

AIDS - Acquired Immune Deficiency Syndrome

I. Introduction.

In 1981, the CDC noticed an unusual a number of cases of pneumonia caused by a fungus.

- This type of pneumonia was relatively rare, and finding it in five people all at the same time got them to pay attention.
- As a result, they discovered more and more occurrences of this odd pneumonia in other cities.
- They also found a number of other strange and rare diseases.
- All cases seemed to be in gay men.
- Further investigations led them to think that the disease may be sexually transmitted among gay men, and the term “gay-related immune deficiency” was coined (GRID).
 - But closer investigation showed that these symptoms also occurred in hemophiliacs, intravenous drug users, and Haitian immigrants.
 - The disease was then referred to as AIDS.
- The problem is, we only discovered AIDS in 1981. It had been around for quite some time already.
 - by 1980, AIDS was already on five continents; no one knew anything about it, so it spread quickly.
 - by 1980, we think between 100,000 and 300,000 people may have been infected already.
- in 2007, AIDS killed 2.1 million people. Another 33.2 million people were living with HIV
 - about 2.5 million people were infected with HIV in 2007.
- since 1981, 25 million people have died of AIDS.
 - estimates are all over the place, though, with some as high as 35 million.

The problem is that the incidence of infection continues to rise. More and more people are getting infected.

II. Cause.

It took a while to identify the cause, but in 1984, several labs identified the virus responsible for causing AIDS.

A retrovirus. Contains two identical bits of DNA, some enzymes, and the usual capsid and

protein coat

- HIV will actually incorporate itself into the host cells DNA.
- HIV includes a special enzyme that will convert RNA --> DNA (it's called "reverse transcriptase")
 - The virus' RNA is converted into DNA. A complimentary strand is added.
 - This short piece of double stranded DNA then merges with the host DNA.
 - the virus becomes a "provirus" a virus that is now part of the host's DNA.
 - this provirus will occasionally be transcribed, and the process follows the usual pattern, except that in this case the stuff being made is new viruses and the necessary proteins.
 - obviously, HIV attacks cells of the immune system.
 - the spikes on the surface of HIV allow it to attach to Helper T cells and other related cells (macrophages).

One problem is that reverse transcriptase makes a lot of mistakes, so HIV is constantly changing. More on this soon.

III. Transmission.

An awful lot has been said about how HIV is transmitted. Generally, blood or sexual fluids need to be transmitted. The most common ways to transmit HIV are:

Sexual intercourse:

- regular vaginal sex (particularly if the genitals have any kind of abrasion, cut, sore, etc.)
- oral sex (very rare, but it has happened).
- anal sex - due to tearing of the anus, this makes transmission more likely.

Intravenous drug use:

- Sharing needles with someone who is infected can transmit HIV

Other ways:

- Blood transfusions/products: in the developed world this has almost

disappeared due to testing of blood

- Mother-child transmission. This can happen either before or during birth. Transmission through breast feeding has also happened.

 - Drugs can reduce the risk of this if the mother knows she's infected (and has access to the drugs!!!)

- Tattoos, piercing - has happened, but if these industries are well regulated then the risk is minimal (i.e., equipment is thoroughly sterilized, etc.)

- Accidental exposure - health workers, dentist, etc.

There's also a lot of misinformation about how to get AIDS. Generally, one doesn't get AID from:

- Kissing (unless both folks have massive ulcers, sores, or bleeding in their mouths)

- Sneezing, coughing, etc. - fortunately HIV is fairly fragile, and doesn't survive outside the body.

- Insect bites - because HIV is so fragile, it doesn't do well in insects, and no cases of insect transmission are known.

Still, the way HIV is transmitted is quite effective, and far too many people are infected.

IV. Course of the disease.

Generally, there's a very long incubation period. Anything from 5 to 10 years (4 years has been mentioned as a minimum, and 20+ as a maximum).

- In developed countries, it's usually at the upper end, in less developed countries, at the lower end.

- This is one of the problems with AIDS - during this entire time a person can be infectious.

At the end of this time, people develop AIDS. This is the stage of the disease where symptoms develop. Until then, we generally just say a person has HIV.

- Generally, symptoms include diseases that are not usually seen (opportunistic infections).

 - initially, symptoms are minor with infections of mucus membranes, and respiratory system.

 - This proceeds to such things as chronic diarrhea, more bacterial infections, and often tuberculosis

- Finally, candidiasis, various pneumonias, cancers, toxoplasmosis of the brain, etc.

- In fact, AIDS is often divided into 3 or 4 stages, which roughly match the lines above (Stage I being asymptomatic, or sometimes with swollen lymph nodes).

It's often not the virus itself that kills, but rather all the infections and stuff that follow the destruction of the immune system.

V. Behind the scenes - the immune system.

So what's happening during the incubation period?

The AIDS virus is slowly destroying the population of helper T-cells.

After initial infection with the virus, the virus often gains entry into immune cells that are near the infection site.

Eventually, the major sites of infection are they lymphatic tissue

- lymph nodes, spleen, liver, etc.

Once the infection has become established, massive amounts of virus are produced every day:

- Estimates are that 100 billion viruses are released every day.

- Most of these have a half life of about 6 hours (i.e., 50% of these are destroyed within 6 hours).

- They're destroyed by the immune system!

- Most of these viruses are produced by helper T-cells (infected T-cells live only about 2 days (normally they live several years).

- The body responds by manufacturing about 2 billion T-cells every day.

- But as time goes on, the body starts losing about 20 million T-cells every day (a net loss).

- This is primarily due to the shortened life span of the helper T-cells and the fact that for some reason the body doesn't compensate by increasing T-cell production.

Eventually the number of helper T-cells falls below a level where the immune system can be effective.

- As a result, the infected individual starts to develop opportunistic infections.

VI. Survival & resistance.

As a general rule, people who are younger or older are more susceptible (their immune system isn't as strong).

But there are a few groups of people who do not seem to develop AIDS:

Some people do not have the right receptor on their cells, so HIV can not attach to the cell surface. This mutation is found in about 1% of people of European ancestry.

Recently, African prostitutes have been found that have unusually effective cytotoxic T cells, and are able to fight off HIV.

In some people, despite being infected, their helper T-cell count stays stable.

This is not understood well; some of these may again have a mutation in their cell receptors, others may have naturally occurring anti-viral compounds that stop HIV replication.

Obviously, these people are being intensively studied!

VII. Testing for HIV.

Tests for HIV have been available for a while, but recently improvements have been made.

- The old test required at least 3 days to complete
- The new test can be done in about 20 minutes.
- Both of these tests look for antibodies, not the actual virus.
 - this is much easier and less expensive than looking for the virus.
- If either test is positive, it's followed up with something called the Western Blot Test which is more accurate and serves as a confirmation.

One problem with testing for HIV in this way is that it can take a while for antibodies to appear in the blood.

- If someone is infected with HIV, but hasn't developed antibodies yet, the test will say negative.
 - it takes about 21 - 25 days for the test to pick up antibodies.
- This is also a problem for blood donated for transfusions.
 - if blood is donated shortly after infection, it will be difficult to detect with these tests.

- fortunately there are other tests that can detect HIV directly, and generally donated blood is screened in this way (but it is more expensive).

Another problem is that HIV mutates so rapidly, that on occasion the test may not detect HIV.

VII. Mutations.

We haven't discussed this yet, but one of the main problems with AIDS is that the virus mutates quite rapidly.

- this makes it very difficult to develop vaccines or treatments.

The main issue is reverse transcriptase. To convert RNA into DNA, the virus uses this enzyme.

- it's not particularly accurate, and it has no way of checking for errors in "reverse" transcription.

- as a result, mutations appear almost every day in an infected person.

- it's estimated that while asymptomatic a person accumulates over a million different variants of the virus.

- during the final stages, this may climb as high as 100 million.

Further, all this has caused HIV to develop into several major groups:

HIV-1:

11 types (or clades). In the U.S. clade B is the most common.

- In Africa, it's clade C, in Asia, clade E

HIV-2:

- HIV-2 is another major HIV type found in West Africa

- fortunately it takes much longer to get AIDS with this type, and people in this area seem to have an almost normal life span.

- remember, though, that the life span in most of West Africa is much lower than here.

VIII. Treatment & prevention.

First, it should be mentioned that there is no cure for AIDS.

If one knows they were exposed, it might be possible to prevent AIDS:

- post exposure prophylaxis - an intense 4 week treatment with antivirals

- has numerous nasty side effects, but it can be effective.

Otherwise, treatments consist of drug cocktails (HAART = highly active antiretroviral therapy).

- This is usually a mixture of three different types of antiviral drugs
- This is done to make sure that the virus doesn't acquire resistance (although it's hardly foolproof).
 - reverse transcriptase inhibitors
 - protease inhibitor (prevent final assembly of new proteins)
- Without treatment, the survival time after developing AIDS (symptoms) is about 9.2 months.
- With treatment, this increases to between 4 and 12 years, though no one seems to know for sure. Some people have lived much longer than that with treatment.
 - The problem is often that the regimen is so difficult to follow that a lot of people make mistakes or simply don't do it
 - That increases the odds of HIV becoming resistant to the treatment.
 - This is particularly true in poorer areas which don't have the same access to health care.
- One thing that has worked fairly well is reducing the viral load during pregnancy and birth (even one or a few drugs seems to reduce the rate of mother-child transmission).

On the other hand, something as simple as daily multivitamin & mineral supplements have been shown to slow down the disease.

Other means of prevention include:

- condoms (both male and female). This is quite effective as the virus can't get through the condom.
 - of course, this has run into serious problems with the Catholic church
 - very recently, the Catholic church is considering allowing condoms for married couples where one partner is infected.
 - Bluntly, it's not nearly enough.
- reducing the number of sexual partners.
 - every time you have sex with someone else the probability of becoming exposed to AIDS increases.

- as everyone knows, you're exposed to everyone that the other person has ever had sex with.
- this had led to many “abstinence” campaigns.
 - All very well and good, but it really doesn't take into account human nature, and human abstinence only campaigns have not been successful.
- very recently, a study showed that circumcision can reduce (but not stop) the transmission of HIV.
 - the results were so successful, that trials were stopped early so that results could be shared.
 - circumcision seems to roughly half the risk of men getting HIV during heterosexual sex.
 - It appears that the foreskin (inner surface) is particularly susceptible to infection, and circumcision obviously removes this.
 - this part of the penis is also more susceptible to minor injuries like tears during sex.
 - It's important to realize that this does NOT prevent HIV transmission, it just makes it less likely.

The really bad news is that despite trying for 20 years, there is no vaccine available for AIDS, and none seems to be in the pipeline.

- Some very promising vaccine trials were recently stopped because they actually increased the risk of contracting AIDS.
- Vaccines are difficult because:
 - HIV is mutating so rapidly, and several types exist
 - HIV hides out deep inside the cell within a cell's own DNA
 - HIV targets the immune system (which is precisely that part that is often stimulated by a virus (though this we should be able to deal with).
 - It's hard to study HIV in other organisms - monkeys work, but they're expensive, have long life spans, and create ethical issues.
 - For some reason, antibodies have a hard time binding to HIV except during very short parts of its life cycle (when HIV is attached to a cell it's trying to infect).

- Some “vaccine” research has focused on trying to stimulate the immune system (which does, after, all, fight HIV, so if it could somehow be given a boost).

IX. Current status.

Since its beginnings in the 70's and 80's (more on the origin of AIDS below), AIDS has spread out to become probably the number one killer (infectious disease) of people in the world.

- Malaria and tuberculosis may come close.

By 2010 it's estimated that 100 million people will have HIV, 90% of these in the third world.

- Deaths are estimated to exceed 8 million a year in 2010.

Sub Saharan Africa is particularly hard hit, though it's growing rapidly in other parts of the world.

- In some countries the incidence is over 20%
 - 24.1% of the population of Botswana is infected
 - life expectancy fell from 65 years in the early 90's to less than 40 now.
 - (incidentally, Botswana is one of the best developed countries in Africa).
 - It's one of the first countries to provide HIV medication for everyone, and because it's better off than most others, it may work better here than anywhere else.
 - 33.4% of the population of Swaziland is infected.
 - life expectancy has plummeted to 31 years.
- This is having a huge impact on society:
 - large numbers of orphans
 - adults are dying in their most productive years
 - women have a higher infection rate than men

But it's not just Africa, other parts of the world are having large problems:

- It's estimated that 4.8 million people in Asia are infected and the number is growing
- Other parts of the world as well are having increases in AIDS

In the United States:

- until recently AIDS was primarily found amongst gay men and intravenous drug users (our blood supply is pretty clean these days).

- still, recently the number of women getting AIDS in the U.S. has increased:

- 25% of new AIDS cases in 2004 were women (75% of which were engaged in heterosexual sex).

X. Final comments.

Origin of the disease:

- As mentioned, it was first really noticed in the early 80's, but it had been around for a while already.

- We have evidence of people dying from AIDS from the late 50's and later. This is just a few people here and there, not any kind of outbreak.

- But the point is that the disease was establishing itself, and no one knew anything about it.

- The HIV-1 virus has been (our best guess) tracked back to chimpanzees. Based on DNA sequencing, it's thought to have crossed into human populations sometime between 1915 and 1941.

- HIV-2 originated in sooty mangabeys (another species of monkey from West Africa) sometime later.

- Incidentally, a lot of people are worried about new diseases cropping up in this way:

- bush meat and meat from monkeys are a staple in many parts of the world, particularly Africa.

- This exposes humans to a huge potential reservoir of new diseases.

- As an aside, it's also having a huge impact on many endangered species.

Stigma:

- Early on, a lot of people weren't particularly interested in AIDS:

- it was a disease of gay men, drug users, etc.

- even today, it's associated with promiscuity, etc.

- it wasn't until what many consider "normal" people started to come down with AIDS that a lot of people finally started paying attention.

- that's when money started to flow into AIDS research.

- one could make an argument that the current crisis wouldn't be nearly as bad if we had started to pay attention a little earlier.

- With disease, it's never a good idea to take a lax attitude because it's not affecting you. One never knows what might happen.

Finally:

TB is a leading cause of death in people with AIDS.

Reason: Lots of people successfully fight off the TB bacteria (prevent it from becoming active). Their immune system is able to deal with it.

If someone with a “latent” infection develops AIDS, they can no longer fight TB, and the disease becomes active. So now we discuss TB.....