many folks get some immunity early on, and since it doesn't mutate quickly, this persists (though not indefinitely).

Influenzavirus C: Infects humans and pigs. It does make people sick, but fortunately isn't all that common.

All strains mutate, which is part of the problem, and the reason we need to get new flu shots every year.

The virus actually contains 8 pieces of RNA.

- negative sense RNA (i.e., the RNA is backwards and must first be transcribed into “normal” mRNA).

- otherwise the virus is fairly typical in the sense that it invades a cell, and makes copies of itself and needed proteins (it's these proteins that will mutate due to mutated RNA).

III. Spread & infection

The virus spreads in a way similar to the common cold - aerosols from coughs and sneezes, and touching infected surfaces.

People are most infectious during the early stages of the disease (2 - 3 days after infections), but can stay infectious for up to 10 days.

There are two flu seasons every year:

- Northern hemisphere - cold months
- Southern hemisphere - cold months

The reasons for the flu being more common in the cold season is similar to the reasons the cold is more common (though, of course, we don't know for sure about the cold):

- huddling indoors
- more sensitive nasal passages
- an interesting hypothesis concerns vitamin D - more vitamin D is available when the sun is around (skin can make vitamin D in sunlight), and there is some evidence that vitamin D helps ward off the flu.

The WHO (World Health Organization) actually recommends two different vaccines each year; one for the northern Hemisphere, one for the southern).

- they base their decision on the flu strains being most likely to be present when the flu season starts.

IV. Symptoms

Symptoms usually appear between 1 and 4 days of being infected (usually about 48 hours).

Superficially, many symptoms are similar to the common cold (in fact, often a re-infection with the flu (or getting the flu after being vaccinated) results in symptoms difficult to tell from the common cold)).

But, here's a list of typical flu symptoms:

- Fever
- Headaches
- Fatigue
- Body aches
- Coughing/sneezing
- Congestion
- Irritated eyes
- Nausea & vomiting

- Reddened eyes & skin

Fever is probably the most useful diagnostic tool, since colds usually don't produce fevers.

Symptoms can be severe enough to force confinement to bed.

While some symptoms are due to the immune system response, tissue damage is much more widespread than with the cold.

Flu can kill.

Usually, folks recover in 1 - 2 weeks, but many develop complications:

- probably the most serious complication is pneumonia (bacterial)
- others include bronchitis, sinus & ear infections.
- the flue can also make pre-existing conditions worse (heart disease, heart failure, etc.)
- smoking can make the effects of the flu worse.

Normally, young, old and compromised individuals are most at risk from the flu.

The Spanish flu is an exception - it killed mostly the healthy 20 - 40 year old population

- Why was the Spanish flu so deadly?
- We don't know all the details, but one reason it killed healthy adults is (paradoxically) because they had the best immune systems.
 - Something called a cytokine storm:
 - This is caused by an overreaction of the immune system
 - Cytokines and other chemical signals cause T-cells and macrophages to overreact.
 - Macrophages can actually accumulate and block airways and other areas of the body.
 - Essentially causes massive inflammation.
 - Older and younger people's immune system isn't as strong, so the cytokine storm isn't as strong.

In normal years, the flu kills about 500,000 people every year.

- in America, it's 36,000 (200,000 hospitalizations).

Approximately, every 10 - 20 years, a pandemic occurs and kills lots more people.

V. Prevention

How can the flu be prevented?

- Most importantly, through immunizations!

- We need to get flu shots every year because the flu mutates so rapidly, and what worked last year may no longer work.

- As mentioned, the WHO analyzes flu strains occurring around the world, and then tries to decide which strains to include in a vaccine for the following year.

- The FDA was meeting only a few days ago to decide which strains of the flu to put into next years next year.

- Usually, the FDA follows the WHO recommendation.

- Unfortunately, every once in a while, the WHO gets it wrong.

- This year, the vaccine is not terrible effective - only about 40% of the flu in the U.S. is a good match for the vaccine.

- But even this year, the vaccine offers some protection as the most infective strain is related to a strain in the vaccine

- this should at least lead to milder symptoms.

- Still, most of the time the WHO gets a match of between 70 and 90% (16 of the last 19 flu seasons).

- Get your flu shot!!! Even for healthy adults this is a great idea!

- about the only time not to get it is when there's not enough vaccine to go around, when the elderly and young really need it.

- Flu vaccines are made by growing the virus in chicken eggs, then either killing or attenuating (weakening) the virus.

- this takes time - up to 6 months to make a good amount of vaccine.

- What else works?

- telling infected folks to cover their mouths when the sneeze/cough

- washing hands regularly

- sanitizing surfaces (alcohol works well)
- possibly shutting down schools or churches, etc.
 - has been shown to slow the spread, but doesn't seem to impact the overall death rate.

VI. Treatment

Basic:

Rest/fluids/avoiding alcohol & tobacco

Medication such as tylenol, other pain/fever reducers

Antibiotics:

Just like with the cold, these are useless.

Probably much antibiotic resistance has come from overprescription of antibiotics for the flu.

However, due to complications, antibiotics are often indicated:

- bronchitis/pneumonia/other infections
- particularly pneumonia (bacterial) is deadly, so antibiotics are important in treating the side effects of the flu.

Antivirals:

There are several antivirals effective against the flu.

As usual, they work best if used early.

Several different kinds

Neurominidase inhibitors

- stop neurominidase, an important enzyme that allows the “new” virus to detach from the host cell.

M2 inhibitors

- stop important ion channels, and prevent the cell from becoming infected
- most of these have become irrelevant - they were overused to treat

poultry in China and now the flu virus is resistant to these.

Not all of these are effective all of the time, and for certain strains the CDC may recommend one or the other.

More research obviously has to be done.

VII. Reservoirs for viruses.

One problem with many flu strains is that they also occur in other animals.

This allows animal populations to act as a reservoir for the flu - while in animal populations the flu can mutate and do other things, and when humans get infected, it might then spread very quickly.

Bird flu:

- A strain highly adapted for birds. Endemic in many bird populations.
- Spreading globally
- Has killed tens of millions of birds, and has caused large number of birds to be culled to try to control the spread (in 2006 over 200 million birds were deliberately killed in order to try and stop the flu - mostly ineffective).
- It has killed people. Fortunately, it seems to spread only to people that handle infected birds. Human - human spread is rare or non-existent.
- The big worry is that it could easily mutate and then spread from human to human.
 - 7.1 billion dollars were authorized by Congress to help prevent/combat the bird flu.
 - Many countries are stockpiling antiviral medications.
 - A flu vaccine is in the works
 - The Chinese also experimented with a flu vaccine to protect their poultry, but due to the way the vaccine works, they've actually increased the diversity of bird flu strains as the flu becomes resistant.

VII. Economic costs

During an average year, the flu is estimated to cost a total of 10 billion dollars per year (note that that's less than the common cold!)

However, should we get a real epidemic, it's estimated this would quickly escalate into over 100 billion dollars.

One study indicated that should we get hit with a flu as serious as the Spanish flu, the total costs would be about 700 billion.

(Strangely, the Spanish flu may have had a positive impact on per capita income since there weren't as many people around).

Costs due to research and prevention are also high.

- for example, the 7.1 billion mentioned above.