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What we know about Aids

‘I have often been asked what it was like to be one of the early Aids investigators. To me, it all began as a medical mystery. As time went on, however, I gradually began to see that what we were studying was much bigger than I had first imagined. Once it was clear that the disease was sexually transmitted, we knew that the disease would not be limited to [men who have sex with men]. And once we knew that the agent was in the blood supply, we knew many more people were at risk. The medical mystery would soon become the global pandemic.’

– Harold Jaffe¹

An epidemic emerges

The cause of Aids has been discovered, been named, become a deadly global epidemic and become treatable, all in less than three decades. In a generation it has evolved into a dreaded scourge and then into a chronic manageable disease. Its spread and growth were made possible by an increasingly globalised world, in which communication, travel and migration have woven the world’s people together. Yet, in contrast to the many plagues of human history, the same factors responsible for its spread have helped raise and spend, often wisely, sometimes not, the billions of dollars that have made HIV infection treatable.

UNAids estimated that 30 to 36 million people were living with HIV in 2007, two million of them children. Well over three million people are

on ARV treatment, and yet another ten million people need it now. Their fates are being decided by a combination of politics and global economic inequality epitomised by the inadequate health systems of the poor countries of the world. Over 25 million people have died of Aids since the start of the epidemic. With the possible exception of the Spanish influenza pandemic, this is the shortest period of time in which so many have died of a single infectious agent in history.

These statistics need to be treated with a great deal of caution. Nevertheless, uncertainty about the precise number of infections and deaths due to Aids should not be mistaken for ignorance. We know that tens of millions of people are infected with HIV, that sub-Saharan Africa bears the brunt of the epidemic and that South Africa has an enormous problem. Perhaps there are not five million people with HIV in South Africa; maybe there are four million, or even seven million. But it makes no difference to this point: that millions of people in South Africa are infected and most of them will die of Aids unless they access ARVs in time. There is ample evidence from waiting lists and death statistics that the number of people receiving ARVs is far short of the number who need it, even if we do not know the exact amounts for either.

This chapter explains the basics of HIV science. Understanding this is essential to understanding why Aids denialism and the quackery surrounding it are factually and morally wrong.

The origin of Aids

Research in the last few years has made it possible to describe approximately when and where the first HIV infections occurred and the route the virus took on its way to becoming an epidemic. First, it is important to understand that there are several varieties of HIV, with a common ancestry: HIV-1 and HIV-2. HIV-1 is the type you almost always read about, while HIV-2 is less easily transmitted and is only occasionally found outside West Africa. HIV-1 is divided into several groups, of which Group M is the one responsible for the worldwide epidemic. The remainder of this book deals with HIV-1 Group M.

Nearly identical viruses to HIV-1 and HIV-2 have been found in captured chimpanzees and sooty mangabey monkeys respectively, both sub-Saharan African animals. This gave scientists clues to the virus's origins. But the vital evidence on the origins of Aids was found in poop. In 2006 a team of researchers from the US, UK and Cameroon, led by Brandon Keele and Beatrice Hahn, discovered a virus almost identical to HIV in the faeces of wild chimpanzees living in southern Cameroon. They compared HIV-1 Group M with it, using genetic sequencing technology, and found that the human virus had most likely evolved from particular chimpanzee communities, probably in the early part of the 20th century as a result of hunting and butchering.²

You might think that for a virus to cross from primate to man is unlikely, but recent research that looked at hunters in Cameroon shows that it is not. This demonstrated that viruses similar to HIV continue to cross over to humans frequently. So it is not so surprising then that there are at least two HIV epidemics, one of which is global in scale. The recent swine and avian flu outbreaks also show that for a virus to cross from animal to human is not unusual.³

Frozen blood and tissue samples from decades ago have helped uncover the pattern of HIV's global journey. An adult man who lived in the Belgian Congo (now DRC) in 1959 is currently the oldest known HIV-1 infection. Nothing is known of who he was or what became of him. We know he had HIV because a blood sample of his was stored and then tested in the late 1990s.⁴

A body fluid sample taken from a similarly anonymous Congolese woman in 1960 was recently discovered to have HIV. Genetically her virus is sufficiently different from the first known infection to lead researchers to conclude that HIV was quite diverse in the Congo by 1960. This suggests that the virus had already begun spreading through the population by then, 'long before the recognised Aids pandemic', as Michael Worobey and his team explain in their fascinating research.⁵

By isolating HIV from the blood of infected people across the world and then comparing how their strains of HIV differ genetically, scientists

have shown that the virus spread from Africa to Haiti in about 1966 and then shortly thereafter to the US. Yet in South Africa, HIV tests of stored blood samples from 1970 to 1974 of over 2,000 miners from Mozambique, Malawi, South Africa, Lesotho, Botswana, Angola and Swaziland showed no conclusive evidence of the virus. So HIV was probably not widely present in southern Africa until at least the mid-1970s, possibly even later. We can therefore be quite sure that HIV is a new epidemic of the last three decades in this part of the world. Southern Africa now has the bulk of the world's HIV-positive population, even though the virus only reached this part of the globe recently.⁶

The origins of Aids and the first cases were only discovered in the last three decades. On 12 December 1977, the first serious clue of this new disease presented itself. A Danish doctor, Margrethe Rask, who had worked in a hospital in Zaire (now DRC), died at the age of 47. An autopsy revealed that the cause was pneumocystis carinii pneumonia (PCP), a rare disease at the time, but one that soon became known as one of the biggest causes of death in people with HIV.⁷

From the last quarter of 1980 to May 1981, doctors and scientists in New York, Los Angeles, San Francisco and Atlanta started to notice strange medical phenomena: young gay men were falling ill with very rare diseases. The news of this was broken in the June 1981 issue of the Centers for Disease Control's weekly *Morbidity and Mortality Report*.⁸ This went on to describe the disease progression of each patient, two of whom had already died. It was the first scientific report of the epidemic. Reports of people dying with similar symptoms started coming out of the UK and France. The disease received the name Acquired Immune Deficiency Syndrome, or Aids, in August 1982. In 1983 a report in *The Lancet*, a leading medical journal published in the UK, described the cases of five men from Zaire and Chad with Aids who had been living in Belgium. At the same time Ugandan doctors started noticing similarities between their patients and the cases being reported from Europe and North America. They called it Slim disease. In 1985 a Ugandan medical report showed that Slim and Aids were likely identical; the symptoms were similar and the only thing that

could explain the transmission of the disease was sex.⁹

This, then, is what the evidence shows about the start of Aids. There are many gaps and some of the facts might be reassessed as new information arises. Debates over the origins and spread of the epidemic are often acrimonious. In his popular book *And the Band Played On*, the late Randy Shilts held a Canadian air steward, Gaetan Dugas, better known as Patient Zero, responsible for the spread of HIV in North America. Shilts described Dugas as a man with a voracious uncontrolled sexual appetite who failed to cooperate with health authorities. Subsequent research has shown that this accusation was unfair. Similarly, the journalist Edward Hooper has proposed the implausible theory that a World Health Organisation (WHO) polio vaccination programme was responsible for the spread of HIV.

The stigma of HIV encourages a search for blame. Deflecting blame for one's disease onto scientists, drug companies, the American government or the WHO is appealing. At its extreme, it seems to me to be often the driving force behind Aids denialism. On the other hand, blaming the disease on gay men or Africans is equally unfair, increasing stigma and promoting the search for conspiracies where none exist.¹⁰

Aids comes to South Africa

“‘Gay Plague’: More victims?’ This was the headline of a story in South Africa's bestselling weekly newspaper, the *Sunday Times*, on 9 January 1983.

The early epidemic was concentrated among white gay men; there are very few accounts about the disease's early progression amongst black people. Apartheid's oppressive environment meant that few people were willing to fight an epidemic that mainly affected marginalised people, and so there are not many written accounts from that time.¹¹

In early 1982, a 42-year-old South African Airways air steward, Ralph Kretzen, whose flight routes included the US, complained to his doctor that he had influenza and was losing weight. By July his condition had worsened. He was coughing and had a fever and diarrhoea. Tests showed that he had symptoms of illness caused by cytomegalovirus (CMV)

infection. His white blood cell count was abnormal. Although there was no HIV test in those days, these were signs that he had the same disease that had broken out in the US and Europe. He improved – ‘dramatically’, according to his case report – after being given various medications. But five days later he was readmitted to hospital, struggling to breathe. He died on 26 August. An autopsy showed that he had PCP. On 1 January 1983 another air steward, Charles Steyn, died of Aids in Pretoria. The *South African Medical Journal (SAMJ)* published the Kretzen and Steyn case reports in July 1983. They were the first two recorded Aids deaths of South Africans. Both were white and gay.¹²

Their stories were known a while before the *SAMJ* article. The front page of the *Cape Argus* three days after Steyn died read, “‘Homosexual’ disease kills SAA stewards’. The report continued, ‘Described by *Time Magazine* as a “mysterious and deadly epidemic”, it was at first thought that Aids was confined to male homosexuals. But developments in the United States over the past three weeks have revealed that Aids has spread to heterosexual drug-abusers, Haitians, haemophiliacs and children.’ On 9 January 1983 the *Sunday Times* ran its gay plague story.¹³

Aids quackery in South Africa started very soon afterwards. On 13 January the *Argus* ran a story headed, ‘Aids can be cured, claim homeopaths.’ ‘Acquired Immune Deficiency Syndrome and homosexuality can be cured through homeopathy, several homeopaths claim.’ The article quotes the spokesman for the South African Homeopathic Society explaining that homosexuality is a psychological problem and therefore treatable. Aids could be treated because homeopathic remedies could build up the body's immune systems. ‘It isn't an easy treatment and would take quite a long time, but there are medicines in our profession that would work.’ He admitted never having seen an Aids patient.¹⁴

Throughout the eighties, Aids continued to kill people, though at a slow rate. By 14 December 1988, only 166 Aids cases had been reported in South Africa, most of them white men. While a handful of people contracted HIV through blood transfusions, the vast majority, 125, did so through homosexual sex; 24 were heterosexual transmissions. Only three were

children. The total number of recorded HIV infections (including people who had not advanced to Aids) was 1,857, of whom more than half were white and almost all were men. (These figures excluded the mining industry for which I do not have data.) There were undoubtedly many more people who were undiagnosed. Because they enjoyed better health services, whites were probably over-represented in the data. Nevertheless, the epidemic was still small and would remain so for a while. The demographics of the epidemic would also soon change dramatically.¹⁵

In 1990, the first antenatal survey was conducted. The Department of Health anonymously tested thousands of pregnant women attending public health clinics. Less than one in 100 women tested positive in the first study. By 2005 the ratio was more than 30 in 100. A large household survey, also conducted in 2005, showed that over 10% of people over the age of two were infected, mostly women. There are now at least 60,000 infants infected annually, mostly during labour and from breastmilk. How Aids in South Africa turned from a seemingly manageable outbreak in the 1980s and early 1990s to the world's largest epidemic in less than a decade is the subject of much unresolved discussion.¹⁶

Incompetence in responding to the epidemic certainly did not start with Thabo Mbeki. The apartheid government was for the most part uninterested in Aids and it was private individuals, mainly in the gay community, who ran awareness programmes in the early years of the epidemic. Considering that homosexuality was illegal at the time, this was not easy. The state response was minimal, particularly in black areas. Sometimes it was destructive. In October 1987, a government regulation banned the employment of HIV-positive foreign workers. It also gave immigration authorities the power to test, detain and deport non-South Africans with HIV. In 1992, a condom awareness campaign developed by the Medical Research Council (MRC) was opposed by the Cape Town City Council, which stopped billboards from being placed at a prominent intersection of the city. A condom awareness advert at the city's Metro train station also caused a furor. At one point the SABC, the public broadcaster, decided to screen condom advertisements, but only after 9 pm out of regard

for public sensibilities. John Scott, a popular Cape Town satirist, cleverly quipped that this 'will persuade many viewers to stay up later than usual, so that they can be disgusted'.¹⁷

This all preceded the era of Aids denialism. More accurately it took place during an era of a different type of government denial, the ostrich-in-the-sand approach. ARVs were unaffordable during this period and in any case were not particularly effective until 1996. Even from 1994 to 1999 under the first democratic government headed by Nelson Mandela, Aids remained low on the radar, something for which Mandela has since expressed regret. Journalist Donald McNeil provides a possible explanation for this. 'In 1991, when [Mandela] endorsed safe sex to some Mpumalanga parents, he said, "I could see they thought I was saying something revolting. After, they came to me and said, "How can you talk about this? You want to encourage prostitution among our children?"' So he quit.'¹⁸

South Africa has never had an effective government HIV prevention information campaign. A useful strategy document developed by the National Aids Coordinating Committee of South Africa was endorsed by the Cabinet in 1994, but it was not adequately implemented. An insipid, only slightly improved, attitude to HIV awareness continues to this day. Useful information about how to avoid contracting HIV was particularly subdued in the era of Aids denialism. Safer sex was promoted publicly, but also obscurely. This was epitomised by very strange billboard messages placed by a government-funded NGO featuring expensively dressed adolescents making meaningless statements like 'Do you love yourself enough?' Condom advertisements, while not invisible, were shown occasionally on television and seemed like a novelty when one saw them, usually after 9 pm.

Finding the cause

After the Centers for Disease Control published its article showing that people were becoming ill from a strange new disease, it set up a small but skilled task force to try to find out what was going on. Harold Jaffe, who was part of this team, has explained the mystery they were confronted with.

Why were men who had sex with men getting opportunistic infections? Was a virus or bacterium involved? If so was it perhaps transmitted through sex? Or was it related to recreational drug use?

As more Aids cases emerged in gay men, recipients of blood transfusions, intravenous drug-users, heterosexual Haitians as well as in five infants, Jaffe's team determined through interviews and tracing contacts of sick people that an infectious agent was very likely involved and that it was transmitted in blood or blood products. They also determined that this agent could be carried by and transmitted from people who had no symptoms of Aids. The incubation period of the disease was potentially long. These were vital clues for laboratories looking for the cause.¹⁹

Every human is made up of trillions of cells. Each cell contains 46 chromosomes. Each chromosome contains DNA, the chemical instructions for making proteins and reproducing the cell. If you look at a piece of DNA, it is composed of two long facing strands of chemicals that spiral around each other. Sections of these encode genes. Each gene is a set of chemical instructions that usually tell the cell how to make one protein. You can think of a protein as a little machine that fulfils a specialised bodily function. One type of protein is an enzyme. These are proteins that speed up chemical processes. The process involved in making a protein from a gene is complex. One of the steps along the way is to construct single strands of chemical instructions from the gene. These single strands are called RNA. So essentially in the process of making proteins, DNA is converted to RNA. At least that's the way it works for humans.

Viruses lack the chemicals to reproduce themselves. They need to use the reproductive machinery of a cell, such as a human one. Many viruses that infect humans, such as herpes and smallpox, are made up of DNA. Others, including influenza and polio, are made up of RNA instead of DNA. There is a subset of RNA viruses called retroviruses. These work by converting their viral RNA into viral DNA, which is then inserted into its host's DNA. There is a viral enzyme that makes this happen. Because it converts RNA into DNA, the opposite direction of the process in humans and most other creatures, it is called reverse transcriptase. It was discovered in the 1970s.

Françoise Barré-Sinoussi, Luc Montagnier and their team at the Viral Oncology Unit at the Pasteur Institute in Paris realised that the swollen lymph nodes of people with Aids most likely contained the infectious agent suspected by Jaffe's team as the cause of Aids. The lymph nodes contain large numbers of white blood cells including CD4 ones and patients were losing CD4 cells, so possibly the virus or bacterium was attacking these. They grew – or cultured, as scientists say – white blood cells. While culturing these cells from people with Aids symptoms, the Pasteur Institute team discovered reverse transcriptase at work, which suggested to them that Aids was caused by a retrovirus. This was striking because retroviruses in humans were unusual.²⁰

The reverse transcriptase activity would stop unless new healthy cells were added to the culture. This suggested that the virus was infecting cells, using them to reproduce but killing them in the process. When a virus invades the body, the immune system generates antibodies to destroy them. Barré-Sinoussi and Montagnier detected antibodies that were specific to a new retrovirus. They showed that healthy blood could be infected by this new virus and named it Lymphadenopathy Associated Virus or simply LAV. On 20 May 1983 they published in the leading journal *Science* their finding that they had isolated a retrovirus from a patient with Aids symptoms, but added, 'the role of this virus in the etiology of Aids remains to be determined'.²¹

The French team also isolated retroviruses from haemophiliac siblings, one of whom already had Aids symptoms. They named this Immunodeficiency Associated Virus (IDAV), just in case it was different from LAV. They studied a range of people and found the same type of retroviruses in those with Aids symptoms or at risk of developing Aids. They could not detect it in people with other diseases or with no known risk factors for Aids.²²

Meanwhile similar work was being conducted by Robert Gallo and his team at the National Institutes of Health (NIH) in the US and Jay Levy at the University of California–San Francisco School of Medicine. In May 1984 Gallo's team published four papers in *Science* which showed clearly that Aids

was caused by a newly discovered retrovirus. Gallo's group also developed a reliable method to detect the antibodies: this was the first HIV test.

The three groups soon realised they were all working on the same virus. In 1985 it was named Human Immunodeficiency Virus, or HIV. For their work Barré-Sinoussi and Montagnier received the 2008 Nobel Prize for Medicine. Unfortunately credit for the discovery of the virus became mired in controversy. Some Aids denialists are obsessed with this to this day, even though it has no bearing on the science of HIV.

Retroviruses, unlike most other viruses, infect you for life. Your immune system usually cannot clear them from your body. The reason is that they insert themselves into the DNA of some of your cells. Whenever infected cells create proteins, they also create new copies of the virus. When these cells reproduce, the viral DNA is copied along with the human DNA into the replicated cells.²³

Over the years, a massive body of evidence has accumulated confirming that HIV causes Aids. Here's a very small selection of this evidence:

- Three laboratory workers, with no other risk factors, developed Aids after being infected with HIV in laboratory accidents.
- A dentist transmitted HIV to his patients and they developed Aids. Genetic analysis showed that the virus his patients had very probably came from him.
- Health workers who have injured themselves with needles contaminated with HIV, but with no other known risk factors, have developed Aids.
- Many haemophiliacs who received blood transfusions contaminated with HIV developed Aids. Those that have not received contaminated transfusions did not, unless they had other risk factors.
- Epidemiological studies in the US, Europe, Uganda and South Africa have shown that people who are HIV-positive are much more likely to get Aids-related illnesses and die younger than people in whom the virus cannot be detected.
- HIV is photographed regularly using electron microscopes. Its genes have been sequenced. Scientists have developed a detailed, albeit incomplete,

explanation, confirmed by experiments, of how it invades the body, attacks CD4 cells and progressively destroys the immune system. HIV is isolated daily in laboratories across the world.

- Tests can measure the amount of HIV in a drop of blood taken from a person. There is a strong correlation between the amount of HIV and the person's health. Also, when people are on ARVs, the amount of HIV drops to barely detectable levels. If the amount of HIV increases again, this is a sign that treatment has stopped working.

It is fair to say that there is no other infectious disease whose cause has been confirmed as thoroughly as HIV.

Scientists have looked for other causes without success. A favourite one advocated by Aids denialists, particularly Professor Peter Duesberg of the University of California at Berkeley, is that recreational drug use in gay communities caused Aids. But studies have been done in gay communities to check this and found too many people who do not use recreational drugs that have developed Aids. By contrast, too many people who do use these drugs do not develop Aids unless they are HIV-positive.

Over a hundred years ago Robert Koch described four postulates that must be met to enable one to say with great confidence that a particular kind of germ is the cause of a disease in an animal. They have been slightly modified over time and some scientists have proposed alternative, perhaps better, conditions. But Koch's postulates are still accepted as the ultimate proof of cause. Slightly modified, here they are:

1. The disease should only occur in animals infected with the germ. Not every infected animal needs to get the disease, though.
2. It must be possible to take the germ from the diseased animal (or isolate the germ as scientists say) and grow it in a laboratory. In other words, it should be possible to culture it.
3. It must be possible for a previously uninfected animal to become sick if it is infected with germs grown in culture.
4. It must be possible to again isolate the germ from an animal infected via postulate 3.

For many infectious diseases, including Aids in its early period, scientists agree on the cause long before all the postulates are met. But HIV has indeed met this high burden of proof. Postulates 3 and 4 have been fulfilled in the tragic accidents in which HIV laboratory workers got infected.

The first postulate is the most important. It means that the germ must be highly correlated with the disease. If it is not, then it cannot be the cause. Yet medical data are full of exceptions in every field. This is because the tools used to measure what is going on in the human body are prone to error. There is always noise in the data, anomalies that cannot be explained and plain old human errors. No medical test is always accurate. Occasionally misdiagnoses are made. (Think of the pregnancy test.) So on extremely rare occasions, people have developed Aids despite testing negative for HIV. Nevertheless with time, the accuracy of the standard HIV testing algorithms has approached, albeit not quite reached, 100%. There are two well-understood exceptions to this: babies younger than 18 months born to HIV-positive mothers and people still in the several-week window period just after infection. The former, because they have their mother's antibodies temporarily, often test HIV-positive when they are not infected and the latter often test HIV-negative because they have not produced sufficient antibodies to show up on the test.

The progress of the virus can be fairly summarily described. HIV progressively depletes the immune system of CD4 T-cells. These are the white blood cells that help coordinate the body's response to infections. They are also therefore known as T Helper Cells. The consequence of their depletion is that people with HIV gradually become more susceptible to a range of infectious diseases. Diseases that attack people with compromised immune systems are called opportunistic infections. People in the early stages of HIV infection might have no symptoms or experience only a higher-than-normal number of minor illnesses. But with time, they are much more likely to get TB, the disease that kills most people with HIV in southern Africa. They are also more likely to get what are otherwise very rare opportunistic infections: PCP, Kaposi's sarcoma, cryptococcal meningitis, toxoplasmosis and many more unpleasant and often deadly

diseases. It is sufficient for an Aids diagnosis for a person with HIV to have any of these. In other words, Aids is simply a stage of HIV infection, the last one. Often when people have Aids, they become ill with multiple opportunistic infections, suffer constantly from diarrhoea and lose far too much weight.²⁴

Without treatment, it takes most people about two to ten years from infection to the onset of Aids. From then it takes about two to three years to die. But there is large individual variability. A UK study showed that about a quarter of people went on to treatment less than two years after being infected. These are known as fast progressors. On the other hand, some very few but lucky people do not show symptoms of Aids even two decades after infection, despite receiving no treatment. They are known as slow progressors, non-progressors or – a term that only medical scientists could have thought of – elite controllers. One's genes appear to be the most important factor affecting the rate of progression, not how well one eats, how much one exercises, to whom one prays or what herbal concoction one takes.²⁵

During the asymptomatic phase of HIV infection, the immune system and the virus are locked in struggle. Millions of viruses are produced daily and destroy millions of CD4 cells. The body counters by producing millions of CD4 cells and destroying millions of viruses. Eventually, for reasons scientists are still grappling with, HIV wins the battle in at least 95% of people, and Aids develops. The battle between HIV and CD4 cells is complicated. HIV infects a minority of CD4 cells, only 1 in 100 to about 1 in 1,000. But those infected cells send signals to uninfected cells to die prematurely. When we are infected with viruses like influenza or one of the common cold ones, the immune system successfully clears the infection from the body. HIV is not cleared and so the immune system constantly detects that it is infected. Therefore it repeatedly produces CD4 cells to fight the infection, but these simply become new targets for HIV to attack. In effect, the immune system behaves like a dog chasing its tail, as a friend of mine put it. Scientists call this immune hyperactivation and it causes a range of health problems. ARV treatment massively reduces the number

of viruses in the body and ends this vicious cycle, allowing the immune system to relax.

Poverty and Aids

A common Aids denialist argument is that Aids in Africa is a new name to cover a range of old diseases caused by living in poverty. Mbeki appeared to agree with this view. Here is an extract of an interview he gave to *Time* Magazine, one of many occasions in which he alluded to it.

Clearly there is such a thing as acquired immune deficiency. The question you have to ask is, what produces this deficiency? ... Now, if you go through the literature, ordinary standard literature available in medical schools, there will be a whole variety of things [that] can cause the immune system to collapse ... Endemic poverty, the impact of nutrition, contaminated water, all of these things, will result in immune deficiency.

Then *Time* asked him, ‘Are you prepared to acknowledge that there is a link between HIV and Aids?’ He answered:

No, I am saying that you cannot attribute immune deficiency solely and exclusively to a virus. There may very well be a virus. But TB, for example, destroys the immune system and at a certain point if you have TB you will test HIV-positive because the immune system is fighting the TB which is destroying it. Then you will go further to say TB is an opportunistic disease of Aids whereas in fact TB is the thing that destroyed the immune system in the first place. But if you come to the conclusion that the only thing that destroys immune systems is HIV then your only response is to give them ARV drugs. There’s no point in attending to this TB business because that’s just an opportunistic disease. If the scientists ... say this virus is part of the variety of things from which people acquire immune deficiency, I have no problem with that.²⁶

This answer exemplifies Mbeki’s statements on Aids from 2000

onwards: confused and equivocal. He reduces the importance of the virus as a cause of Aids and elevates other causes, in this case the effects of poverty: contaminated water, poor nutrition and TB, which is a disease much more likely to occur in poor people. As his words show, this was his justification for withholding ARVs from the public health system. Mbeki’s comments were not merely a misrepresentation of truth. He fudged the cause of Aids by denigrating the role of ARVs and appealing to genuine concerns about the role of poverty. The nonsense of his response in *Time* is made worse by his misunderstanding of how TB is treated. It, too, is treated with drugs, different ones from ARVs. Mbeki’s description of the causal relationship between HIV and TB is particularly confused.

Andile Madondile took me to his tiny shack in Khayelitsha which he shares with his wife and two children. There is barely any privacy. Dirt roads crisscross almost randomly between houses. When it rains heavily, those roads become rivulets. But on the day we were there, the sun was baking his shack. There are no shady trees; there is hardly any vegetation at all. Just ugly dilapidated shacks cobbled together from wood and corrugated iron, one after another, packed together nearly on top of each other. And this is not the worst part of the area. There is even more dense ‘housing’ just down the road from Andile which he says has a lot of people with TB. There is no tap in Andile’s shack. The one a few metres from it was vandalised by *tsotsis* and Andile’s ward councillor has not done anything to repair it despite promising to do so. So the nearest tap is about 100 metres from his shack. The nearest toilet is even further. His shack, the tap and toilet make a triangle of inconvenient town-planning with devastating public health consequences.

How is poverty related to Aids? For one thing, as Andile’s circumstances show, it makes day-to-day living with the virus and opportunistic infections difficult. Diarrhoea is a part of life in the advanced stages of HIV. For many people it occurs often enough at all stages of HIV infection. There is also compelling evidence that poverty increases the risk of HIV infection. Until there’s evidence to the contrary, it seems prudent to assume that food insecurity puts people at higher risk of contracting HIV. Aids affects far

more poor than middle-class people. And malnutrition worsens the decline of the immune system after HIV infection.²⁷

But there have been too many well-off people who have died of Aids for poverty to be its cause. Many scientific studies have debunked this notion, but one in particular is worth describing. Nelson Sewankambo and his team of scientists at Makerere University in Kampala have done a series of important epidemiological studies in the Rakai district of Uganda. Over a period of more than three years they followed nearly 20,000 adults under the age of 60. This was long before ARVs became generally available in Uganda. Slightly more than 16% of their cohort was HIV-positive. People with the virus were more than seven times likelier to die during the study period. Babies of HIV-positive mothers were more than twice as likely to die. Younger adults were more at risk of dying from HIV-related illnesses than older ones. None of this is surprising, except for this: HIV deaths were higher among better-educated adults and civil servants, a finding that demolishes the notion that poverty is the cause of Aids.²⁸ And contrary to Mbeki's theory, studies from Thailand, Côte d'Ivoire, Uganda and Tanzania show that, if anything, Aids exacerbates poverty.²⁹

TAC has since its inception in 1998 produced T-shirts which say 'HIV-positive' in bold letters on them. They are worn by HIV-positive and HIV-negative people. The purpose is to show solidarity with infected people, encourage openness and destigmatise the disease. Each edition of the T-shirt has a different message on the back. TAC's response to Mbeki's suggestion that poverty caused Aids was to produce an edition of the T-shirt with the slogan 'Aids causes poverty'. As with Mbeki's view, it was an oversimplification, but it was designed to make an important political point. Most poverty existed before Aids, but the evidence shows that the HIV epidemic has made many people poorer and even thrown well-off people into poverty.

There is one particularly crucial way in which poverty exacerbates Aids that Mbeki almost entirely ignored except, so far as I can find, for one fleeting reference in a speech that otherwise expressed his deep scepticism about HIV as the cause of Aids as well as the benefits of ARVs. Poor people

do not have access to the health services of the well-off. Besides having poorer health facilities, they cannot afford to buy expensive medicines. Until ARVs and other medicines for opportunistic infections were widely available in the public health system – and even since – the poor died of Aids in large numbers in South Africa precisely because it was much more difficult for them than for well-off people with medical insurance to get ARVs.

Finding the first treatment

The search for a cure or treatment for HIV began in earnest once it was shown to cause Aids. Samuel Broder, the clinical director of a special Aids task force established at the US National Cancer Institute (NCI), requested pharmaceutical companies to send drugs which might be effective against HIV to his institute for testing. Drug companies store thousands of compounds in the hope that they might one day be beneficial and potential money-spinners.³⁰

Broder's lab ended up testing over 180 compounds. The most promising was azidothymidine, popularly known today by its abbreviation AZT and also by the more pronounceable name zidovudine. It killed the virus in laboratory tests. In 1985, a small trial was carried out on 35 patients with HIV to work out what the dosage for AZT should be. The trial also concluded that it was safe enough for testing to be taken further.

The process of testing a drug is complex, expensive and time-consuming. The thalidomide scandal of the 1960s, in which thousands of deformed babies were born to women who took the drug, precipitated stringent standards for the testing and approval of new medicines. Typically a new drug must be designed, then tested in a laboratory, then tested on animals, then tested on a small number of healthy volunteers to establish dosage and safety (a step skipped in the case of AZT but incorporated in the next step), then tested on a small number of ill people to determine what dosage, if any, is effective against the relevant disease. Finally, a large study comparing the drug with the best available standard of care must be carried out. If there is nothing available to treat a disease, as with Aids in 1987, then the drug must

be compared to a placebo that is inert but looks and tastes like the drug. This is the decisive step, often called a phase III clinical trial, although in the case of AZT it was the second phase of the human clinical trials. The group taking the real drug is called the intervention or test arm. The group taking the placebo is called the control arm.³¹

Phase III trials need to be randomised, which means that anyone selected to participate in the trial must have an equal chance of being allocated the placebo or the real thing. This is critical. If, for example, the placebo arm had only women and the test drug arm only men, one could miss problems with the drug that are specific to women. Randomisation helps distribute evenly over the two arms of the trial all the factors that could confound the results, so that neither arm is likely to be biased. Analyses of trials show that those that are not properly randomised tend to produce results heavily biased in favour of the test drug.³²

Ideally, trials should also be blinded, meaning that the patients do not know which arm of the trial they are on until it is finished. Even better, trials should be double-blinded, meaning the doctors or nurses treating the patients do not know which arm they are on either. Trials that are not double-blinded tend to produce results biased in favour of the test drug. Not all trials can be blinded, however, sometimes for ethical reasons and sometimes for practical reasons. For example, three randomised controlled trials have looked at the effect of circumcision on HIV transmission. They could not be blinded because it would be somewhat challenging to administer a placebo circumcision.

If a drug outperforms the placebo better than can be explained by chance, then the trial has what is called a statistically significant result. It means, all other things being satisfactory, that one can assume the drug is effective. Unfortunately, even if a trial delivers a statistically significant result, this does not mean one can be absolutely sure the drug is effective, but it is likely. Sometimes, unluckily, a clinical trial produces the wrong result and scientists might not realise it for decades or for ever. There are no absolute guarantees in medicine. However, the better the drug performs compared with the placebo, the more confident we can be. Moreover, if

multiple clinical trials confirm each other's results, we can be even more confident. As we shall see, with ARVs we can be extremely confident.

Safety must also be considered. No drug is entirely safe, because to be effective it has to have some effect on the complex chemistry inside the human body. If a product claims that it has no side-effects – a commonly made claim for quack remedies – it either is false or probably has only a placebo effect. Homeopathic remedies are an example of the latter. When you read a claim that says 'No side-effects', replace this in your head with 'Very likely to be complete bullshit'.

The trial researchers and regulatory authorities, such as the FDA or the South African MCC, decide on all the available evidence if the benefits of the drug outweigh its safety concerns. If so, and if the drug can be manufactured according to strict quality-control standards, it is registered for the treatment of the ailment it was tested on. After a drug is registered, reports of serious or previously unknown side-effects have to be tracked. The registration can be reviewed if a previously undetected problem occurs. Registration is important to drug companies – at least it should be. In South Africa it is illegal for someone selling a medicine to claim that it treats a viral disease, such as Aids, unless it is registered for the treatment of that disease. In chapter 8 I explain why this law is often ignored.

The registration procedure is there to ensure that the medicines people take are acceptably safe, effective and of good quality. It is a reasonably good system that works well much of the time. But despite the numerous checks and balances, things can go wrong, sometimes because of greed and corruption. Tragically, despite the lessons of thalidomide, there continue to be scandals such as that surrounding the painkiller Vioxx, which is thought to have caused nearly 30,000 heart attacks or sudden cardiac deaths in the US alone. It is incidents like this, which are too common unfortunately, that erode public confidence in the pharmaceutical industry and fuel conspiracy theories that lead to Aids denialism.³³

The blinded placebo-controlled trial for AZT, known as BW002, commenced in 1986. All 282 HIV-positive patients were ill, either with Aids or nearly there. The study was terminated early because, within six months,

19 patients out of 137 on placebo died versus only 1 out of 145 taking AZT. The odds of this result having been obtained by luck are less than one in a thousand: AZT is effective. AZT was therefore registered by the Food and Drug Administration (FDA) on 20 March 1987. It took less than three years from the NCI experiments on AZT to registration, extraordinarily quick by drug development standards. This was a consequence of pressure from Aids activists and a realisation by scientists and the FDA that finding treatments for Aids was an emergency.³⁴

The AZT trial was a critical moment in the history not only of Aids but also of Aids denialism. Although it was a breakthrough for people with HIV, the combination of several problems soon undermined public confidence in the drug.

The drug was simply overhyped by its manufacturers and doctors. AZT was not a cure for Aids – and was never marketed as one – but even its efficacy as a chronically taken treatment proved to be double-edged. The trial lasted less than six months. Only 27 subjects were on it for more than four months. Had it continued a bit longer, one problem with the drug would have become apparent: HIV develops resistance to AZT quickly, within months in most patients. The benefit the drug conferred was transient. Even in the trial this had started to become apparent, but it did not last long enough to reveal how serious the problem was.

Resistance is a serious problem. The reason it occurs so readily when patients only take one ARV is that HIV often makes mistakes when reproducing itself. These mistakes are called mutations. Most of the time mutations are actually a problem for the virus, not the infected human. But occasionally some mutations help the virus by making a drug like AZT ineffective against it. Copies of the virus with this resistant mutation have a huge survival advantage over other viruses that are being wiped out by AZT. Soon the resistant viruses become dominant and AZT no longer works. While resistance occurs with all viral and bacterial infections, HIV's replication is speedy and particularly error-prone. This results in resistant strains developing quickly when patients take only one ARV or with suboptimal treatment.

To make matters worse, AZT in those days was prescribed in extremely high doses. Patients were given 1.5 grams of the drug daily. Today the adult dosage is just over a third of that. The drug elicited serious side-effects, which for people with advanced HIV and poor immune systems were sometimes deadly. The perception developed among people with HIV that they faced the possibility of certain death by Aids or likely death by AZT. Moreover, AZT was often prescribed to people with HIV long before they had symptoms of Aids. The problem with this is that resistance would evolve and the drug would then be useless by the time Aids developed. In fact, a clinical trial called Concorde demonstrated that it made more sense to defer treatment with AZT until Aids.³⁵

And then there was the price. It cost \$7,000 to \$10,000 per patient per year. Burroughs Wellcome had patented the drug, effectively giving it a monopoly on its production and sale. American activists protested against the company and Congressional hearings were held over the extortionate prices being charged to people facing death.

All these problems with AZT fuelled public scepticism of Aids researchers and, even more so, scepticism of pharmaceutical companies, primarily in the US and other countries where AZT was available. Much of this scepticism, especially of the drug industry, was healthy and justified, but extreme versions manifested as Aids denialism and the claim that AZT, not Aids, was killing people. Duesberg was at the forefront of this claim. He had made important discoveries on cancer in the 1970s. In March 1987, a few weeks before AZT was registered by the FDA, he published a long article in the journal *Cancer Research* contending that HIV was not the cause of Aids. He began writing prolifically on the subject, becoming the scientific face of the Aids denialist movement. Soon he began to allege that AZT was one of the causes of Aids.³⁶

A common denialist argument is to attack the findings of the BW002 trial. As a recent example, an article was published in the March 2006 issue of *Harper's*, a highbrow American magazine, by Celia Farber, an Aids denialist and Duesberg disciple. In it she said: 'Members of the control group began to acquire AZT independently or from other study participants, and

eventually the study was aborted and everyone was put on the drug.’ This implies that the study was ‘aborted’ because it became unblinded. But that is not why the study was stopped. The FDA explained that the study was stopped in September 1986 ‘after preliminary data strongly suggested that AZT prolonged short-term survival in Aids patients who received it’. In other words, it was stopped because people on placebo were dying and those on AZT were staying alive, and therefore it was unethical to continue giving people a placebo when a life-saving drug was known to be available.³⁷

AZT has been compared against a placebo in 15 clinical trials for people at various stages of HIV infection. Not a single trial has shown that it is worse than the placebo and several show that it is much better.³⁸ Also, many observational studies of AZT in practice have been carried out. They too found that people who had access to AZT had fewer opportunistic infections and increased life expectancy. Duesberg’s claim that AZT causes Aids is unsupported by evidence.³⁹

Duesberg’s arguments have been rejected by his scientific peers. His steadfast refusal to change his dogmatic views has resulted in his scientific star waning. While once he was considered an outstanding scientist, he has for nearly two decades been regarded as an intransigent cuckoo who courts controversy instead of making scientifically tenable arguments. Mbeki used Duesberg’s scientific authority to promote Aids denialism, a role Duesberg happily fulfilled. Consequently, he shares at least some responsibility for the misery caused by his dogma. Thus, though Aids denialism would find its most powerful adherent at the helm of South Africa, its roots were American.

HIV becomes a chronic manageable disease

After AZT was registered, it took a few years before new drugs were added to the ARV arsenal. Didanosine was registered in 1991, zalcitabine in 1992. Clinical trials showed that patients who used one of these drugs together with AZT were less likely to get sick or die. Then two more drugs followed, stavudine in 1994 and lamivudine a year later. Except for zalcitabine, whose side-effects are worse than the others, all of these remain in use today. One

of the sites for the phase III trial of lamivudine was in South Africa and was run by local clinicians.⁴⁰ I make this point as a counter to the nationalistic view, promoted implicitly by Mbeki, that ARVs are a Western import and that Africa must find its own solutions to Aids. Science has become a global enterprise and Africa certainly contributes, albeit not nearly enough. Lamivudine (known to many people by the trademark 3TC) is still one of the most commonly prescribed ARVs because it seldom causes serious side-effects.

From 1991 until 1995 standard ARV treatment involved taking two drugs. But the effects of treatment were still time-limited, although less so than with one drug. While the life expectancy of people with HIV with access to treatment had been extended, it was still a fatal disease and the drugs merely delayed the inevitable. Then came a major breakthrough. A drug in a new class of ARVs was registered by the FDA in December 1995. It was called saquinavir. Its development is described by Merrill Goozner in *The 800 Million Dollar Pill: The Truth behind the Cost of New Drugs*. Read it to find good reasons for being sceptical of the pharmaceutical industry.⁴¹

Up to that point all ARVs worked by hampering reverse transcriptase, the enzyme that converts the virus’s RNA into viral DNA. AZT and the drugs in its class bind to the end of the viral DNA as it is being generated by reverse transcriptase. This stops the viral DNA from being completed and it becomes useless, like a half-written computer programme. But if the viral DNA is successfully created, it is inserted into the human cell’s DNA. Now the human cell’s DNA contains the code for making HIV. Therefore when the cell makes proteins, it also inadvertently makes the component parts for new viruses. These parts are assembled by another viral enzyme called protease. This is essentially HIV’s equivalent to a robot in a car manufacturing plant. Saquinavir is called a protease inhibitor because it stops protease from assembling the viral parts.⁴²

In 1996 several more protease inhibitors were registered as well as a third class of ARVs. By 1997 the death rate from Aids in the US had dropped by nearly half. Yet it would be another seven years before it became government policy in South Africa to provide ARVs.

Clinical trials as well as research from ARVs used in practice show that using three drugs, preferably from two different classes, substantially increases the time until resistance develops. With one drug, a virus only has to mutate to be resistant to that drug. If a person takes three ARVs, a virus will require more mutations to be resistant to all of them. Also, by using more ARVs the amount of virus in the blood is reduced to very low levels. Few new viruses are produced and so this lessens the chance of resistant mutations developing. If people on ARVs take their drugs daily at about the same time, the probability of a mutated virus emerging in their bloodstream is small. It is therefore possible to take the same regimen for years.

Today there are over 25 different ARVs available. More are being developed. While the early ARVs were renowned for their dreadful side-effects – partly because of the dosages prescribed – the side-effects of the new regimens are much more manageable and for many people are not a problem at all. Patients who become resistant to one regimen should be able to move on to a second line of treatment, and even third and fourth salvage regimens if need be. However, each successive regimen change usually makes treatment increasingly difficult and expensive.

An enormous number of studies have looked at the effectiveness of ARV treatment. A meta-analysis conducted by Rachel Jordan and her team at the University of Birmingham found that in clinical trials, taking two drugs versus just one resulted in a 40% less chance of disease progression or death. Taking three drugs reduced the risk by a further 40%. Taken together, ARV clinical trials show that taking triple-drug treatment reduces the risk of disease progression or death by about 75%. In practice, the results are often better because only the best regimens found by clinical trials need be used. On the other hand, second-rate regimens are also often used because they are cheaper.⁴³

Taking three, sometimes four, ARV drugs a day is now the standard of care for people with HIV whose immune systems have declined to the point where they have Aids or nearly have Aids. It is called Highly Active Antiretroviral Treatment, or Haart. Haart is not a cure for Aids; there is

none yet. Currently, it has to be taken for life.

Aids denialists argue that Haart has not been proved to work in a randomised controlled clinical trial and therefore has not met medicine's golden standard. This is not true. The trials of three drugs against two analysed in Jordan's meta-analysis, for example, disprove this. You might ask why Haart has not been tested against only a placebo. In other words, why are some patients taking three ARVs not compared to a similar group of patients taking only placebos? This would generally be unethical. People who participate in clinical trials are entitled to the current standard of care. When scientists in the mid-1990s thought that three drugs might do better than two, it was already known that two drugs were better than one or none. This is an important point, not only for ARVs. If you have a medicine that you think can treat HIV, you can only get approval to run a clinical trial testing that medicine if you ensure that all patients participating in the trial get the accepted medical standard of care.

Nevertheless, as it happens, an ethical trial was recently conducted that did in fact compare Haart to nothing (not placebo), although this was not its primary intention. In the early 2000s there was much talk amongst scientists and patient groups about the possibility of what is called structured treatment interruptions. Because taking Haart daily for life is a schlep and is also associated with side-effects, scientists and patients wondered if it was possible for patients to take a temporary break from Haart when their immune systems recovered. Besides improving adherence, they reasoned, this would also save on the cost of drugs. So the NIH funded the largest ARV study planned, with over 5,000 patients. It was known as SMART and it tested whether structured treatment interruptions could be used without being detrimental to health. There was great excitement about SMART. My colleagues and I were really hoping it would show that interruptions were not harmful. One South African mining company which started covering the cost of treatment for its workers saw treatment interruptions as a potentially huge cost-saver.

Unfortunately SMART showed that structured treatment interruptions, at least as they were used in the trial protocol, could not work. People on

the interruption arm were more than twice as likely to get sick or die. This was not what was hoped for or expected. But think about what this means: patients on Haart all the time did better than patients on Haart some of the time. If Haart was poisonous, patients taking it more often should do worse. The SMART trial showed precisely the opposite. It debunks the notion that the toxicity of Haart outweighs its benefits. Three other treatment interruption studies in adults have reached similar conclusions to SMART.⁴⁴

Hundreds of studies collectively involving tens of thousands of adults and children on Haart from Africa, Europe, the Middle East, South America, Haiti and the US have been published. They have found that the benefits of ARV treatment are enormous, extending life expectancy, reducing opportunistic infections and allowing people who previously faced a near-certain early death to resume their lives with the reasonable expectation of dying in old age, probably of something unrelated to HIV.⁴⁵

Blinded placebo-controlled trials have also shown that ARVs reduce the risk of pregnant women passing the virus on to their babies. The science of this has advanced swiftly over the past decade. A protocol that reduces mother-to-child transmission to less than 2% has been developed. Without any health intervention, the combined risk of transmission due to pregnancy, labour and breastfeeding is in the region of 30% to 40%.⁴⁶

While for practical and ethical reasons it is not possible to do clinical trials showing that ARVs are effective in reducing the risk of an HIV-negative rape survivor contracting the virus, an accumulation of data from health facilities comparing women who received ARVs within 72 hours after rape with women who did not shows that very likely they do work for this purpose. ARVs also most likely reduce the risk of hospital workers contracting HIV after they have been injured with contaminated hypodermic needles. And relatively new evidence shows that HIV-positive people on ARVs are less likely to pass the virus on to their sexual partners.⁴⁷

All ARVs achieve the same goal: the number of viruses diminishes to very low levels, allowing the body to replenish its CD4 cells. Consequently the risk of getting an opportunistic infection becomes much smaller. ARVs

work incredibly well, often bringing people on the verge of death back to life. They work irrespective of whether a person is male or female, black or white, gay or straight, child or adult, health fanatic or intravenous heroin user. They work for fast progressors too. But ARVs do have two serious problems: side-effects and resistance.

ARVs are obviously not the panacea for the Aids pandemic. Many other health interventions are essential, such as condom distribution, mass public information campaigns, campaigns that promote HIV testing, offering heterosexual men in high-prevalence epidemics circumcision, and sex education in schools, to name a few. Improving the living conditions of poor people could also help lower the HIV transmission rate.

I have dwelt in detail on how we know that ARVs are safe and effective because the success of these medicines elicits the crux of what is wrong with Aids denialism and Aids quackery. The evidence is immense that by and large people who test HIV-positive and then either develop Aids-related illnesses or have low CD4 counts do extremely well on Haart, much better than those who do not take them. Yet Aids denialists have disputed and continue to dispute this. Aids quacks dispute it implicitly by offering unproven alternatives to ARVs. It is therefore on this aspect of the debate, the benefits of ARVs versus alternative remedies, that the central battle for life and death was fought during the era of Aids denialism.

Side-effects

In March 2002 the President's office released this statement: '[Mbeki] said he was aware that there was some controversy in the country about the issue of ARV drugs. He had no desire to enter this debate. This was because he did not believe that drugs were central to the fight against Aids. Even in the US, various complications relating to these drugs had not been resolved.'⁴⁸

Thabo Mbeki does not like AZT. On 28 October 1999 he addressed the National Council of Provinces about South Africa's high incidence of rape. There was already evidence, albeit limited, at the time that AZT could reduce the risk to a person who had been raped of contracting HIV. Some had begun calling for the drug to be made available to rape survivors. The

TAC had also called for AZT to be made available to pregnant women. Mbeki vetoed the idea:

Concerned to respond appropriately to this threat, many in our country have called on the Government to make the drug AZT available in our public health system.

Two matters in this regard have been brought to our attention. One of these is that there are legal cases pending in this country, the United Kingdom and the United States against AZT on the basis that this drug is harmful to health.

There also exists a large volume of scientific literature alleging that, among other things, the toxicity of this drug is such that it is in fact a danger to health.⁴⁹

As far as I can tell, the legal cases he referred to had been initiated by Aids denialists and they were dismissed. Two weeks later, the Minister of Health announced that she had asked the MCC to review the safety of AZT before it could be used to prevent mother-to-child transmission. In February 2000 she rejected their findings, which had endorsed AZT. The arrogance of this was breathtaking. At the time the MCC's impartiality and expertise were still respected. The institution's ability to determine the safety and efficacy of AZT outstripped any other source the Minister of Health might have consulted.⁵⁰

Mbeki wrote a letter to world leaders who were giving him a hard time about his Aids policies, including Kofi Annan and Bill Clinton:

Demands are being made within the country for the public health system to provide ARV drugs for various indications, including mother-to-child transmission.

We are discussing this matter, among others with our statutory licensing authority for medicines and drugs, the MCC.

Toward the end of last year, speaking in our national parliament, I said that I had asked our Minister of Health to look into various controversies

taking place among scientists on HIV/Aids and the toxicity of a particular ARV drug.⁵¹

Here is an exchange between Mbeki and a caller in a BBC radio interview on 6 June 2000:

Mark Rolfe, Scotland: Why do you deny pregnant women the use of AZT during pregnancy and labour when there is solid evidence it reduces the transmission of HIV from mother to child?

President Mbeki: This is part of the discussion that is now taking place. The latest circular from the World Health Organisation was specifically on AZT. It says when you dispense AZT, it must be done under close medical supervision, bearing in mind the contra-indications and potential toxicities. The idea you can just give out this ARV without the proper health infrastructure – because in many instances you've got to check this patient every day – you cannot do it in a rural district hospital. This infrastructure does not exist. One of the issues that the scientists are looking at is – where you have to dispense these ARVs to large numbers of people in a poor country, with a weak health delivery system? What the WHO is warning about – is that if you don't do it properly, you might kill the pregnant mothers because of the toxicity in the drugs.⁵²

The side-effects of ARVs have become the stuff of legend in South Africa. One of the most frequent and hardest tasks that TAC members face is to convince people sick with Aids that they need to start Haart. Doctors frequently complain that their patients leave Haart until too late, when they have become very ill, because they are scared of the side-effects. I have even seen this apprehension of side-effects in colleagues and friends who have reached the point where they need to start treatment. They know the benefits of Haart, they teach about HIV, yet even they are nervous. Fear of the side-effects of Haart is, I suspect, one reason why people are dying of Aids now in South Africa without ever getting treated, even though the medicines might be available in a clinic nearby. The myth created by Aids

denialists, that it is ARVs and not HIV that kill, permeates our society. It is a dangerous and deadly illusion.

The patient information sheets that come in ARV pill boxes list dozens of side-effects. Aids denialists love quoting them. Many side-effects are indeed dangerous. The most commonly reported serious ones are lactic acidosis, peripheral neuropathy (this feels like numbness or bad pins and needles in fingers, toes, hands or feet), rashes, anaemia, lipodystrophy (the redistribution of fat to different parts of the body), and lipoatrophy (loss of body fat from the face, legs and arms). Of these, peripheral neuropathy, lipodystrophy and lipoatrophy are not deadly, but they are serious and can make treatment intolerable.

The deadliest and scariest side-effect is lactic acidosis. This is a build-up of lactic acid in the blood and tissues. The symptoms are tiredness, pains in the abdomen, weight loss, an enlarged liver and lots of vomiting. Unfortunately, these are the same symptoms for many other diseases and it usually requires a test to confirm the diagnosis. I knew two TAC members who died of this side-effect, partly because they lived miles from their hospitals and did not have access to decent transportation to get them help in time. It comes on quite suddenly and a person can reach the point of no return quickly. But it can be picked up in time if clinics can test lactic acid levels. This is not expensive and it is done in resource-poor settings like Khayelitsha. If it is not picked up in time, the person will have to be hospitalised and there's a high risk of death. It is caused primarily by an ARV called d4T. This is a cheap drug that is used as part of the standard of care in the South African public health system. For years, activists have been trying to get the government to phase it out and replace it with a better drug, yet Tshabalala-Msimang, who claimed to be terribly concerned about ARV side-effects, alternately ignored and resisted these calls.

What is the risk of getting a serious side-effect if you are on Haart? It differs widely from place to place because of the different stages at which patients are getting treated, quality of care and other local factors. We have seen that the risk of dying from not going on Haart is very much higher. A 2003 analysis of US patients showed that about 30% of patients

who had been on treatment for three years had had a serious side-effect. A small fraction died from these, but without Haart nearly 100% would have died.

Dealing with side-effects is usually straightforward: you change your drugs. There are quite a lot of ARVs, so patients usually have options. The copious reports on Haart coming out of the South African public health system show that our health professionals, be they nurses or doctors, generally handle side-effects remarkably well, whether in the centre of Johannesburg or the remote rural village of Lusikisiki, where thousands of people are on Haart and doing well. Arguably the most critical factor is that patients should be treated in clinics that are an affordable and convenient travelling distance from where they live, but even if this is not possible, the benefits of Haart still far outweigh the risks.

Side-effects in children whose mothers took ARVs while pregnant

At the South African Aids Conference in 2009 a pamphlet produced by Aids denialist Anthony Brink was distributed by an elderly man to the delegates as they entered the conference hall. 'Why do Zackie Achmat, Nathan Geffen and Mark Heywood want pregnant African women and their babies to be given AZT?' The pamphlet reproduced quotations from about 15 medical studies, most of them of good quality. The quotations read alone would lead you to believe that ARVs for pregnant women are extremely dangerous for their unborn children.

Brink's pamphlet is misleading because the three people referred to in its title advocate AZT and other ARVs only for HIV-positive pregnant women and we do so irrespective of whether they are African or not. Moreover, none of us are scientists, but what we advocate is firmly supported by scientific institutions across the planet, as well as many HIV-positive women in TAC who have healthy babies today thanks to ARVs.

Far more misleading is the selectivity of Brink's quotes. Nearly every study from which he quotes actually supports the provision of ARVs to pregnant women. It is true that babies born to HIV-positive women who took ARVs while pregnant can experience side-effects. But the question to

ask is whether the baby is likely to have been better off if the mother had not taken ARVs.

The Cochrane Collaboration is an independent organisation that evaluates the evidence for different medical interventions. It is respected for its independence and for the high quality of its reviews. In fact it is fair to say that it is the most respected evaluator of medical evidence there is. Using the best experts in a particular field, Cochrane reviews make recommendations after examining all the available relevant high-quality evidence.

In 2007, the Cochrane Collaboration reviewed ARVs for the prevention of mother-to-child transmission (PMTCT). Its conclusion was unequivocal. It 'found that short courses of certain ARV drugs are effective in reducing mother-to-child transmission of HIV, and are not associated with any safety concerns in the short term'.⁵³

What about long-term side-effects? This is a bit trickier. There are long-term concerns. The most serious of these is that there is evidence that ARVs damage the foetus's mitochondria. Exactly what the consequences of this are we do not yet know. Some researchers suspect it might put these babies at higher risk of cancer. But given that this intervention only started in the 1990s, it is too early to tell. More long-term data on children whose mothers took ARVs while they were pregnant are still needed. Nevertheless, the largest and best-conducted follow-ups so far reveal that very few children have suffered serious side-effects attributable to the drugs.⁵⁴

Consider that nearly half of all babies born with HIV die by the time they are three years old unless they get Haart. Consider also that even in an excellent health system in which HIV-positive children receive Haart from the day they are diagnosed, at least 4% will die at a young age. Finally, consider that so far very few serious side-effects have been seen in children born of mothers who took ARVs when they were pregnant, despite 15 years of AZT use and over 10 years of Haart use. Taken together, these points make the case for PMTCT very compelling. Then there is also the crucial point that many pregnant HIV-positive women need Haart for their own health.

That is why Zackie Achmat, Mark Heywood and Nathan Geffen, as well as nearly every HIV activist and scientist in the world, want HIV-positive pregnant women to get ARVs.

Micronutrients and Aids

The last topic we need to consider in this chapter on the science of Aids is the value of micronutrients for those with Aids. Multivitamin or micronutrient supplements have been touted by many, including Matthias Rath, whom I shall deal with at length in later chapters, as a preferred treatment instead of ARVs and we need to consider briefly the scientific evidence for their claims.

Micronutrient supplements are a huge multibillion-dollar industry. Exaggerated claims and aggressive advertising characterise the marketing of these products. Often they are marketed as a natural, non-pharmaceutical solution to healthcare, but they have to be artificially manufactured, just like any other pharmaceutical product. Moreover, despite the anti-drug company approach of advertising for these products, some of the big drug companies, such as GlaxoSmithKline and Pfizer, are also major sellers of multivitamin pills, with substantial markets in developing countries like India. Micronutrients are cheap and easy to manufacture and very easy to sell at a high price, hence the size of the industry.

So what is the evidence for Rath's claim that micronutrients reverse the course of Aids? To answer this, it will help to take a brief look at the evidence when HIV is not considered. Numerous clinical trials have been and continue to be conducted on micronutrients, far too many in fact. This plethora of trials is driven less by health needs and more by the potential for large profits. The outcomes of these trials are a complex mesh of contradictory results. Unsurprisingly, trials conducted by the micronutrient industry or by researchers with close links to it tend to find positive results. Large, well-conducted trials on the other hand tend to find minimal or no benefits from micronutrient supplements and sometimes even find that they are harmful.⁵⁵

The Cochrane Collaboration has also reviewed micronutrient

supplements for people with HIV. The trials in adults give inconsistent results. Some showed no benefit from vitamin supplements; others show small benefits on progression to Aids and mortality. Two small trials of vitamin A in children with HIV showed reduced mortality, improved growth and reduced diarrhoea.⁵⁶

One of the studies considered was carried out by Harvard researchers in Tanzania. It is the best of the vitamin trials that found positive results. At the time of the trial, Haart was not available in Tanzania and the researchers wanted to see if vitamins could delay the onset of Aids in a poor country. It was never their intention to promote vitamins as an alternative to Haart and the modest results of the trial, albeit positive for vitamins, show unequivocally that they cannot be used as an alternative. The trial researchers' conclusion was straightforward and honest; 'Multivitamin supplements delay the progression of HIV disease and provide an effective, low-cost means of *delaying* the initiation of [Haart] in HIV-infected women' [my emphasis].⁵⁷ The lead author of this study, Wafaie Fawzi, has also stated, 'It is important to underscore that multivitamin supplements should not be considered as an alternative to [Haart] in developing countries but as a complementary intervention that is part of a comprehensive care package.'⁵⁸

Although Rath has consistently overstated the findings of this study in his advertisements, the Cochrane reviewers took a cautious approach when examining this and other controlled trials. 'There is no conclusive evidence at present to show that micronutrient supplementation effectively reduces morbidity and mortality among HIV-infected adults. There is evidence of benefit of vitamin A supplementation in children. The long-term clinical benefits, adverse effects, and optimal formulation of micronutrient supplements require further investigation.'

I went to my local pharmacy and found that a month's worth of a leading multivitamin brand was just under R100 (many times what they cost to manufacture). They will not fill you up or alleviate your hunger in any way. They come with no carbohydrates, fats or proteins. You will therefore not get any energy from them. If you are a healthy person, HIV-negative or -positive, you are better off spending the money on a selection of foods,

for example liver, eggs, oranges and milk (if you are a vegetarian there are many other options). These will give you the micronutrients you need and a lot of macronutrients to boot.

As one of the authors of the Cochrane review has wisely said: 'The most that micronutrient supplementation can have been demonstrated to achieve in people with HIV is to assist recovery from malnutrition, delay the onset of Aids, or improve the response to ARV treatment. However, further research is needed to determine conclusively whether or not they achieve this.'

* * *

This book is not the appropriate place to traverse every detail of HIV science or address every false argument given by Aids denialists. But I hope this chapter has given you an understanding of why Aids denialism is wrong. I have referred to many excellent scientific papers. If you want to know more, they are a good place to start. The aidstruth.org website also debunks most of the common myths spread by denialists and the explanations are usually easy to follow.