It's the virus, stupid

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Does HIV cause AIDS? This *Backgrounder* explains the relationship between the virus and the disease, and the scientific basis that our knowledge is based upon.

From time to time you may read stories in the media or on the internet which suggest that the link between HIV and AIDS is less than clear or that there is insufficient evidence to conclusively prove that HIV causes AIDS.

These stories often highlight the views of individuals, often with scientific qualifications, whose claims can range from the extreme (“ HIV is harmless and AIDS doesn’t exist”) to the nearly uncontroversial (“ AIDS is caused by HIV, but won’t occur unless some other cofactors are present.”)
The arguments put forward by these people often seem very convincing, and may be supported by impressive-sounding scientific evidence, so how can we be sure they aren’t right?

To understand the process by which science has determined that AIDS is caused by HIV infection, we need to go back to 19th-century Berlin.

Heinrich Hermann Robert Koch was a German physician and Nobel laureate who is remembered (along with Louis Pasteur) as one of the founders of the science of bacteriology. Koch’s work gave us a set of criteria for determining what causes infectious illness, and what doesn’t.

Koch was a precocious and inquisitive child (he taught himself to read and write at a young age by studying newspapers) and quickly developed a life-long interest in biology and travel. After graduating from university in 1866 with a medical degree, and a stint in the army during the Franco-Prussian war, Koch was posted as the district medical officer to a farming community where regular outbreaks of anthrax were threatening the local cattle industry.

The late 19th century was a period of feverish scientific and medical exploration and new discoveries were being made all the time. But the causes of infectious disease remained poorly understood. Most people, including physicians, believed that infectious diseases were caused by *miasma*, a noxious form of ‘bad air’ which came in the night, bringing disease. Diseases like cholera, smallpox, and tuberculosis were all thought to be caused by miasma. The idea lives on in the name of the disease malaria, which literally means ‘bad air’.

Other scientists had shown that anthrax could spread between cows in the same herd, and Koch set out to discover the mechanism by which this disease was transmitted. With only limited resources and equipment, Koch performed experiments which showed that the anthrax bacillus could be found in the blood of infected cows, and it could be transmitted to other animals if it got into their blood.

After publishing his discovery, Koch was recruited [1]The act of signing up participants into a study. Generally this process involves evaluating a participant with respect to the eligibility criteria of the study and going through the informed consent process. by the German government and moved to Berlin, where he set to work to understand the cause of tuberculosis (TB), the cause of one in seven deaths in Europe at the time. Koch isolated the bacterium which causes TB, *Mycobacterium tuberculosis*, in 1882, and a year later he found the cholera bacterium, *Vibrio cholerae*.

In 1905, Koch won the Nobel prize for medicine for his work on tuberculosis and for outlining a set of rules, called **Koch’s postulates** , which must be satisfied before it can be accepted that a particular micro-organism (such as a bacterium or virus) causes a particular disease.

Does HIV satisfy Koch’s postulates?

Through his work with anthrax, tuberculosis, and cholera, Robert Koch showed that, in order to be accepted as the definitive cause of a disease, the organism:

Must be found in every person who has the disease;
Must be isolated from people with the disease and cultured in the laboratory;
When the cultured organism is introduced into a susceptible, uninfected individual, it must cause the onset of the disease; and
It must be able to be found in the newly-infected individual and cultured again.

Now back to modern times. After the first cases of AIDS were diagnosed in the early 1980s, the race was quickly on to isolate and identify the responsible organism. Dr Luc Montagnier of the Pasteur Institute in Paris was the first to find the cause, a virus he named LAV, for lymphadenopathy-associated virus. Not long afterwards, an American researcher, Robert Gallo, claimed he had found the cause: another virus he called HTLV-III, for human T cell lymphotropic virus type III. Eventually, both viruses [2]A small infective organism which is incapable of reproducing outside a host cell. were shown to be one and the same and they were renamed HIV.

Despite the discovery of HIV, some people (popularly known as ‘ AIDS denialists’) still insist that the link between

1. Nearly every person who has been diagnosed with AIDS has been shown to have antibodies to HIV. In people who do not have HIV antibodies, sophisticated PCR (polymerase chain reaction) testing has been able to find the virus itself. PCR tests have shown the presence of the HIV virus in people at all stages of disease.

2. Although culturing HIV in the laboratory initially proved difficult, modern co-culturing techniques have enabled researchers to culture HIV from blood taken from people with AIDS at all stages of disease.

3. There have been numerous cases of laboratory workers and clinicians who have developed HIV infection and AIDS after accidental occupational exposure to HIV (‘needle-stick injuries’). There have been at least three laboratory workers, with no other risk factors for HIV/AIDS, who developed sever immunosuppression and AIDS after accidental exposure to cloned, cultured HIV in the laboratory.

4. In the three cases described above, HIV was subsequently isolated and cultured in the laboratory, satisfying the last of Koch’s postulates.

Other evidence that HIV causes AIDS

Medical research carried out on chimpanzees and other animals has demonstrated the link between HIV and AIDS. When animals with similar DNA to humans are inoculated with cultured HIV, an AIDS-like condition invariably develops with loss of immunity and development of opportunistic infection.

Some people occasionally develop diseases characterised by severe immunosuppression but have no evidence of HIV infection, however these people do not have AIDS. People who are elderly, malnourished, have cancer or tuberculosis or who are undergoing radiotherapy for cancer may have a severe loss of immune function similar to

A condition does exist, called idiopathic CD4+ T-lymphocytopenia (ICL) which is very similar to AIDS but does not result from HIV infection; however this condition is very rare and has several clinical [3]Pertaining to or founded on observation and treatment of participants, as distinguished from theoretical or basic science. features which distinguish it from AIDS.

Epidemiological studies also provide evidence. In countries and regions where HIV infection levels are low, AIDS is rare, while in countries where HIV is highly prevalent, so is AIDS. Sub-Saharan Africa remains the region most severely affected by both HIV and AIDS, yet just 250 miles to the east of Africa, the island nation of Madagascar has reported very few cases of AIDS despite economic, social and racial similarities with many of the worst-affected countries in Africa.

Additional evidence comes from ‘blood donor pair’ studies. Before screening of donated blood for HIV antibodies, many thousands of people worldwide became HIV-positive after receiving blood transfusions. Studies have shown that people who received donated blood products from the same HIV-positive donor later developed

But is there more to the picture?

It's true that not everybody who is HIV positive develops AIDS at the same rate or in the same way. Some people have quickly progressed from HIV infection to AIDS while others, known as 'long-term nonprogressors' have been able to go many years without treatment and without developing AIDS. This raises the question about whether something else additional to HIV — a 'co-factor' — is needed beforeAIDS can develop.

There is much research still being done on co-factors, and the evidence of long-term nonprogressors holds out the promise of learning new ways to stop HIV from developing into AIDS, however numerous studies have shown that AIDS can and does develop from HIV infection with no identifiable co-factors.

Large cohort [4]In epidemiology, a group of individuals with some characteristics in common. A cohort study is a special kind of clinical trial which looks at a treatment or treatment strategy in a cohort of people. studies of people with AIDS have looked at possible co-factors like simultaneous infection with bacteria [5]A microscopic organism composed of a single cell. Many bacteria can cause disease in humans. or other viruses, sexual behaviour patterns, drug use and nutrition in people with AIDS including men, women, homosexuals and heterosexuals, injecting drug users, sex workers, children, haemophiliacs and other people with medically-acquired HIV. The only common factor is HIV.

The proof of the pudding

Perhaps the strongest and most immediate evidence we have of the link between HIV infection and AIDS is the effect of treatment. HIV treatments have been specifically designed to target HIV, and this has been confirmed in laboratory experiments. In people who are not HIV-infected, taking antiretrovirals [6]A medication or other substance which is active against retroviruses such as HIV. produces no beneficial effect whatsoever, but in people who do have HIV, in almost every case these drugs slow the individual's progression to AIDS.

In countries where treatments are not available, HIV-positive people continue to develop AIDS and die, while in countries where treatments can be obtained, deaths from AIDS have slowed to a trickle of what they once were.

The link between low or undetectable HIV viral load [7]A measurement of the quantity of HIV RNA in the blood. Viral load blood test results are expressed as the number of copies (of HIV) per milliliter of blood plasma., measured independently with PCR testing, slowed progression to AIDS and improved survival has been conclusively demonstrated in hundreds of clinical trials. Likewise, people whose HIV viral load remains low but who are not on treatment have been shown to have a much lower risk of developing AIDS.

Working through the evidence and following in the footsteps of scientific pioneers like Robert Koch, it's clear that the evidence is overwhelmingly strong: AIDS is caused by HIV infection, and while HIV infection in different people will sometimes take a different course or move at a different speed, there's one common thread which runs through every case of AIDS we've ever seen: HIV.

- HIV/AIDS basics

Links:
[1] http://www.napwa.org.au/glossary/term/489
[2] http://www.napwa.org.au/glossary/term/125
[3] http://www.napwa.org.au/glossary/term/475
[4] http://www.napwa.org.au/glossary/term/477
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