

# THE WHITE DEATH

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This online version of *The White Death* differs from 1996 print edition in several respects, including pagination, minor textual details, new material in chapter 12 and omission of the prologue, photographs, appendices and index. The appendices are available online at

<http://www.uow.edu.au/arts/sts/bmartin/dissent/documents/AIDS/Curtis92ul.html> and

<http://www.uow.edu.au/arts/sts/bmartin/dissent/documents/AIDS/Hamilton94/AIDSvsLawsuit.html>

## Portrait of a Catastrophe

David Carr suffocated to death in Manchester Royal Infirmary, UK, on 31 August 1959. His end was the outcome of an horrific lung infection caused by two rare organisms, *Cytomegalovirus* and *Pneumocystis carinii* along with a host of other bizarre symptoms. The doctors who attended him were baffled, regarding the character of his disease as almost freakish.

Carr was just twenty-five years old at the time he died. He had grown up amid the working class surrounds of Reddish, a suburb of Manchester, in the industrial English Midlands. A popular figure, like other boys of his background he had been a keen footballer, playing for the local club, Central Rovers. After leaving school, he went to work as an apprentice linotype operator for the *Manchester Evening Chronicle* but was called up to do his two years national service in the armed services. On 7 November 1955 he had reported for duty with the Royal Navy as a rating, and after a tour in shore service at various British naval bases, was ordered on a voyage to Gibraltar aboard HMS *Whitby*.

While there, it was believed, he obtained a leave pass and went on a brief excursion by ferry across the straits to Tangier in Morocco, North Africa, notorious at the time as a flagrant centre of the sex trade, and consequently a cherished resort for sailors of all nationalities. It was in Tangier, doctors later came to suspect, that Carr acquired the seeds of his doom.

On his return to Britain, he received his discharge from the Navy on 6 November 1957, returned to his home in Manchester and became engaged to be married shortly thereafter.<sup>1</sup>

But all was not well with David Carr. Since the last months of his service with the Royal Navy his gums had been giving him trouble, and, within a year, some large, brownish spots appeared on his back and shoulders, for which he was given X-ray treatment. In spite of this, his health continued to deteriorate. His symptoms became ghastly: by December 1958 he was breathless, wasted, tired and feverish. He was afflicted by a heavy cough which produced purulent sputum flecked with blood. He suffered from haemorrhoids, and in February a painful fissure opened up around his anus, extending for ten centimetres. A small pimple in one nostril rapidly grew into a second ulcer. On admission to the Royal Infirmary he was found to be severely emaciated and febrile. Doctors noticed his immune white cell count was abnormally low,

yet his lymph glands seemed fine and his heart and lungs were otherwise normal. But the scaly brown lesions had spread across his back and shoulders.

After admission to hospital, and even under treatment, the ulcer which had begun in his nostril grew into his upper lip and mouth, dribbling a constant stream of pus down his throat which caused the surface of the tongue to slough. The anal fissure spread remorselessly until it ulcerated a large area of both buttocks. His body was colonised by organisms: cytomegalovirus, golden staph and the parasite pneumocystis honeycombed his lungs. His fingers became clubbed and small abscesses dotted his skin. Severe pneumonia set in. In spite of massive doses of antibiotics, it eventually claimed his life.

The doctors at the Royal Infirmary, pathologist George Williams, registrar Trevor Stretton and senior registrar John Leonard, did not know what to make of this bizarre array of symptoms. At first they were inclined to suspect tuberculosis, but tests rapidly eliminated that possibility, along with several other less common conditions. They then opted for an extremely rare disease, Wegeners granulomatosis, which was their prevailing opinion at the time Carr died. Finally, after extensive post-mortem examination, they concluded the culprit was cytomegalic inclusion disease (CID), a rare viral condition in which infected cells form into giant units. Strangely, though, CID is a disease of infants and scarcely ever kills an adult.

Although Carr's death certificate attributed his demise to Wegeners granulomatosis, the post-mortem found that he had suffocated from a massive lung infection. The case was sufficiently unusual for Williams and his Royal Infirmary colleagues to record in detail for *The Lancet*. Their report appeared in October 1960.<sup>2</sup>

Specimens were taken from Carr's corpse and preserved. His other remains were cremated and the ashes scattered at Manchester Crematorium, whose Book of Remembrance sombrely records "cherished memories of the happiness he gave".

At the time of Carr's death, of course, nobody had ever heard of a disease called AIDS. Nobody even dreamed that such a disease could exist. Its discovery lay more than two decades in the future.

\* \* \*

In 1979, twenty years after David Carr's demise, a sharp-eyed Los Angeles doctor named Joel Weisman began to observe in certain of his patients a cluster of puzzling symptoms which included fever, loss of weight, diarrhoea, fungal infections and

swollen lymph glands. The other common thread was that patients were all young, male and homosexual.

It was the heyday of gay liberation, an era when male and female homosexuals across the western world finally began to scent victory in their long struggle against stigma and prejudice. California, as in so many social trends, was the bow-wave of an attitudinal revolution that was starting to ripple around the globe. Many gays were celebrating their new-found freedom of sexual and individual expression by aggressive promiscuity, a symbolic defiance of the puritanical principles by which society seemed bound: "An unplanned outcome of the gay liberation movement of the 1970s was a vast business of gay bath houses and sex clubs. These establishments capitalised on the prevailing ethos, in which pressing beyond the limits of conventional sexual behaviour was a political act, proof positive of ones freedom from repressive social norms. At the same time this institutionalization or commercialization of sex led to a tremendous increase in sexually transmitted diseases...."<sup>3</sup>

The symptoms in Dr Weisman's patients multiplied. Sometimes they appeared to get better, at other times worse. The best guess seemed to be cytomegalic disease -- the same one that David Carr's doctors had suspected as the primary cause of his demise -- coupled with some other infectious agent such as the Epstein-Barr virus (EBV). The problem was complicated by persistent fungal infections and diarrhoea.

One patient, in particular, went into a decline, suffering rapid weight loss and heavy lung infection. Early in 1981 he was admitted to the California University Hospital where Dr Michael Gottlieb recollected a similar case he had treated in late 1980. Both patients had severely impaired immune systems, both suffered the same lung infection, both were male, both were gay. The puzzle was why two mild and relatively common viruses should have such a severe effect on this small group of patients. Checking the state medical records, the doctors located a third case, and then another. By May 1981 five cases had come to light and the first patient had died two months earlier of severe pneumonia.<sup>4</sup>

What particularly seized the attention of medical workers was the catastrophic nature of the complex of otherwise relatively harmless infections, and the terrible suffering they inflicted. "In June of 1981," recalled Dr Samuel Broder, "we saw a young gay man with the most devastating immune deficiency we had ever seen. We said: We don't know what this is, but we hope we don't ever see another case like it again. But it was already far too late for

that." <sup>5</sup>

By that same month the suspicions of researchers at the United States Centers for Disease Control (CDC) in Atlanta, America's disease watchdog, had been alerted by the growing trickle of reports of unusual infections and rare cancers which had begun appearing in New York, Los Angeles and San Francisco over the previous two years. All the cases reported to that point were young, male and homosexual, and all were afflicted by the same agent, pneumocystis. The CDC scented a possible epidemic and decided that sufficient grounds already existed to issue a national alert. This duly appeared in the CDC weekly bulletin on 5 June 1981.

"The appearance of pneumocystis in these five, previously healthy individuals without a clinically apparent underlying immunodeficiency is unusual," they commented cautiously, and went on to note "an association between some aspects of homosexual lifestyle or disease acquired through sexual contacts and Pneumocystis pneumonia in this population ... All the above observations suggest the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections such as pneumocystis and candidiasis."

This was the first hint that a new, completely unknown, killer was on the loose. It was, as medical historian Dr Mirko Grmek later dubbed it, the birth certificate of AIDS.<sup>6</sup>

According to United States records, the first patient to die had been diagnosed in 1978 as suffering from Hodgkin's disease - his symptoms were swollen lymph glands, weight loss and fever, but the post-mortem examination revealed no trace of this complaint. However, this clearly raised the possibility that he had contracted the agent which led to his death as early as 1978, although it was only from 1981 onwards that the disease became at all widespread in America. In its July bulletin, the CDC reported twenty-six cases of the rare cancer, Kaposi's sarcoma, coupled with pneumocystis and other infections. Eight had already died.<sup>7</sup>

Medical authorities argued about whether the symptoms were the product of a synergy between two or more microbes, the use of recreational drugs such as amyl and butyl nitrate inhalers or "poppers" intended to intensify sexual experience, excessive rectal exposure to semen (which was thought to undermine immunity in some way) or to an agent previously unknown to medical science. Many cumbersome names were proposed for the new condition, including GRID (Gay-related Immune Disease), SIDA (Syndrome

d'Immuno-Depression Acquire), GCS (Gay Compromise Syndrome) and even SPID (a Russian acronym).

As doctors gradually became aware of the existence of the new disease, many began to back-track through their records for earlier cases which had puzzled them at the time. In North America, the earliest confidently diagnosed case known was in 1978. On the strength of this, Dr Grmek and others considered it probable that the first American victims had contracted the virus around 1976. So, by the time the CDC became involved in 1981, the disease had already begun to spread quite widely, entering the heterosexual community through injecting drug users and bisexuals and, not long afterwards, surfacing among haemophiliacs and other recipients of donated blood transfusions. Adding to the social stigma which initially attached to it, the condition had also shown up among prison inmates, and among Haitians visiting the United States.<sup>8</sup>

Yet there had already been straws in the wind. On 12 December 1977, a 47-year-old Danish doctor, Margarethe Rask, died in a Copenhagen hospital of an appalling lung infection. She had suffered from rampant colonisation by fungi, bacteria and parasites, and her immune T-cell count had been abnormally low.

Dr Rask had devoted the previous five years of her life to her medical work in Central Africa, first at a primitive rural hospital at Abumombazi in northern Zaire from 1972-'75, and then from 1975-'77 as chief surgeon in the Danish Red Cross hospital in the Zairean capital, Kinshasa. Her colleagues testified that she was an individual of incredible persistence and dedication with an unwearying capacity for hard work. Day-long she laboured, and often much of the night too, under conditions most medical workers would shudder to see: equipment and drugs scarce, needles constantly reused, surgical gloves often torn and disinfection inadequate. There were stark warnings of what these conditions could lead to: not far from where Dr Rask had worked in rural Zaire, at a town on the Ebola River called Maridi, erupted one of the most horrifying new diseases to come to medical attention, the so-called Ebola Fever. Spread initially by contaminated needles, the contagion slew 153 people before it finally subsided.

During much of her time in Africa Dr Rask suffered from chronic diarrhoea, which responded reluctantly to treatment. From 1976 on she began to experience growing fatigue, wasting and swollen glands, symptoms which had greatly disturbed her medical friends. Sometimes the condition abated, but the tiredness only increased. A brave and skilful doctor, she knew only too well what

was to be the inescapable outcome of her symptoms: "I'd better go home to die," she frankly informed her friend and colleague, Dr Ib Bygbjerg.

Taking a long-due holiday in South Africa, Rask suddenly found herself choking, unable to breathe, and, strapped to an oxygen bottle, she was hastily flown home to Denmark for treatment. In hospital in Copenhagen, X-rays had revealed her lungs to be densely infected. Two weeks later a glutinous white fungus invaded her mouth.

When it became clear that no treatment could help her, she asked to be discharged from hospital in order to return to her home at Hjardemaal. There, nursed by a close friend, she lingered for three months before yielding to entreaties to return to hospital. When she did so, they found that her body was heavily invaded by thrush, golden and white staphylococci, *Escherichia coli* and pneumocystis. After a valiant struggle Margarethe Rask succumbed to suffocation, caused by the solid proteinaceous mass of millions of organisms which had clogged her airways. At the time of her death, the case of Margarethe Raske, like that of Carr, baffled her doctors.<sup>9</sup>

While Rask was fighting her final battle, a 34-year-old airline secretary from Kinshasa, Zaire, flew with her 3-month-old daughter to Belgium to seek treatment for the child's persistent fungal infection of the mouth. Two of her three children had already died: one from a lung infection, the other of septicaemia, and both had suffered severe oral thrush. The third child had been found to have a low T-cell count.

In Brussels, the mother herself began to suffer from fever, fatigue, headache and infected sinuses. In September she was admitted to hospital suffering a temperature of 39 degrees, rigors, signs of lung infection, swollen glands, weight loss and general aches and pains. Over the next four months her mouth was colonised by fungus, her genitals and anus by herpes and her body generally by cryptococcus, golden staph and candida. Afflicted by severe diarrhoea caused by salmonella and urinary infections of *E. coli* and pseudomonas, the woman deteriorated rapidly, and in January 1978 she asked to be flown home to Kinshasa, where she died the following month. The doctors who examined her thought there ought to be some back-tracking into the history of her disease in Kinshasa.<sup>10</sup>

In 1982 the son of a Congolese government official from Kinshasa died in Stockholm at the age of eight. His blood subsequently tested positive for HIV. The boy had been sick all

his short life, probably contracting the virus at birth in 1974.<sup>11</sup>

In September 1978, a French geologist, Claude Chardon, suffered a serious car smash while working in Haiti. Taken by ambulance to the hospital at Port-au-Prince, his arm was amputated and he was transfused with fresh blood drawn from local volunteers. Over the next four years he developed all the classic symptoms of the new disease and, in October 1982, he died. He was a heterosexual and was never known to use drugs.<sup>12</sup>

Growing awareness of the puzzling cluster of symptoms led European doctors to recall the case of a Portuguese taxi driver, Monsieur Fel. Between 1977-'79, while living in Paris, Fel had received regular treatment for a range of infections including depressed immunity, pneumocystis, thrush, a plague of warts and the terrible brain parasite *Toxoplasma gondii* -- a battery of symptoms that had greatly puzzled his doctors. At the end of this period he returned to Portugal, where he died. Subsequent investigations revealed that Fel was a heterosexual and had lived in Africa during the early 1970s. From 1973-'76 he drove trucks across the Congo, then Zaire.

Then, in September 1980, a 37-year-old Danish agricultural engineer succumbed in Copenhagen with symptoms almost identical to those of Dr Rask. He had never been near Africa or Haiti. But he was a homosexual and, in 1977, had paid a visit to New York.

From 1980 on, cases began to come to medical attention across Europe -- first in Denmark, then France, Britain, Italy and Spain. By the end of 1981 there were thirty-six European cases on record. On the face of it, they seemed to bear out the emerging hypothesis that this was predominantly a disease of male homosexuals.

The first the United States public learned of the mysterious disease came with an article by Lawrence Altman, medical writer for the *New York Times*, which was published on 3 July 1981, less than a month after the appearance of the CDC bulletin warning. Titled "Rare Cancer Seen in Forty-one Homosexuals", the single-column story fell like the initial pebble heralding the landslide -- quietly.

Discreetly avoiding any suggestion of a new disease, the first international scientific paper describing the perplexing symptoms was published by three American scientists in *The Lancet* in September 1981.<sup>13</sup> To begin with, the disease prompted scientific interest rather than alarm. Newly-discovered diseases has always been a font of scientific publication -- the chief means by



which scientists earn their reputations and obtain promotion -- and is useful for prising open the lid of the tightly locked research funding coffer.

A few Cassandras warned that these early cases represented only the tip of the iceberg but, by and large, they were ignored. After all, the number of patients was very small.

How and when the North American epidemic began remained obscure, but with New York emerging as a primary focus, several authorities speculated it had originally been introduced by sailors arriving for America's birthday party, the United States Bicentennial Celebrations on 4 July 1976. How it spread was less equivocal: an exceptional piece of sleuthing by CDC investigators David Auerbach and William Darrow traced clusters of cases in Los Angeles and New York to a flagrantly promiscuous Air Canada airline steward, Gaetan Dugas. Everywhere he flew Dugas had sexual contacts, averaging around 250 partners a year. He estimated his lifetime tally at around 2,500. When his disease was finally diagnosed as fatal, Dugas was consumed by a kind of dark fury, refusing to take any precautions and continuing to have unprotected sex liberally, telling his partners afterwards: "I've got gay cancer: I'm going to die and so are you." In all, the horrified CDC team concluded, he had directly infected at least forty of the 248 American AIDS victims diagnosed by mid-1982. In the end, Dugas was dubbed "patient zero" of the North American epidemic.<sup>14</sup>

Speculation about the origins and cause of the disease ranged widely. Early theories included the suggestions that it was a variant of the strange sheep disease scrapie, that it was related to African swine fever, that it was a new form of syphilis -- perhaps interacting with another microbe -- that it was due to mysterious factors in the blood, and that it was due to certain homosexual practices.

But as time went by researchers became convinced they were dealing with a new agent, and they began to search for one. The hunt was greatly influenced by the recent discovery of a new kind of microbe known as a retrovirus. The first of these ever to come to light was isolated from Japanese samples by Dr Robert Gallo and colleagues at the National Cancer Institute of the United States National Institutes of Health (NIH). He christened his discovery HTLV -- Human T-cell Leukaemia Virus -- because of its link to blood cancer. Seeing the emergence of a new disease, researchers naturally began to seek a new agent, a retrovirus, as the possible cause.

In February 1983, a French team led by Dr Françoise Barré-Sinoussi and Dr Luc Montagnier took the world's first pictures of the agent under the electron microscope at the Pasteur Institute in Paris, whose august halls had for almost a hundred years sheltered some of the world's most gifted microbiological minds. At that time, many scientists suspected viruses to be a primary cause of cancers, and Montagnier's team had been in pursuit of an agent which they suspected was linked to breast cancer. Because of the Pasteur Institute's superlative diagnostic skills, a colleague approached Montagnier with a request to examine the blood of a certain Zairean, Monsieur Elomata, who exhibited similar symptoms to the United States cases, to see if it contained any of the newly discovered retroviruses. Montagnier was intrigued by the proposition and expanded his search to include samples taken from the lymph nodes of a homosexual, Frédéric Brugière. On 25 January 1982, after a fifteen-day culturing process, Barré-Sinoussi was able to produce convincing evidence for the presence of a retrovirus -- although it took over a year before the laboratory was finally able to pinpoint and photograph it.<sup>15</sup>

It was during this year, however, that medical researchers finally agreed what to call the disease. Because it was by now clear that it involved irrevocable breakdown of the immune system due to some externally-acquired cause, and was clearly no longer confined to the gay community, they decided to name it Acquired Immune Deficiency Syndrome -- or AIDS.

For much of the past four years, doctors had considered AIDS to be a product of Western society, because that was where the majority of early cases had been observed. But in 1983 French doctors reported that a disease with almost identical symptoms was blazing across central Africa. It was widespread, affecting both women and men, and its effects were invariably lethal. Convinced by now that humanity had fallen victim to a totally new plague, laboratories in Europe and America embarked on a frantic race to expose the biological agent responsible.

What drove them, as much as the quest for knowledge and professional laurels, was a rising tide of public hysteria: the speculative fears expressed by many doctors and enlarged in the media that AIDS, like hepatitis, could be spread by poor kitchen hygiene, social contact, by kissing, by mosquitoes and even on lavatory seats. Such alarms were inflamed by prejudice against the groups who seemed initially to be most affected -- homosexuals, prison inmates, Haitians, drug users -- and by the evident

connection between the new disease and those potentially atavistic human talismans, blood and sex.

In May 1982 the French scientists Barré-Sinoussi and Montagnier had reported their discovery in the leading United States scientific publication *Science*, and in November they announced to a World Health Organisation (WHO) conference in Geneva that they had detected virus-like particles in the lymph nodes of several patients with early symptoms of the disease. The particles appeared to bud from the surface of infected white blood cells and were tiny, from 80-120 nanometres (billionths of a metre) across. On the basis of their appearance, Montagnier assigned them to the family of retroviruses and named them LAV -- lymphadenopathy-associated virus, meaning a virus linked with swollen lymph nodes. But his professional caution got the better of him and he stopped short of claiming that the particles were indisputably the cause of AIDS.

Coincidentally, in the same issue of *Science*, Dr Bob Gallo reported findings which seemed remarkably similar. He had persuaded himself that the strange new condition, AIDS, was linked to his team's earlier breakthrough discovery of the first retrovirus, HTLV-I. Gallo had fewer hesitations than Montagnier: he was convinced he had found the AIDS agent -- and that it was HTLV-1, not LAV. He was wrong. Just weeks later, a Californian group led by Dr Jay Levy also reported finding viral particles in San Francisco AIDS patients, and, with greater empathy for the by now mystified public, called it ARV or AIDS-related virus. Then a British researcher, Professor Alex Karpas, photographed a virus in the blood of an AIDS patient. Finally, in the face of mounting evidence, Gallo shifted his ground, deciding that the causative agent was not HTLV-I but a variant which he named HTLV-III. At a press conference stage-managed by the United States Health and Human Services Secretary Margaret Heckler, on 23 April 1984, Gallo claimed victory. "Today we add another miracle to the long honor roll of American medicine and science," Heckler declaimed.

As it gradually became evident that all groups were dealing with the same pathogen, the International Committee for the Taxonomy of Viruses stepped in to hose down the haggling over who held the right to christen the new agent, decreeing that henceforward it was to be known as HIV -- the human immunodeficiency virus. Reluctantly, the contestants submitted. At last, the monster had a name.

Smarting at having been denied credit for being first to discover the AIDS agent, the French accused the United States

NIH researchers of pirating their virus (they had exchanged samples) and using it to develop the hugely profitable American HIV antibody test. It was a dispute which was to sour international collaboration, to remain unresolved for several years and to cast a long shadow over what was to follow.

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Unresolved too was the question of the origin of the disease: HIV seemed to have exploded out of nowhere, a killer without a past. All that scientists could be certain was that HIV was a virus, one of the simplest and most primordial forms of life. The Latin word virus means, literally, sap or juice and, by derivation, a poison. A tiny capsule of genes, composed of DNA or RNA encased in a protein coat, a virus is hardly alive in any sense that most people would recognise at all, but seems to inhabit a half-world somewhere in between. In the graphic words of author Richard Preston, "Viruses are obviously ancient and perhaps primeval. They are molecular sharks, a motive without a mind. They have sorted themselves into tribes and they infect everything that lives."<sup>16</sup>

HIV's appearance indicated that it was a member of the retrovirus family, a smaller sub-group of the vast virus lineage. Retroviruses have all of their genetic code in the form of RNA or ribonucleic acid. RNA is a single strand of nucleic acids, while DNA is a double strand wound helically. The usual task of RNA is to carry the cell's internal messages. Because its genetic code is entirely made from single-strand RNA, before a retrovirus can reproduce, the RNA must first be copied to form the double-stranded DNA and the new genes inserted into the cell's own DNA. As parasites, viruses have no means of reproduction outside their host cell. There are three kinds of retroviruses: the cancer-causing oncoviruses, the foamy viruses and the slow-acting lentiviruses. HIV is a lentivirus, because the symptoms of disease are very slow to emerge.

Outside its host cell a virus can remain dormant, sometimes for many years, a lurking, crystalline time bomb. Once in contact with the host, however, it goes furiously into action, docking, penetrating, commandeering the cell's genetic machinery and compelling it to mass-produce new virus. Eventually the cell may become clogged with masses of viral material and rupture, or else sustain a catastrophic breakdown in its internal function. Alternatively, having detected that the cell has gone haywire and ceased to perform its proper task, the immune system sends it a terse command to commit suicide. Either way, the cell usually dies

-- but not before releasing a swarm of virions (viral particles) which make off in search of fresh prey.

Viruses seldom kill their natural host -- especially quickly - because to do so would jeopardise their own survival. Despite the media scares, ultra-lethal agents like Ebola rapidly burn themselves out; because the virus is so swift to disable and kill, infected people have few opportunities to spread it widely.

Viruses also grow weaker over time. Former killers, like measles, have over centuries evolved far less virulent behaviour in a process known as attenuation. At the same time, communities exposed to the virus simultaneously developed protective immunity which is sometimes passed on to their offspring. In this way the virus becomes weaker and the host stronger.

But newly-emerging viruses are quite often highly infectious and very lethal. Whether HIV was a totally new virus, or had simply never come into contact with most of the human population before, remained unclear. Whatever was the case, it had certainly evolved a peculiarly subtle strategy. Though fragile and easily destroyed outside its natural host, it had chosen to colonise one of the key agents of the body's immune system, a type of white blood cell (or lymphocyte) known variously as the helper T-cell (Th), the T4 or CD4-positive cell.

Several different kinds of cells are involved in mounting a defensive response against an invading microbe. The task of the helper T-cell is to co-ordinate the army. In the typical sequence of events, when a virus invades your body its presence is detected by a white blood cell called a macrophage, which digests it and then presents recognisable fragments to the helper T-cell. Thus alerted to the presence of an invader the helper T-cell distributes chemical warnings to other immune-system cells telling them what to look out for. Once activated, the B-cell, for instance, begins to churn out antibodies which go in search of the enemy, bind to it like glue and neutralise it. Memory T- and B-cells remember the invader from the first infection so that the next time the body is attacked, the system can mount a rapid immune response. The killer T cell acts as judge and executioner, ordering body cells which have been colonised by virus to self-destruct, so as to arrest the multiplication and spread of the infection. While there is a lot of toing and froing between the various units of the defensive army, the helper T-cell forms a central link in the chain of command and control. In football terms, the helper T-cell behaves like the half-back. Wipe enough of them out, and just about anything can get through.

Scientists found that once HIV particles came in contact with the body they hunted for a helper T-cell to invade. Anywhere there was a cut or infection, there would be many T-cells performing their defensive duties and the opportunity for the virus to lock onto a host cell would be quite high. The virus would dock with its host cell by binding a molecule on its own outer coat to a special receptor molecule on the T-cell's surface known as CD4, which could be thought of as a kind of ship's mooring buoy.

They discovered that after binding to the T-cell, the virus was engulfed and its outer coat stripped off, releasing the viral heart, its RNA, into the cells interior. Once inside, the viral RNA came in contact with a pair of enzymes called reverse transcriptase and integrase. These copied the RNA into a double-strand of DNA and plugged it directly into the hapless T-cell's own genetic code. The innocent T-cell was thus reprogrammed as a factory for making viral RNA. New strands of viral RNA were rugged-up in little protein coats comprising host cell membranes modified by the viral envelope proteins. These newly coated virions then budded from the cell's outer surface and drifted off in search of fresh T-cells to infect. It also became apparent that cells infected with HIV remained so for the rest of their lives, pumping out fresh virus. (See diagram.)

Doctors also found that while all this intracellular treason was going on, the newly infected person seldom knew anything about it. The process of infection was usually silent, meaning that, in two thirds of cases, there was no outward indication that any disease had been contracted. The others experienced symptoms resembling glandular fever two or three weeks after becoming infected, at the time when the virus was first starting to multiply and their body was attempting to fight back. This fever was usually acute enough to prompt most sufferers to see a doctor, though it seldom lead to hospitalisation and seemed to depart of its own accord, leaving them outwardly, perfectly healthy. Inside however, the virus was on the march and the immune system's defensive antibodies were also in evidence. By testing for these, researchers found, it was possible to diagnose HIV infection.

Their studies showed that the period of good health might continue for months, or even many years, until enough of the vital helper T-cells were lost to undermine the immune system as a whole. Deprived of its defence co-ordinator, the body then lay open to a range of opportunistic infections, most of which presented little threat to a healthy person. The early signs of this invasion were rather non-specific: fever, night sweats, malaise,

persistent diarrhoea and loss of weight. The lymph nodes also became swollen in several places.

Doctors established that as HIV infection took hold, the number of helper T-cells in the blood dropped from a normal level of 950 per microlitre to under 200 -- and in most countries this became the technical definition of AIDS.

One of the great puzzles was how the HIV virus actually managed to achieve this wipeout among the helper T-cells, as, unlike other common infections, it did not seem actually to kill the cells it infected. It was also curious how AIDS could appear within 18 months in some victims, and in others, not for 20 years. In a tiny handful of cases it did not appear at all. Researchers were stumped by this bizarre behaviour and tested all sorts of theories, the most popular of which was that it required infection by another sort of virus to trigger HIV into action. In the end however this was demonstrated to be incorrect: American scientists showed that, as fast as the virus could replicate, the immune system was churning out new T-cells and killing off the old, infected ones. This unleashed a titanic struggle between the virus's ability to mass-reproduce and the immune system's ability to keep up with it, with millions of new cells being made and destroyed daily. In the end this marathon struggle exhausted the immune system, the T-cell count collapsed -- and AIDS developed.<sup>17</sup>

As the disease progressed towards AIDS and the immune defences collapsed, the patient began to suffer persistently from infections caused by bacteria, other viruses, fungi and parasites. Two characteristic cancers, Kaposi's sarcoma and Non-Hodgkin's lymphoma, were observed in many cases. The main invaders included the viruses cytomegalovirus, herpes simplex, parvovirus and varicella, the parasites toxoplasma, pneumocystis, cryptosporidium and certain amoebae, the fungi candida, cryptococcus, tinea and aspergillus, the bacteria salmonella, golden and white staphylococcus and streptococcus, and the mycobacteria tuberculosis and mycoplasma.

Breakdown of the immune system could be swift or slow, researchers found, taking from months to many, many years. For individuals infected in the late 1970s, the average time from infection to the appearance of AIDS was nine years, but it could be as short as one year, and as long as nineteen years. In the face of mounting evidence, AIDS was deemed by medical scientists to be a 100-per-cent-fatal condition. This made it vastly more lethal than any disease of humans yet known, with the sole exception of rabies -- and with the salient difference that rabies could be arrested

if treated early enough.

This singular lethality was seen by some virologists as powerful evidence that HIV was a virus new to humans and had not had time to evolve attenuated (weaker) strains. This view was supported up by the virus's fantastically rapid rate of mutation: HIV-1 (the commonest of the two major types) had two subtypes, which divided into eight or more substrains. Even among these strains researchers discerned phenomenal genetic diversity and as well as evidence that different kinds of HIV could recombine their genes with one another to create fresh mosaic strains. Some scientists predicted this process would eventually give birth to a third superstrain, HIV-3. Research also indicated that many victims were infected with more than one strain of HIV.<sup>18</sup>

Furthermore the virus rapidly developed resistance against drugs used to treat it. In a recent case, a single drug was found to provoke a 1000-fold increase in resistance both to itself and to six other drugs of the same class. These examples demonstrated why HIV might prove exceptionally difficult to block, either with drugs or by vaccination.<sup>19</sup>

As a clearer picture of the disease emerged, it became evident that there were several pathways by which HIV could travel: by direct injection of blood containing the virus, by sexual intercourse -- vaginal, oral or anal -- with the virus entering through minor wounds or the mucosal tissues, and from a mother to her baby, either during pregnancy or in her milk during breast feeding. In spite of all the media scares and community prejudice, no good case was ever made for any other mode of transmission.

Armed with this formidable array of biological talents, HIV stealthily extended its sway from a handful of individuals in the late 1970s, to tens of thousands, ultimately to more than twenty million in the space of two decades. A completely new disease never before seen in humans, its origins were still an enigma which, despite all the scientific effort, remained clouded in mystery.

## Endnotes

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## The Cruel Sculptor

DISEASE has constantly reshaped the human destiny. Though it is seldom appreciated, the rise and fall of entire civilisations can often be attributed to the interaction between communities and the diseases or parasites which they encountered or fostered.

The handful of Spanish conquistadores who triumphed over the Aztecs in the sixteenth century did so, it is now believed, not because of the superiority of their firearms or their military prowess: Cortez, Narvaez and their followers were far too few to stand against the might of millions of enraged Mexican warriors. What saved the invaders was the Angel of Death passing over the Aztec capital, Tenochtitlan.

They were protected neither by firepower nor armour. Their most potent weapons were the microscopic smallpox particles carried by a single individual from the Old World to the New -- and the Spaniards' own immunity to them.

A Spanish monk recorded: "At the time that Captain Panfilo de Narvaez landed in this country there was in one of his ships a negro stricken with smallpox, a disease which had never been seen here. At this time (1520) New Spain was extremely full of people, and when the smallpox began to strike the Indians it became so great a pestilence among them throughout the land that in most provinces more than half the population died; in others the proportion was little less.

"For as the Indians did not know the remedy for the disease and were very much in the habit of bathing frequently, whether well or ill, and continued to do so even when suffering from smallpox, they died in heaps, like bedbugs. Many others died of starvation, because, as they were all taken sick at once, they could not care for each other, nor was there anyone to give them bread or anything else. In many places it happened that everyone in a house died, and, as it was impossible to bury the great number of dead, they pulled down the houses over them in order to check the stench that rose from the dead bodies, so that their homes became their tombs."

The epidemic rampaged along the coast from Vera Cruz, reaching the capital of Tenochtitlan (modern Mexico City) where, following the death of Montezuma while in their captivity, Cortez and his band were at the point of flight in the face of a furious local uprising. Yet within the space of hours the pestilence blazed

through the Aztec capital, slaying the leaders of resistance and many of their followers. It went on to destroy the greater part of the population including most of the men of military age, rendering the survivors easy prey to the invader. The deaths were never accurately totalled, but it is now estimated that between seven and twelve million perished in Mexico alone.

Four years later smallpox found its way to the mountainous land of the Incas where it slew at least 200,000, including the Emperor and his heir, decapitating the nation and exposing it to external predation. Lured by the Inca gold, Ferdinand Pizarro and his small band of cutthroats made short work of the conquest and plunder of the capital, Cuzco.<sup>1</sup>

In his book *Plagues and People*, William McNeill argued that when Columbus first set foot in the New World, there may have been as many as a hundred million inhabitants of the Americas. Less than eighty years later, perhaps ten million remained. Nine out of every ten had perished from the battery of unfamiliar pestilences which the invaders brought with them.<sup>2</sup>

Smallpox was not the sole destroyer, though it was the most spectacularly potent. In its wake came equally lethal invasions of measles, diphtheria, yellow fever, mumps, typhus and influenza -- diseases which the native Americans, isolated on their island continents for 20,000 years, had never encountered and against which they consequently lacked any immunity. These contagions were undoubtedly compounded in their effect by famine, the breakdown of family structure and social order, the collapse of individual morale leading to the neglect of children and the sick, and finally to military conquest, oppression and inquisitorial zeal. The fact that the conquistadores themselves seemed immune to these afflictions, which to the superstitious on both sides were plainly a manifestation of divine approbation of their deeds, set the seal on the conquest. Who could fight the will of God?

Smallpox was also an instrument in the European settlement of Australia where it eradicated the greater part of the native populations, leaving the land vacant for invaders and colonists. The disease was observed among aborigines living near the first settlement at Sydney Cove in 1789, only a year after the landing of the First Fleet -- but probably did not originate with the Fleet itself, as the colony had no cases. As white explorers pushed out into the bush, everywhere they found evidence of smallpox raging among the native tribes. Over the ensuing decades the disease eliminated a very large part of the aboriginal population,

leaving the continent apparently empty. Modern scholars consider it possible the aboriginal population -- perhaps once as high as two or three million -- was devastated by disease to such a degree that European settlers found the continent largely empty, seeing it as land free for the taking. This opinion was reinforced at law in the now-infamous doctrine of Terra Nullius, in which the British judiciary decreed Australia to be "no man's land", so avoiding the need to make a treaty with the native occupants.<sup>3</sup>

In return, the worst that Europe gained in exchange for its early colonial adventures seems to have been syphilis, probably imported from the Americas by Columbus' sailors on the first returning ship. The disease erupted first in Italy in 1494 in the army of Charles VIII of France as he was besieging the Italian city of Naples. At the time, syphilis was widely regarded as an affliction entirely new to Europe: it was spectacularly virulent and ugly in its florid symptoms which did not weaken into its present, less malign, form for more than a century. Within four years of its emergence in Europe, da Gama's sailors had borne the disease to India, and by 1505 traders and travellers had imparted it to peoples as far away as China and Japan. So, if syphilis was truly a disease newly introduced to the Old World from the New, then it took scarcely a decade to blaze from Western Europe to the eastern extreme of Asia even with the sluggish transport of the age.

Ironically, if it was immunity to the common infectious diseases which enabled Europeans to complete the conquest and subjugation of the Americas and Australasia, it was only because they had acquired that immunity the hard way, by themselves suffering almost two thousand years of plagues and contagions which broke out time and again following the opening of trade routes to India, China and the Far East. The routes which operated following the Mongol conquest and the Silk Road in particular became highways for death.

One such famous bacterial invasion began in 1347 when a Tartar Kipchak army commanded by Janibel Khan, laying siege to a Genoese trading outpost called Kaffa in the Crimea, catapulted over the walls the stinking bodies of plague victims in what was, by then, an accepted mediaeval germ warfare tactic for bringing a tedious investment to a speedy conclusion. Panic-stricken, the merchants fled the town and took ship, rats and all, for Italy. The consequence of their flight was the Black Death, a relentless pestilence that engulfed the whole of the European continent, including Scandinavia, in less than three years, erupting again and again in lesser outbreaks for more than two and a half centuries.

The disease consisted of bubonic (lymphatic), pneumonic (lung) and septicaemic (blood) infections caused by the same organism, *Yersinia pestis*, which was spread by fleas and rats. In countries such as England it may have been aided in its deadly work by the effects of ergot poisoning from a harvest spoiled by rain: it is thought this deadly fungus undermined the immune systems of the people who were thus made doubly susceptible to the plague itself. Mortality varied from region to region between one eighth and two thirds of the population.<sup>4</sup>

"Men died, and women and children, the baron of the castle, the franklin on the farm, the monk in the abbey, and the villein in his wattle-and-daub cottage. All breathed the same polluted reek and all died the same death of corruption. Of those who were stricken, none ever recovered, and the illness was ever the same -- gross boils, raving, and the black blotches which gave its name to the disease. All through the winter the dead rotted by the wayside for want of someone to bury them. In many a village no single man was left alive."<sup>5</sup>

The bubonic plague took its name from the swollen lymph glands (buboes) in the armpit and groin, and from the black bruise-like marks which appeared on the faces and bodies of the dying as a result of blood-congestion.

Entire communities expired. Ships at sea became derelict when their crews perished. Corpse collectors trundled their grisly wains over the cobbled streets of London, Paris, Berlin, heaped with the bodies of the dead and dying. Fear of the monstrous carnage led many to experiment with weird rituals in their attempts to assuage divine malevolence: animals were sacrificed, and witchcraft, Satanism, astrology and alchemy were rife. Physicians recommended the drinking of liquid gold, ground emeralds and menstrual blood in the desperate search for a remedy. Dried toads were applied to the swollen glands and people covered themselves with excrement or bathed in urine in the belief that "stinks" would defend them. In Warsaw, plague victims were fed on the boils of those who had already died in what must surely have been an early attempt at vaccination. Gambling, lewdness, sexual orgies and drunken revelry became rampant as society, fatalistically certain of its doom, abandoned itself to debauchery. Bands of flagellants roved from town to town whipping themselves to a frenzy of

pious self-abuse in the belief this would appease the divine wrath, and stirring such a fanatic following they threatened to overturn the established social order. Crazy chorists danced hectically in the streets in the belief this would ward off infection, until they too expired - from exhaustion.

In the end it is estimated that more than twenty-five million perished in Europe alone. The Asian death toll, in the plague which preceded and ignited it, has never been tallied. It was 150 years before the population recovered its numbers: wars, commerce, agriculture and civic affairs ground to a standstill. Aided by other infections, child mortality reached horrifying proportions. Superstition and morbid fears arose which halted progress towards cultural, religious and scientific enlightenment for generations, immuring society in a dark age of ignorance, superstition and prejudice which was only finally to be dispelled in the Renaissance.

The consequences of the Black Death were at least as severe as those of World War I. In both cases contemporaries recorded economic chaos, social unrest, inflation, profiteering, moral depravity, loss of production, frenetic gaiety, wild spending, avarice, maladministration, debauchery, social and religious hysteria and the decay of manners.<sup>6</sup>

Plague had also taken a fateful hand in ancient Greece, during the Peloponnesian war between the confederations of Athens and Sparta. In 429 BC, after some indecisive engagements elsewhere, the Spartan army invaded Attica and laid siege to Athens. Plague broke out in the city, killing about one in four and leaving survivors immune. It sapped the military power and the will to resist of the Athenian people as well as inflicting losses on the marauding Spartans beyond the walls. Its ravages wrote an abrupt coda to the golden age of Classical Greek civilisation.<sup>7</sup>

If plague brought Greek civilisation to its knees, it may also have delivered the knockout blow to an entity more vast and potent still -- the Roman Empire. According to McNeill the fall of the western empire was primarily the consequence of two major epidemics which swept the Mediterranean in 165-180 AD and 251-266 AD. From the west of Spain to Hadrian's Wall, from the Rhine to the Danube, the Euphrates to Egypt, the boundaries of Roman Imperium were watched by thirty legions, more than 150,000 troops plus their auxiliaries and administrative tail. The cost of maintaining this immense standing army was colossal and fell ultimately on two groups -- the farmers of the fertile Mediterranean basin and the merchants. The prodigious mortality

caused by plague among farmers and slaves who worked the foodbowl as well as its direct impact on the economies of cities like Rome itself, dried up these essential streams of revenue. By the end of the second century discipline in the unpaid frontier legions had largely collapsed and the Empire been rent among local warlords, leaving it easy prey to barbaric hosts from the east. By 290 AD the Emperor Diocletian was passing laws in a vain bid to keep landholders down on the farm, so alarming had the failure in imperial sustenance become.<sup>8</sup>

The emergence of modern medicine in the twentieth century provided no insurance against pandemic disease, chiefly because it was accompanied by a global upsurge in travel and trade which greatly assisted the spread of contagions. This was never more evident than in the final months of World War I, when a new strain of influenza erupted among the war-weakened populations of Europe and America. To begin with the epidemic attracted little attention, as 'flu seldom kills any but the old or very young, but soon it became clear that many of its victims were in their prime. Although it appeared to have started in America, the contagion spread quickly to Europe where ironically it became known as the Spanish 'flu, because Spain was one of the few nations where wartime censorship did not prohibit the mounting death toll from being reported in the newspapers.

During the middle months of 1918 the malady exploded around the world, inflicting vastly more deaths than had ever before been seen from such a cause. By August the death toll had doubled and tripled and health services in many countries were overwhelmed. A second wave arose towards the end of the year, sending to their sickbeds millions who had escaped the first assault. Then, in early 1919, a third wave raged across the globe succeeded in 1920 by a fourth.

In India alone the Spanish 'flu is said to have slain more than twelve million, and in the United States over half a million lives were lost. In isolated countries such as Western Samoa, nearly one person in five perished, placing it on a par with the Black Death. Early estimates indicated that the infection had claimed at least twenty million lives and made nearly one third of the world's population sick.

However the toll was were revised upward after historians delved through records from Asia, Latin America and Africa. The final number of deaths was never known for certain -- probably it exceed twenty-seven million -- but researchers considered that in terms of total mortality it was the most severe event ever to afflict

humanity, far worse than the War to End All Wars which had preceded it.<sup>9</sup>

Because the memory of disease often perishes with its victims, awareness of its fundamental role in shaping the human destiny is muted. Except for very spectacular plague events such as the Black Death, disease affects only a modest proportion of the population at any one time. People of the pre-medical era accepted this and seldom bothered to record what was, for them, a commonplace of the human condition. So historians have tended to focus on events more immediate, dramatic and colourful, attributing to them greater importance than may be their due: rulers and regimes, battles, technological, social, religious and cultural advances.

Also, quite significant epidemics take place over many months or even years and so lack the sensational character of an instant disaster such as the destruction of Pompeii, the Great Fire of London, the San Francisco earthquake, the explosion of the *Hindenberg* or the loss of the *Titanic*. It is a perversity of human nature that we barely notice disasters vastly greater in scale when they take place beyond our limited perception of the present. Yet disease is more influential over historical outcomes than any empire, any discovery, any belief.

Some authorities consider that the success of Christianity and Buddhism, two of the world's greatest religions, is founded on their acceptance of the apparently random and arbitrary cruelty of death by disease. Europe was constantly invaded by hideous plagues travelling the Eastern trade routes from Roman times on, and the appeal of a doctrine which preached acceptance of mortality and reward in the afterlife was not to be compared with the faltering pagan beliefs and religions of the Roman Empire. In China and India, whose civilisations had been ravaged by continual epidemics over centuries, Buddhism served a similar function, holding out the promise of reincarnation in exchange for saintliness in the first life, however horribly it might end.<sup>10</sup>

Disease, therefore, has had an impact even more profound on human culture, creed and development than merely upsetting the plans of the occasional conqueror or causing an economic hiatus. From time to time it had levelled entire civilisations and established the preconditions for the emergence of new orders and systems of belief. The appearance of a major new disease in the world population cannot be dismissed purely as an inconvenient and costly medical event. It has to be seen for what it is: a consequence



of human behaviour and a profound and permanent shift in the path of human destiny.

The Black Death, smallpox and the Spanish 'flu were the three most devastating plague events in history. Now they had been joined, and may well be surpassed, by a fourth in the form of AIDS.

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AIDS is a pandemic -- a universal plague. But because of its slow-burning character and the effect of this on public perceptions of the scale of the epidemic, the World Health Organisation has dubbed it "a catastrophe in slow motion".

The outbreak may have been ignited with a handful of cases in Africa, America and Europe but by the early 1990s HIV infection had been reported on all continents and in nine out of ten of the nations on earth. It achieved this universal distribution in scarcely a decade, extending its lethal tendrils from twenty nations in 1981 to 192 just thirteen years later.

Over the same span it had spread from probably a few thousand infected people to almost twenty million, delivering one new death sentence every 24 seconds. More shocking still was the trajectory of the disease: by the mid 1990s the infection rate had climbed to one new death sentence every nine seconds and was poised to redouble.

Neither political frontiers nor social mores keep it at bay. The HIV agent is unstable, volatile, exploding in fresh outbreaks among susceptible societies and constantly evolving novel strains. These factors meant that the status of the pandemic was ever-changing in all countries, communities and societal groups, noted the first head of the WHO Global Program on AIDS, Dr Jonathan Mann. Even in the first-affected areas, AIDS has continued to extend the range of its victims, while at the same time it has made inroads into societies which have never seen it before. "The second importance consequence of the newness of the HIV/AIDS pandemic is that its major impact is yet to come," Dr Mann said in 1992.<sup>11</sup>

Though western society had long regarded it as a disease affecting mainly homosexual men, even from its early days on a worldwide scale nearly three quarters of all HIV infections were contracted by heterosexual intercourse. Only fifteen per cent were the result of sex between homosexuals, seven per cent by drug injection and five per cent by blood transfusion. AIDS is a people's plague.

By the early 1990s scientists were generally persuaded that

the pandemic had been spawned somewhere in sub-Saharan Africa during the 1960s-70s. In no time it had reached Haiti and thence had been carried to North and South America. It had reached Europe direct from Africa through the former colonial ties. By 1979 it had struck across Oceania and the Caribbean and within three years was ravaging the people of the south-eastern Mediterranean. In 1982 it had surged into Eastern Europe and swept across Russia, penetrating as far as north-east Asia. A year later the tinder was fired in southeast Asia. The AIDS circumnavigation was complete. It had all taken just seven years.

By 1995, only eighteen countries in the world had yet to report their first AIDS case. In most instances the epidemiological blank was attributable to poor diagnostic facilities and worse medical records, in others to isolation. Yet others were the result of official refusal to acknowledge reality, or simply to conservative sexual customs which slowed its spread. Such countries included Afghanistan, Mongolia and Bangladesh at one end of the scale to the Cook Islands, Nauru, and Tuvalu.

Studying its progression, the World Health Organisation has identified three main patterns to the spread of HIV/AIDS around the globe.

Pattern one can be found in developed, industrialised societies, chiefly North America, Western Europe, Australasia and urban Latin America. It is characterised by extensive infection during the late 1970s and early 1980s initially among homosexual and bisexual men and injecting drug users, travelling rapidly to haemophiliacs by transfusion and then, more slowly but with increasing momentum among the heterosexual community. The first wave has been followed by a second, as infected mothers have passed the disease to their unborn babies.

In a few countries with well-educated populations and advanced health care systems there have lately been signs of the epidemic levelling off due to public awareness and education, although it has continued to rise among injecting drug users, their partners and babies.

Pattern two countries lie in sub-Saharan Africa and Latin America. Here the disease spread like a brushfire during the mid-to-late 1970s and 1980s, predominantly among heterosexuals. In the worst-hit communities, one quarter of all sexually active adults became infected, along with a majority of prostitutes. Transmission to babies is a growing nightmare, with from five to fifteen per cent of pregnant women found to be infected.

Pattern three countries in Eastern Europe, North Africa, Asia and the Pacific islands experienced the spread of HIV/AIDS from the mid to late 1980s, in some slowly, in others like wildfire - especially where there were large sex and sex-tourism industries. As a result of their late start, the initial death toll in Asian communities is lower than elsewhere but health officials fear that it is here, among very large populations with scanty medical and public education facilities, that the most ghastly impact of the epidemic will ultimately be felt.

By 1995, WHO estimated that a cumulative 19.5 million people -- including 1.5 million children -- had been infected with HIV.<sup>12</sup>

There were more than one million diagnosed cases of AIDS, but poor records and medical services made it probable there were actually 4.5 million people with full-blown AIDS.

The lion's share of the world's cases of both HIV infection and AIDS are to be found in sub-Saharan Africa: this region was estimated to have eight million of the global total of fourteen million HIV-infections in 1995 and nearly three quarters of the 4.5 million cases of full-blown AIDS. The worst affected region is central and east Africa where up to one quarter and, in places, one third of the population in some communities are infected. The worst-hit nations in terms of total numbers of reported AIDS cases are: Uganda, Tanzania, Malawi, Zimbabwe, Kenya, Zambia and Zaire. In South Africa, previously comparatively free of the disease, 850,000 people, or 2.1 per cent of its population had been infected by 1995 -- and the number is doubling every 13 months.

One of the gravest difficulties in monitoring the early phases of the pandemic was the inadequacy of medical records, a situation which for a long time caused global misconceptions about the location and severity of the worst outbreaks. This was underlined by the fact that of the 1 million *recorded* AIDS cases at the end of 1994, the United States had 39 per cent and Africa 34 per cent. Yet of the 4.5 million *estimated* AIDS cases in the world, Africa had 70 per cent and the United States nine per cent. Likewise, Europe had 13pc of the recorded cases but only 4pc of the estimated true number, while Asia had two per cent of recorded cases and six per cent of the true number. The understandable focus by both the media and health officials on what was happening "at home" thus obscured, to a degree, both the extent and character of the global pestilence.

Dr Michael Merson, who was head of the WHO Global Program on AIDS (GPA) from 1990-95 saw, at first hand, the

blossoming of the plague. In many cases, too, he witnessed the wilful blindness with which societies and religious and political leaders greeted it. In an interview given when he stepped down, he recorded his concerns:

"Our first aim was to build on what had been achieved. Dr Mann (former director of GPA) had brought about an unprecedented global mobilization. He had a broad vision as to the factors that were fuelling the epidemic and the type of response that was needed. His focus on human rights and on the discrimination experienced by HIV-positive persons was particularly important. It was essential to continue this focus, for example, by encouraging the greater involvement of HIV-positive persons at national level and in GPA's work.

"Our second aim was to better articulate the impact the epidemic was having on developing countries and on women. We were starting to see the epidemic reaching many parts of Asia and Latin America.

"Another thing that was clear was that while we were very much into the HIV epidemic, we were only at the very beginning of the AIDS epidemic. Many policy-makers I met really did not grasp this. Even today, we are still at the start of the AIDS epidemic in many ways, and the consequences are still not appreciated by many political leaders. They tend to respond only to problems that are right in front of them.

"The long delay between HIV infection and AIDS continues to handicap efforts. It is still causing some of the denial and complacency around the world. (At first) I did not realize how much more difficult it would be for countries to deal with AIDS than other public health problems. With cholera, immunizable diseases or heart disease, for example, there are few political or cultural impediments to control efforts. But with AIDS, moral and religious barriers and social and cultural taboos have been much greater impediments than I expected.

"I have been to some African countries where one third of young adults are infected in the capital city and many people are dying from AIDS. Yet they are still not able to broadcast AIDS prevention messages that promote the use of condoms. The extent of such inhibition in the face of an epidemic of a fatal disease surprised me.

"But we are not going to eradicate HIV or have a magic bullet in the foreseeable future, so we must learn to live with the virus," Merson warned. "And even if we did have a highly efficacious vaccine, it would not halt this epidemic."<sup>13</sup>

To begin with Asia had far fewer reported cases than Africa, Europe or the Americas -- but the 250,000 officially diagnosed by 1994 nevertheless represented an eightfold increase in the space of just one year. Merson and others were profoundly alarmed at what this portended.

In the United States, where the disease has been most intensively studied and tackled by medical, public health and education programs, it has been estimated that more than one million people and possibly as many as two million had contracted HIV by 1995. In that event, the AIDS death toll by 2005 was likely to exceed that of the American Civil War or the 1918-20 'flu epidemic, previously the two worst disasters in American history.

For Europe, with a cumulative total of more than half a million infections from 1979-94, the cost in lives will be three times that of the battle of Verdun. A sad footnote to the European tragedy is that half of the children in that continent with AIDS are from Romania, victims of contaminated blood transfusions or the use of unsterilised needles before the fall of communism and the introduction of improved healthcare in 1989.

In 1990 WHO had forecast that, by the end of the century, between fifteen and twenty million people around the world would be infected with the AIDS virus and some five to six million would have full-blown AIDS.

One year later they had doubled their estimate, putting the number of HIV infections at forty million by 2000 and actual AIDS cases at ten million. This is a rate of ten thousand new cases every day.<sup>14</sup>

The first year of the third millenium will open with two million AIDS deaths. To this unimaginable toll of human suffering will be added a further ten million HIV-infected children to be born by then, and five million orphaned.

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The ultimate impact of AIDS on our common future as a species is no more predictable than the impact of that anonymous West African slave with a few smallpox sores on the history of the Americas. Whatever his name, his contribution to history in one sense exceeds that of Genghis Khan, Josef Stalin or Adolf Hitler.

There is no conqueror like disease.

Nor is it deniable that AIDS will greatly influence the pattern of civilisation in the coming centuries. From a handful of cases in the mid-1970s, forty million women, men and children will carry the deadly particles by the year 2000, having acquired them in just a quarter of a century. How many by 2050 -- two hundred million? Five hundred million? Some researchers even say one billion.

The difference between AIDS and smallpox or The Black Death is that its timeframe as an infection exceeds the average human power of imagination. If people were dropping in the streets hour by hour, society and governments would be galvanised, but because the disease usually takes years, as opposed to days, to disclose itself and because most cases are in the Third World where people die constantly from unpleasant things society's perception of the scale of the epidemic has been diminished.

This in spite of the fact that AIDS has already demonstrated itself to be three times deadlier than the Black Death. Historians have recorded how bubonic plague retarded European population growth, society, trade, religious and intellectual enlightenment for centuries. How smallpox and other infections virtually obliterated the Amerindian civilisations. How measles and plague undermined the Roman Empire. It is valid to ask: what will be the long-term consequences for civilisation of AIDS?

Every disease has a cost which is not obvious, either to economists or historians. Apart from the direct costs of treating and caring for the victims of AIDS the productive labour of tens of millions of people in the prime of their lives is lost, both from the sick and those who nurse them. By the early 2000s, the global economic impact of the AIDS pandemic will be greater than the loss of an entire country the size of England, South Africa or South Korea. And there will be lower growth, less trade, fewer jobs and reduced capacity to overcome poverty and human misery.

Because of its relatively inefficient modes of transmission and long lead-time, AIDS does not resemble one of the Horsemen of the Apocalypse. It is a slow-burning catastrophe whose direct effects will in all likelihood be confined to a relatively small proportion of humanity -- currently fewer than 1 per cent, and probably never more than four or five per cent at any one time. Yet it has the potential to lock up a further five or ten per cent of people simply in compensating for its impact. The indirect effects of AIDS, in other words, could potentially consume a significant

part of the combined productive output of humankind -- and this will inescapably alter the path of history.

According to Lynn Brown of the International Food Policy Research Institute (IFPRI) there are numerous largely unanticipated impacts of the epidemic besides the obvious one of increased healthcare costs. By reducing lifespans, AIDS will lower the social returns on investments made in health and education. It will make more individuals dependent and less productive for a greater proportion of their lives: on average, each case of HIV represents a loss of nine to ten productive years of life.<sup>15</sup>

If parents believe their children unlikely to survive long as adults to support them in some cases they may reduce their investment in preventative healthcare such as immunisation, Brown believes. They may also be tempted to invest less in education -- because families who are desperate for income will send their children out to work.

"If AIDS strikes at the more educated, productive worker, a skill shortage may be created increasing the wages of skilled workers. AIDS will produce increasing numbers of orphaned children who will either be cared for by the extended family or by the state," she says, citing Tanzanian evidence that such orphans are less likely to receive an education. The result of this lower investment in human capital will be lower economic growth down the track; and stagnant economies are liable to remain so. So far there is every indication that the incidence of AIDS, at least in Africa, is highest among the educated and among professionals -- the military, teachers, nurses and public servants -- and lowest among rural workers. The elimination of so many skilled workers from society will cause national savings to plummet, and so reduce investment in social infrastructure -- industry, roads, bridges, ports, irrigation schemes, water and electricity supplies, schools and hospitals.

But it also sucks slender medical resources into cities, leading to a general decline in the health of farmers and rural people as well. Since agriculture is usually the first-stage engine of economic development, this has serious consequences for the capacity of countries to attain the point at which they can establish secondary and tertiary industries capable of generating export income.

Brown also foresaw AIDS would prove a major threat in the struggle of poor countries to achieve food stability, because it was spreading fastest in the richest, most populous and most productive farming regions. "AIDS and malnutrition will thus work

hand-in-hand to sabotage food security," she warned. Such rules apply not only in Africa but also increasingly in Asia and Latin America.

Poverty, we now know, brings many other evils in its train -- famine, political instability and insurrection, wars both civil and international. Paradoxically, poverty also brings excessive human population growth. It is by now well attested that once household incomes rise beyond a certain critical point, birth rates begin to drop quite sharply as children become a cost to the family rather than a source of income. The driving force behind the global population problem is poverty -- both its cause and, potentially by overcoming it, its solution. If AIDS exacerbates poverty, it will also lead to increased birthrates.

This may appear a contrary notion to many who have swallowed the "grim reaper" images of the epidemic and imagined AIDS as some kind of cruel Malthusian answer to human population growth. This is quite wrong. AIDS will seldom incapacitate or kill more than a small percentage of any population at one time and will often make little appreciable impact on the birth rate, especially if impoverished families respond by having more babies. Brown demonstrates that for population growth rates to fall from 3 per cent to zero would require a constant HIV infection rate in the adult population of the order of 48 per cent. Even though it strikes adults in their most productive years, the populations of the worst-affected African countries are still expected to double by 2020.

But the economic damage inflicted will be out of all proportion -- and that affects everyone. The division of society into haves and have-nots, the erosion of government and the rise of anarchy in so many developing countries today -- and even in the troubled cities of the western world -- may eventually lead to a state of strife and economic decay equivalent in cumulative impact to a global war. Indeed, some observers contend the Third World War between the haves and the have-nots has already broken out in many of the world's mega-cities where governments and police forces have lost control over crime, violence, vandalism, drugs and anarchy. AIDS can only compound this process of disintegration, soaking up resources, diverting wealth, consuming labour, aggravating human fear, misery and resentment. In the larger sense, we are all AIDS victims.

What then do the economic losses triggered by AIDS forebode? Lower growth, reduced world trade, fewer jobs than otherwise, greater demand for food and medical aid -- certainly. But



much more. It is commonly accepted that a sustainable future depends on our being able to safeguard our natural resources of soil, air, biodiversity and water and pass them intact to our children. It is equally evident that poor countries are less able to protect their resources than rich ones. So the economic cost of AIDS is also an environmental cost. It postpones, for an unknowable period, the time when humans can live in balance with the earth's natural systems.

Those who would argue, apocalyptically, that AIDS is the Earth's vengeance on an improvident humanity ought to think again. It may simply help us wreck the place.

The burning question is: can we prevent it from happening twice?

### Endnotes

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## Out of Africa

AS the quest to uncover the agent responsible for AIDS gathered momentum, the world began to demand answers to the crucial questions: was it new? Where it had come from? How it had managed to invade the human race?

These were primal issues: an understanding of the origins of the disease might provide doctors with the knowledge necessary to overcome it. The discovery of its fountainhead might help yield a vaccine or a treatment on the basis that, in their native setting most forms of life have some natural parasite, predator or factor which keeps them under control. Understanding how the disease had disseminated initially could provide epidemiologists with clues to contain its spread or to prevent similar epidemics in future.

In an article published in *Scientific American* two of America's leading AIDS researchers, Max Essex and Phyllis Kanki of Harvard School of Public Health, explained that their goal in seeking the origin of the virus was "to learn more about viruses related to HIV and so understand how HIV has evolved the unique and deadly properties that lead to AIDS".<sup>1</sup>

The reason for the search has been articulated by many scientists in many ways: Robert Gallo, the discoverer of the first human retrovirus and co-discoverer of HIV, advocated a quest to see if there existed a monkey virus which was so similar to HIV-1 as to be a credible precursor. If so it was important to understand how it had jumped species. "We may never know for certain the answer to these questions," he wrote, "but they are of more than academic interest, because answering them may help avoid further zoonotic catastrophes -- that is, transmission of disease from lower animals to humans."

Even in the lay press the significance of the quest for the origin of the AIDS pandemic did not pass unheeded. *The Economist* magazine wrote: "...questions about the origin of AIDS are not worthless. AIDS will not be the last disease to attack mankind. Knowing about the origins and evolution of disease in general is clearly worthwhile -- and might conceivably help studies of the present epidemic. And there may well be lessons to be learned..."<sup>2</sup>

Despite the first cases actually being identified in America, the focus of attention soon shifted as it became clear that, however grave the United States epidemic, something far, far worse was

unfurling its dark wings over sub-Saharan Africa. Already a disturbing trickle of cases, especially those being diagnosed in France and Belgium, seemed to point in new directions. Five of the original twenty-nine French cases were heterosexuals who had links with Haiti or the Caribbean. A further four heterosexuals had lived in equatorial Africa and appeared to have contracted their infections before the United States outbreak manifested itself. And even in the United States itself, a significant proportion of early cases were found in Haitians or those who had paid a visit to the Caribbean island.<sup>3</sup>

In 1981, Tanzanian regional medical officer Dr Katende Kashaija recalled, "...the regional commissioner alerted us to the fact there was a strange disease around which the people were calling "hella's disease". *Hella* is a Swahili word meaning money and they called it that because they noticed it was rich traders and fishermen who were coming down with it. We physicians thought this was a funny thing: we'd never read anything about a "disease of money" in our textbooks, so we asked the district medical officer to investigate..."

Despite their amusement the medical officers had kept a sharp eye on it nonetheless. Over the ensuing months they had noticed that the disease was disseminating ever more widely and its symptoms becoming increasingly complex. It seemed distributed through much of the Lakes region of central Africa, especially in communities engaged in trade or smuggling: in eastern Uganda it was dubbed "slim", because that was the most obvious of its symptoms, in another district "Juliana's disease" after some brightly coloured cloth with the name Juliana printed on it which prostitutes in one town bought from a trader, before they began to fall sick and die. The local people believed the cloth was cursed but the medical staff knew better, as they tried to track its spread. About that time they also began to read strikingly similar accounts in American medical reports: the thing that had puzzled them was that in Africa the victims included virtually no homosexuals, drug users or haemophiliacs.<sup>4</sup>

In Paris, French immunologist Jacques Leibowitch and colleagues at the Claude Bernard Hospital for infectious and tropical diseases recollected similar cases. Of three cases seen by the French doctors, two had originated in Republic of Congo and one in Senegal. Danish physicians, too, recalled the death of their colleague, Margarethe Rask, after her self-sacrificing labours in Republic of Congo.<sup>5</sup>

In Antwerp, a gifted expert on sexually transmitted

diseases called Dr Peter Piot remembered the case of a Greek fisherman he tended in 1978: the man had fished Lake Tanganyika from a base in Republic of Congo for a number of years before coming down with dreadful symptoms. His return to Europe came too late to save his life, but the doctor was never to forget the sight which had met his eyes when he performed the post-mortem: "The fisherman appeared to be in his late 30s, an outwardly healthy man. But when Piot opened the body, the stench and sight of "pure and complete rot" greeted him. Every organ, each bone, all the tissues were covered with some type of mycobacterium..."<sup>6</sup>

The microbe could not be identified but Piot -- later to become head of the WHO Global Programme on AIDS -- traced three more cases in the files of Africans from Zaire, now the Republic of Congo, who died under treatment in Belgium of strange and horrific infections. He later confirmed the Greek had indeed died of AIDS.

As the number of cases swelled in America, Europe, Africa and Australia, scientists stepped up the worldwide search to pinpoint the origins of the contagion. This quest consisted chiefly of a hunt through old medical records and samples to try to trace the earliest victims of AIDS as a potential signpost to the source of the affliction. In 1983 an international medical team including Dr Piot visited the Mama Yemo Hospital in Kinshasa and diagnosed thirty-eight AIDS cases over a three-week period, a quarter of whom died during this same time. The startling conclusion from this study was that, contrary to experience in America and Europe, in Africa AIDS was almost exclusively a heterosexual disease. Incredulous scientific journals for a long time refused to publish the discovery, so firmly entrenched was the image of the "gay plague".

The crescendo of reports in the medical literature prompted Dr Ib Bygbjerg, colleague of the Danish doctor Margarethe Rask, to write to *The Lancet* warning that America was unlikely to be the only focus of the disease. "Little attention has been paid to the hyperendemic focus of Kaposi's sarcoma in central Africa," he chided his fellow doctors, pointing out that the scarcity of immunological labs in that region meant that there was virtually no prospect of any cases being diagnosed. Rask had almost certainly died of AIDS, he said, yet she had never visited America or Haiti and did not abuse drugs. In Africa, however, she had encountered cases of Kaposi's sarcoma and had been heavily exposed to blood and other secretions. Bygbjerg went one bold step further: he suggested that AIDS had *originated* in Africa.<sup>7</sup>

In the same year the virus was identified another expert, Dr

Kevin De Cock, advanced the argument in the *British Medical Journal* that AIDS might be an ancient disease of African genesis, probably originating in Republic of Congo or one of the countries of the equatorial region.<sup>8</sup> The widespread character of the African epidemic was underlined when an investigator from the CDC visited northern Tanzania: AIDS in the United States was still a comparatively rare condition, but in just one small African rural hospital he had witnessed no fewer than two dozen full-blown AIDS cases.

Support for the view that the AIDS epidemic had erupted in Africa long before it had reached America or Europe soon began to trickle in. In 1986 American researchers Nahmias, Kanki, Essex and colleagues ran tests on 1213 stored blood samples which had been collected in Africa over the preceding thirty years for immunogenetic studies.

Using a range of different techniques they screened the samples for HIV viral proteins -- and obtained a hit. One sample, taken from an Bantu man in Zaire, formerly the Belgian Congo (and now the Republic of Congo) was positive for HIV. The blood sample, one of the oldest in the group, had been collected in 1959.

Cautious, because such tests can return false positives, the team employed four different methods of analysis, besides asking three outside laboratories to probe the blood sample independently. All three labs concurred in the original result -- that the blood was positive for HIV.

"We have demonstrated that at least one individual from central Africa had been exposed to a virus similar to human HTLV-III [HIV] more than a quarter of a century ago," the Harvard team triumphantly reported.

"The identity of the donor is no longer known. Our results show that the prevalence of HTLV-III [HIV] was very low in central Africa in 1959. No evidence of infection was found in sera taken in rural areas of the Belgian Congo or South Africa (1959), Mozambique (1969), the Congo (1982)."<sup>9</sup>

The second candidate, more enigmatic still, came from Britain and was to have a profound and, as it turned out, untoward impact on medical opinion with respect to the origin issue. It was the case of 25-year-old apprentice printer and former Royal Navy national serviceman David Carr, described in Chapter One, who had died in Manchester Royal Infirmary in 1959 of a massive infection by cytomegalovirus and pneumocystis -- both by this time regarded as classic signatures of AIDS.<sup>10</sup>

In 1990 researchers Williams, Corbitt and Bailey of

Manchester University decided that Carr's remnants merited a second look.

More than forty samples of his tissues had been preserved, embedded in paraffin wax, and six of these they subjected to DNA amplification in an attempt to find tiny amounts of HIV genetic material in target cells. As a blind check, they also included samples taken from a road traffic accident victim who died about the same time. Each sample was given a code number, the key to which was known only by Williams, though not by those performing the tests.

Four samples proved positive for HIV, and when correlated with the secret list held by Williams they were found to be from the kidney, marrow, spleen and pharynx of the sailor, David Carr. His brain and liver, and all six organ samples from the accident victim, returned negative results.

"We conclude that the patient who died in Manchester in 1959 with an unexplained immunodeficiency and overwhelming pneumocystis and cytomegalovirus co-infection of the lung had HIV infection," Corbitt and Williams reported.<sup>11</sup>

The result of their investigation caused a medical sensation and was lauded internationally for the light it threw on the origins of HIV and the timing of its emergence among humans. Poor David Carr became "patient Zero", the index case or earliest-known victim of the AIDS pandemic: the first of seventy million to tread that dark path.

Outside Britain, the earliest European case of AIDS to appear in the scientific literature came from Norway -- about the last place one might expect. The name of the victim was Arvid Noe and he, too, was a sailor who had visited several African ports and had contracted sexually transmitted diseases at least twice before his AIDS symptoms emerged. The case also illumined one of the saddest dimensions of the AIDS tragedy.

Since 1966 Noe had suffered from a complex of symptoms including pain, aching joints, inflamed lymph nodes and recurring lung infections. Placed on drugs, his condition had stabilised for nine years until 1975 when he fell into a sharp decline. Lung disease, growing weakness and paralysis of the legs, loss of motor control, incontinence and finally mental derangement had followed in quick succession, bringing his death in April 1976 at the age of 29.

Noe was married and his wife had given birth to three daughters. From 1967 on his wife also began to undergo bouts of upper and lower airways inflammation, bladder disease, fever and

stubborn fungal infection. In 1973 she became seriously ill, suffering severe loss of weight, behavioural disturbances and symptoms of brain inflammation. Her condition was diagnosed as leukaemia and she was given anti-cancer therapy. After a brief improvement she too deteriorated rapidly, suffering paralysis of the legs and dementia. She died just eight months after her spouse.

The youngest daughter, born in 1967, had developed normally for two years before becoming ill with recurrent bacterial infections of the bones, joints, blood and respiratory tract. *Haemophilus influenzae* (HiB, a bacterial infection, not to be confused with 'flu) and golden staph had both been found, while her airways had become clogged with candida fungus which resisted all treatment. Eventually she died -- of chickenpox -- in January 1976, three months before her father, the first-known child victim of the new plague.

Blood samples from all three patients were preserved and tested a decade later by Dr S.S.Frøland at Oslo National Hospital. All proved positive for HIV.<sup>12</sup> Subsequent investigation of Noe's case by British writer Ed Hooper established that the sailor had indeed visited Africa, on two occasions. From August 1961 to May 1962 he had sailed on the merchant vessel *Hoegh Aronde* to ports along the West African coastline as far as Douala, in Cameroon. During this trip he caught gonorrhoea and was treated for it. Then, again, in 1964 he visited the port of Mombasa in Kenya, on the other side of the African continent.<sup>13</sup>

The suspicions of researchers that Africa had more than a casual connection with the origin of HIV/AIDS hardened sharply in 1987 when two Belgian doctors, Jean Sonnet and Jean-Louis Michaux, published details of seven cases which they had observed in Central Africa between 1962 and '76.

The first was that of a 50-year-old black woman, Helene, who had been admitted to the University Hospital of Kinshasa in Zaire in February 1962 where Sonnet and Michaux were in charge of internal medicine. She was suffering from a grisly purulent infection of the mouth, fever, swollen cervical lymph glands, breathing distress and severe wasting. Her body was piteously emaciated, weighing just thirty-six kilos, her face puffy and her legs covered with pitted swellings. Massive treatment with antibiotics failed to save her, and after death doctors found her lungs, lymph nodes and spleen to be heavily infiltrated by Kaposi's sarcoma. A quarter of a century later Sonnet and Michaux concluded retrospectively she was probably the first known African victim of AIDS.<sup>14</sup> It was later established that the woman came from Lisala,

one of the main ports on the Congo river, but had moved to Kinshasa. Lisala is about 150 kilometres from Yambuku, where five HIV+ cases were detected in blood samples collected in 1976.<sup>15</sup>

So far as Sonnet and Michaux were concerned, she remained an isolated example until the mid-1970s when they observed a shotgun spatter of HIV/AIDS cases across the heart of Africa. These included a Belgian building contractor who had lived in the little country of Burundi on the Congo's eastern border for five years from 1971, and his African wife who came from the neighbouring country of Rwanda. The husband began to suffer persistent skin infections in 1976 and travelled to Brussels for treatment where he was found to have lost about six kilos, and to be weak and feverish. After a temporary improvement, he returned to Africa to resume his work but was soon flown back again to Belgium complaining of fever and pain in the lungs. Grotesque warty growths formed on his penis and fungi colonised his nails. After treatment with antibiotics the patient experienced a second remission and returned to Burundi but there he became deranged from acute abscesses of the brain. Finally, he died in Belgium in June 1981.

The builder's widow lingered in Belgium after his death and did not remarry. After a few years, she too began to feel tired, weak and feverish. In 1984 she tested positive for HIV and the diagnosis was confirmed when the virus was found in cultures taken from her lymph glands. On the strength of this, the doctors concluded that her husband, too, was an early AIDS case. The couple's three children, however, remained free from infection.

Case four was a Belgian mining engineer who had worked in the Copper Belt of the Congo since 1964 and who had developed AIDS symptoms in 1975, dying two years later after flying to Brussels for emergency treatment. He had suffered from acute toxoplasma infection which destroyed his sight, caused palsy, epileptic seizures and finally coma. After death his brain was found to be riddled with abscesses.

This case was followed by that of a divorced 37-year-old Belgian aid worker who had been posted on voluntary service to the Congo from 1976-78, where he regularly availed himself of local prostitutes. His own virus was never directly diagnosed, but three surgical patients who were transfused with his blood were later found to be HIV-positive within six months. He died of AIDS in Brussels in September 1989.

Finally, an elderly Belgian colonial officer, a cartographer,



and his African wife were both been diagnosed as HIV-positive in the early 1980s, although they had quit the Congo to settle in Belgium as early as 1968, on the husband's retirement, and neither had since returned. They stated they had never taken drugs or received transfusions (though the husband underwent a hernia operation)> The wife said she had not had extra-marital sex since marrying in 1952, whereas her husband admitted to some heterosexual liaisons. The wife died of AIDS in May 1987, followed by her husband who died of AIDS in July 1988.

Like De Cock, Sonnet and Michaux concluded from these cases that AIDS was an old disease in Central Africa which, because of lack of clinical definition, had remained undiagnosed until the present outbreak. Yet despite its presumed antiquity, they added the conflicting observation that during a nine-year stint in the Congo from 1957-'66 they had seen no other AIDS-like cases and only two cases of Kaposi's sarcoma among the estimated 10,000 patients they treated.

In the earliest known perinatal AIDS case, the son of a Congolese Government official from Kinshasa died in Stockholm of AIDS in September 1982 aged just 8, after suffering from the disease for almost all his short life. The boy's symptoms first appeared within five months of his birth in Kinshasa in 1974. Stores samples of his blood were later tested and proved positive for HIV.<sup>16</sup>

In any event, during this period the AIDS epidemic was still pupating in its chrysalis and was at levels so low as not to arouse clinical alarm. However, there were several important clues that it was poised to hatch: the 1959 Congo blood sample, the 50-year-old Congolese woman who died in 1962, an upsurge in cases of Kaposi's sarcoma in Central Africa and the Norwegian sailor whose symptoms first became manifest in 1966. Given the nine year average period required for symptoms of the disease to appear in a healthy person, it was possible that cases four and six, the mining engineer and the colonial official, had also contracted the virus during the 1960s.

This possibility was reinforced when a retrospective survey of 805 blood samples collected from healthy women in the capital Kinshasa in 1970 revealed that two were HIV-positive. Then, samples taken from a slightly smaller group ten years later in 1980 revealed fifteen people as HIV-positive and hinted at the widening ripples of disease. In the same time frame, blood samples from 659 rural inhabitants of northern Republic of Congo collected in 1976 during the outbreak of haemorrhagic fever on the Ebola

river -- not far from where Dr Rask had worked -- revealed five had HIV at this time.<sup>17</sup>

Bearing out such evidence was the clinical observation of Congolese AIDS expert Dr Kapita Bila Minlangu that, from 1975 onward, there was an explosion in cases of aggressive Kaposi's sarcoma and cytomegalovirus. More remarkably still, doctors working in Uganda and Tanzania reported a dramatic upsurge in cases of KS among children in 1969, documenting 51 cases.<sup>18</sup> KS is exceptionally rare in children – indeed this group represented a 235 per cent increase on the total number of examples reported in the world medical record hitherto. As an example, the first case was a young boy, aged two-and-a-half, who had been suffering from swellings in the groin for six months. He was grossly emaciated, weighing only 17.5 pounds. His lymph glands were massively enlarged and his face was “ringed in a collar of swollen tissue”. Despite treatment, he deteriorated rapidly and died. The epicenter of this new outbreak of Kaposi’s sarcoma, in its particularly malignant form, lay “in eastern Zaire and adjacent countries” where rates were from 3 to 10 times higher than elsewhere in Africa.<sup>19</sup>

These cases, along with a steady stream of reports from other African and European doctors began to arouse suspicion that, like humanity itself, AIDS had come out of Africa. That it was an artefact of the tropical rainforest, one of the richest wellsprings of life on the planet. Every known species of life has viruses, and concealed within the tropical forest's biological largesse were agents which made it also the last great reservoir of unknown plagues. Several times in the twentieth century contagions of appalling virulence and lethality had erupted from the dwindling rainforests and -- with the exception of AIDS -- had mysteriously subsided.

To begin with, African governments and medical officials were deeply angered at what they felt was the accusatory finger of western medicine pointing their way, blaming their people for starting the epidemic. Their objection appeared particularly well-founded when it transpired that the early AIDS tests had been inaccurate when used on patients suffering malaria or other infections, leading to inflated estimates of the incidence of AIDS among the population. Giving added offence, teams of western "safari" doctors flew in and out of central Africa with an aloof kind of postcolonial arrogance, demanding assistance from governments, taking blood samples and then flying out again with scarcely a word to their offended hosts. These doctors had then, it seemed to the Africans, turned round and foisted the blame for the AIDS epidemic on Africa and its people, using erroneous test results to

reinforce their claim. For a long time there was ill-feeling between African doctors and their American or European counterparts, but by the latter part of the 1980s strenuous efforts were being made to iron out the awkwardness and collaborative links were being re-established.<sup>20</sup>

The discovery of more and more strains of SIV in wild African monkeys represented the clinching argument for most researchers. By 1990, Cambridge University's Professor Alex Karpas was able to summarise world scientific opinion on the source of the disease: "There is now little doubt human AIDS began in Africa. Not only is the disease widely spread in central Africa, but only in Africa are the monkey species naturally infected with lentiviruses related to HIV.....there is no evidence for the existence of HIV in Europe, the Americas or Arabia during the past century, or even the first half of this century, which argues strongly that the widespread HIV infection in Africa is a recent event.

"All in all the epidemiological evidence thus points to the spread of HIV infection from Africa since the Second World War. The spread seems to coincide with the widespread introduction of syringes and needles from the West, together with vaccination programs."<sup>21</sup>

For some years other scientists had had their suspicions. Max Essex and Phyllis Kanki of Harvard School of Public Health had reported the discovery of a similar retrovirus to HIV in African green monkeys -- in fifty per cent of all green monkeys they tested, to be precise.<sup>22</sup>

"Present evidence suggests that the acquired immune deficiency syndrome (AIDS) emerged in Central Africa as a new disease in recent decades," they stated. "This disease has recently approached epidemic proportions in many parts of the world.

"The etiologic agent of AIDS is believed to be the virus HTLV-III/LAV, which is proposed as having originated from a recent simian-human transmission in Africa." Kanki and Essex were pleased at their discovery of an HIV-like agent in monkeys because they believed it would provide a model for understanding the nature of the disease and so lay the groundwork for the development of a vaccine or treatment.

"These data indicate that healthy African green monkeys are infected with a retrovirus closely related to HTLV-III, designated STLV-III," they concluded. Subsequent testing of thousands of wild-caught and captive green monkeys revealed that from thirty to seventy per cent of them were infected with the

virus.

The Harvard team also added an important warning to their report. "African Green monkeys," they said, "are commonly used for biomedical research, diagnostic virology, and the production of biologic reagents; much of the oral poliovaccine (OPV) used throughout the world is produced on primary cultures of kidney cells from this species."

Another scientist who seemed to share these concerns about a medical origin for the AIDS pandemic was Dr Gerald Myers, head of the HIV sequence database and analysis project at Los Alamos National Laboratory in the US where he was exploring the genetic family tree of the immunodeficiency viruses. In an article published in 1993 in which he discussed possible origins, he wrote: "First there was a sharp increase in the exportation of monkeys from Africa in the 1960s, largely for the purposes of medical research. Second there was also, in the 1960s, a valiant push to vaccinate Third World populations. In particular, many countries began using live polio vaccines ... creating some small but finite opportunity for the introduction of passenger viruses through contaminated vaccine lots..."<sup>23</sup>

In the upshot, it was to emerge that not only African green monkeys (*Cercopithecus aethiops*) but also six other species of cercopithecine monkeys as well as sooty mangabeys, colobus monkeys, mandrills, yellow baboons and the chimpanzee<sup>24</sup> all carried various simian immunodeficiency viruses, known henceforward as SIVs. All the African primates appeared naturally immune to their own viruses and showed no ill effects from having them. In fact the monkeys were notably successful in ecological terms.

But there was a shock in store: SIV was also found in captive Asian rhesus macaque monkeys in the United States and it was far from benign. In fact, it caused a form of AIDS -- and it killed. The infection appeared far from natural, and was undoubtedly transmitted when African and Asian monkeys were housed together in United States holding facilities awaiting medical experimentation. "The fact that a virus that seemed to be quite harmless in African monkeys was wreaking havoc in the newly-exposed Asian monkeys indicated that at least some strains of SIV still had potential for great virulence," Essex and Kanki wrote.<sup>25</sup>

A team from Georgetown University which studied the outbreak of SIV among captive (Asian) macaques held in the United States concluded that "African nonhuman primates are the natural reservoir for SIV, and that SIV was introduced to North

American macaques by way of cross-species transmission." If any further proof was required, this demonstrated beyond doubt the ability of this cryptic virus to leap from one kind of primate species to another.<sup>26</sup>

The Georgetown researchers also noted a quite remarkable diversity among the various strains of SIV they had isolated: whether this was because there had been many strains to start with, or a small number of strains had undergone rapid change upon entering new hosts was hard to say. But it was an important point, hinting at the virus's powerful ability to mutate and develop new varieties.

Subsequently, it was determined by other teams of scientists that monkeys and apes could be infected with HIV<sup>27</sup> -- and a laboratory accident involving a technician demonstrated humans could also become infected with SIV.<sup>28</sup>

The essential question which researchers could no longer avoid was: how and when did SIV become HIV? How did a "harmless" monkey virus cross into humans with such devastating effect as to become, in all likelihood, the world's fourth Great Death, the scourge of the twenty-first century? And, more importantly, would attempting to discover answers to this issue help to save lives and to protect humanity against future transmissions of disease?

## Endnotes

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## Speculations

To begin with there was much armchair conjecture in the letters' pages of the medical literature and the growing shelf of learned books on AIDS about how the virus had entered humans -- but few serious endeavours to find out. After a while, even this debate died away. On the whole, researchers seemed content to accept the fact of HIV without applying scientific method to its origins.

Many scientists argued, reasonably, that history was none of their business. There was more than sufficient work on their hands simply in attempting to understand and contain the emerging pandemic. To inquire into the actual origin or means of transmission of the virus to humans seemed, to some at least, a purely academic exercise of little immediate relevance to the task of defeating it.

The origin of AIDS might well be untraceable, they argued, lost in the thickets of time and the rainforest. Searching for it was dismissed by others as a task of such complexity and costliness as not to be worthwhile. Yet neither difficulty nor expense had deterred science from attempting to recreate the conditions of the Big Bang, to emulate the fusion processes of the sun or to place humans on the Moon. Was striving to uncover the origin of probably the most devastating pandemic ever to strike humankind less noble, less significant, less relevant, less profitable to knowledge and understanding, less worthwhile? When they heard the issue of the origin of AIDS dismissed in such terms, a few scientists felt it was time to ask why it was being so dismissed.

Theories advanced for the origin of AIDS ranged, literally, from the sublime to the ridiculous. A few were highly plausible, wanting only solid data to strengthen and sustain them. Others were quite bizarre. The mounting public hysteria, anger, prejudice and political controversy surrounding the emerging pandemic, fanned by the media, made it a fertile breeding ground for conspiracy notions.

Two main categories of theory emerged: those which sourced AIDS to an African monkey origin on the strength of the accumulating fragments of scientific evidence -- and those which asserted that it arose under quite different, sometimes credible but frequently ludicrous, circumstances.

At the extreme end of the conspiracy spectrum was the theory that AIDS was spawned in the super-secret biological



warfare labs of one or other of the Cold War gladiators -- and then escaped or was released into the wider community. The accusation was levelled at both the United States and former Soviet military establishments and their targets were variously claimed to have been: one another, the gay community or the coloured population.

The prime originators of this idea appeared to have been either the western anti-war lobby, out to discredit its own military establishment, or the former STASI or East German intelligence service in an imaginative disinformation campaign targeted at the United States and NATO. A third version attributed it to the KGB Fifth Directorate, seeking to discredit the Western military, possibly in riposte to American accusations that the Soviets were using Middle East conflicts as a testing ground for their chemical and biological weapons. The theory was also widely embraced by American coloured activists resentful of the white establishment and by homosexual activists seeking to vent their frustration over the health industry's alleged dawdling in the search for a cure.

A graphic example of this mischievous theory appeared in the Soviet journal *Literaturnaya Gazeta* in October 1985. Quoting an Indian newspaper, the article asserted that AIDS was a biological weapon devised by the United States that was being field-tested in Africa. The Indian report turned out to be non-existent, but the story soon took on a life of its own when a report based on it was circulated at a meeting of non-aligned governments in Harare, Zimbabwe. One of its assertions -- that the appearance of AIDS coincided with the opening with an American military biological lab at Fort Detrick, Maryland -- seemed to lend it credence in the eyes of those who wished to believe such claims. In one form or another the theory was subsequently rehashed and embellished in various western media.<sup>1</sup>

Provocative versions of the germ warfare theory were also advanced by Jakob Segal, a professor at Humboldt University in the former East Germany, and Dr Robert Strecker, an American anti-vivisection campaigner. Segal theorised that HIV was an artificial lifeform compounded from the sheep virus visna and HTLV-I by United States army biological warfare researchers in either 1977 or 1978. This virus supposedly escaped by accident after being tested on prisoners. Strecker proposed that HIV was formed from visna and BLV (Bovine leukemia virus) by American researchers in the 1970s after years of developmental work. This new virus was then deliberately introduced into the United States homosexual community through hepatitis vaccination. In support of their arguments, Segal and Strecker claimed visna and HIV were

very similar, while the United States military had recently conceded in evidence given before a Congressional hearing that it was interested in making biological agents against which humans had poor immunity. They argued that HIV's sudden appearance in America in the late 1970s lent weight to their case.

Another variant of the same idea – that HIV was a variant of the sheep virus, visna - provoked several commentators to speculate it might have been contracted in Europe or America as a consequence of people having sex with sheep or other farm animals.

These ideas fell down on several grounds: first, they were originally proposed at a time when nobody had a clue where HIV had sprung from, before the primate SIV viruses were discovered and widely accepted as being the genetic ancestors of the HIVs. Second, the deliberate creation of a new virus by splicing of two separate viruses to create a viable new agent was scientifically unattainable in the 1970s. And third, the ideas conformed with the early, but erroneous, view that AIDS was a disease arising in the United States gay community instead, as subsequently shown, in central Africa, where its traceable origins went as far back as 1959.

In any event, AIDS would have made a useless biological weapon, as the generals would have to wait from five to ten years for it to take effect in the enemy population and even then its universal spread was unlikely. It would only affect the promiscuous and intravenous needle users, and then only after a considerable lapse of time. It would not have choked even ordinary medical facilities. Besides, virologists pointed out, Nature had generously provided an infinitely greater selection of agents more suited to the creation of quickfire biological mayhem without having to synthesise them. This theory also presupposed that the Dr Strangeloves of the military manufactured HIV years before the virus was actually identified by the far more generously resourced civilian medico-scientific fraternity. Yet not one of the Strangeloves leaked to a civilian colleague. The theory also implied horrendous field trials somewhere in equatorial Africa, New York and California, which surely carried some risk of a breach of secrecy. This theory has not been disproved, but, as Cold War paranoia recedes, will probably die a natural death.

The second non-primate explanation for AIDS was based on the proposition advanced in 1986 by former British Astronomer Royal and popular science author Fred Hoyle that viruses could come from outer space. The discovery of organic molecules in the tails of comets passing close to Earth rendered this

not quite so outlandish a notion as might, at first sight, appear. In Hoyle's view up to thirty per cent of the mass of material in a comet could consist of elementary prebiotic molecules of various sorts including sugars, amino acids and nitrogen-rich compounds, which were continually being reprocessed chemically and by heat, cold and radiation. He and his colleague, Chandra Wickramasinghe, argued that life on Earth may originally have been seeded from space by these means and was periodically topped up by new lifeforms, some of which had produced abrupt outbreaks of epidemic disease such as the 1918 'flu and the plague of Athens. The view that epidemics resulted from sudden mutations of existing disease, Hoyle regarded as "not well proven".<sup>2</sup>

Why life should have arisen in those illimitable cosmic reaches, where it would be exposed to lethal extremes of temperature and radiation, rather than in the temperate womb of the Earth where all the right chemicals and preconditions already existed was not clear from Hoyle's argument. However most biologists considered it exceedingly doubtful that comets have either primates or lymphocytes in which HIV might be transported safely, or if the rigours involved in space travel would permit the survival of an otherwise highly-fragile virus even in a dormant state. Also, as Earth is constantly passing through the tails of comets (the annual Perseid meteor shower is such an event), humanity should in theory be subjected to large douches of totally unknown diseases every few months, which it plainly is not. Potentially, however, Hoyle's proposition is at least testable by sampling the upper stratosphere for strange organic molecules or lifeforms following the recent passage of a comet.

A third theory was propounded by a noted United States scientist, Professor Ernest Sternglass, who held the chair in radiological physics at the University of Pittsburgh Medical School. Sternglass was an outspoken critic of the safety of nuclear technology and had for some years argued that low-level radiation leaks from power plants and weapons factories were partly to blame for many of society's emerging chronic ailments, including genetic defects, mental retardation, lung disease and perinatal deaths. In hypothesising about the origin of HIV, Sternglass contended that the dispersal of radioactive compounds from French atmospheric bomb tests in the Sahara had generated a mutation in a previously harmless virus present in both humans and monkeys.

AIDS historian Dr Grmek dismissed his theory as being without

factual basis -- though similar objection could have been raised to any of the AIDS-origin theories and was not, of itself, an argument for dismissal. The notion was at least conceivable because the virus had plainly undergone dramatic mutation, though it was difficult to see why such an agent should have become virulent and lethal for humans exclusively while remaining harmless to other African primates.<sup>3</sup>

The fourth non-primate theory was advanced by Peter Duesberg, a professor of molecular biology at the University of California at Berkeley. Duesberg was an eminent figure who had pursued the AIDS pathology from the very beginning, puzzling over why the virus was so hard to detect in AIDS patients, why it seemed not to harm the cells it infected and why it did not appear to build up even when the disease itself became grave. In the end he concluded AIDS was an endemic condition brought on by a cocktail of sexually-transmitted infections, recreational drugs, anti-AIDS drugs and a wild lifestyle which undermined the immune system, and he published a paper to this effect in *Cancer Research* in March 1987. Duesberg further argued that HIV was merely an indicator of promiscuity, not a cause of AIDS. He anchored his claim on the fact that HIV failed to satisfy "Koch's postulates", the four criteria set by the great microbiologist Robert Koch, discoverer of the tuberculosis bacillus, by which an agent of disease can be recognised:

1. the organism must be found in all cases of the disease
2. it must be isolated from the host and grown in culture
3. it must reproduce the original disease when passed to a susceptible host
4. it must be present in a host so infected.<sup>4</sup>

Duesberg pointed out that HIV was not found in all AIDS cases. Grown in culture it killed its host cells, but not those in the body, and there was no other animal to which it could be readily transferred for testing. In a series of polemically-worded letters to the mainstream scientific press he defended his call for an open mind on the cause of AIDS. He even volunteered to have himself injected with HIV, provided it was "clean" of other viruses.

The great majority of medical scientists disagreed with Duesberg, objecting among other things that virtually every case of AIDS seen appeared to be accompanied by HIV infection or at least by HIV antibodies, while not all AIDS victims (especially the children) took drugs, had sexual infections and led a wild life. But Duesberg was correct in that there was for a very long time, technical difficulty in explaining exactly *how* HIV caused AIDS

especially as it appeared not to kill the white blood cells it invaded.<sup>5</sup> Duesberg's theory was also important for the interest it evoked in the media and among sections of the gay community who believed that the medico-scientific establishment was dragging its heels in the hunt for a sufficiently profitable cure.

The second category of explanation, and that subscribed to by most researchers, was that the disease came to us from monkeys or apes probably by means of the transfer of blood, tissues or other substances. This opinion was significantly influenced by the genuine fright which the world received when it was discovered that contaminated blood donated by HIV-infected people was spreading the virus among tens of thousands of haemophiliacs and other plasma recipients. Because of the very high likelihood of infection (ninety five per cent) resulting from a transfusion of contaminated plasma, blood thus became the favoured route of transmission for the original introduction of the virus to humans from primates -- and even for its initial spread. In 1985 British researcher Dr Peter Jones had even suggested that the American epidemic was seeded, not by sex, but by the shadowy international trade in plasma products operated by drug companies and blood brokers from places such as Africa and Haiti to the United States.<sup>6</sup> But this only attempted to explain the virus's spread -- not how it had originally leapt species.

The first theory for the actual transmission of the virus to humans by blood involved medical experiments intended to curb the scourge of malaria, which took place in America and probably in Africa or Belgium between 1922 and 1955, according to Dr Charles Gilks of Oxford's Radcliffe Hospital.

"Direct inoculation of fresh blood is the most efficient way to transmit the AIDS virus," Gilks wrote. "No-one has suggested any circumstances under which fresh monkey blood could have been injected into humans in a systematic fashion and this has not been considered as a mechanism. But the malaria literature describes many instances in which humans were injected with primate blood containing viable malaria parasites."<sup>7</sup>

Gilks went on to detail numerous cases in which humans had been either directly or indirectly injected with monkey or chimpanzee blood: "Thus at least 34 people have received...injections of fresh blood taken from 17 chimpanzees. A further 33 received blood from people given primary chimpanzee blood injections...perhaps two, are described as being given direct inoculations of mangabey blood. In addition, three people have received blood from macaques infected with mangabey malaria

parasites passaged via a baboon. All of these recipients of primate blood must be considered at risk of developing retroviral infections if the hosts were infected with SIV..."

Some of the experiments were carried out by doctors in the United States, and some of them by Belgian doctors, presumably in either Belgium itself or the Belgian Congo. Most of them took place during the 1930s, with only a handful in the 1950s. Many of the patients who received monkey blood were suffering from neurosyphilis, and it was by now believed that the presence of other sexually-transmitted diseases increased the risk of HIV infection. Malaria parasites from chimpanzees were also given to volunteers in United States gaols, though it was not clear how many recipients were involved.

Gilks argued that, at least, his theory had the virtue of being testable: surely blood samples from these experiments were preserved and could be examined for SIV/HIV? He hoped colleagues with access to such samples would take the idea seriously enough to have a closer look.

A second plausible explanation for a blood transfer was advanced by a Dr F. Noireau in *The Lancet* in 1987. He cited a book, *Famille Sexualite et Culture*, written by Anicet Kashamura, a member of the Idjwi tribe of the Lake Kivu area of the eastern Congo, which dealt with the sexual customs of the people of the African lakes region. Kashamura wrote: "To stimulate a man or a woman to intense sexual activity, male monkey blood for a man or she-monkey blood for a woman, was directly inoculated in the pubic area and also into the thighs and back."

"Such practices," commented Cambridge's Professor Karpas, "would constitute an efficient means of trans-species transmission and could be responsible for the emergence of SIV infection of man, and thus AIDS." Karpas went on to suggest that this explained the close similarity between one strain of SIV and HIV-2 in West Africa, and to predict that eventually an SIV sufficiently similar to HIV-1 would be found.<sup>8</sup>

It was not clear whether the ritual of pre-coital blood inoculation was also practised in West Africa as well as the lakes region of central Africa, which lie more than 2000 kms apart and have markedly different cultures. There was no evidence in the scientific literature. However the appearance of at least two distinct strains of HIV in the human population in Central and West Africa simultaneously suggested to some researchers that the same mechanism of transfer might have been at work.

There was a second flaw to the sex-rite theory. If blood

inoculation for ritual or sexual purposes were a truly long-standing tradition and a route for cross-species infection then the disease would almost certainly have transferred at some time in the many, many thousands of years preceding, given the wide distribution and frequency of SIV among African monkeys. In cultures in which permissiveness, polygamy and intermarriage between widely separated communities were all commonplace the disease would certainly have spread around quite quickly -- as it was doing in many contemporary societies, or as syphilis did in the early days. Also, since African monkeys were immune to SIV, it was probable that if constantly inoculated with the virus in this fashion for centuries, Africans would also have developed some broad population immunity. Yet there was no evidence that this was the case.

Similar objections applied to the early contention of researchers such as De Cock, Sonnet and Montagnier, that AIDS was an ancient disease which has existed in Africans for centuries, millennia or even millions of years. In all the preceding five hundred years of European contact with Africa, including the enormous slave trade in which over ten million people were shipped to the Americas as well as Arabian slaving to the east, there was not a single credible case of AIDS reported. Also, no AIDS was found among West Indian immigrants entering Britain forty years ago, suggesting that that region, too, was free of the disease at least up until the mid 1950s. Research into the genetic family tree of the AIDS virus and its proliferating strains has recently also lent strong support to a view among leading researchers that it was a new disease which had evolved rapidly since around 1960.<sup>9</sup>

Until 1959, the scientific record is silent on HIV/AIDS.<sup>10</sup> Karpas himself acknowledged that the absence of AIDS worldwide prior to this date represented a powerful argument that the epidemic was recent: "All in all, the epidemiological evidence thus points to the spread of HIV infection from Africa since the Second World War."

Nevertheless, the idea of transmission via a ritual inoculation involving contaminated blood carried a strong potential risk factor, and so merited closer investigation of such practices among African tribes and some attempt to see if behavioural patterns coincided in any way with the epidemiology of the disease in Africa. Doing this would require sensitivity: no country or culture wanted to be stigmatised with giving birth to the AIDS epidemic.

Karpas's suggestion irked Professor Mike Lecatsas of the Medical University of South Africa, and prompted him to write in reply: "To single out Africa and its people and customs as essentially pivotal in this tragic pandemic is decidedly biased, and in view of the possible social and related repercussions one would urge extreme caution before embarking on such generalizations." There were other, far more likely methods of transmission, he noted cryptically.<sup>11</sup>

The most provocative version of the monkey-origin theories was articulated by an American journalist who asked a senior Congolese health official at a press conference whether Africans had sex with monkeys. The Congolese doctor, with a keen sense of repartee, told her that in Europe and America, so he understood, films were made showing women having sex with dogs. No, he said, Africans were not in the habit of cohabiting with other primates. Technically, of course, it has never been established whether SIV can or cannot be passed from monkey to human by sexual contact, but the odds of it happening seem rather small.

Another theory advanced by Guy de The mirrored that of Sternglass but without invoking the atom bomb: humans and monkeys had carried harmless retroviruses in their systems all along. At some point the viruses had come into contact with one another and recombined their genes to produce a lethal strain -- rather like the deadly 1918 strain of 'flu was thought to have done. Again, it seemed paradoxical the recombinant virus should prove deadly to humans yet harmless to chimpanzees or African monkeys. Subsequently no research has emerged either to support or rebut this theory.

By far the preferred theory among the medico-scientific community for the origin of AIDS is that of the chimp hunter or monkey bite. The chimpanzee is the particular subject of this theory because, in 1989, it was found to carry a strain of SIV which had a good (up to 84 per cent) resemblance to HIV-1 type M, the American/European strain of the AIDS virus.<sup>12</sup> But chimpanzees and monkeys are interchangeable for the purposes of the theory.

At a conference of the Australian Academy of Science in 1991 Professor Roger Short outlined the main version of the theory as follows: "Chimpanzees inhabit tropical rainforest areas where human population densities are low, and they have been traditionally hunted and eaten by the indigenous people of these regions. It would only require an accidental cut on the hunter's



hand whilst skinning a dead chimpanzee to transmit the infection from chimpanzee to man, and isolated acts of transmission could have been occurring for hundreds or even thousands of years. The hunter, and maybe his wives and some of his children, would ultimately die of the infection, but at low human population densities the chances of the disease spreading to other individuals would be slight.

"But in recent years, with increasing human population density, and the opening up of the rainforest, coupled with increased mobility of the human population, the stage was set. An infected hunter might have been able to buy a bicycle for example, and this would have enabled him to cycle into the nearest village of an evening, and have sex with one of the local bar girls, who in turn might subsequently have sex with a passing truck driver. And so perhaps a match was struck, and put to the kindling. Where will it end?"<sup>13</sup>

The chimp hunter-monkey bite theory had a range of variants, which tended to be dragged out whenever objections were raised to one version of the story or other. These included oral transmission by the monkey biting someone, oral transmission by the eating of uncooked monkey meat, and blood transmission via the use of monkeys in magical or sexual rituals.

A related hypothesis for the origin of AIDS was championed by the discoverer of the agent, Dr Luc Montagnier, who considered that the disease had existed for "quite a long time in certain isolated African tribes without causing the least damage". The reason, he argued, was that the tribe had developed immunity, and the virus did not become lethal until it got out into the wider human population who were not immune. Then, perhaps recognising the weakness of this theory -- that Africans, patently, aren't immune to HIV -- he, too, postulated a sudden evolutionary mutation had then given rise to the most lethal bug known to humankind. The problem with this idea was that the mutation had to have occurred several times, in different SIVs, in the same time frame in order to create both HIV-1 and HIV-2 and their major subtypes.

De Cock elaborated on his theory of an ancient origin for AIDS in 1988, arguing that HIV infection had remained low and stable and thus latent in rural Congo, while it rose sharply in the cities. This suggested that the rural mores and the way of life were less conducive to the spread of infection and that in the countryside it might have festered away quietly for decades or centuries without spreading. However, he proposed, in regions

swept by profound social change following the end of colonialism during the 1960s the virus was able to escape and spread, to become epidemic.<sup>14</sup>

The monkey hunter and "ancient AIDS" theories proved attractive to medical science in many ways. They placed the origin and transmission of AIDS back in the distant past, with an anonymous chimp-hunter or isolated tribe somewhere vague and far away, well out of the reach of modern medicine. They were not sustained by a single shred of concrete evidence, yet they were plausible, even possible -- and probably untestable. They offered comfort because they sidestepped all suggestion of responsibility. They evaded the necessity to ask: *How?*

That both the medico-scientific establishment and the scientific press found the chimp-hunter theory appealing was illustrated by an article published in *New Scientist* in 1990, by Dr Myra McClure, a virologist at the London Institute of Cancer Research. After dismissing other theories she wrote: "But is it possible that monkeys could have infected humans with an HIV-like virus? The answer is yes...because transmission might have been possible via a number of routes such as monkey bites, scratches, eating monkey meat or taking ritual preparations obtained from primates."<sup>15</sup>

But the chimp or monkey hunter theory also had a significant flaw. Humans and chimpanzees have both evolved in Africa over the last four million years. Before that time, the genetic evidence suggests, we had a common lineage. As mammals, we are very much alike and based on the latest DNA findings some researchers have even suggested we are so similar (97-98 per cent) in our genetic makeup that we ought to be classified as the same genus. That is, that chimpanzees should be reclassified as *Homo*, rather than we as *Pan*.<sup>16</sup>

Humans and chimpanzees are both omnivores, and anthropology has many records of human hunters preying on chimpanzees and other primates. Indeed chimpanzee hunting is something of a specialty among certain Central African tribes, while monkey appears on many a menu throughout the tropics.

Chimpanzees, too, eat meat and while their diet is normally restricted to smaller game, they are quite capable of co-operating to mount hunts for larger animals. Primatologist Jane Goodall witnessed the Gombe Stream chimps hunting and devouring bushbucks, bushpigs, redbellied monkeys, blue monkeys and colobus monkeys and even baboons. Indeed hunting appeared to be an important way in which aggressive young males rose in the colony

hierarchy.<sup>17</sup> "And there are two authentic cases on record of chimpanzees in the area actually taking off African babies -- presumably as prey, for one infant, when recovered from an adult male chimpanzee, had had its limbs partially eaten," Goodall recounted.

So chimps have eaten people and people have eaten chimps and both have certainly eaten monkeys for much of the two species' considerable co-existence, which spans at least 4.2 million years. If SIV was transmitted from chimp (or monkey) to human as a result of a cut, a scratch or a bite, the opportunity for this to occur would arise, literally, on millions of occasions, over millions of years. Some virologists contended that this merely raised the odds that, one day, the infection *would* cross from one species to another -- but there was no particular reason why this should have taken place in the 1950s rather than any other decade in the previous 420,000. Also, there was also no obvious immunity in humans resulting from constant exposure to the virus.

But there was a piece of conflicting scientific evidence which rendered the chimp hunter hypothesis hard to sustain: odd cases of HIV/AIDS were showing up in the central African cities and densely populated areas from 1970 onwards -- however blood samples collected from Congo pygmies between 1975-78 and again in the 1980s revealed no trace of HIV-1 or HIV-2. Pygmies are the most inveterate hunters and eaters of monkeys, chimps and other primates in the Central African region -- and if anybody was going to catch a monkey virus by cutting themselves, eating monkey meat or getting bitten, then surely it was a pygmy. Yet, according to studies conducted by both America's CDC and the Pasteur Institute, these pygmies were free of HIV at a time when cases were burgeoning in the cities and rural areas of the Congo.<sup>18</sup>

The scientific weight of evidence was that AIDS was a new disease, for four reasons:

- First, because humans appeared totally unresistant to HIV whereas chimps and monkeys had clearly grown to tolerate their own SIVs without ill effect.
- Second, the spectacularly fast rate of mutation and evolutionary divergence which scientists found among the various strains of HIV was highly indicative of a new virus blazing through a virgin population, evolving as it went.
- Third, because there was not one but two kinds of HIV - HIV-1 and HIV-2 -- and both appeared to have mutated and entered humans in the same time frame, the odds of which happening naturally appeared extremely small.

- And finally, because no substantiated cases of either HIV or AIDS had been found prior to 1959.

Not even in Africa, the scientifically-agreed hearth of the AIDS pandemic, was there any clear evidence that humans had historical immunity to HIV. Yet the opportunities for passing HIV among the African population would have been legion, and epidemiology and immunology commonly accept that if a disease, however virulent, has been circulating in a population for a couple of centuries or more, a fair proportion of people will have developed immunity to it, while the virus itself will have tended to weaken as both host and parasite grow used to one another.

The great flaw in the argument of those who wished to believe that AIDS was an ancient, endemic African complaint was their ignorance of African history. It is common for many westerners to assume that, prior to the dawn of European awareness of Africa with the adventures of Stanley and Livingstone in the late 19th Century nothing much happened in that continent -- the continent which cradled humankind and populated the earth. This naive view flies in the face of Central African history, which is a rich and vibrant tapestry of river and land travel, tribal migration, intermarriage, trade, warfare, slaving, nomadism and other forms of human intercourse. The African saga, in other words, is every bit as turbulent, complex, vital and interactive as that of Europe or Asia. If a new sexually transmitted disease arose, there was no reason at all for it not to spread across the continent in just a few years, as syphilis had done in both Europe and Africa.

A letter by Leroy Vail of Harvard to the *New England Journal of Medicine* in 1988 suggested that not all researchers were prepared to swallow completely the notion that AIDS somehow propagated its way out of "lost tribes" isolated in the rainforest as a result of demographic change in the 1970s.

"Zaire, like other countries in Central Africa now affected by AIDS, has a long history of disruption of rural life by forces of economic and social change and colonial administrative policies dating as far back as the 1880s and 1890s," he pointed out. "One of the general consequences of these disruptions was a widespread movement of men from rural areas to places where they were employed as migrant workers, usually mines." The men returned home, bringing their sexual infections with them, then went off to work somewhere else. By the 1930s, Vail stated, "nowhere in rural Zaire was isolated enough to be accurately described as having a population that was living in accordance with traditional village

life". And by the 1940s urbanisation was in full swing.<sup>19</sup>

The inference was plain: if AIDS was an ancient disease it would have come out of the rainforest into urban populations and spread round the world at least fifty years – most probably centuries – before it actually did. It should be borne in mind it had taken just fifteen years to move syphilis from the Americas to Europe, to Africa, and thence to China in the 1500s.

Furthermore, rural Africa's sexual customs seemed not to favour the idea that they were abstemious: according to two surveys, the typical pastoral Nilotic male enjoyed an average of twelve female sexual partners a year and some had more than fifty. The typical heterosexual male Briton, in contrast, averaged but one conquest in a twelve-month.<sup>20</sup>

In the light of such evidence, to suppose that a lethal sexually-transmitted infection might constantly invade communities or tribal groups in the rainforest, and sit there patiently for centuries or even millennia before modern transport and urban growth arrived to deliver it to the "outside world" taxed credulity. This did not, of course, render the chimp hunter and lost tribe hypotheses untenable – merely unlikely. And, more particularly, unsupported by scientific evidence.

Then, on a New York radio program broadcast on WABC on 31 May 1987, a San Antonio doctor, Eva Lee Snead, claimed AIDS had indeed leapt species from monkeys to humans. But it was not via a cut or monkey bite, she suggested. According to Snead, AIDS had entered the human race through a contaminated polio vaccine.

Of all the origin theories, this was the easiest to test. Vaccine stocks and possibly stored blood samples still existed from the time when the vaccinations took place.

If Snead was correct, then AIDS was a product of modern medicine.<sup>21</sup>

## Endnotes

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<sup>1</sup> Grmek, M. *History of AIDS*, Princeton University Press 1990, pp 151-152

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<sup>3</sup> Sternglass E., *Secret Fallout: low level radiation from Hiroshima to Three Mile Island*, McGraw Hill 1984; and Grmek, M., *ibid.* p147.

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- <sup>4</sup> Adams J., *The HIV Myth*, St Martin's Press, 1989.
- <sup>5</sup> Later work in both the United States and France greatly clarified this process -- it is the immune system which kills infected lymphocytes, so undermining itself. See Research shows how HIV exhausts the body, *British Medical Journal* 310, 21 January 1995, p145 and Wain-Hobson S., Virological Mayhem, *Nature* 373, 12 January 1995, p102.
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- <sup>8</sup> Karpas A., Origin and spread of AIDS, *Nature* 348, 13 December 1990, p578.
- <sup>9</sup> Li W-H., et al 1988, Cited in Sharp P.L., Robertson D.L. and Hahn B.H., Cross-species transmission and recombination of AIDS viruses., *Philosophical Transactions of the Royal Society London* 349, 1995, pp41-47.
- <sup>10</sup> Several earlier cases have been argued for an AIDS diagnosis based on patients suffering from the opportunistic infections often associated with AIDS, the most popular being that of Robert R., from St Louis, USA, in 1968/69 and a case from New York in 1959. None of these are supported by a confirmed test result for HIV, and most have reasonable alternative explanations. See Hooper E, *The River*, Penguin Press 1999, pp129-150.
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- <sup>15</sup> McClure M., Where did the AIDS virus come from?. *New Scientist*, June 30, 1990.
- <sup>16</sup> Eastal S. et al, *The Mammalian Molecular Clock*, Springer-Verlag NY, 1995.
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- <sup>18</sup> Rouzioux et al, 1986, cited in Myers M., MacInnes K and Myers L., Phylogenetic moments in the AIDS epidemic, *Emerging Viruses*, Oxford University Press 1993, p122.
- <sup>19</sup> Vail L., HIV infection in Zaire, *New England Journal of Medicine* 319, 1988, p309.
- <sup>20</sup> Konings E. et al, Rates of sexual partner change among two pastoralist southern Nilotic groups in East Africa, *AIDS* 3, pp 245-247 and May R.M. & Anderson R.M., The transmission dynamics of human immunodeficiency virus (HIV), *Philosophical Transactions of the Royal Society* 321, pp 565-607.
- <sup>21</sup> Pascal L., What happens when science goes bad. *University of Wollongong Science and Technology Analysis Research Programme, working paper No. 9*, December 1991, p10.

## Mission of Mercy

Polio, like AIDS, is a ghastly disease. Throughout history it has afflicted virtually every society on earth, becoming increasingly prevalent with the spread of urbanisation. The earliest known example was found by archaeologists in the twisted 4500-year-old skeleton of a woman unearthed from a bronze age communal tomb at Tell Abraq in the ancient kingdom of Magan in the southeastern part of Arabia. Its crippling effects were also depicted on an Egyptian grave stele dated to 1400 BC and showing a young priest with a shortened left foot.

Polio infection takes two forms: a trivial infection of the gut, which causes mild fever and produces immunity, and paralytic poliomyelitis, once known as infantile paralysis. This acute condition develops when poliovirus escapes from the gut into the bloodstream and then starts to inflame and destroy the nerves. Infection may be silent (without obvious symptoms) or accompanied by fever and other minor ailments, and in infants, protected by the mother's immunity passed in the milk, often goes no further. In older children and adults, however, if infection spreads to the central nervous system, the spine and brain, the effects can be fearsome: acute fever, meningitis, extreme weakness in the muscles and paralysis. When breathing muscles are paralysed, death by asphyxiation often follows. The limbs of those who recovered were frequently distorted for life due to the unequal pull of partially-paralysed muscles on the child's growing bones, and wasted by the permanent atrophy of the nerves. In many societies, these physical deformities inflicted by polio also bred stigmatisation, isolation and loss of self-worth.<sup>1</sup>

History does not recollect much about polio because its incidence, relative to other child killers such as measles, diphtheria and smallpox or various kinds of plague, was low. But it was a constant companion, and, as cities grew, an omnipresent one, especially during the summer months. Major epidemics smote Britain and America in the 1830s and Europe and America in the 1890s. In 1911 a savage outbreak erupted in Sweden and was followed in 1916 by the worst United States epidemic, which caused 12,000 cases of paralysis in New York alone, affecting two per cent of all children under five years old. From the 1920s on, United States cases fell away as the disease ebbed and flowed, before rising to a new peak of 40,000 cases a year in the early



1950s.

Paradoxically, by the early twentieth century, polio had come to be thought of as a disease of the upper classes in society. One of its most notable victims was the United States President Franklin D. Roosevelt, scion of one of America's wealthiest families, who contracted the virus at the age of forty when he was already a father of five and a distinguished politician. More than any other factor, it was his personal misfortune which lent impetus to the drive to develop a polio vaccine.

The reason paralytic polio seemed more prevalent among the loftier social strata was that the virus was passed from faeces to mouth as a consequence of poor hygiene. Ordinary people, who had little notion of the microbial jungle in which they lived and whose standards of domestic and personal hygiene were consequently not high, became infected as tiny infants and so developed immunity early on. In privileged households, however, where parents, nannies, cooks and children were taught to wash their hands after going to the toilet and before preparing food or eating, individuals could sometimes even reach adulthood without ever being exposed to the virus. When they finally became infected, the effects were all the more horrific.

One of polio's most distressing features was that it seldom killed but left its young victims pitifully maimed and paralysed, sometimes for years, occasionally for life. Though planned immunisation has since banished it from most communities round the world, millions of sufferers from the pre-vaccine era remain permanently disabled even today. Thanks to successful vaccination the disease today carries only a dim horror for the larger community who recall with a shudder the macabre term "iron lung" -- and it is virtually unknown to the young. Polio has now been eradicated in the western hemisphere and WHO hopes to exterminate it from the earth in the early 21st century.

Because polio could be both mild and severe, no-one was ever able to estimate how many infections occurred each year, and few epidemics were chronicled in detail. It was usual to record only the small minority of cases which resulted in paralysis, not mere infections, which mostly passed undiagnosed.

Although polio had been recognised as a human disease throughout history, the agent which caused it was not identified until 1908 when a brilliant Viennese researcher, Karl Landsteiner, induced paralysis in a monkey which he had infected with spinal tissue from a child who had died of the disease. By further passing extracts of infectious material through ultra-fine filters, Landsteiner

was able to demonstrate that the cause was not a bacterium as doctors had supposed, but that invisibly minute and mysterious agent, a virus.<sup>2</sup>

Compared with other epidemic diseases, polio had two great vulnerabilities: first it had no animal host to provide a permanent reservoir for re-infection of humans; and second, a mild infection induced lifelong immunity. These two qualities rendered it an ideal target for vaccine immunisation, because if an entire community could be made immune, the disease would die out, a fact recognised by medical science as early as 1910. This led to the first attempt to develop a vaccine by a German colleague of Robert Koch, Paul Romer. But when administered to monkeys, Romer's vaccine caused polio, and when given to mice, it failed to protect them. It was a foretaste of the terrible difficulties that lay ahead. Discouraged, he abandoned his endeavour.

On and off for the next 25 years researchers pursued the dream of a vaccine for polio, but far too little was known about the behaviour of the virus and how it was transmitted from person to person, while the technology of the day did not permit the manufacture of large, cheap batches of safe inoculant. For several decades scientists argued over whether polio was passed in the air, in food or by insects, whether it was a generalised infection affecting most of the body or one which exclusively attacked the nervous system, and whether there was one kind of poliovirus or many.

The latter question was resolved by two Australians, Macfarlane Burnet and Jean Macnamara when they demonstrated in 1931 that an Australian strain of the virus was decisively different to one found in the United States. From then on, it became clear that there were several strains of polio, which meant that, to be effective, a vaccine had to offer protection against all of them.

Meanwhile, the effect of Franklin D. Roosevelt's polio suffering began to exert its impact on the public imagination. Roosevelt had been stricken by the disease while holidaying at Campobello Island, New Brunswick, in 1921. He had probably contracted the virus when he stopped for a brief visit to a boy scout camp on the way.

"I first had a chill in the evening which lasted practically all night," Roosevelt later wrote. "The following morning the muscles of the right knee appeared weak and by afternoon I was unable to support my weight on my right leg. That evening the left knee began to weaken also and by the following morning I was unable to

stand up. This was accompanied by a continuing temperature of 102 and I felt thoroughly achy all over. By the end of the third day practically all the muscles from the chest down were involved. Above the chest the only symptom was a weakening of the two large thumb muscles making it impossible to write..." The doctor could not determine what was wrong and prescribed massage, which only made matters worse. By the time his condition was finally diagnosed as polio, Roosevelt was completely paralysed from the waist down.<sup>3</sup>

Despite this grievous setback, and encouraged by his family, Roosevelt maintained a cheerful insistence, which some privately felt bordered on self-delusion, that he would both recover the use of his legs and resume his political career. Tended by his devoted secretary -- some say his mistress -- Missy LeHand, he exercised and swam constantly, taking advantage of the restorative powers of the mineral-rich waters at Warm Springs, Georgia, a health-spa since Indian times.

While still convalescing Roosevelt took a lively interest in the rehabilitation of other polio victims, corresponding with them and sharing novel ideas for restoring the wasted muscles. In 1926 he purchased Warm Springs, encouraging fellow "polios" to come and experiment with the restorative powers of its waters. The following year he established the Georgia Warm Springs Foundation to assist polio patients in their rehabilitation from paralysis. Eventually, Roosevelt was sufficiently well recovered to take up his political career from a wheelchair and automobile -- assets which prematurely seemed to endow him with elder-statesman status. He was elected Governor of New York and then in 1932, President of the United States. Following his inauguration, a group of enthusiastic friends and admirers formed the "President's Birthday Ball Committee" to raise charitable funds for the foundation and for the scientific research into polio which it had begun to sponsor. In 1938 the committee changed its name to the National Foundation for Infantile Paralysis (NFIP) under the chairmanship of Roosevelt's legal partner and long-time friend, the redoubtable Basil O'Connor. Then, in a moment of inspiration, it adopted the campaign nickname "The March of Dimes", the idea being that even humble contributions -- the coins sometimes laid in rows at collecting points across the country -- could grow into substantial funds for overcoming the scourge of polio.

Among Roosevelt's earliest policy initiatives as President was to set in place an array of measures designed to alleviate the effects of the Great Depression on America and its citizens. It was

the cornerstone of what was to become his "New Deal". The primary goals were to restore prosperity to farmers through a system of subsidies and adjustment assistance, and to industry and the workforce through a massive \$US3.3 billion spending program on public works. The New Deal conflicted stridently with the prevailing American social order, imposing heavy taxes on the rich in order to generate employment for the poor, who had been hardest hit by the Depression. Millions who had been out of work, sometimes for years, found themselves in worthwhile jobs on big public construction projects, such as the United States's magnificent public highway network, flood mitigation, reforestation, soil conservation, slum clearance and new electric power stations. Wealthy America, outraged at Roosevelt's "soak-the-rich" tax approach and labour reforms, became embittered at this perceived betrayal by one of their own and the President was occasionally jeered by pampered youngsters, which only helped to entrench his growing popularity among the masses.

The "March of Dimes" gave poorer Americans now in work an opportunity not only to express their personal gratitude to the President but also a repartee to the hissing brats of high society. Thousands volunteered as collectors, and cans were rattled from one end of the country to the other on street corners, in milk bars, at sports grounds and private gatherings. That great social innovation, the cinema, became a major collection point for the war on polio following the production of a ten-minute tear-jerker depicting paralysed children being kept alive in their coffin-like iron lungs.

"As the film ended, the movie star narrator would be shown in a pediatric polio ward, patting the paralyzed children and staring directly into the moist eyes of every person in the audience," historian Allan Chase explained. "Her voice, her nostrils, her entire body quivering, she would inform her viewers that the medical care, the iron lungs, the braces, and above all the scientific research on vaccines were all paid for by the billions of dimes contributed by ordinary and often very poor people like the lucky men, women and children listening to her voice. The lights would come up, and ushers would pass up and down the aisles with jingling collection cans."

The movie theatres at times became the arena for political confrontation over the New Deal too. When Roosevelt's features appeared on the cine news, they were greeted by a storm of boos and hisses from the affronted rich in the audience, whose pockets had born the brunt of his new taxes. The poor, on the other hand,

responded by redoubling their contributions to the President's charity.

The trickle of dimes rapidly swelled into a flood worth millions of dollars which, in turn, stimulated large donations from wealthy philanthropists. Each year the March of Dimes raised an average of \$US25 million and in its most successful year, 1957, it grossed \$US44 million, an immense sum. To begin with this money was spent on treatment to alleviate the suffering of its victims such as the purchase of iron lung (Drinker) respirators to keep those with paralysed lungs breathing. But with advances in scientific understanding of the disease and the pressure of an acute shortage of research money in the wake of the Depression, increasingly the funds began to flow towards research aimed at developing a safe vaccine. In all, some \$US69 million was devoted to this goal between 1938-62, a figure which highlighted the sheer scale of the resources which the United States was able to throw into the challenge of defeating polio.

In September 1935, a severe polio epidemic in Raleigh, North Carolina, provided a trigger for the testing of a new vaccine developed in the New York City Health Department laboratories by William Park and his talented young Canadian associate, Maurice Brodie. The vaccine was made from a potent strain of the virus which had been killed by immersing it in formalin. Park and Brodie proclaimed its safety by the courageous act of injecting it into themselves and several volunteers first, without ill-effect. When they announced their success, the newspapers responded with adulation. The only sour note came from a colleague, Rockefeller Institute director Dr Tom Rivers, who claimed the vaccine was ineffective and would not provide sufficient protection. Nevertheless Brodie and Park set to work injecting it into 10,000 children in New York and other centres.<sup>4</sup>

What goaded them into action, besides the urgency of the Raleigh outbreak itself, was their knowledge that a colleague, Dr John Kolmer of Temple University, Philadelphia, was quietly working on what he considered a superior answer -- a vaccine made from a chemically weakened live virus. Two days after Brodie and Park publicly revealed their achievement, Kolmer announced he had successfully tested the new vaccine on himself, his own children and forty-two others. Confident of his product, Kolmer pressed ahead with plans to administer it to 12,000 children in various parts of the country.

This was the unleashing of the vast competitive forces which were to shape the politics, economics and even the science

of polio vaccination for the next twenty-five years, to drive its pioneers at an always-relentless and occasionally reckless pace as they vied with one another for the prize of producing the first effective vaccine. Thrusting them onward was the giant machinery of public expectation, the fascination of the media, the interest of politicians like Roosevelt, the huge commercial windfall from the sale of millions of doses of vaccine which pharmaceutical firms were now beginning to anticipate, the promise of fresh scientific funds, the urgings of their peers, the lure of discovery, the dream of saving lives and the lustre of personal glory.

In the wake of these first bold experiments twelve of the treated children became paralysed and six died. Whether the vaccines were to blame, or whether the children became infected with wild strains of poliovirus against which the vaccines gave no protection is unclear. At that stage no-one was even certain how many different strains of polio existed.

Nevertheless, at an emotion-charged meeting of the American Public Health Association in November 1935, Dr James Leake of the United States Public Health Service, whose investigations had convinced him the vaccines were to blame, passionately accused the researchers, according to one account, of murder. In the rather more discreet official record, he addresses Kolmer crying "I beg of you, Dr Kolmer, to desist from the human use of this vaccine".<sup>5</sup>

Rising to his feet, Kolmer replied with great dignity: "Gentlemen, this is one time I wish the floor would open up and swallow me." A bitter Park retorted "It looks as though, according to Dr Rivers, my vaccine is no good, and according to Dr Leake, Dr Kolmer's is dangerous."

The vaccines were recalled and destroyed. Destroyed too were the reputations of the men who had made them. Maurice Park abandoned his work in disgrace and died heartbroken in 1939. Brodie lost his job at New York University Medical School. Kolmer returned to his post but moved on to other fields of research. The outcome of this minor disaster was to bring a virtual halt to work on polio vaccines for the next fifteen years, and to cast a long shadow over what was to follow.

Today vaccination for many diseases is so universal it is easy to forget that until World War II only three truly effective antiviral vaccines had been developed -- Edward Jenner's original smallpox vaccine, which first emerged in the late eighteenth century, Louis Pasteur's rabies vaccine and Max Theiler's yellow fever vaccine. It is also easy to forget that vaccines have since

saved many more human lives than all the antibiotics and other drugs put together.

The post World War II period was indisputably the Arcadian age of modern medicine: scientific and surgical advances came in rapid succession, breakthroughs against previously intractable ailments were headline news, and antibiotics radically altered the pattern of human mortality. Before their advent forty per cent or more of deaths in developed countries were attributable to bacterial infections -- afterwards, fewer than ten per cent.

To many it seemed as if there was no condition which medicine, household hygiene and public health could not ultimately defeat if the will was strong. In a world wearied by inhumanity and slaughter, this vision ignited a global explosion in medical research prompting many experiments on human subjects. Some of these carried considerable, if not extreme, risks and would be adjudged cavalier if not unethical and downright foolhardy in today's litigious and censorious age.

Yet, in the space of a few decades, life expectancy for people living in advanced societies extended by almost half. It was the age of heroic intervention in public health, in which individual preferences were firmly subordinated to the common weal with few daring to openly question or challenge measures seen to be taken in the public interest. It was also the age of medical heroes, when fame brought money and money spelt more breakthroughs.

Between Fleming and Florey, the developers of penicillin, and Henderson, Arita and Fenner who masterminded the world crusade to stamp out smallpox, there came a veritable throng of giants. Among them strode three Americans: Jonas Salk, son of a Russian immigrant garment worker, and two Polish migrants, Albert Sabin and Hilary Koprowski. All three were of Central European extraction, gifted with high intelligence and powers of insight, perseverance and lateral thought beyond most of their fellow researchers. Between them a fierce rivalry, at times bordering on antipathy, developed.

The choice faced by vaccine developers of the 1950s was whether to use a preparation of highly potent but killed virus, in the hope that its molecules would provoke sufficient of an immune response to give protection -- or to use a live attenuated (weakened) strain, which would certainly confer protection provided it did not revert to its former virulence. The goal was made more complicated by the fact that there was not one, but three strains of poliovirus, which meant that, to be of any lasting value, a vaccine had to offer protection against all three. Also, until

this time it had been immensely difficult for researchers to grow, extract, prepare and purify the virus. Laboratory accidents were frequent and being a vaccine researcher meant that your life, health and wellbeing were constantly on the line. It was not a profession for the faint of heart.

The production problem was solved in 1948 when American John Enders first grew polio virus in a tissue culture made from human foreskin cells at the Boston Children's Hospital - a feat which ultimately gained him and his co-workers a Nobel prize. Others soon adapted his technique using monkey cells. It was one of the great dividing moments in history, a watershed which made possible the defeat of a wide range of common diseases, so liberating humanity from the main constraint to population growth under which it had laboured for millennia. Coupled with the invention of the electron microscope this meant that, for the first time, viruses could be cultured in human cells and could be identified by appearance. Their patterns of infection and the damage they inflicted could be closely studied. It was the foundation of modern virology.

The ability to grow alien viruses in human cells and human viruses in animal cells may also have been a watershed in another sense: it opened up a completely new avenue by which viruses could pass from one species to another provided they had the genetic wherewithal to make the necessary adaptations. It was a back door into humanity.

Enders made a second discovery which was nearly as important: he resolved the longstanding argument about how polio was transmitted by showing it was really a gut disease which entered via the mouth and did not exclusively infect the nervous system after travelling via the lungs, as many researchers had supposed. This closed off several blind alleys up which polio workers had long been labouring, clarified their thinking and laid the groundwork for its defeat. Of equal importance was the discovery, by yellow fever researcher Max Theiler, that a weakened (attenuated) strain of polio virus could be created by passaging it successively through laboratory mice. The result was a virus which had the power to infect and immunise -- but not to paralyse.

The idea behind attenuation was to reproduce artificially what tended to happen naturally over time to the virus in a host population: a depletion of its virulence, or ability to cause serious disease. The introduction of measles into Spain by the Moors in the eighth century is a good example of this process: to begin with the contagion was highly virulent and very deadly, cutting great



swathes among the European populace who had not been exposed to it before. After a century or so, however, the virus lost its virulence and became much as we know it today -- an unpleasant but seldom lethal childhood disease which still infects most people, but to which they develop immunity early on. Theiler demonstrated polio could be weakened by passing it through successive generations of mice, so artificially accelerating the normal process by which a virus adapts to its host. The idea was that a weak live vaccine would not only protect those who received it, but also be harmless for those who might accidentally be infected through contact with the vaccinees. The great uncertainty in this process was whether the virus would revert to a more virulent and dangerous form while passing through one of its new hosts, and thus help to spread deadly strains of polio among those infected by accident.

These momentous advances by Enders and Theiler flagged the start of a dramatic race between competing teams of researchers and laboratories to be first to develop a truly effective, safe and cheap polio vaccine. They were egged on in their endeavours by the extraordinary public enthusiasm and high expectations which had been generated by the March of Dimes. Ordinary Americans had put their hard-earned dollars on the line, and, abetted by the media, they were vitally interested in the outcome which they saw as saving the lives of their children.

Quick off the mark was Jonas Salk. Son of a migrant, Salk had attended New York University Medical School during the 1930s, where the disgrace of Brodie and Park no doubt left a deep impression on him. During the 1940s he worked mainly on influenza at Michigan University. Then in 1947 he moved to the University of Pittsburgh, becoming Professor of Bacteriology in 1949 and adopting the new techniques described by Enders. Like Brodie and Park, he was committed to the notion of a killed vaccine. Salk's first undertaking was to find the most potent strains of poliovirus he could and neutralise them by immersion in formaldehyde for up to thirteen days. This gave him, in theory, a generous safety margin as he was unable to discover live virus in the preparation after three days and concluded that by six days it would be 100 per cent safe. With the panache that so often characterised these great researchers, Salk injected himself and his three sons with the killed virus, with no ill effect.

To test its efficacy, Salk then injected the killed virus into sixty-nine children who had already been stricken by one strain of polio, inmates of the D.T. Watson Home for Crippled Children in

Leetsdale, Pennsylvania. He then monitored their antibody levels to see if they had developed immunity to the new strain. Sixty of the children showed evidence of protection. Encouraged by these results, Salk then extended his trial to a home for mentally retarded children at a state school in Polk, Pennsylvania, where, once again, the antibody results proved highly encouraging. Better still, not a single child suffered any form of polio subsequent to receiving the vaccine.

Greatly heartened by this evidence of success, Salk's supporters pressed for a large-scale field trial in the face of objections from other quarters. Those who protested included Enders and Sabin, who argued that the killed vaccine would prove ineffectual because it was the wrong type, and also there was evidence that some live virus might survive the killing process. Pressure for a major trial was augmented by a premature report of the success of the research which leaked into the press, much to Salk's irritation, and which prompted a flood of public donations to the National Foundation for Infantile Paralysis (March of Dimes) along with cries for the new vaccine to be released as soon as possible.

The unworldliness of the dedicated scientist was seldom more plain than in Salk's demand for a special press conference in which he proposed to put the case for more time. He spoke with great modesty and caution on both radio and television -- and managed to achieve precisely the opposite effect to what he had intended. The media and public became instantly infatuated with the image of the modest, cautious scientist, hailed him as their hero and redoubled the pressure on him to release his vaccine. Salk had become a prisoner of his own publicity.

With the foundation also breathing down his neck for a public proof to sustain the vast money-raising enterprise it had become, Salk finally relented and arranged for a huge trial involving 400,000 children across the United States to take place in early 1954. The results were spectacular, with 80-90 per cent of them developing immunity. This success gave Salk the confidence to advocate an even larger trial involving the vaccination of nine million children from April 1955 onwards -- one of the epochal events in modern medicine.

"To the millions of people who, in the darkest years of the great depression, had contributed dimes, then dollars, and had given years of their lives to help the March of Dimes to collect hard-earned contributions from ordinary concerned people like themselves, the announcement that those dimes and dollars had

yielded a safe vaccine which would protect their children and grandchildren against polio was possibly the greatest moment in American life since the end of the killing in World War I," Allan Chase recorded.

"Now, as in November 1918, church bells and, in many cities, trolley bells and factory sirens hailed the development, the testing and the licensing of the Salk vaccine as the great step forward for humankind that it was."

Expectations of the prodigious benefits promised by the new technology were so high that NFIP president Basil O'Connor placed orders with pharmaceutical companies for twenty-seven million doses of the vaccine, even before the results of a careful analysis of the outcome of the first major field trial were in. The authors of the report were stampeded into an early release of their findings which were emblazoned across the nation in newspaper, radio and television headlines by a horde of news hounds who raced to the telephones in a frantic battle to break the embargo. In this way an air of terrific drama and emotion built up surrounding the forthcoming trial, exacerbating the problems faced by the vaccine manufacturers who were struggling vainly to meet the NFIB's deadline against multiplying quality-control difficulties.<sup>6</sup>

Less than a week into the campaign disaster struck: reports came from California of children becoming paralysed within days of vaccination. In all, two hundred and four vaccinees or their contacts were infected. Eleven died. Other reports of paralysis started to flow in from Idaho, Georgia and Louisiana. The public began to panic. A frantic investigation traced the main problem to a single source, Cutter Laboratories in Berkeley, California, which had prepared part of the batch under inadequate filtration, permitting live virions to clump together and so survive the formalin and get into the vaccine. But the fault was not Cutter's, for they had closely followed Salk's recommendations.

Triumph turned to terror as a major media-scare ensued. In the end much of the blame was sheeted home to the unseemly haste with which the NFIP had urged the trial. Safeguards were immediately put in place and after vigorous argument in which he pointed out that none of the other batches of vaccine produced by Cutter or other laboratories had caused a single case of polio, Salk persuaded the Congress and health officials to press ahead with the trial. Seven million children were injected -- without any further sign of disease. In fact, over the following two years 200 million doses of the Salk vaccine were administered in several countries without a single case of paralysis and accompanied by a dramatic

fall in the incidence of polio in all cases.

American children alone were spared some 16,000 cases of paralytic polio in the year following the trial as a result. In Sweden and Finland, the disease had totally vanished by 1962. But in the longer run the results were seen to be less than perfect: cases of paralytic polio began to crop up, with increasing frequency, even among populations largely protected by the vaccine.

In spite of Salk's success, some scientists considered that a live vaccine would prove far more effective. Their arguments were technical but, broadly, it was felt the killed vaccine did not protect a high enough percentage of recipients, it needed at least two booster shots making it both cumbersome and costly to administer, it did not provide gut immunity, which meant that immunised people could still act as carriers of infection to others, it was dangerous because of the extreme potency of the strains used, it was unstable and needed to be kept refrigerated at all times, and it was expensive. For these reasons they continued to work quietly away on the ideal of a live, attenuated vaccine.

In the vanguard of the field were Herald Cox and Hilary Koprowski. Cox was the director and Koprowski assistant director of viral and rickettsial research at the Lederle Laboratories of the giant American Cyanamid Company. One of the leading chemical and pharmaceutical enterprises in the United States, indeed the world, Cyanamid's activities at the time encompassed everything from synthetic fibres to antibiotics and fertiliser to plastics. But its biggest and most profitable division by far was Lederle, originally an independent pharmaceutical concern set up in 1906 and acquired by Cyanamid in 1935. Its success was largely founded on the enormous boom in antibiotics which had eventuated since World War II, and on an unwavering commitment to excellent research and development.

The Pearl River, New York, laboratories where Cox and Koprowski worked were "of a most impressive size and scope. The buildings might easily be mistaken for those of a university, were it not for the Lederle flag flying above them and the fact that the whole area is completely sealed off by means of a high wire fence, with policemen at the gate at the only entrance. It is impossible to get in without a pass, but once you do, the atmosphere is idyllic," a contemporary account rhapsodised. "The Administrative Building is clean red brick, pleasantly proportioned, with a green campus stretching around it for acres. The production plant is cleverly hidden behind it. There are ponds with ducks on them. The research buildings are dotted about the

campus, of varying age, some stone built and covered with ivy, others of more modern construction...one of the largest of these buildings houses the Virus Research Department."<sup>7</sup>

Cox and Koprowski had been quietly exploring the potential for a polio vaccine since 1946. Fascinated by Theiler's discovery that polio virus could be artificially weakened by passing it through mice, they set out to improve on his work by producing two attenuated strains which they repeatedly passaged through cotton rat brains. On the strength of highly promising results, they persuaded Cyanamid that a live polio vaccine was a goal well worthy of pursuit -- a goal in which the company was ultimately to invest the astounding sum of \$US13 million. From this point on the principal challenge was to devise tests rigorous enough to ensure the safety and stability of the attenuated virus. It was no easy task.

Born in the Polish capital, Warsaw, in 1916, Koprowski matriculated from the Nikolaj Rej Gymnasium of the Lutheran Congregation then went on to study medicine at Warsaw University. A youth of rare ability he also trained as a concert pianist, first at the Warsaw Conservatory of Music and then Santa Cecilia Academy in Rome, before deciding that his heart lay in science and accepting a post as research assistant in Warsaw University's Department of Experimental and General Pathology. In 1939, sensing the import of the gathering war clouds, he emigrated, working first at London's Lister Institute then on the staff of the Yellow Fever Research Service in Rio de Janeiro, where he served for much of the conflict. In 1944 he joined the American Cyanamid company in 1944 to work in its famous Lederle pharmaceuticals laboratory at Pearl River. There, at the remarkably youthful age of twenty-eight, he was promoted to be Lederle's assistant director for viral research under the gifted yet self-effacing Cox.

To those who knew him, Koprowski was an impressive individual of formidable scientific gifts bordering on brilliance, coupled with a great personal charm which was reflected in his cosmopolitan manner, eloquence and wide erudition. An extrovert, he was by no means averse to parading his intellect in his scientific presentations, sprinkling them liberally with quotes from the classics, philosophers, playwrights and novelists in French, English, German and Italian. Besides his native tongue and English he was fluent in Spanish and Portuguese. Though his home and car were modest, as if in faint disdain of materialistic American culture, his social converse was rich in fields such as music, art, literature

and travel. In a sphere liberally endowed with egos, Koprowski was no shrinking violet: "If his self-confidence seemed at times a little overpowering, it was at least founded on an impressive record of achievement," one chronicler recorded.<sup>8</sup>

On 27 February, 1950, Koprowski claimed a world-first by feeding a naturally attenuated live poliovirus to a six-year-old boy in a mental institution, Letchworth Village, run by the New York State Department of Mental Health.<sup>9</sup> When the child did not become ill after forty-four days, the virus was administered to a second child, and then to eighteen more. In all cases it proved harmless. The conditions of absolute secrecy under which the trial was carried out underscored not only the sensitive character of the experiment but also the immensity of the financial windfall which big pharmaceutical firms could scent if a vaccine were to be successfully developed.

At a meeting of the NFIP immunization committee held in chocolate town, Hershey, Pennsylvania, one year later on 15-17 March, 1951, Koprowski disclosed his achievement to the scientific world for the first time with the theatrical flair that was to become his hallmark. Asked by the chairman, Dr Paul, whether he had any data to present he took the floor, responding, "The data I want to acquaint you with represent a summary of clinical trials based on oral feeding of children with TN strain of polio (living virus)...Twenty children and two adults were fed the TN virus...In many instances the infectious material was mixed with milk and 5% glucose or chocolate milk and sometimes it was given on a spoon."

The sweetener was given to disguise the flavour of the vaccine which "tasted like cod-liver oil and was in fact a suspension of cotton-rat cord and brain tissue which had been recently infected with three million mouse lethal doses of the TN strain".

"This represented the first successful trial of immunization of man against poliomyelitis," Koprowski later declared. "Because of its nature, knowledge of this trial was at first confined to Dr Jervis, Mr Norton and myself. No-one else knew of the study during the period between February 27, 1950, when the first child was fed the virus and late January, 1951, when observation of the first series of 20 subjects was nearing completion and preliminary evaluation of the procedure indicated that it was harmless."<sup>10</sup>

News of the experiment caused a sensation. Koprowski later recalled: "I reported just after lunch, and everyone was somnolent. Tommy Francis listened to me droning away and said

to Jonas Salk, "What's this - monkeys?" and Salk answered "Children!" Francis sat up and gasped "What?" Albert Sabin got all perturbed and said to me later, "Why have you done it? Why? Why?"<sup>11</sup>

If the move was deemed by some of the polio pioneers to be premature, it certainly awoke them to the seriousness of the competition which was now brewing -- and established an experimental precedent. The following year Salk himself conducted his first human trials with his killed vaccine on polio victims at Leetsdale Home for Crippled Children and on mentally-retarded children at Polk state school.

Koprowski's vaccine was subsequently tested on other groups of mentally-retarded children at Sonoma State Home in California and elsewhere in a series of trials which seem ethically questionable by today's standards. But as author Allan Chase pointed out: "The prevailing and very eugenically oriented American medical ethics of the first half of this century considered mentally and physically handicapped children to be desirable subjects for medical experimentation."<sup>12</sup> To this should be added the fact that, in the past, mental asylums were hotbeds of polio infection, owing to the fact that among their inmates excrement was frequently the missile of choice for the unambiguous expression of displeasure, disagreement or sheer exuberance. They were therefore a suitable place both to attempt protective vaccination and to field-test its efficacy. And finally, as Koprowski himself later observed, the experiment had to be done and somebody had to do it.

Nevertheless, even in those robust days a few were perturbed by the ethical issues. Rockefeller Institute director Rivers observed tartly, "An adult can do whatever he wants but the same does not hold true for a mentally defective child". What was acceptable in pre-war America was no longer so readily tolerated: by the start of the 1950s, world conscience on the issue of medical experimentation was undergoing rapid revision, having been acutely pricked by the disclosures at the Nuremberg War Crimes trials of the wicked and inhumane arts practised in the Nazi concentration camps.<sup>13</sup>

When he reported his success in the *American Journal of Public Hygiene*, Koprowski dealt obliquely with the issues, referring throughout to his subjects as "volunteers". This provoked a coyly satirical response from the editor of *The Lancet* who observed "One of the reasons for the richness of the English language is that the meaning of some words is constantly changing. Such a word is "volunteer"." In future scientific reports, he

speculated, one might well read about "volunteer mice". Others were more unsettled: nearly a decade later Koprowski was still directing scornful retorts at individuals rash enough to question his principles.

At the time, however, there is little doubt that Koprowski was seized with the urgency of the challenge and the importance of saving as many lives and preventing as much misery as possible. In a paper ornate with literary allusion published a decade later he recounted his achievement, identifying the various phases of his work with the twelve labours of Herakles. Attenuation of the virus to a non-dangerous condition he compared with subduing the Ceryneian hind, evaluating field trials with garnering the golden apples of the Hesperides. The stage which involved purging the vaccine of virulent strains of viruses he likened to the cleansing of the stables of Augeias. Justifying the presumption of contrasting his own achievements with those of a Grecian demigod he quoted Fabr : "History records the names of royal bastards, but cannot tell us the origin of wheat." Koprowski clearly was of a mind this should not be the case with polio vaccine.<sup>14</sup>

Finally, in a dart aimed at rivals who had challenged the safety of his vaccines and which exemplifies the bitterness of the professional enmity prevailing during those early days, he concluded "The history I have just given of the development of live virus vaccine is my attempt to 'tell you the origin of wheat'. I should not be surprised, however, if you at some time or other hear a different version, put forth by those scientists who follow Schopenhauer's advice on merit: "There are two ways of behaving in regard to merit: either to have some of one's own, or to refuse any to others"."

But the early lead which Koprowski had opened up over his competitors in 1951 was fated to evaporate in a startling and distressing manner. To begin with, Salk, financially backed to the hilt by the March of Dimes and fortified by a blaze of publicity, had already launched into major field trials. Secondly Koprowski was starting to have disagreements with his superior, Cox, over the best means of growing the virus. Cox was convinced that chick embryos were the most economical and productive method, whereas Koprowski was an acolyte of Enders' view that monkey kidney tissue and human embryo tissue were superior. At the same time he was also extremely anxious to widen his trials beyond the United States to places untouched by the Salk vaccine and had been on the lookout for a suitable site for several years.

In 1956 he was delighted to receive an offer from George



Dick, Professor of Microbiology at Queens University, Belfast, in Northern Ireland, to conduct a limited trial on his behalf. Northern Ireland was a clever choice because it meant the experiment could be run under tightly controlled first-world medical conditions, but could sidestep the red tape that would impede it in England or other developed countries. The Lederle laboratory at once set to work to furnish sufficient vaccine, and the trial was constructed according to the most rigorous principles.

Dick first tested the vaccine to ensure it was as Koprowski claimed, then dosed himself, his staff, some student volunteers and finally a group of children, in all 206 individuals. He then analysed the results with meticulous care while Koprowski waited impatiently for news.

When it came, it was with all the shock value of a bucket of ice water. Although none of the subjects came down with polio, their stools contained large amounts of a markedly virulent virus which caused paralysis in the monkeys it was tested on and accidentally infected an adult and a child. Dick's damning results appeared in the *British Medical Journal* where there could be no avoiding them. Koprowski hastened to Europe, seeking to allay the concerns of the British doctors in a meeting at the Savoy Hotel, but Dick remained adamantly opposed to the vaccine. The disastrous outcome to the trial appears to have further strained relations between Koprowski and his superior, Cox, and shortly afterwards Koprowski quit Cyanamid to assume the position as director of the prestigious Wistar Institute of Anatomy and Biology, taking with him several of his highly skilled staff.

The result of this dismaying episode was to set back both Cox and Koprowski, obliging each to rebuild his research program virtually from the ground up, developing fresh strains. In the meantime, Jonas Salk had assuaged public doubts about his killed vaccine and was basking in the warmth of international acclaim, while the meticulous tortoise of this tortoise-and-hare contest, Albert Sabin, quietly slipped into pole position in the race to develop a live attenuated vaccine.

Sabin had already earned himself a measure of notoriety in the wake of the Cutter Incident, when he had publicly urged the abandonment of the entire Salk program on the grounds that the virus used was far too dangerous. Given that he was engaged in a competing project, some colleagues were inclined to dismiss this as sour grapes. Nevertheless, Sabin had already earned a reputation as a scientist of the highest principle and exacting standards and was not an easy person to ignore.

Born in Bialystok, Poland, in 1906, Albert Bruce Sabin had migrated to the United States with his parents at the age of fifteen and, like Salk, studied medicine at New York University before joining the Rockefeller Institute of Medical Research. From there he moved to Cincinnati University where he was appointed Professor of Pediatrics. His genius had already emerged in his discovery of the herpes B virus and early work on a vaccine for dengue fever.

Sabin was convinced that a live polio vaccine would offer greater protection than Salk's inoculant and had been working quietly away on one for a number of years with limited support from the NFIP. Among its advantages were the capacity for it to be administered by untrained staff such as nurses or teachers acting under supervision, that it was cheaper to make and that it spread immunity to non-recipients of the vaccine through mild infection to produce the so-called "herd immunity" which is so vital to the successful immunisation of a community. In 1956, at the pinnacle of Salk's triumph and Koprowski's discomfiture, Sabin emerged from the shadows with the news that he had successfully vaccinated 133 people with attenuated strains of *all three* kinds of polio, grown in cultures made from monkey kidneys.

However, with America committed to the Salk vaccine -- the use of which would in any case interfere with the proper field evaluation of a new inoculant -- and the public still wary of the risks inherent in such massive experiments, the big question was where could he conduct his trial? Sabin opted for an audacious and imaginative scheme, given the politics of the day and his own ethnic background: a mass trial in the USSR with the backing of the Soviet government, as well as seven other countries. In Russia neither the finding of volunteers nor sufficient manpower to perform a trial on the largest scale were liable to pose much of a problem. Obtaining enthusiastic Soviet approval, Sabin teamed up with Dr Valentin Soloviev and by 1959 was able to document the results of more than 4.5 million vaccinations which had been carried out in perfect safety, and without any reversion to virulence on the part of the virus. So vast was the success of this campaign that by the end of 1960 polio was virtually extinct in the USSR and Eastern Europe.

Soloviev and Sabin proclaimed their triumph at the International Scientific Congress on Live Virus Vaccines in Washington in June 1959, co-hosted by the World Health Organisation and the Pan-American Health Organisation. The effect was galvanic: from this day forward the Sabin oral vaccine

was destined to sweep the board as the world's polio immunogen of choice and was finally adopted, after much learned argument, by the United States itself in 1961.

Koprowski's determination to develop an effective live attenuated vaccine was in no way diminished in spite of his discouraging setback over the Belfast trial. For the past few years he and Sabin had been in virtual lock-step as the rivalry between them intensified. Now installed at the Wistar Institute, he threw his protean energies into attenuating other polio strains descended from the ones which had been so harshly criticised by Dick, finally arriving at one designated CHAT-1. (CHAT was apparently derived from the surname - Charlton - of the child who produced the virus, an inmate of Sonoma State Home in California. 1 stood for type one polio.<sup>15</sup>)

CHAT-1 was the offspring of Koprowski's original SM strain which had been attenuated by intraspinal passage in mice, and then fourteen serial passages in chick embryos at which point it had been fed to humans. The virus excreted by these human guinea-pigs had been passaged four times in humans and then had undergone five successive passages in monkey kidney in order to fully deplete its virulence. The virus was then injected into the brains of monkeys and spines of chimpanzees to see if it produced lesions, a sign that it was still potent enough to infect the nervous system. It did not. The result was "a remarkable degree of attenuation".

Even had it shown some tendency to revert when tested in monkeys, Koprowski was not convinced this constituted a serious objection to its use. At a meeting of the New York Academy of Sciences in 1957 he expounded a hypothetical case: "Let us again play at *advocatus diaboli* and let us suppose, for instance, that an increase in virulence for intracerebrally injected monkeys should occur in the course of transmission from man to man. Are the conditions changed thereby in endemic areas? These represent vast sections of the world. What actually would take place in this very improbable and hypothetical case is that one more strain would be added with properties not much different from those of the viruses already present and prevalent in endemic areas, areas in which "wild" poliomyelitis viruses, virulent for monkeys, are more often than not recovered from asymptomatic children."

Koprowski's case was far from hypothetical. He had already decided, nearly two years earlier, to attempt a mass trial in Africa. Its initial phases were already under way.

Characteristically, he opened his address with a delicate

barb directed at his arch rival: "Sabin's excellent presentation reminds me of the description of John Donne's greatness by C.S.Lewis in his *English Literature in the 16th Century*: "These diverse excellencies are usually held together by Donne's adoption of the role of pleader - by his argument. The argument may be on different levels... fanciful... or serious." Since most of Sabin's arguments were, I hope, in the serious category, in equally sober mood I shall try to present, for comparative purposes, some of the results of our work..."

Characteristically, too, he concluded his address with a literary flourish, in this case from the philosopher Bertrand Russell: "There are, I think, several factors that contribute to wisdom. Of these I should put first a sense of proportion: the capacity to take account of all the important factors in a problem and attach to each its due weight".

But Koprowski unaccountably qualified this sage counsel with a flippant piece of homespun philosophy: "As for the rest -- "you pays your money and you takes your choice"."<sup>16</sup>

## Endnotes

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<sup>1</sup>Wyatt H.V., *Cambridge World History of Disease*, Cambridge University Press 1993, pp942-949

<sup>2</sup>Chase A., *Magic Shots*, Wm Morrow & Co 1982, p278.

<sup>3</sup>Gould A., *A Summer Plague: Polio and its Survivors*, Yale University Press, 1995

<sup>4</sup>Chase A., op. cit.; Gould A., op. cit.; and Fisher P.J., *The Polio Story*, Wm Heinemann Ltd, 1967.

<sup>5</sup>Ibid.

<sup>6</sup>Fisher P.J., op. cit.

<sup>7</sup>Wilson J.R., *Margin of Safety: the poliomyelitis vaccine story*. Collins 1963, pp 135-6

<sup>8</sup>Ibid., p139.

<sup>9</sup>Elswood B.F., Stricker R.B., Polio Vaccines and the Origin of AIDS, *Medical Hypotheses* 41, 1994 pp347-354. Also Chase A. op cit. Also Wilson J.R. op cit. Also Curtis T., 1992 q.v.

<sup>10</sup>Koprowski H., Historical Aspects of the Development of Live Virus Vaccine in Poliomyelitis, *British Medical Journal*, July 9 1960 ii pp85-91.

<sup>11</sup>Koprowski H., Vaccination with Modified Active Viruses, Poliomyelitis: *Papers and Discussions, Fourth International*

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*Poliomyelitis Conference 1957*, p122. Cited in Gould H., op cit, p125.

<sup>12</sup> Chase A., op. cit. p295.

<sup>13</sup> Paul J.R., *A history of Poliomyelitis*, Yale University Press, 1971, p452.

<sup>14</sup> Koprowski H., *Special Publications of the New York Academy of Sciences*, 1957, p128

<sup>15</sup> Hooper E, *The River*, Penguin, 1999, p419.

<sup>16</sup> Koprowski H., *Special Publications of the New York Academy of Sciences*, 1957, p133.

## War on a Killer

In terms of disease, Africa in the 1950s was still the dark continent. Its jungles, savannas and river valleys harboured a festering multitude of afflictions which constantly felled its native inhabitants and foreigners with impartial spite: malaria, bilharzia, blackwater fever, yellow fever, amoebiasis, elephantiasis, trypanosomiasis. From among the ranks of pathogens with which it had traditionally scourged humanity, every so often it managed to throw up something new and especially hideous. Medically speaking, it was the last frontier.

The Belgian Congo, the modern-day Republic of Congo and formerly known as Zaire, is the belly of Africa. Its glittering-dark girdle is the mighty Congo River, draining a basin more than three and a half million square kilometres in extent, its waters stained with the fecund silts of the scarp and the rainforest. Surpassed in its flow only by the Amazon, the Congo at its flood peak flushes almost two million cubic feet of water to the sea each second. To the lordly river hundreds of great and thousands of lesser streams add their tribute, a sprawling skein of bright waters which in the level heartland combine to produce one of the most navigable and readily traversed regions in the world -- an aquatic highway network unmatched by man-made roads. Embracing this immense, shallow amphitheatre a series of escarpments rise like giant steps down which the rivers plunge and race. Through the western wall of the bowl the Congo has carved its outlet to the sea, thundering in its final few hundred kilometres down the Livingstone and Inga Falls to dissipate its energy in a torpid, swampy estuary.

The climate of Central Africa is perfect for the cradling of new forms of life: warm, wet and biologically opulent. Over much of the Congo catchment sprawls a verdant evergreen rainforest which annually flushes its humic black waters into the river system. Beyond this rules the lordly gallery rainforest, and beyond that the dry forest takes charge of the landscape. From its outer fringes the savannas roll in tawny profusion, sparsely decked with wizened trees, an open country bearing the scars of ten thousand years of slash-and-burn farming. To the east the basin drops into the Great Rift Valley, birthplace and fountainhead of humanity. To the south the Shaba hills of Katanga gleam with the earthen tints of copper, cobalt, managanese, zinc and tin, and the magpie glitter of gold and diamonds.

The eastern part of this region, and probably much of the centre, has been inhabited by humans and proto-humans for four million years. Its valleys, mountains and arid plains formed the anvil on which our kind was shaped. It saw the human and chimpanzee genera divide and go their separate paths. It witnessed the first hesitant bipedal steps of a hominid child, watched *Homo habilis* shape his rudimentary implements in Olduvai, and saw the gradual rise of social order, language and a co-operative division of labours that soon lofted the new species far above its origins. It observed the birth and flourishing of *Homo erectus* and their craftsman-like Acheulian culture, the eruption of fully modern humans bent on world conquest 120,000 years ago, the advent of primitive cultivation and finally, about 10,000 years ago, the origins of farming and the practice of a new mode of economics that was to transform the face of the earth.

The early farmers of Africa discovered that when a piece of the wild white yam was discarded, very often it regenerated into a new plant -- and that this miracle could be performed to order. It was the first faint pulse in the tidal surge that was to become the human population explosion. At the time that modern people forged their way out of Africa the entire population of the earth may have numbered no more than 10,000 hunters and gatherers. With the dawn of agriculture these numbers swiftly grew to millions. The great river valleys of Central Africa, along with the Middle East, India and China became regional epicentres of the rolling human explosion.

In Africa the farming of the yam was followed by that of the banana, a plant rich in culinary potential and other uses, and then by millet. The art of fishing grew contemporaneously and the "fish stew revolution" brought with it not only protein but also technology, in the form of artistically decorated earthenware. These innovations brought about the rise of settlements as the Africans, like their hunting counterparts in Europe and China, discovered the food supply could be more readily sustained by farming and fishing than by the chase. And villages led inevitably to the complexities of social order, politics, religion, trade and warfare.

That great migrations and social interconnections also took place in prehistoric times is known from the spread of the Bantu languages out of West Africa and into the Congo basin more than 2000 years ago. Bantu was the lingua franca of trade and was probably disseminated largely through the marketplace. Although some of the region's indigenous tribes, like the pygmies, for a time

clung determinedly to their own tongues and cultures, regular exchange of forest goods for the manufactures of village society soon eroded even these linguistic islands, illustrating that even in the heart of the Congo, no groups were truly isolated.

The advent of the iron age, some time around 2500 years ago, brought with it the same revolutionary changes in African society as elsewhere. Percolating down the Nile from Egypt, iron not only raised technological skills but gave superior weapons to the warrior and hunter and tools to the farmer. It was not an innovation which any group could, or did, ignore, and the iron masters of Central Africa were revered with an almost superstitious awe. There had been no earlier copper or bronze age in the Congo, so the metals epoch arose full-fledged with the advent of iron. Copper, in particular, became a source of gorgeous adornment for both the living and the dead, and lent its resonant music to African ritual and ceremony.

The spread of metal encouraged the growth of trade. Soon communities in every corner of equatorial Africa were exploring their local resources to see what they had which might be valuable enough to exchange for the substances they lacked but coveted. Salt from both east and west coasts was traded to agricultural dwellers in the heart, becoming a source of wealth and power to tribes such as the coastal Kongo, who controlled it. Dried fish provided valuable stored protein and were traded far beyond the rivers and lakes where they were caught. Textiles and raffia were highly prized as storable or transportable wealth and as a bride-price in a society whose cultural response to the hazards of inbreeding was to encourage its young men to seek spouses from distant clans rather than locally. In this way small communities often hundreds of kilometres apart became linked by a complex web of blood ties.

For centuries the political landscape of Central Africa remained local, based on villages and communities rather than states or empires. However in the fifteenth century the outside world finally intruded with a vengeance: Arab slavers arrived from the north and east, and Europeans from the west. In the 1470s a Portuguese sugar settlement on the offshore isle of Sao Tome became so profitable to its investors that it established the precedent for the vast, brutal trade in human misery that was to found the Americas. In 1565 the Portuguese launched an expedition of 600 musket-armed conquistadors which vanquished the ancient kingdom of Kongo, overthrew its monarch and commenced to mine its human ore. The Portuguese were followed by eager Spaniards, Dutch and French in succession, and no part of the Congo basin,



even the most remote of the rainforest dwellers, remained untouched by the voracity of their demand for ivory, slaves and precious substances. In the centre, empires arose to satiate this cruel new appetite.

The once-numerous population of the Congo region dwindled sharply due both to the rapacity of the slavers and to the diseases which the trade helped to disseminate: smallpox, measles, yellow fever, influenza and malaria. In spite of great changes in the outside world, slaving continued right up until the 1880s when the Belgians, belated last of the European powers to pillage Africa, established the notorious Free State.

The Congo Free State was created as a kind of private European gentleman's fiefdom by a group of rich investors under the patronage of Leopold II of Belgium, who became interested in the area as a consequence of the explorations of the adventurer Henry Morton Stanley between 1874-77, which he had funded. In the way of native peoples the world over, the 450 African tribal communities who signed treaties with the innocent-sounding *Comité d'Études du Haut Congo* soon discovered they had in fact pledged away their autonomy in favour of Belgian despotism.

To begin with, the deal did not seem entirely a bad one, as one of the Belgians' earliest acts was to declare war on the Arab slavers who had for generations preyed on the Congolese. However the Africans soon found they had exchanged one form of bondage for another, worse kind, as Leopold's rapacious task masters began the systematic plunder of the African heartland of wild rubber, palm oil, ivory, minerals, diamonds and gold, lashing their new subjects into submission with a brutality that became legendary. During this period alone, it is said, the population of the Congo dwindled from twenty-five million to around eight million people.

European outrage finally forced an end to these feudal excesses, compelling Leopold to cede his personal power to the Parliament of Belgium. The sadly misnamed Congo Free State was abolished and replaced by the Belgian Congo in 1908. From this time on the rule was somewhat less brutal, with indenture and forced labour replacing outright slavery, but remained highly paternalistic: the Africans were to be treated as children, trained, cared for and denied any say in their own future. During the 1950s, when Britain and France had acknowledged the inevitable and were readying their African possessions for independence, the Belgians clung stubbornly to the claim that theirs was a model colony illustrative of the parent/child relationship between Europe and Africa. This purblind opinion was adhered to in the face of an

increasingly vigorous and potent Congolese independence movement led by Patrice Lumumba which would sweep them abruptly away in 1960.<sup>1</sup>

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It was to this Africa that Hilary Koprowski came in 1955, in search of a place to test his live polio vaccine. Throughout the latter part of his time at Lederle he had travelled widely, keeping a keen eye open for a suitable trial site. He had explored the possibilities of Kenya, South Africa, his native Poland and even Tristan da Cunha, so far without success.

But Koprowski was a man of more than ordinary determination and powers of resolve. In an account of the early days of polio vaccine, John Rowan Wilson described his appearance as "interesting without being handsome, dark and of medium height, thickset and turning in middle life towards portliness. He dressed well, in a fashion certainly not American or even English, but more vaguely Continental, the trousers slightly tapering, and double-breasted waistcoats, with lapels."<sup>2</sup>

He spoke with a marked central European inflection, but in a powerful, persuasive and charming manner: "If he wished you to do something it was difficult to deny him; the reasons he gave were so good and so perfectly marshalled, and it so obviously never entered his head you would refuse. He seemed never to have a moment's doubt in the correctness of his own opinion.

"When he wished to charm, he was gay and confidential, his eyes flashed warmly, he used your Christian name like a caress, he would take you by the arm as if you and he were the only people who mattered, two superior beings in a rather ridiculous, muddle-headed world. He obviously thought so well of himself that to include you with himself in this fashion was like the most outrageous form of flattery. A warm glow went through you...it was a tremendous temptation not to disappoint him..."

Koprowski's assertive persona was exercised on groups as well as individuals: Wilson described him as an impressive speaker with a fluent and powerful delivery, a perfect command of his subject and a wide general knowledge on which he drew to make his material more interesting. "He was also surprisingly lacking in inhibitions, and had a way of attacking the capacity of his opponents which was startling by British or American standards."<sup>3</sup>

Halfway through a learned discourse Koprowski would break off and direct "a contemptuous harangue" at one or other of his rivals. Though there was no doubt that these excursions amused

and delighted many among his audiences, others "feared his gift of invective and the power of his tongue" and this may have further acidified the spirit of competition that had by now arisen amongst the polio pioneers. As with his speeches, so with his scientific papers, which were larded with literary, artistic and philosophical references, subtly needling other scientists' secret social anxiety, their lack of cultural accomplishment. In the end, Wilson speculated, such potent gifts may have worked to the virologist's own detriment, although "it was agreed by everybody that, whatever else you might think of Koprowski, he was certainly a remarkably clever fellow."

Koprowski had served in the tropics and he understood how primitive the health services and clinical treatments available in these vast regions were, and also how acute was the human need. He knew the nature of the pestilences with which the equatorial regions flayed humanity. Profoundly challenged by the task of overcoming them, he was fearless of any personal consequences.

Testing a new vaccine is not easy. After small-scale trials on animals and people to determine its safety and efficacy, the only real way to establish how much protection it confers is to conduct a mass experiment in the field involving thousands of people -- and then study what happens to the incidence of the disease. That was what Salk had done in the United States and Sabin was now secretly undertaking in Russia. The urgency of the contest to develop the world's first truly effective polio vaccine was bearing down on all three researchers.

For the clearest results, the trial had to be conducted in a virgin population which had never before been vaccinated and in a place where recurrent outbreaks could be expected frequently to test the efficacy of immunisation. Africa, with its perennial minor scourges of wild polio in remote areas and lack of previous vaccination history was just about perfect.

In recognition of his contribution to the development of a rabies antiserum some years before, Koprowski had been appointed to the rabies committee of the WHO, a job which gave him opportunity to rove far and wide. While taking part in a WHO rabies workshop in Kenya in 1955, Koprowski made the acquaintance of Dr T.J.Wiktor, a member of the veterinary service of the Belgian Congo, who in turn furnished him with an introduction to the director of the Laboratoire Médicale in Stanleyville, Dr Ghislain Courtois. Ever alert for a suitable testing ground for his new vaccines, Koprowski at once seized the opportunity to outline his plans. <sup>4</sup>

The government of the Belgian Congo was more than happy to volunteer its citizens for Koprowski's experiment, in view of an annual incidence of paralytic poliomyelitis which sometimes exceeded 1,450 cases. Courtois immediately agreed to help Koprowski to establish a chimpanzee farm at Lindi Camp, near Stanleyville, for the purposes of testing the vaccine.

One of the first steps was to administer the vaccine to the chimpanzees' caretakers in order, the scientists claimed, to protect them against possible exposure to the virulent strains of polio that would then be used to "challenge" the immunity levels of experimentally vaccinated animals. By his own account, Koprowski says this immunisation of the chimp minders was so successful that it "prompted us to undertake clinical trials in the Belgian Congo on a much larger scale than had been attempted so far."

It would be remarkable if the idea of a mass human trial had not occurred either to him or Courtois prior to setting up the chimp farm. Nevertheless they applied to Dr Charles Dricot, physician-in-chief to the government of the Belgian Congo and duly received authorisation for human trials "in the second half of 1957".

Official sanction may have been granted in the face of a fait accompli. Though their report in the *British Medical Journal* is vague as to exact dates of some trials, it is precise on two points: the largest mass trial commenced on 24 February 1958, and 4,228 infants, children and adults of both European and African origin had been vaccinated with CHAT-1 and FOX-3 in Stanleyville "during the previous 12 months".<sup>5</sup>

From the information presented by Courtois, Koprowski and others it is reasonable to infer that vaccination of the first Africans (the chimp minders) may have taken place as early as 1956 and the first trial mass vaccination campaign may have begun in Stanleyville (modern Kisangani) as early as February 1957. Formal authorisation to proceed with the trials was not granted until later in 1957.

The CHAT-1 and FOX-3 strains of virus were selected for the trials, as they represented the strains of polio most prevalent in the region. The pools of vaccine were prepared in the laboratories of the Wistar Institute, Philadelphia, and tested for lack of virulence by injecting them into the brains and spines of rhesus monkeys and chimpanzees. To test for the presence of other dangerous viruses, the vaccines were also injected into rabbits, infant mice, guinea pigs and adult mice and careful tests performed

to ensure sterility. As a final test of the vaccine's efficacy, it was administered to a small group of infants and adults in the United States, probably at the Philadelphia Children's Hospital.

Temporary vaccination stations were established near clinics, schools or other centres, often under canvas, and long lines of Africans were martialled beneath the beating sun and swarming flies to receive their allotted dose of live virus. This was administered to them either as a capsule, by squirting one millilitre into the mouth from a pipette, or else on a tablespoon. Since the most prevalent infection in that part of Africa was caused by polio virus type 1, priority was given to the CHAT-1 strain.

The first field trial (after Stanleyville itself) began at Aketi, a town lying north of the Congo and not far from the Ebola river. Here, 1,978 school children, mostly aged between five and fifteen, received the CHAT-1 live virus. Blood samples were initially taken to check on their immune status. Those who had initially shown no antibodies to type one polio were bled again two months later to see if they had developed protective antibodies. All except two had done so -- and none had shown any signs of illness. It was an extraordinarily promising result, repeated six months later with the FOX-3 strain. (See Map)

Then came the first real chance to show what modern medicine was made of. Between November 1957 and early January 1958, eight cases of paralytic poliomyelitis were reported from the small town of Banalia, to the north of Stanleyville. It was decided to go in and vaccinate the entire population in the face of what could be an emerging epidemic. Courtois and Koprowski were careful to state the decision was made "following the recommendation of the (WHO) Expert Committee on Poliomyelitis" and at the request of the provincial health authority. They fed CHAT-1 virus to "every inhabitant of Banalia", a total of 4,182 people.

"Not a single case of paralytic poliomyelitis was observed in Banalia following oral vaccination with the Chat type 1 strain of virus," they reported. On the face of it, a triumph -- and one that was hailed as such by international authorities such as Dr Russell Ritchie of Oxford University. The only loud dissent came from Belfast's Professor Dick, by now a committed antagonist of Koprowski's strains, who attacked the WHO for allowing the vaccinations to go ahead. In the course of this, the WHO made a startling admission: it had reservations of its own, and it did not support the Congo trial.<sup>6</sup>

In the field however, Banalia seemed not merely a triumph,

but a repeatable one. Less than three weeks later outbreaks of paralysis were reported from three more rural centres, Gombari, Watsa and Bambesa, which lay further to the north and northeast of Stanleyville, not far from the Ugandan border. Once again the team moved in and administered the life-saving vaccine to every inhabitant, a total of 18,704 recipients. Once again the pestilence seemed to halt in its tracks.

It was good enough. On 24 February, 1958, the largest trial hitherto conducted with a live polio virus in Africa got under way. Under orders from their chiefs, the population assembled in long lines at the designated vaccination stations where between 3000 and 11,000 people received the virus daily. By 10 April, the two teams had administered vaccine to 215,504 inhabitants of the Ruzizi valley, which lies between Lake Kivu and Lake Tanganyika, at the conjunction of the Congo, Rwanda and Urundi (modern Burundi). The vast majority received CHAT-1, while 2511 were given FOX-3.

"No sickness was reported following administration of the virus," Courtois and Koprowski recounted.

According to the map published with their report, the main vaccination effort centred on the towns of Bukavu, to the south of Lake Kivu, Kabunambo at the southern end of the Ruzizi valley, and Usumbura (modern Bujumbura) in Burundi, on the northern shores of Lake Tanganyika. To assess the safety of the vaccine they selected two missionary schools, giving one group of students the virus and the other a placebo to see if any sickness resulted. None did. Medical authorities were asked to monitor for any signs of illness connected to the vaccine in the wider community, but none was reported.<sup>7</sup>

Koprowski and his colleagues had done a fine thing. They had immunised nearly a quarter of a million people in susceptible communities and they had apparently proved the power of polio vaccination to stop an epidemic dead. It was an achievement well worth reporting to the world scientific community and one which led to personal honours for Koprowski. In 1959 he was invested as a Chevalier of the Belgian Order of the Royal Lion.

It was also by no means the end of the African campaign. These trials had taken place for the most part in rural or semi-rural districts. The signal test lay in the cities, densely thronged with humanity, often living in squalid conditions in which contagions could blaze up like brushfires.

Leopoldville, now Kinshasa, stands abreast the Congo some 500 kilometres inland from the Atlantic, the main riverport

and gateway linking central Africa to the world. In many ways emblematic of the forces and contradictions which have shaped modern Africa, across its wharves and along its streets passed the commerce, the immigrants and emigrants, the expatriates and the colonialists of that era. Those making for West Africa followed the river to Leopoldville, bypassed the Congo falls by rail or road to the port city of Matadi and thence took a coaster. Others followed the same route by ocean to Haiti and the Caribbean islands or Europe. The Europeans and Americans whose trade, government or missionary activities drew them to this corner of the world traversed the city in large numbers. The Africans, whom the winds of change were sweeping off the land and out of the forests, thronged there by tens of thousands.

The city stands just below Malebo Pool (once known as Stanley Pool), a forty kilometre-long expanse of water named after the nineteenth century explorer, where the Congo's dark brown currents suffuse into tranquillity after their tumultuous passage of the gorges in the Cristal Mountains. Standing on the shores of this glittering lake in 1877, Stanley at once grasped the potential of a site which had been inhabited by traders and fisherfolk since ancient times, and hastily sealed an agreement with the ruler of one of the main litoral villages, Kintamo. Then he set to work to open up the trade route along the middle river as far as Stanleyville by having prefabricated steam boats delivered from Europe and manhandled past the rapids on the lower river. His newly founded trading outpost he christened Leopoldville in honour of his patron, Leopold II of Belgium.

For the next forty years or so, however, the town of fewer than 5000 inhabitants remained sleepily remote from the outside world until the completion of a railway linking it to Matadi and the Congo estuary, and the introduction of the first air services. From that time on its population expanded rapidly despite a climate oppressively hot for much of the year, the maddening heat punctuated by infrequent, violent downpours and heavy winter rains. In 1923 the administration of the Belgian Congo relocated its headquarters there and Leopoldville at once began to flourish, before long emerging as the first city of Sub-Saharan Africa.

In the 1950s Leopoldville was an entrepôt, a meeting place, a crossroads, a trade, transport and administrative hub, a place one passed through on the way to somewhere else. Populated by some 346,000 people in 1958 it consisted of three distinct sections: the Ancienne Cité, old, densely packed and squalid where 126,000 huddled under grass shacks in mediaeval conditions of hygiene, the

Nouvelle Cité, where 130,000 people dwelt in more gracious and salubrious European colonial surroundings (though still with backyard privies) and six other suburbs which fell somewhere in between. By African standards of the day it was well served in public health terms, with twelve hospitals, forty-five clinics, fifty doctors and the considerable resources and skills of the Belgian medical service. This made it an ideal locale for the conduct of a major vaccine field trial, because the results could be monitored and patients followed up by the medical system more readily than they could be in rural areas.

In one other respect Leopoldville vividly represented the new Africa: during the nineteenth it had housed fewer than 5000 people and by 1935 its population had only reached 26,000. Barely two decades later however it had boomed sixteenfold as formerly rural communities uprooted and flooded in to the city. At its peak in the early 1950s the population exceeded 400,000. This vast surge of urban migration produced an unnatural gender ratio: some fifty-five per cent of the inhabitants were males, mostly young, who had moved to the city in search of work. Prostitution naturally flourished.

Not surprisingly, given the limitations of its public hygiene Leopoldville suffered more than its share of polio outbreaks. From 1951 to 1958 there had been an average of sixty-three cases of paralysis a year, about nineteen cases for every 100,000 people. The vast majority had been in children under three. Because of this, it was decided to vaccinate the susceptible child population, aged five years and less.

The virus of choice was Koprowski's CHAT-1, pool 13 which, according to the official account had been tested "for bacterial and fungal sterility and for the presence of extraneous viruses". To make sure it was safe, it had been injected into the brains of forty-five monkeys and the spines of five chimpanzees. Nothing was found other than some mild polio lesions in one monkey.

"The vaccine was administered in 1-ml doses by means of a semi-automatic syringe. The ball of the syringe was placed in the bottle containing vaccine and vaccine was sucked through a rubber tube into the barrel of the syringe. Each pressure on the piston then delivered 1 ml. An attempt was made to squirt the vaccine into the back of the child's throat so that swallowing was involuntary. If the material was not swallowed, a second dose was administered. For children under 30 days of age, the dropper bottle was used and the 1-ml dose was delivered by dropping into the



child's mouth," they said.<sup>8</sup>

The operation began on 18 August 1958, in community centres, schools and infant health clinics to which the population was summoned, street by street, by the Belgian authorities. By April 1959 a total of 45,726 African children -- rising later to 76,000 -- had swallowed CHAT-1.

But after the initial triumphs in Stanleyville, the rural townships and Ruzizi valley the results of the Leopoldville experiment were a disappointment.

When 3400 vaccinees were followed up later, no polio disease was reported, but when bled, only about 60 per cent had developed protective antibodies. This was a very poor figure compared to the previous trials which had achieved protection as high as 90-95 per cent. There was also a sharp upsurge in illnesses among vaccinated children, with the total sick climbing by 64 per cent in the fortnight after they received the virus, although none showed symptoms of paralytic poliomyelitis. Two months after the vaccination campaign began, wild polio broke out in Leopoldville and of the 99 cases, ten proved to be among children who had been vaccinated.

Koprowski's Wistar colleague Dr Stanley Plotkin embarked on an urgent investigation to discover the reason for these disturbing results. His first conclusion was that the vaccine itself had not caused the children to contract polio -- the interval of time elapsing between vaccination and the appearance of symptoms in the patients was too long.

From followup studies of 7200 vaccinated children he also concluded that the vaccine had not been responsible for any upsurge in serious illnesses, although he did observe "a significantly greater incidence in total illnesses during the 15 days after vaccination, than in the seven days preceding it". These were mainly upper-respiratory infections which seemed *a priori* not to be related to poliovirus. He attempted to explain this spate of sickness by arguing that infants attending for vaccination would, naturally, only be brought in by their mothers if they were in good health. Over the ensuing weeks they would develop the usual proportion of coughs and tummy bugs, resulting in an apparent increase in ill health. Had the vaccine been responsible, he claimed, the upsurge would have been seen in the second week after vaccination, not the first. No further monitoring was performed after fifteen days, so the infants' subsequent disease history was not known. The argument rang a little hollow, as the report also made it plain the mothers were rounded up, street by street, by

paternalistic Belgian health officials. Undoubtedly, they had little say in whether or not their baby was vaccinated -- or understanding of the medical implications.

However, the vaccine had plainly failed to provide the hoped-for protection against wild polio. In the Ancienne Cité, where endemic polio was worst, Plotkin estimated that only 53 per cent of vaccine recipients had been protected. The figure was rather higher in the Nouvelle Cité -- around 71 per cent -- and other districts where it was 68 per cent. Since the Nouvelle Cité had received some natural immunity in the form of a recent epidemic, Plotkin calculated that the overall rate of protection across the whole experiment was no more than 60 per cent.

"The low serological response to vaccination was surprising, considering the results obtained with the CHAT strain, both in carefully controlled groups and in field studies using exactly the same pool of virus material as was used in Leopoldville," he wrote. "In these studies the serological efficacy of the CHAT strain was 90%-95%. The explanation for this disparity in results is obscure."

Rejecting as possible explanations loss of potency in the vaccine under tropical conditions and faulty administration (since the first 10,000 doses had been closely observed), Plotkin concluded that the most attractive theory was that wild gut viruses which already infected the vaccinees had somehow interfered with the polio virus in the vaccine and prevented it from taking.

Citing a number of colleagues who had reported similar observations, he wrote "Coxsackie, Echo and heterotypic polioviruses have all been implicated in interference with the response to live polio vaccine," and quoted a Mexican study in which only 28 per cent of a group of vaccinated children, who were all infected by various gut viruses, developed antibodies to the polio in the vaccine. Gut viruses were a part of life in Leopoldville, he noted.<sup>9</sup>

The equivocal results from the Leopoldville campaign did little to aid Koprowski in his quest to develop the world's most effective oral vaccine. Even before they were fully analysed and published in the scientific press, Albert Sabin had disclosed his sensational results in the USSR, and his live, attenuated virus rapidly became the world's preferred polio vaccine, progressively supplanting even the Salk vaccine.

The vaccinations in Kinshasa were by no means the end of the campaign, as Belgian health authorities led by Courtois and Ninane, took up the task of spreading CHAT vaccine ever more

widely. According to research by writer Ed Hooper, there were no fewer than nineteen additional vaccine trials conducted throughout the Congo, involving a total of more than 600,000 recipients.<sup>10</sup> These included:

- a further 321,000 in Burundi,
- 137,000 more in southern Rwanda
- 64,000 in the town of Lubudi in the copper mining region of Katanga to the south
- up to 5000 in the Congo river port-town of Lisala
- an unknown number of recipients in the city of Kikwit and
- Matadi, the port at the mouth of the Congo.

In all, Hooper estimates, close to one million people were fed CHAT vaccine between February 1957 and March 1960.

Then, in early 1960, the Congolese rebelled, tumbling the heedless Belgians out of the country and proclaiming their independence. Chaos ensued. It was the end of the experiment. There could be no question of any attempt to follow up on the polio trials and observe what happened to recipients in the longer term.

Never one to surrender in the face of adversity, Koprowski immediately initiated fresh trials in Poland, Croatia and elsewhere, but the laurels in the polio war had long gone to Sabin.

Today the African immunisation trials lie almost half a century in the past. Polio, like smallpox before it, has largely been defeated and expunged from most continents. If the WHO's global campaign succeeds, another vicious killer andcrippler of little children will be consigned to history's rubbish bin. That could never have been without the courage, expertise and dedication of the polio pioneers.

The only question was whether something far, far worse had inadvertently been let loose.

## Endnotes

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<sup>1</sup> *Encyclopaedia Britannica*, various references.

<sup>2</sup> Wilson J.R., *Margin of Safety*, Collins 1963, p140.

<sup>3</sup> *Ibid* p141.

<sup>4</sup> Courtois, Flack, Jervis, Koprowski & Ninane, Preliminary Report on Mass Vaccination of Man with Live Attenuated Poliomyelitis Virus in the Belgian Congo and Ruanda-Urundi, *British Medical Journal*, July 26 1958, pp187-190.

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- <sup>5</sup> Ibid. p189.
- <sup>6</sup> Wilson J.R., op cit p186.
- <sup>7</sup> Courtois, Koprowski et al. op cit.
- <sup>8</sup> Lebrun A., Courtois G., Koprowski H. et al. Vaccination with the CHAT Strain of Type 1 Attenuated Poliomyelitis Virus in Leopoldville, Belgian Congo. *WHO Bulletin* 22, 1960, p203-214.
- <sup>9</sup> Plotkin S., Lebrun A, Koprowski H., Studies of the Safety and Efficacy of Vaccination. *WHO Bulletin* 22, 1960, pp215-234.
- <sup>10</sup> Hooper E., *The River: a journey back to the source of HIV and AIDS*, Penguin Press 1999. See, especially the table on pp 742-743.

— 7 —  
**Inklings**

MISFORTUNE seemed to dog Koprowski's footsteps in those days. Its baleful stare fixed upon him once again on Saturday, 14 March 1959, when the latest issue of the *British Medical Journal* hit the streets.

This contained a long and meticulously detailed article by Albert Sabin entitled "Present Position of Immunization Against Poliomyelitis with Live Virus Vaccines", which laid the ground for Sabin's sensational announcement of the Soviet trial results three months later. In particular, the article dealt with ways to ensure that live vaccines were safe, and uncontaminated by virulent strains of polio or other viruses. Sabin explained the methods by which he had tested his own vaccine samples and his recommendations as to the best way to puncture a monkey's spine in order to verify the preparation was indeed safe. He also described the results of certain of the tests performed.

"For the identification of the virus in each vaccine, as well as to check for the absence of non-poliomyelitic cytopathogenic viruses, specially potent rabbit antisera were used," he wrote. "These rabbit antisera, in 0.1 ml. amounts, were capable of neutralising approximately 10 million TCD<sub>50</sub> of homotypic poliovirus, so that it was possible to test the undiluted vaccine for the presence of other cytopathogenic viruses. No extraneous cytopathogenic virus was found by this method in any of the large lots of [Sabin's] vaccine.

"The efficacy of this method was emphasised when similar tests on the large lot of Koprowski's type 1 "Chat" vaccine used in the Belgian Congo trials (Courtois et al, 1958) revealed the presence of an unidentified, non-poliomyelitis cytopathogenic virus."<sup>1</sup>

Essentially, Sabin was attempting to ensure that his own vaccines were as free as possible from any form of contamination. Almost inadvertently, in the process, he revealed that Koprowski's CHAT-1 vaccine fed to nearly a third of a million infants, children and adults in the Belgian Congo had been contaminated with an unknown virus.

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"Virology today is at the same stage as bacteriology was at the beginning of the twentieth century. New pathogenic organisms are constantly being discovered... The ingenuity of

a host of research workers is being put to the test by the antigenic lability of viruses, by their existence in masked forms in reservoir hosts (still mostly unknown), where they escape current methods of investigation, and by our ignorance of the pathogenicity of many of those found in man or beast.”

In this curious fashion began the WHO’s commentary on Koprowski’s Belgian Congo vaccination campaign, during which more than a third of a million people had been fed the live, attenuated CHAT-1 and FOX-3 polioviruses.<sup>2</sup>

The article, published in mid-1960, was a remarkably candid admission of the limitations at that time of scientific knowledge of the nature, behaviour, extent and diversity of members of the virus clan. It also sounded a prophetic warning.

WHO went on to cite a paper by Dr J.Tobin of the Biological Standards Laboratory in Britain’s Medical Research Council Laboratories who opened his remarks as follows: “Viruses known to be carried by monkeys and which may be encountered during the production of vaccine made from monkey tissues include B viruses, miscellaneous simian viruses, “foamy agent”, “measles-like” agent, haemadsorption viruses, lymphocytic chorio-meningitis (LCM) virus and arbor viruses.

“These agents have been isolated either from intact animals or from cell cultures prepared from them. B virus, LCM, measles and the arbor viruses are definite human pathogens.

“In vaccine production these viruses will be of no account unless they are transferred from animals to the cell cultures used in vaccine manufacture and safety testing. In producing live vaccines this transfer must be eliminated...”<sup>3</sup>

Tobin could hardly have put it more succinctly. There was a veritable jungle of invisibly small creatures out there in kidney-country—some dangerous, some deadly and many still unknown—which could easily be transferred to vaccines and thence to humans. These simian viruses grew readily in monkey cell cultures. It was something every worker in the field was critically aware of: the untoward contamination of a vaccine culture could kill the person working on it and, not infrequently, did. At the time he was writing, more than ten such deaths had been reported in the previous few years.

But if you wanted a live virus for your vaccine, you had to live with the risk that unwanted, unknown hitch-hikers might come along for the ride. Much of the research involved in developing a

new vaccine went into testing, testing, testing, in an endeavour to eliminate this threat.

Prior to the invention of the electron microscope in the late 1930s, viruses could not be seen. Their very existence had not even been guessed at until 1891 when the Russian scientist Dimitri Ivanovski filtered through porcelain some fluid made from a plant contaminated with tobacco mosaic virus, and proved it could infect healthy plants. This was the first real clue that mysterious particles which were invisibly small—far smaller than bacteria—could cause disease. By the beginning of the twentieth century scientists had managed to demonstrate that several human infections, including yellow fever and rabies, were produced by these sub-microscopic agents. To begin with, it was assumed that viruses were simply tinier versions of visible bacteria—very small living organisms. But in the early 1950s, it was demonstrated that infectious virus could arise from inert substances and must therefore be a far more basic form of life, if life was the right word for it. That debate was never satisfactorily resolved: on the one hand, a virus could be as inert as a sugar crystal, on the other, it could commandeer a cell's genetic machinery and force it to make fresh virus. A virus is the perfect illustration of our imperfect understanding of what it means to be alive.

Viruses have probably existed since the very earliest times. Some biologists consider they are survivors from the probiotic era more than three billion years ago when the earth was an experimental alchemist's brew of organic molecules. Others believe that sex evolved in other organisms in a riposte to the parasitic impact of viruses: by allowing us to reassort our genes in more varied combinations, sexual reproduction dramatically enlarged our chances of producing offspring which were virus-resistant in comparison to simple animals which reproduced merely by splitting into two genetically identical and hence equally vulnerable offspring.

The advent of the electron microscope enabled viruses to be readily imaged for the first time during the 1940s, but even after that instrument came into common use, if an unknown agent was present, chances were researchers wouldn't even know it was there or recognise it if they saw it. Seeing a new virus was harder than locating the proverbial needle in a field full of haystacks.

In 1932, a researcher at Bellevue Hospital in New York had been bitten by a monkey. He became paralysed and died. Anguished at his loss, the young Albert Sabin set out to track down the culprit, rejecting suggestions from a far more senior

colleague that it was ordinary herpes. Two years later Sabin managed to establish the cause was an entirely new kind of agent, which he named Herpes B virus. Fifteen years later, Sabin encountered the foe anew when another vaccine worker perished. Then, as the mass production of Jonas Salk's killed poliovirus rolled into action in the early 1950s came a veritable string of fatalities among lab workers and monkey handlers, ten in all. Some still occur, infrequently, today. In monkeys, B virus causes insignificant illness. But to humans, it is death.<sup>4</sup>

B virus was a plain warning of what could happen if a virus leaped from monkey to human. The old host, having developed natural immunity, might carry the agent with little or no inconvenience, but the new host might be eaten up with it. A good analogy on a larger ecological scale was the devastation wrought when a new pest, the European rabbit, was introduced to Australia. Lacking the predators to keep it in check the rabbit devastated two thirds of the continent and became a primary cause of the world's worst rate of mammalian extinctions among Australia's native marsupials. That is what happens when something new gets loose in a naive ecosystem—even something as apparently innocuous as a bunny rabbit.

Another more telling example of what happens when a virus leaps into a virgin species, occurred in 1978 when a cat parvovirus, feline panleukopenia, suddenly appeared in dogs—with appalling results. In under two years the disease spread to every dog population ever tested for it in the world, and later infected even wild populations of wolves and coyotes. Where it originated was not clear, but the disease was first noticed in Belgium and the Netherlands in 1977/78. During the following six months it exploded across Denmark, Australia, the United States, Japan and New Zealand, where it killed millions of puppies through an acute inflammation of the heart and older dogs through fever, vomiting and diarrhoea. How the disease spread was easy to explain—dog faeces which had stuck to travellers' shoes would have done the trick. But how the virus crossed from cats to dogs was far more mysterious.<sup>5</sup>

Cats and dogs have, after all, shared human dwellings for at least 5,000 and possibly 10,000 years. They have been fighting, biting and scratching presumably for all that time, yet the cat virus never crossed to dogs. What many veterinary virologists now believe is that FPLV jumped species during vaccine experiments, in which live cat virus was inoculated into a tissue culture made from dog cells. There it became adapted to its new host. Exactly



where this occurred is not clear, but attempts to backtrack the disease through the examination of preserved blood samples found three seropositive cases from Greece dating to 1974.<sup>6</sup>

Because monkeys and apes are very close to humans in an evolutionary sense, their viruses may be far more dangerous to us than those of a genetically more distant mammal such as a dog or rabbit, as primate viruses are already well-adapted to our genome. For the very same reason, monkeys and apes are also ideal as experimental animals in the mass production, attenuation and testing of human viruses as vaccines. In virological terms, then, primates are a two-edged sword.

The crucial question was: could a vaccine ever become contaminated by an unknown live monkey agent and then, unintentionally, be administered to tens of thousands of people?

This is precisely what happened in the late 1950s with the polio vaccine developed by Jonas Salk, Koprowski's old rival, and to several other vaccines. Some time between 1954 and early 1961 – when the problem was finally exposed—virus pools made on Asian rhesus monkey kidney cultures became contaminated with a previously unknown agent, christened simian virus 40 (SV-40).

This occurred on at least four separate occasions: first, among about 100 volunteers to an experimental study of a respiratory virus; secondly among more than 100,000 United States army conscripts being immunised against adenovirus with a licensed vaccine; thirdly, among 10,000 volunteers in live oral polio vaccine trials; and fourthly among 98,000,000 people vaccinated with the Salk licensed killed polio vaccine in the United States alone and untold millions more in Europe and elsewhere.<sup>7</sup>

Ninety-eight million is a great many people to expose to an unknown biological agent in any country. In the case of the United States, it was half the population at the time and included virtually every person born between 1941-61 who received the Salk vaccine. In East Germany, 86 per cent of all babies born in the years 1959-61 received contaminated vaccine.

For a long time after its discovery, medical science feared that SV-40 might be a killer. When the mistake was finally picked up in 1961, panic ensued behind tightly closed doors: for it was thought that SV-40 caused brain cancer.

SV-40 is a papovavirus, a member of a family responsible for causing tumours, warts, vacuoles and other growths in animals and humans. Injected into newborn hamsters it causes cancer a few months later. It can also turn human cells cancerous in culture and causes warty lumps in the skin of human subjects.

The virus entered the poliovaccine via the kidney cell cultures used to grow it, which came from the 200,000 Asian rhesus and cynomolgus macaque monkeys imported into the United States each year for vaccine manufacture. Subsequent investigation showed that few of these were originally infected with SV-40: probably most of them caught it while housed for a few weeks in “gang cages” before being sacrificed to donate their kidneys to medicine. The kidneys were mostly prepared as monolayer (a single cell-layer) cultures for growing polio virus, and these later proved to be heavily contaminated by SV-40: anywhere from 20-100 per cent carried the invading virus, depending on the source of the kidney material.

It is not clear exactly how many people were injected with live SV-40 in their polio shots, but Keerti Shah and Neal Nathanson of Johns Hopkins University School of Hygiene and Public Health who investigated the issue came up with “an educated guess based on our interpretation of the data on vaccine contamination” that from ten million to thirty million of the total of ninety-eight million Americans vaccinated against polio had received live monkey virus as well. This was founded on a study of the level of contamination in vaccine batches administered to nine million 6 to 8-year-old children in May/July of 1955. The presumption was that many millions more around the world had been similarly dosed, wherever the Salk vaccine was used. In Australia, for example, it is thought some 5 million were so exposed.

To begin with, there was little evidence of any adverse effect. Indeed, there were few signs that anyone had even been infected by SV-40 -- infection being the point at which a virus begins to multiply in your body cells and the body to muster its immune defences against it. The first follow-up, of the nine million children, did not disclose any untoward increase in cancers. However antibody to SV-40 was found in blood samples in 20 per cent of cases taken from children in Maryland who had been vaccinated with killed poliovirus.

Whether this was a reaction to killed SV-40 or to live SV-40 being passed in the vaccine was moot. But the fact that the children continued to put out constant levels of antibodies against SV-40 for several years thereafter indicated they had indeed been infected by the live virus, which had remained active in their bodies.

Then, in the late 1970s, two teams of researchers reported SV-40-like antigen in nearly a third of brain tumour cases which they studied, suggesting that SV-40 had indeed entered the human

population and prospered. Later still, SV-40 was isolated from the brains of two patients with PML (progressive multifocal leukoencephalopathy) and from a skin cancer sufferer. A German team could not find any increase in brain tumours among children vaccinated with the contaminated Salk vaccine—but it *did* discover a four-fold increase in skin cancer incidence.

At the same time an Australian report linked higher cancer rates in children over one year old who had been vaccinated against polio, while further research indicated higher incidences of brain tumours among groups known to have received SV-40 contaminated vaccine. An early study had found thirteen times more brain tumours among children of mothers who had received the Salk vaccine, but a follow-up failed to find any trace of SV-40 in their blood samples. The reviewers, Dr Franz Rosa and colleagues, felt the cancers were probably due to an unidentified infection from the vaccine “which was known to be contaminated with numerous monkey viruses”.<sup>8</sup>

Finally in 1996, nearly four decades later, came the shocking discovery that SV-40 was indeed implicated in cancer. Researchers at the US National Institutes of Health and at Baylor College of Medicine in Houston, Texas, found traces of SV-40, and finally the virus itself, in the tissues of people dying from the asbestos cancer, mesothelioma.<sup>9</sup>

Further research confirmed that the virus was responsible for disabling one of the key genes which protect people against lung cancer. They concluded that the virus would make the development of mesothelioma far more likely in people exposed to asbestos, and might also be the cause of the cancer in the 20 per cent of cases who had never been in contact with asbestos. The death toll from mesothelioma is projected to reach 80,000 in the United States alone by 2015.

Whether polio vaccine was the only source of the killer monkey virus SV-40 and of mesothelioma remains unknown. But the discovery certainly demonstrated the capacity of early vaccines to transmit potentially-lethal live monkey microbes to tens of millions of people round the world.

(Subsequently, too, US researchers were to claim that the so-called “stealth viruses” found in patients suffering from Chronic Fatigue Syndrome (CFS) and various disabling and lethal brain disorders also originated with African Green Monkeys, and were probably transmitted in polio vaccines.<sup>10</sup> Their claims met with a similar official cold shoulder to the HIV/polio vaccine theory: “The concepts that certain stealth viruses may have arisen as

contaminants of live viral vaccines, and that vaccinations may have had untoward consequences, have not been embraced by either vaccine manufacturers or Public Health agencies,” John Martin, Professor of Pathology at the University of Southern California told a scientific conference in 1996. “If a vaccine program were to be initiated today, one would surely not import wild monkeys from Africa, create short-term primary kidney cultures, add a human virus and administer the crude garnish derived from the virally infected cells to virtually every child in the country... Yet this is essentially the situation with live polio vaccine.”)

In an extraordinary sidelight on the SV-40 issue, the researcher who had made the discovery that the Salk vaccine was contaminated, Dr Bernice Eddy, was pilloried by the United States Government. Eddy, a talented researcher at the US National Institutes of Health (NIH), discovered in 1959 that monkey kidney cell cultures of the type used to make vaccine also had cancer-causing properties and this was ultimately traced to a virus present in them, SV-40. For two years, her government employers suppressed her findings, refusing her the right to publish them. Then in 1961, when it was clear her research was well-founded, they finally relented—and ultimately punished her for publishing her conclusions by confiscating her laboratory and equipment, cutting her staff and demoting her. Credit for her discovery was then given to researchers from a private drug company.

By mid-1963 the United States NIH had belatedly decided the risk was too great, and ordered manufacturers to withdraw the SV-40 contaminated polio vaccine from use in that country. Despite this, the Salk vaccine continued in use in countries such as Australia for some years afterwards.

The SV-40 scandal also illustrated an important point about the transfer of a virus across the species boundary, from monkey to man: like the Cutter Incident, only a part of the total vaccine administered was contaminated. And out of those millions of contaminated doses, it seems that only a small number of people became infected with the virus. But if a disease is infectious, it requires only one case to start an epidemic. And if the disease is lethal, the toll may be great.

For a long time, the scientific world believed it had escaped a potentially terrible event by a slender margin. In its wake, the leading United States scientific journal *Science* commented:

”Who could have argued against the benefits of polio vaccine in the 1950s - yet the vaccine received by millions

of people in the United States is now known to have been contaminated with SV40, a monkey virus which causes tumours in hamsters, though not, as luck would have it, in man.”<sup>11</sup>

Luck was the operative word. When Eddy’s findings were finally published and the public became aware that both killed and live poliovaccines had been contaminated with SV-40, there was outrage. The United States Congress convened an enquiry.

One of the experts who presented his views on the issue, in the form of a letter dated 14 April 1961, was Dr Hilary Koprowski, who had been serving as director of the Wistar Institute of Anatomy and Biology since 1957. He wrote:

“As monkey kidney culture is host to innumerable simian viruses, the number found varying in relation to the amount of work expended to find them, the problem presented to the manufacturer is considerable if not insuperable. As our technical methods improve we may find fewer and fewer lots of vaccine which can be called free from simian virus.”<sup>12</sup>

It was Tobin’s point exactly. Koprowski was arguing for the replacement of monkey tissue cultures with human foetal-cell cultures, which he considered far safer for the purposes of vaccine production because they carried no risk of introducing an alien virus from another species unintentionally.

\* \* \*

That there were wicked things still lurking in monkey-kidney country was horrifically illustrated six years after the SV-40 scare in an outbreak of disease among vaccine technicians using African green monkey kidneys in the German cities of Marburg and Frankfurt, and also Belgrade in former Yugoslavia.<sup>13</sup>

In its worst manifestations the disease began with blinding headaches, fever and muscular pains. Soon followed nausea, violent vomiting, cramps and diarrhoea. Then came blood, seeping from the eyes, the nose, the mouth, the anus, as the unknown agent shredded the delicate capillaries.

The victims’ bodies would then develop clots which clogged the skin, the eyes, the lungs and the gut, filling them with blood. As clots packed the brain, their faces grew expressionless and mask-like. They became sullen, at times lapsing into fits of psychotic fury, as gradually the disease deleted their personality and self-control centres.

At the same time, the blood cells, ruptured by the fast-breeding virus, refused to coagulate. Blood issued in streams from every orifice and filled the spaces of the body. Vomito negro, a gruel of black blood and stomach lining laced with bright arterial bleeding was expelled from the mouth in spasms so violent they sometimes stripped the lining off the tongue.

Their skin grew speckled with clots and erupted in bubbles, then ripped open and bled. Inside, the liver grew hard and yellow, and split. The intestines shed their inner lining and evacuated it in rushes of bloody diarrhoea. As cell after cell burst, the body's proteins drained away in the urine. In men, the testicles grew peeling blue-black, and rotten. Their semen was radiant with virus. In pregnant women the foetus erupted in blood and was cast out.

In the agonal—or final—phase the victims went into violent seizures that sprayed virus-laden blood in all directions. Afterwards, their hospital rooms were said to resemble slaughter houses. Following death the ravaged cells of the corpse's connective tissues, skin and organs began to dissolve and liquefy, and the fluids which streamed from the body were alive with virus.

The condition was known as severe or fulminating haemorrhagic fever, and it is one of the most virulent, repulsive and deadly forms of disease known to man. It has been seen in several parts of the world, caused by different agents. In this case, the pathogen responsible had never been seen before and was named after the town in which it first made its appearance: Marburg.

Marburg was the first of an entirely new family of viruses, the filoviridae or thread viruses. In that particular outbreak there were thirty-one cases of the disease, twenty-five of which were caught from handling contaminated monkey kidneys and six of which were transmitted human-to-human. One man passed Marburg virus to his wife by sexual intercourse. Seven people died.

The outbreak was followed in 1976 by explosive epidemics of another, even more deadly, agent with identical symptoms which took place in Zaire (now the Republic of Congo) and Sudan. This too proved to be a filovirus, and was named after the Ebola River, which ran close to Maridi, where the Zaire infection arose. Fatality rates ranged from 53-85 per cent. In all, 400 people died, virtually the entire populations of two hospitals and several villages. The origin of the virus remained obscure—it may have come from bats—but it was originally circulated to the local population by means of contaminated needles which were used on an infected individual and then not properly sterilised, a not-uncommon cause of epidemic disease in Africa.

The threat posed to humanity by these new agents was graphically underscored by a second major outbreak of Ebola fever in the republic of Congo (then Zaire) during mid 1995. Erupting in the city of Kikwit, the plague quickly spread to other centres, causing more than a hundred deaths and triggering a worldwide scare in which several countries sealed their borders against travellers from Congo.<sup>14</sup>

Like HIV and the lentiviruses, the filoviridae are RNA viruses. Like all viruses they are parasites, only able to reproduce by invading a host cell and commandeering it as a factory for virus. A feature which adds to their peculiar virulence is their ability to infect a wide range of the body's different cell types. They can probably be passed from one person to another in several ways—in blood, semen, body fluids, faeces and possibly by air transmission.

That their ability to cause disease can range widely was demonstrated in 1989 when an infection closely resembling Ebola fever broke out among monkeys housed in a quarantine facility at Reston, on the outskirts of Washington DC. The source of this disease seems to have been Asia rather than Africa. Four humans who were infected with the virus suffered no ill effect, but scores of monkeys died and the rest were put down by United States Army vets. In this case, the disease appeared to have been air-transmitted.<sup>15</sup>

Marburg and Ebola are the most virulent agents known to medicine, due largely to the speed with which they strike. Yet they are only from 30-85 per cent lethal. AIDS, by contrast, is thought to kill close to 100 per cent of those who contract the virus and develop the disease.

Marburg and Ebola were the warning that the rainforest regions of the world still harboured unknown agents of extreme lethality.

As leading United States virologist Dr C.J.Peters put it: "We were fortunate that the high infectivity of the Reston Ebola strain was not combined with the human pathogenicity of the 1967 Marburg virus".<sup>16</sup>

Once more, fortunate was the operative word.

\* \* \*

Sabin's revelation that the CHAT-1 poliovaccine was contaminated by an unknown virus was less than pleasing to Koprowski. In a stiff letter to the *British Medical Journal* of 23 May 1959, which underlined the intensity of their professional rivalry, he struck back.

“The purpose of this letter is to take issue with the results reported by Sabin...” he wrote.<sup>17</sup>

“On page 678 Sabin states that tests of the Chat strain in his laboratory revealed the presence of “an unidentified, non-poliomyelitis, cytopathogenic virus” in the pool. He made a similar report to me in May, 1958, after he had tested the attenuated Fox III virus obtained from our laboratory, but no further elucidation has come from him—the inference one is left with is that further studies had disclosed it to be the same type III poliovirus which “broke” through the neutralisation test in the lower dilutions.

“Two laboratories apart from our own have performed identity tests on the large Chat pool mentioned by Sabin with rabbit immune homotypic sera, and have failed to discover another “agent”.

“It was impossible to make a direct check on Sabin’s results because he failed to forward his “especially potent polio virus rabbit antisera” to our laboratory.”

After taking further issue with Sabin on other matters related to safety of polio vaccines, Koprowski concluded that large-scale field trials “are the only effective means of evaluating the safety of attenuated virus vaccines.”

A year later he made his views plain in the *Journal of the American Medical Association* in an article commemorating the tenth anniversary of his original successful trial of live virus. Still smarting under the criticisms of Sabin, Dick and others, Koprowski wrote: “Protagonists of live virus vaccination often search in vaccine preparations for viruses other than polio and usually find them in the products of their colleagues but not in their own, thus subscribing to the dictum of the fourth Earl of Chesterfield that “most people enjoy the inferiority of their friends”. (They often tend to forget Benjamin Franklin’s advice “Clean your finger before you point at my spots”.”<sup>18</sup>

“Indeed,” he continued, “a simian agent not related to poliovirus has been found in all the lots of vaccine prepared with the attenuated strains LSc ab, P-712 and Leon KP-34 and probably will be found in all other lots of vaccine prepared from freshly explanted monkey kidney tissue cultures. But this should hardly deter anyone from accepting the product.

“The idea of disqualifying a live virus vaccine because it contains an extraneous virus not known to be a human pathogen immediately suggests the following considerations: 1. Almost every attempt to isolate viral agents that lie dormant in the cells of living organisms and which can emerge when such cells are



cultivated under conditions freeing them from the restraining influence exerted by the organism as a whole will succeed. As a self-perpetuating project it is a good one for the next thousand years.”

Smallpox vaccine had been used for two centuries and doubtless harboured unwanted organisms, he said. Vaccines prepared in chick embryos could well contain chicken cancer viruses, yet this apparently did not preclude their use. He went on: “The poliomyelitis vaccine is administered orally and many viruses find their way into the human body through the mouth. If one wishes to be a purist in this entire matter, then the licensing authorities should require all food items which are eaten uncooked to be tested for the presence of viral agents.”

However, while being lighthearted there was no excuse for being lightheaded, he added. Any vaccine to be fed to millions of people throughout the world should be as free as present scientific knowledge could possibly make it from any virus other than polio. He went on to suggest that one way around this problem might be to grow the virus in lines originating from human embryo tissue, although this raised the alternate problem of possible contamination by human cancer viruses.

In concluding, Koprowski displayed once again the eclectic character of his library and its power of reproof to his adversaries: “The greatest detective of them all, Sherlock Holmes, was less impressed by the mysterious stranger on the premises than by the failure of the dog to bark in the night. Perhaps in the “Case of the Spiked Potion”, too, the mysterious agents encountered in our laboratories are less significant than all those healthy children who never complain!”

Koprowski knew the risks. Salk knew the risks. Sabin knew the risks. But none of them had ever heard of lentiviruses, nor of HIV nor of SIV. Those discoveries lay twenty years in the future.

Koprowski’s letter of rebuttal to the *British Medical Journal* was published in mid 1959, more than two years after the trials of oral poliovaccine had commenced in the Belgian Congo and just before Sabin announced his epic results from Russia which were to sweep all other contenders from the board.

It was in this same year, 1959, that a sample of blood was collected which, decades later, tested positive for HIV-1 -- the earliest-known case of the disease in the world. That sample was taken from an unknown Bantu man in Leopoldville, now Kinshasa, where almost 76,000 people had been inoculated with CHAT-1

vaccine over the preceding twelve months.

Kinshasa — where Belgian doctors were to conclude an old woman dying of Kaposi's sarcoma and immunodeficiency in 1962 was Africa's, and maybe the world's, earliest known AIDS victim.

Kinshasa - where a Congolese baby boy contracted HIV at his birth in 1974, dying eight years later from AIDS.

Kinshasa — where two cases of HIV were detected in blood taken from 805 healthy women in 1970, and a further fifteen HIV-positive cases recorded in 1980.

Kinshasa — where the Portuguese truck driver and the Belgian aid worker perhaps availed themselves of the thriving sex industry before dying of AIDS.

Kinshasa — former capital of the Belgian Congo, where thousands of French-speaking Haitians had been employed to keep the wheels of government spinning following independence in 1960. And Haiti, in less than 20 years' time was to become a center of the emerging AIDS pandemic.

Kinshasa — where the Danish doctor, Margarethe Rask, who also died of AIDS after serving as chief surgeon in the Red Cross hospital from 1975 to 1977.

Kinshasa — where the airline secretary and two of her three children had died of AIDS by 1978.

Kinshasa.

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## The Smoking Gun

San Antonio physician Eva Lee Snead, the first person to voice the idea that AIDS might have crossed to the human species via a contaminated polio vaccine, had arrived at the idea independently in the light of the SV-40 incident. Snead knew that African green monkeys were heavily infected with SIV, that oral polio vaccine was made from their kidneys and that millions of doses of vaccine had in the past been contaminated by SV-40 by this route. (She also ventured, incorrectly, that SV-40 might possibly have been the precursor to HIV.)

Listening with interest as she expounded her theory in a radio broadcast in May 1987 was a New York ethics scholar named Louis Pascal. "I thought her claims about African green monkeys having been used to make vaccine and about other monkey viruses having contaminated numerous vaccine batches, were straightforward factual claims which I could prove or disprove easily enough -- and they were extremely important, if true," he later recounted.<sup>1</sup>

"It did not take long to verify these claims. The SV-40 incident is well-known. And the principal early article tying SIV to green monkeys, published in *Science* on 22 November 1985, contains this line: "Much of the oral polio vaccine (OPV) used throughout the world is produced on primary cultures of kidney cells from this species"."

Pascal was puzzled. Admittedly a radio program canvassing alternative views about health was hardly likely to be regarded as a source of serious scientific ideas by the medical research establishment. But surely the warning by Essex and Kanki, two of the most respected AIDS authorities in the world at the time, ought not to have passed without comment or enquiry, he thought. He decided to investigate for himself the early history of polio vaccination – with spectacular results.

"It was I who discovered the completely unexpected location of the first campaign, the contamination of that batch and the fact that the same batch had been used in Kinshasa in the year before the earliest AIDS-positive blood sample was taken there. And I discovered much else," he stated. "It was the smoking gun. The evidence was too much to be ignored, too striking to permit any further stonewalling. Or so I thought."

Pascal prepared a paper setting out his theory of an oral

polio vaccine origin for HIV, citing all the references which he had found in the mainstream scientific and medical literature, and mailed it out to six biologists, seven AIDS researchers and several others in early December 1987.

In only one instance did he receive a reply: a note of thanks from a colleague on behalf of Luc Montagnier, acknowledging receipt. Surprised and rather irked, he submitted the paper to three scientific publications, *Nature*, *The Lancet* and *New Scientist*, all of whom rejected it. He then submitted it to two multidisciplinary journals. They both advised that his paper really belonged in a scientific journal.

*The Lancet* gave no reason, while *Nature* said "while the theory cannot be ruled out, it does not seem readily to fit the epidemiology of AIDS". *New Scientist* took two years to reply, saying only that it had sent out the paper for review. Nothing more was heard.

Pascal decided he would fare better among the profession of philosophy, and wrote to several colleagues whose work had been published along with his own and luminaries such as John Stuart Mill (1806-73) and David Hume (1711-76) in the Oxford University Press publication *Applied Ethics*, edited by Australian Professor Peter Singer. Here he was received much more open-mindedly, and one associate was sufficiently impressed to forward a copy to the *Journal of Medical Ethics* in England.

Due to a mail mixup the response from the *Journal of Medical Ethics* took some months to reach Pascal, but it was encouraging, stating that although the article in its original form was unsuitable, the journal was prepared to consider a cut-down 3,500 word version giving an outline of the theory, but focusing mainly on the treatment meted out to it by the scientific press.

By now Pascal was becoming frustrated and had just reworked his original document into a 19,000-word monograph in which he not only detailed his theory but also launched an intemperate attack on science, scientists, scientific publications and their editors in general. He piled it, together with supporting documentation, into an envelope and mailed it off to the editor of *The Journal of Medical Ethics* asking that it be considered as an independent submission.

It is a deeply indignant document, opening with an account of a famous research "conspiracy". This was the story of how the ultra-aggressive HeLa cancer cells contaminated researchers' cell cultures worldwide, thereby invalidating millions upon millions of

experiments upon which countless scientific reputations were based -- and how the profession had hushed it up. On the face of it the story had little to do with the polio vaccine idea, but Pascal apparently felt it said much about the reluctance of medical researchers to confront unpalatable facts when professional reputation was at stake.

He then outlined his theory, pointing out that, even in the 1950s, there had been grave reservations about the use of live virus vaccines because of the risk of them reverting to a virulent form and because the culture process used to grow them was almost assured of contamination by foreign viruses. Koprowski, he noted, had declared that anyone who probed the strains of live virus vaccine then available might find non-polio viruses in all of them. This, Pascal contended, was an unsatisfactory response, because no vaccine could be made free of such viruses with the technology of the day; any pathogens present were likely to be monkey viruses and so especially dangerous to humans; and viruses which cross species can sometimes produce deadly epidemics.

He went on to argue that Africa was selected for the first major field trial of live polio vaccine because the United Nations had suggested trials should be conducted in an undeveloped country and, in the 1950s, Central Africa did not even have UN representation. "Thus when Belgium volunteered its Central African territories of Ruanda-Urundi and the Belgian Congo for the first test, everyone was happy. I suspect even the Africans were happy, since I suspect they knew nothing of these reservations [about the safety of live virus vaccine]," Pascal wrote.

Those who had planned the Congo experiment simply did not lend due weight to the possible consequences if the vaccine turned out to be a carrier of other dangerous agents, Pascal claimed. The gravest objection to their defence of the early vaccines, he wrote, was that it was not accompanied by the caveat: "I realise that if I am wrong, hundreds of millions may die as a result of my error, but I have taken this into account and I still believe the risk is too slight to justify abandonment of the vaccine".

By vaccinating with live viruses made in monkey kidneys "It was completely predictable that monkey viruses would get started in a new species never exposed to them before. And it was almost completely predictable that not all of them would be harmless. And now this completely predictable disaster has occurred. This very first batch of vaccine gave us AIDS," he affirmed.

This was over the top. There was no evidence that the

mystery virus found by Sabin in Koprowski's CHAT-1 vaccine was SIV, the HIV-precursor, or anything harmful to humans. The most it demonstrated was what the SV-40 incident had later proven: unknown agents can get into batches of vaccine -- and be widely distributed to people.

Pascal pointed out that the geographical areas in which the polio campaigns had been conducted coincided in an extraordinary way with the places which today have the world's highest incidence of HIV infection and are recognised as the epicentres of the outbreak.

He also advanced another, subtler argument: when scientists wish to transfer an alien virus into a new species experimentally, they do so by knocking out its immune system with drugs or radiation, or by injecting the virus into new-born or very young animals whose immune systems are undeveloped. During the Congo campaign, it was documented that live CHAT vaccine had been administered to around 149,000 children and babies, some as young as three weeks, as well as an equivalent number of adults. Because the immune systems of babies under thirty days are not fully developed, they were given an extra-massive dose of live virus -- 1,500,000 units, seven to fifteen times the standard doses of 100,000 or 200,000 units.

It was also inevitable that many of these African babies and children would have oral sores, teething inflammation, herpetic lesions and other possible sites for transmission, as well as the mucosal cells of the mouth and the respiratory tract, where the virus could find host T-cells to infect.

Medical researchers who argued for the monkey bite (or chimp hunter) theory of transmission were hardly disinterested parties, Pascal claimed. "If they are wrong, and if monkey diseases such as AIDS are indeed getting into the human population through contaminated vaccines, then other new diseases are likely to get started in the same way in future and hundreds of millions of additional lives will be risked," he said. "Nowhere do they say "I realize that if I am wrong, hundreds of millions of people may die as a result of my error. Nowhere do they show any inkling of grasping the importance of this question"."

Pascal conceded that the early polio pioneers had no knowledge of SIV, and there was no test for it until twenty-eight years after the campaign began. Manufacture consisted of little more than growing the virus in cultures of monkey kidney cells and then straining the liquid through a filter fine enough to remove bacteria, but which would permit the passage of viruses. "There

were no methods used to prevent those viruses already present in the monkey kidneys from contaminating the vaccine and no methods to kill the viruses after contaminating."

He was working up a head of steam. "Practically every AIDS researcher around the world who was remotely interested in AIDS' origin would have read the 22 November 1985 *Science* article tying AIDS to SIV, tying SIV to green monkeys, and tying green monkeys to polio vaccination," he charged. "Why did the article's authors (Essex and Kanki) not pursue this obvious important lead? Why did no single one of the thousands of AIDS researchers who would have read the article pursue it?"

What Pascal, in his wrath, had made little allowance for was the fact that most AIDS researchers were at full stretch under the lash of public anxiety, trying to figure out how the virus worked, why it was mutating and how to disrupt its life cycle or make a vaccine against it to probe too deeply into its prehistory. Also, there is no doubt that it was a deal easier to obtain research funding for an AIDS cure than to discover its origins, especially if the answer might reflect negatively on medical science.

"What the research scientists should have done themselves a long time ago, I did for them," Pascal thundered. "They had nothing to do but check it out, using the references I supplied them, references from their own medical journals. Even this was beyond them."

He then supplied an answer to his own rhetorical question: "No one should be surprised by the response of the scientific community to the information that it had started AIDS. When large mistakes are made in any field, they are almost always covered up. It is entirely predictable. How many of the tobacco companies have admitted their product causes lung cancer?" He then switched targets and delivered his second broadside at scientific editors.

"The editors of the world's learned journals are the gatekeepers of knowledge... Their power is enormous. Their responsibility is enormous... It is my strong view that these editors are entirely culpable. Against this mass of evidence the editors did not raise a single concrete objection. They did not question a single point of fact or reasoning. Yet they rejected it anyway, thereby sending who-knows-how-many people to a horrible and pointless death.

"And it is not a matter of a single editor or scientist being particularly stupid or irresponsible. It happened over and over. Unless one is prepared to argue that those journals and scientists I sent my work to were a few rotten apples entirely



unrepresentative of science as a whole, one must reach the conclusion that people of this calibre typify science.

"We take the kidneys from great numbers of SIV-infected monkeys, add a little polio virus, grow whatever will grow for several days, filter the solution, and feed it to hundreds of millions of children around the world.

"Then, a quarter century later, when we discover SIV now infects humans too, we say, "What could have happened? It must have been a monkey bite!"

\* \* \*

"Bearing in mind that many thousands of doses of the original Salk vaccine produced in the 1950s were contaminated with SV.40, a simian agent, one wonders whether monkey kidney tissue might not be the source of AIDS viruses in man...

"Consequently while it would be simplistic to assume and even more difficult to prove that polio vaccine is the source of HIV infection in man, it would be equally naive to ignore the possibility.<sup>2</sup>

These words appeared on 21 October 1989, while Pascal was still striving to get into print. The fact that they were published in the *Medical Journal of South Africa* might help explain how they apparently failed to generate international scientific attention. The authors were two South African virologists, Professor G Mike Lecatsas of the Medical University of Southern Africa and Professor Jennie Alexander of the University of the Witwatersrand in Johannesburg. Their letter was written to express their concern at the practice of using green monkey kidneys for the manufacture of live vaccines, which continued in use worldwide in spite of the discovery of the lentiviruses HIV and SIV and in spite of the existence of safer technologies. It contained the additional arguments that HIV-2 appeared closely related to SIV, that both appeared to have diverged in the past thirty years and that other monkey viruses such as SV-40 and B virus could successfully infect humans.

Their words did not escape all attention, however. In fact, they brought a booming denunciation from the director of the South African National Institute for Virology, Professor Barry Schoub, whose establishment was still using monkey kidneys to make polio vaccine.

"The letter by Lecatsas and Alexander is scientifically,

factually and conceptually incorrect, and in view of national and international efforts to control poliomyelitis is reprehensibly irresponsible misinformation," Schoub and his collaborators stormed in a letter to the next issue of the *South African Medical Journal*.<sup>3</sup>

"To suggest that live polio vaccine may carry the potential danger of AIDS because of contamination with simian immunodeficiency viruses (SIV) or unknown dangers associated with other primate retroviruses is recklessly wild and unscientific speculation."

Schoub argued that monkey kidney cells could not become infected with SIV, even in SIV-positive animals, and if the culture was free of white blood cells there was no way the vaccine could be contaminated. He rumbled on, charging that the claims of Lecatsas and Alexander "served only to misinform, confuse and mislead and do little to help" global efforts to eradicate polio by the year 2000.

Years after, Alexander is still faintly mystified at this colossal over-reaction to what she considered an eminently reasonable and logical idea, an idea which was probably testable. But just as other enquirers into the polio vaccine theory were to find themselves deflected, reprimanded and even sued by the medical establishment, scientists who raised it found themselves under personal attack, usually without much scientific basis.

"We were vilified in the extreme," Alexander said later. "No reasoned consideration was given to our points -- instead we, and not our ideas, were essentially attacked." As a consequence, she felt constrained to abandon all work on HIV because the letter had made her too controversial. Anyone who pursued such an issue as the possible transfer of SIV in polio vaccine would soon find themselves "begging on the street corner" for funds to support their research as the medical establishment closed ranks against them, she vividly explained.<sup>4</sup>

Yet neither South African was easily intimidated. In May 1991, Lecatsas went so far as to air the idea in *Nature* -- a place where it certainly could not escape the scrutiny of the world scientific fraternity or even the media.<sup>5</sup>

Responding to the letter by Cambridge University's Professor Karpas, who was advocating the sex-ritual theory of transmission, Lecatsas wrote: "A combination of tribal customs involving African monkeys carrying HIV-like agents as the probable origin of AIDS in man is essentially speculative.

"However the use of tissues from such animals for live

human vaccine production is a fact and should be considered as a possible source of the virus. Such vaccines were also a post-Second World War development as was the introduction of syringes to Africa. The reference to "more than a dozen such cases of herpesvirus simiae (B virus) infection in man", with no mention of millions of cases of SV-40 transmission to man via polio vaccine prepared in monkey tissues is misleading."

The cat was out of the bag, scientifically speaking. The idea that AIDS had got its start in a contaminated batch of polio vaccine had appeared in the world's most prestigious scientific publication. It was on the common-room table in every decent scientific institution in the English-speaking world. It was right under the noses of medical researchers globally.

Studiously, they ignored it.

\* \* \*

The possibility that SIV might contaminate polio vaccine had clearly crossed the minds of officials at the World Health Organisation as far back as 1985, as soon as the existence of the monkey virus was made known by Essex and Kanki, but the concern was for the safety of present and recent vaccines, not those developed thirty years earlier.

Professor Arie Zuckerman of the London School of Hygiene and Tropical Medicine noted: "These findings are particularly important in relation to the production of vaccines and reagents in monkey kidney cell cultures and the use of these cultures in diagnostic virology.<sup>6</sup>

"For example, most of the oral attenuated live poliomyelitis vaccine used throughout the world is produced in primary kidney cultures from African green monkeys and in some countries from rhesus monkeys."

Suitably alarmed, the WHO launched an urgent but quiet investigation to determine the implications. The results, said Zuckerman, proved reassuring: vaccines made during the 1970s had been tested for the presence of unknown retroviruses and had been found to be free of them. WHO then went on to test current seed stocks of vaccine for all three types of polio and examined twenty different current batches of vaccine in Europe and North America for retroviruses. None were found. They then tested 250 vaccine recipients for HIV or SIV antibodies and failed to find any. Long-term follow-up of earlier recipients likewise failed to reveal any signs of adverse effects. In the end WHO decided that monkey kidney cultures would contain "few, if any" T-cells capable of hosting SIV.

A senior WHO official, who must remain unnamed, conceded that when the theory first surfaced there was furious debate behind closed doors and it was "looked into in great detail". In the end it was determined that no public comment would be made on the issue (though results of the tests were reported in WHO's weekly record) because of the harm that might be caused to public perceptions of the safety of polio vaccines and vaccines in general and the setback it might inflict on world plans to curb or eradicate preventable disease.

There must also have been a second consideration: hundreds of thousands of people had already contracted AIDS from transfusions of contaminated blood, tens of millions had been given SV-40, hundreds had been paralysed or killed by vaccines that simply went wrong. The track record was starting to look decidedly shaky. One more scandal might place in jeopardy the public credibility of vaccine research and manufacture, not to mention its future funding.

There was doubtless a third consideration, barely voiced: the very model of American health science was on the line. The highly interventionist approaches which American doctors had used to tackle health problems worldwide, epitomised in the big polio campaigns, might come under scrutiny. American prestige was at stake. Quite apart from the scientific implications, could the United States medical establishment afford the stigma of suspicion of having unleashed -- even by accident and with the kindest of intentions -- the AIDS pandemic?

The issue of possible contamination of polio vaccine cultures by SIV was not laid to rest by the WHO tests, however. Quietly, it continued to trouble researchers' consciences. In 1989, a Japanese team at Tokyo University reported that they had killed a couple of African green monkeys which were infected with SIV and tried to detect the virus in cultures made from their kidneys, but failed. They then tried to infect two normal kidney cultures with SIV and failed. Finally they tested polio vaccine stocks for SIV, once more with a blank result. In a paper which proved greatly reassuring to many researchers, they wrote "From these results poliomyelitis vaccines may be considered not to be contaminated with SIV<sub>AGM</sub> even though they are prepared in primary kidney-cell cultures from SIV<sub>AGM</sub>-infected African Green Monkeys".<sup>7</sup>

So limited a test was unlikely to provide a definitive answer as to whether polio vaccines could carry SIV. This possibility increased in 1992 when a spokesman for Lederle, the United

States' sole manufacturer of polio vaccine, acknowledged in the media the company had discovered SIV in monkey kidney tissues used to make vaccine – and as a result had discarded that batch of vaccine.<sup>8</sup>

An Australian polio vaccine expert proposed a way in which some batches of vaccine might be contaminated with SIV but not others: if the monkey which donated the kidneys had recently contracted SIV while caged with other monkeys, it would carry extremely high levels of virus in its white blood cells from 5 to 35 days after infection. These white blood cells would be incorporated into the tissue culture at a rate, theoretically, of 1.5 million infectious units per monkey. "This consideration points strongly to the most likely source of an SIV/HIV contamination being monkeys cross-infected by exposure to other (infected) monkeys in an interval between caging for shipment to the USA and sacrifice by the vaccine manufacturer," he suggested.<sup>9</sup>

That the international science press was alive to the implications of the polio vaccine theory was evidenced in June 1990 when the ordinarily open-minded magazine *New Scientist* dumped on it. In an article entitled "Where Did the AIDS Virus Come From?", London Institute of Cancer Research virologist Dr Myra McClure wrote: "More discomfoting was the suggestion that HIV might have started life as a "harmless" contaminant of a human vaccine which, once injected into people, changed its properties and became a lethal disease. There are no grounds, epidemiological or biological, for believing that this has happened with HIV."<sup>10</sup>

It is hard to know which error in this statement to amend first. To begin with, SIV is not harmless: it can infect humans and it causes something very like AIDS in Asian monkeys. Secondly, the vaccine in question was administered orally, not injected. Thirdly, it is misleading to suggest that the virus had "changed its properties" to become deadly: it may well have been lethal to humans from the outset, though it subsequently underwent dramatic evolution in its new host. Fourthly, there are many epidemiological grounds – place, timing, patterns of spread, patterns of evolution etc. – for believing it may have so started. Fifthly, as six of America's most eminent microbiologists later acknowledged, there exist sound biological grounds, albeit of low probability, and using monkey kidneys is an inherently dangerous practice for this very reason, as researchers such as Koprowski, Tobin, Lecatsas, Alexander as well as many others had been warning since the 1950s.

McClure persisted. "But there are two good reasons for considering the possibility long enough to be able to discard it with an easy mind." She acknowledged contaminated vaccines were not unheard of and accepted that viruses can jump species when inoculated into a new host experimentally. She conceded the opportunity for such an incident existed, "theoretically at least", because polio vaccine was grown in cultures of green monkey kidneys, and green monkeys harbour SIV.

Nevertheless, she dismissed the notion on two grounds: "First, the epidemiology -- the pattern of HIV infection and its timing -- argues emphatically against such a possibility. Secondly, now that SIV<sub>AGM</sub> has been cloned and sequenced, we know that it is not sufficiently close to HIV in its make-up to support the argument."

She offered no evidence, emphatic or otherwise, to support her epidemiological argument. Her second claim that, because *one strain* out of many strains of SIV, known and unknown, did not resemble HIV-1 then contamination could not have occurred, was feeble. But the article was accurate in one respect: it presaged that no matter how persuasive the circumstantial evidence, it was liable to be discarded "with an easy conscience".

\* \* \*

Meanwhile, Louis Pascal's impassioned opus continued to fall on stony ground, although it is not hard to imagine why his assertions were so coolly received by the very people he had lambasted as "stupid and irresponsible". While adopting a quasi-scientific approach in carefully documenting and citing the evidence in support of his theory, he had shot himself in the foot by the tone in which he had elected to deliver it.

Regrettably, in the pressure cooker of public anxiety, media scares and policy vacillation of the 1980s, AIDS had become an issue awash with conspiracy theories of various kinds. These ranged from paranoid speculation about its origins to allegations that the authorities were letting it rage unchecked as part of a "back-burn" on the gay community. There were also claims of "propaganda, profiteering and genocide from the medical-industrial complex" in which governments were asserted to be in league with big pharmaceutical firms bent on squeezing out the most profitable rather than the quickest solution to the epidemic.<sup>11</sup> Among the most disturbing findings were polls of middle- and working-class black residents of Washington taken between 1988-90. These revealed almost two thirds believed AIDS had probably been developed as a tool of genocide against the black race.<sup>12</sup>

Professor Peter Duesberg, a molecular biologist at the University of California at Berkeley argued that AIDS was not caused by HIV, but due to immune system breakdown stemming from a heady mixture of drugs, sexually transmitted disease and a fast life-style.<sup>13</sup> This theory, which achieved wide coverage in the press and support in sections of the gay community in turn spawned fresh conspiracy theories about the motives of the scientists, public health officials and drug companies involved in the epidemic.

Highlighting the climate of paranoia, *The Economist* wrote: "One London doctor points out that many of his AIDS patients truly believe the disease to have been created by the CIA, however much he tells them that the idea is nonsense. They need something to believe in, someone to blame."<sup>14</sup>

In such an emotion-charged atmosphere it was difficult for a controversial theory about the origin of HIV in polio vaccine to receive objective consideration from the scientific community, especially when it arrived encased in similar invective to other, far less credible and well-researched hypotheses.

Pascal persisted in his efforts to get his ideas into scientific print. His first stroke of luck came in 1990 when Richard Sylvan, a philosopher at the Australian National University, forwarded a copy to Dr Brian Martin, an academic at Wollongong University in Australia, who specialised in the study of the nature, impact and management of science in society under the university's Science and Technology Analysis (STA) research program. One of Martin's particular interests was what he termed the "scientific straitjacket", the suppression of dissenting or alternative ideas by academic institutions, governments and industry. He was also interested in the dynamic of how society received and dealt with controversial and challenging notions.

"In my studies of the suppression of dissent, I have come across many cases similar to Pascal's, in which an unorthodox idea is prevented from being heard, especially if it is threatening to a powerful interest group," Martin said. "I find Pascal's case particularly well documented and persuasive. To my knowledge, his arguments have not been refuted. I believe (his) ideas deserve a wider hearing because a free society needs a much freer dissemination and discussion of controversial ideas than present social mechanisms allow."<sup>15</sup>

Martin considered there were three principal reasons for the refusal of the scientific press to publish Pascal's monograph. First, he was not a scientist, he had no advanced degree, nor did he

hail from a recognised scientific institution. Second, his articles were not written in the "dry, concise and passionless style" demanded by such journals but displayed more emotion and concern that was commonly permitted. And third, his ideas were enormously threatening to the medical research community. They could cause public loss of faith in vaccines and lead to stricter controls over medical research itself.<sup>16</sup>

But if nobody else would print it Martin, at least, was as good as his word. In December 1991 he published Pascal's monograph as Science and Technology Analysis working paper No 9. He then mailed copies to a wide selection of international medical researchers, scientists, philosophers and a handful of journalists inviting response, then sat back to study the reaction.

A characteristic response to Pascal's monograph came from a prominent researcher, Dr Robert May -- then of Oxford University, later to be appointed Chief Scientist for Great Britain and knighted for his services to science -- who described it as "a ranting tract, blending ideas (interesting but unsubstantiated) about the origin of HIV, less-interesting maanderings about the epidemic and self-centred emotional prose that raves on and on." May added: "Of course no-one would publish this in a sensible journal." Nevertheless, he conceded Pascal's ideas were "potentially interesting" and carried implications for vaccine development.

In spite of such reactions, a handful of scientists, some of them eminent, seemed willing to brave the wrath of their peers and venture an opinion that Pascal's theory had a few things going for it.

May's colleague, the eminent evolutionary biologist Professor William Hamilton, received a copy in December 1991. As Royal Society Research Professor in Zoology at Oxford, Hamilton had international credentials, including the Darwin Medal, the Linnaean Society medal and numerous other awards for his work on social behaviour, sex ratios and genetics. His academic career spanned Cambridge (UK), the London School of Economics, London University, Imperial College and the University of Michigan, before he assumed his Oxford chair in 1984

Pondering the import of Pascal's paper, Hamilton wrote back: "It is a strange paper and a strange style, but as I read I came to realise almost all of this is well justified. Refusal by the academic world for so long to publish the perfectly reasonable and plausible theory that you describe does seem quite extraordinary."<sup>17</sup>

Most original thinkers in science encountered something of



the sort during their careers, he observed, but what fanned the flames of Hamilton's concern was "the extreme practical importance of the matter in question".

"Your scenario accords with everything I believe likely about the origin of new diseases and about the *evolutionary* sequence such interspecies invasions are likely to go through," he wrote. "It seems to me that medical science tends to neglect the evolutionary aspects as if believing tacitly in a pre-Darwinian fixity of the pathogen entities they deal with." By this he meant that doctors were often unappreciative of the sudden and dramatic changes an agent might undergo when subjected to evolutionary pressure and of the scope that existed for previously stable agents to invade new ecological niches when an opportunity opened up.

Hamilton also saw the matter from a pragmatic perspective: "I must say that had I known...that they were injecting or making me eat *raw extracts of the tissues of a primate with nothing done to eliminate or incapacitate other viruses*, I would immediately have refused the inoculations." With a certain irony, he likened the practice to "borrowing money from the Devil to pay off polio, thereby incurring a debt the Devil will call in with another disease later."

Besides anticipating the cold shoulder that attempts to publish the idea were likely to receive, Hamilton was prophetic in another regard: he saw that the credibility of the theory would come to turn on the question of the Manchester sailor, David Carr -- and what strain of HIV he carried.

He went on to note that if the chimp hunter theory was the correct one, then Africans ought over generations to have selected for resistance to HIV as a result of being continually exposed to it. In concluding, he found Pascal's hypothesis "fascinating and frightening" and urged him to be stoic. If proved correct, he suggested it was worthy of a Nobel prize, though he preferred that some action be taken which would prevent future harm to humanity.

In South Africa, Professor Jennie Alexander, who had arrived at her own suspicions independently and with the insights of an expert virologist, also received a copy of the paper. "I don't see Pascal's idea as being "unorthodox"," she commented. "It seems an eminently reasonable and logical idea -- and it is probably testable.

"Stored serum samples must exist from persons vaccinated with attenuated polio virus in Central Africa in the late 1950s. These sera could be tested for HIV antibodies," she suggested.

"The Belgians probably have stored sera.... notably from the Kinshasa district. If the stored sera of 10,000 vaccinated Central Africans from the 1950s/60s could be tested together with the same number of sera from patients in eg the USA during the same period, one might find support for Pascal's claim.

"Another test would be to subject any remaining samples of the early attenuated polio vaccine to the polymerase chain reaction test using HIV probes directed against the conserved regions of the viral genome."<sup>18</sup>

Alexander felt that Pascal's failure to achieve a reasonable hearing for his theory in the scientific journals might be due in part to his accusatory style, to the fact that it was presented as *fait accompli* unsupported by the necessary facts, figures and research results, and because his delivery was more evocative of popular journalism than of scientific writing.

"The idea has merit, but those who hear it do not understand. Most scientists these days are not men and women of vision. Their world and their work is driven by technology and tunnel vision. They have ink in their veins and shrug off ideas or concepts that do not appear in their textbooks." Editors of scientific journals, she suggested, were highly dependent on such people to help them decide what to publish and what not. Finally, Alexander concluded that were Pascal's claim to be shown as valid, it would seriously impact on the medical profession, eroding its self-image of greatness, invincibility and knowledge.

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Meanwhile the editor of the *Journal of Medical Ethics*, Raanan Gillon of London University, rejected Pascal's paper on the grounds of length, but followed up its publication by Wollongong University with a favourable two-page editorial entitled "A startling 19,000-word thesis on the origin of AIDS: should *JME* have published it?"<sup>19</sup>

In the editorial, Gillon rehearsed Pascal's arguments and then summarised them as: "...in a nutshell, that AIDS is an iatrogenic disease, ie caused by doctors".

He explained the protracted negotiations which had taken place, Pascal's refusal to cut his opus down to a more concise 3500 word article on request and his failure to appreciate that the *Journal of Medical Ethics* was dedicated to the discussion of ethical issues, rather than original scientific hypotheses. However, he conceded, there were important ethical issues embedded in the story. Gillon hinted at his dismay when the paper came back, longer than ever, challenging him with the view that its publication

"might well help save millions of lives".

Gillon dismissed this argument "in retrospect perhaps rather too swiftly" and upped his offer to 7500 words. Pascal turned him down and instead accepted Martin's offer of complete, unedited publication in a form that was ultimately to achieve international circulation in excess of 500 copies. But the theory had obviously been bothering Gillon, because he generously decided to write his editorial to make the existence of the monograph known to those interested in the ethical questions it raised.

"*If it were true* it would certainly have very important implications, not least for AIDS scientists, for makers of live vaccines grown in monkey tissues (or indeed in tissues of any other species) and doubtless too for lawyers specialising in allegations of medical negligence," he wrote.

"The thesis of Mr Pascal's paper is essentially based on circumstantial evidence, but an impressive amount of it."

Gillon considered Pascal's reasoning and evidential chain "impressively coherent and entirely consistent" with his thesis that HIV started in a polio vaccine, but noted "consistency does not show causality".

"It is not the role of the *Journal of Medical Ethics* to opine on the truth or falsity of Mr Pascal's thesis. What does seem clear is that it is an important and thoroughly argued one and ought to be taken seriously by workers in the AIDS field."

Five years' passionate research and campaigning had finally paid off for Louis Pascal. But he was not to achieve the limelight of recognition when the theory finally surfaced in the public domain.

## Endnotes

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## In the Open

It was neither scientist nor scholar who laid the polio vaccine theory squarely before the general public, but an American reporter named Tom Curtis. A freelance investigative journalist and former senior editor with *Texas Monthly*, Curtis was working on a story about bioremediation when a chance acquaintance with a medical professor on an airliner prompted him to get in touch with a researcher and AIDS-activist called Blaine Elswood, at the University of California at San Francisco.

The contact led to Elswood faxing Curtis several items from the scientific literature, including Lecatsas' letter to *Nature*, suggesting that polio vaccine might be the source of AIDS. "Here's a bombshell story just waiting for an investigative reporter," Elswood wrote on his fax.

Curtis was intrigued by the idea, but didn't initially feel confident he could master the technical detail necessary to investigate the story: "I'm not a trained scientist. My degree is in political science," he explained. But Curtis had behind him a long and gutsy career in the investigation of complex and thorny issues such as civil rights, pesticides and police corruption, and his journalistic instincts gnawed away at him. This was far too important a story to ignore, he felt. Finally, he compromised, suggesting that Elswood write an article for a scientific journal which Curtis could then report in the general press. Elswood told him up front that he didn't think any scientific or medical journal was going to touch it, no matter how well reasoned or substantiated, because the medical research fraternity couldn't face up to the implications and no specialist publication would risk affronting its readers. The ball was back in Curtis's court.

"Ultimately we convinced one another," he said. "Elswood began to prepare a paper on how it might have happened, and I began checking it out also."<sup>1</sup>

Curiously, at this time, neither investigator had heard of Louis Pascal nor of his monograph. Elswood and Curtis were working purely off the few tantalising hints which had begun to trickle into the mainstream science literature. Coincidentally, they and Pascal were treading an almost identical scientific paper trail in complete unawareness of one another.<sup>2</sup>

Elswood broke the scientific ground. He had access to a superb medical library and the time to pursue his investigations,

carefully checking each of the references cited in the scientific literature and then relaying the results to Curtis. When he saw the evidence amassing, Curtis was inspired. "I got pretty interested and started to follow up, myself, in the Texas Medical Library."

Browsing the *Wall Street Journal* over breakfast one morning, Curtis's attention was rivetted by a report of the discovery by researchers at Baylor College of a monkey virus in the tumour of an AIDS patient. Significantly, the AIDS sufferer had never had contact with monkeys.

"I thought: whoa! This was the thing that really impressed me. So I went to see the researchers and asked them if they had any idea where it came from. They told me, no, none at all. I asked had they considered oral polio vaccine? It was like a light went on. It was a very interesting idea to them, because polio vaccine was ancient history by then."

Curtis continued to hunt through the scientific literature and ran across the SV-40 story. The fact the polio vaccines *had* transferred an unknown, potentially deadly, monkey virus to millions of humans impressed him still more forcibly. He decided to consult an expert and went to call on Joseph Melnick, one of the great polio pioneers along with Salk, Sabin and Koprowski, at the Warm Springs, Georgia, headquarters of the National Foundation for Infantile Paralysis. Melnick was quite candid: "SV-40 scared the hell out of us," he told Curtis. "We thought we'd given a whole generation cancer."

The polio pioneers were terrified that they had exposed millions upon millions of people to a virus which, even then, was suspected of being a major cancer culprit. Melnick's reaction gave Curtis confidence in another way, too. He began to appreciate that, despite its apparent aura of sophistication, the whole polio vaccine business was not some arcane, high art practised by geniuses and beyond the comprehension of mere mortals, but basically low-technology. "It became clear to me that these were human beings who didn't entirely know what they were doing, working in the dark, fallible. This emboldened me," Curtis recalled.

Something else also encouraged him. Each expert he consulted started by presenting an insurmountable reason why poliovaccine could not possibly be the source of the AIDS epidemic. But every reason put forward was different. "And when you came to look closely at each of them, they weren't so insurmountable after all. Everyone kept saying: "That's it. End of story. A complete refutation." But every explanation had holes in it, and it wasn't hard to find them -- but there were so many AIDS

conspiracy stories about then, it wasn't difficult for them to tar this theory with the same brush." Furthermore, as he delved into it, the history of polio vaccine seemed strewn with accidents, close-shaves and disasters.

While Curtis worked on his article, Elswood and a colleague, Dr Raphael Stricker, wrote up the hypothesis in a scientifically-presentable fashion and submitted it for publication in the *British Medical Journal*. As Elswood had anticipated, it was rejected.

They then submitted it to *Research in Virology*, a journal published by the Pasteur Institute, and received a more encouraging response. But the prevarication which followed meant that Curtis's article for the popular press beat Elswood and Stricker into print by more than a year.

Curtis's promised bombshell, "The Origin of AIDS -- A startling new theory attempts to answer the question 'Was it an Act of God or an Act of Man?'" was finally published in the 19 March 1992, edition of *Rolling Stone* magazine after six months of in-depth research and interviews with many of the top polio and AIDS experts in America and elsewhere.<sup>3</sup>

Curtis opened his account by depicting his own family, queued up in 1962 along with millions of their fellow Americans "like communicants in some universal mass", to receive the life-protecting vaccine. He conveyed both something of the terror which polio held for people in those days, and the public's trusting infatuation with science and technology in the halcyon post-war era. He recounted how Elswood had tipped him off about the vaccine theory, and of his first confrontation with one of the polio giants, the late Jonas Salk who, in the twilight of his career, was labouring to develop a vaccine for AIDS.

"I don't think I can be helpful to you," Salk had harumphed at Curtis, "other than to try to dissuade you from pursuing that kind of hypothesis, because what value is it? What value is it to anyone to try to imply such a cause and effect relationship?"

It was a response to be encountered again and again, in various guises, by journalists and other investigators seeking answers on the matter from senior virologists. What's the point of all this? Why do you want to know? It isn't important.

Salk had told Curtis he thought AIDS was a very ancient virus, but he could not cite any sources or evidence for his view. "It seemed like an article of faith. He didn't want a legacy of an unintended contaminant, even attached to someone else's vaccine". Gradually it had dawned on Curtis that he was likely to encounter much the same response whomever he spoke to, if they were

involved in vaccine.

In his magazine piece Curtis reviewed a variety of alternative theories for the cross-species leap, pointing out that each of them had problems. He then ran through the circumstantial evidence for a poliovaccine transmission: SV-40, Herpes B, Marburg, the Belgian Congo vaccination trials, and Sabin's discovery of a contaminating virus in CHAT-1. In search of answers he had decided to beard the great man, Koprowski's old sparring partner and merciless critic Albert Sabin, in his lair.

"You can't hang Koprowski with that," Albert Sabin growls at me," Curtis recounted. "He's sitting at the desk in his study. The walls are covered with testimonial plaques, certificates of commendation and achievement, photos of him with several presidents. Sabin insists that the AIDS virus won't survive swallowing. He's certain of it."

Curtis then referred to some scientific findings suggesting that Sabin's point was no major impediment: other researchers had found evidence, correct as it turned out, that HIV could be transmitted orally. He put the same question to Dr Tom Folks, chief retrovirologist at the CDC in Atlanta, and quoted him as saying that any time a person had a lesion (cut, bite or sore) in the mouth, transmission could occur if there was sufficient virus. Others had suggested the act of squirting the vaccine into children's mouths would create aerosol droplets that would pass to the lungs and blood stream.

Most perplexing were the contradictory statements made to him by scientists of international standing. When Curtis interviewed Gerald Quinnan, deputy head of the Food and Drug Administration, he had been told that there was no possible way that HIV could grow in a culture made from monkey kidney. "He said he'd done the experiment. Well, that seemed like the end of the story." But then he interviewed Folks who told him that, of course, HIV could get into a kidney culture if there were traces of blood in it, and there nearly always were when the culture was first minced up. "And the fact that it is a live vaccine would indicate they had not gone through any inactivation procedures to denature the AIDS virus, because it would probably denature the polio virus," Folks had told him. "So the polio virus is kept alive and the SIV virus would just travel with it. The theory, the possibility is real. And I don't think anybody would deny it." (To compound the confusion, both scientists subsequently reversed their views: Folks recanted, accusing Curtis of selective reporting, while Quinnan later qualified his categorical claim, admitting small amounts of virus



might get in.)

Curtis acknowledged that there was a missing factor in the equation: nobody seemed able to recall what sort of monkey kidneys were used to make the CHAT-1 vaccine -- whether Asian rhesus, which was the most common sort used until the SV-40 scare, or African green monkey, or both. Koprowski's papers simply stated the vaccine was grown on monkey-kidney monolayer.

However, in passing, Curtis also noted the fact that large lots of CHAT-1 used in the Belgian Congo were prepared at the Wistar Institute itself, whereas subsequent smaller batches used elsewhere were made at Wyeth Laboratories -- indicating there were multiple sources for the vaccine, as had been the case in the Cutter incident.

Finally, Curtis had gone to call on Koprowski himself at the Wistar Institute which, he recalled, was "a kind of spooky place... parts seem almost unchanged since the 1950s. You go in and there's this large stairway leading up; the hall has this Gothic appearance. It's rather old in its public face, modest and, it seemed to me, a little bit anachronistic. But then it's also very modern, a fully functioning research institution."

Koprowski had greeted him in a plainly furnished, unostentatious conference room. He was wearing an old sweater with a moth-hole in it, as if to underscore the informality of the meeting. "He struck me as avuncular. Charming, very articulate, cosmopolitan and media-savvy," Curtis remembered. "He was in his late seventies, but mentally pretty sharp. He struck me as a very socially skilled person, and he evidently had his eye on history in speaking with me. He was very interested in talking about the history of his polio vaccines. He seemed to enjoy the interviews and I have to say it was a fascinating conversation."

Koprowski's chief concern had been that Curtis not delve too deeply into the question of his original human trials, which had been conducted in a home for mentally retarded children and which had stirred up ethical debate at the time. He had explained that the director of the home had approached him for help because the children were throwing faeces at one another and infection was rife. So it was a good place to try a vaccine. Curtis was not entirely persuaded: "Everyone knew there was a race going on. He was extremely eager to find somewhere to run the trial."

After canvassing the history of his work, Curtis had asked Koprowski about Sabin's finding of an unknown virus in CHAT-1 and Koprowski had responded with much the same answer he did

in 1959: two other labs besides Wistar couldn't detect it. However, he had conceded that there was a problem in detecting unknown agents: "the viruses which lurk, for which there is no test, obviously you can't do anything about."

Curtis had then asked him what sort of monkeys had been used to make the vaccine. According to Curtis, Koprowski originally had insisted to him that the team had used African green monkey kidneys for producing the CHAT-1 virus. Koprowski checked his records and could not find an answer. He had then said he had a suspicion the original virus was grown in rhesus kidneys, and green monkey kidneys were used later on. However they had arrived at the lab from the supplier already excised, and possibly no-one knew for sure. In any case, the actual species was probably not that important, as it was by then known that green monkey SIV could infect rhesus monkeys if they were housed together.<sup>4</sup>

After much interlocution, Curtis had broached the idea with Koprowski that his vaccine may unintentionally have transferred the AIDS virus: "Koprowski dismisses the idea with a deep laugh: "Ho, ho, ho, ho, ho."

""I'm asking the question, I say.

"He laughs again, this time longer and deeper. "By then you would have plenty of opportunity to see AIDS in the vaccine," Koprowski says. "You have started in 1960; now its thirty years. The latency period of AIDS is nine years.""

Koprowski had pointed out there was no sign from any other part of the world of any virus in polio vaccine causing problems. Why insist AIDS began with polio vaccine in Africa, rather than anywhere else it was used? He had observed that HIV did not grow in monkey kidney cells, but only in white blood cells and had concluded by telling Curtis: "You're beating a dead horse. My opinion is that this is a highly theoretical situation, which...does not make sense."

In his article, Curtis disputed that AIDS would have been seen in the Congo nine years after the vaccine was administered. In underdeveloped, argely rural countries like the Congo, Rwanda and Burundi, AIDS-style infections might easily pass unnoticed among the swarm of other afflictions that carry people off. Clinical skills and resources were poor. It was a point later underlined by the WHO, which stated in 1994 that "where expertise and blood testing facilities are lacking, it may be difficult to differentiate AIDS from other common diseases. And in remote parts of the world, people fall ill and die without ever coming into contact with modern health services."

Curtis then cited the Belgian researchers Sonnet and Michaux who had identified seven cases of HIV/AIDS retrospectively from the Congo and Burundi between 1962 and 1976. He also attempted to close the gap between Africa and America, pointing out that, in his authoritative *History of AIDS*, Mirko Grmek had reported that after Congolese independence in the early 1960s many Haitians crossed to the newly-named country of Zaire. Being well educated, French speaking and black, they were a first choice to fill the void left by the departing European civil servants. Haiti was close to the United States and used to be regarded as a sex-holiday destination.

Finally, having elicited from Koprowski the information that seed stocks of the CHAT-1 and Fox-3 vaccines were still kept at the Wistar Institute, Curtis had suggested that it would be easy enough to settle the matter by testing them. Koprowski had doubted this would settle anything.

After some further argument about the phylogeny of the various strains of HIV and SIV -- a jungle becoming thicker and bushier by the year -- Curtis put the question to America's (then) AIDS hero, Dr Robert Gallo, whom he found "intellectually open-minded to the possibilities... in the best tradition of science".

"It could happen," Gallo conceded after initially arguing against the theory, due to the absence of a credible HIV precursor. He had concurred with Curtis's suggestion that one way to check would be to test the Wistar stocks. He had also provided a rationale for trying to find out: answers about the origin of AIDS may help us avoid future catastrophes. But Gallo, too, was ultimately to backtrack and come down strongly against the idea.

The suggestion the theory might help avoid future disasters held little appeal to Dr David Heymann, research director of the WHO Global Programme on AIDS, when Curtis rang him in Geneva: "The origin of the AIDS virus is of no importance to science today," he had bluntly declared. "Any speculation on how it arose is of no importance."

Other researchers were adamantly opposed to the notion. Professor William Haseltine of Harvard refused even to discuss it with Curtis, saying "It's distracting, it's non-productive, it's confusing to the public, and I think it's grossly misleading in terms of getting to the solution of the problem. It's over, it's done with, it's very, very unlikely it happened that way."

Curtis made it plain that he regarded the poliovaccine issue as unproven, neither true nor false but worthy of closer investigation. He had taken care to quote numerous scientists who

opposed it, as well as others who viewed it as conceivable. Should it ultimately prove to be true, he insisted that no blame should attach to Koprowski, who, he said, was acting from the highest of motives in wanting to eradicate a deadly scourge. Nevertheless, he concluded, "there was a certain hubris involved in the rough-and-ready campaigns to conquer polio".

\* \* \*

Around the same time that Curtis's article appeared in *Rolling Stone*, something came out of left field. An American lawyer, Walter Kyle, wrote to *The Lancet* saying that he had learned that in 1976 official United States tests on live polio vaccine Lederle lot 3-444 had revealed the presence of previously unknown C-type RNA viruses in numbers from 1000 to 100,000 per dose. Other lots were also implicated. After some deliberation, the United States Bureau of Biologics had cleared the vaccine for general use provided that it contained no more than "100 organisms" per millilitre, or dose.

Kyle knew that green monkeys carry SIV and that HIV probably crossed from them. But he did not appear to have heard of the Belgian Congo polio vaccine theory. His argument then took a curious twist. During the 1970s multiple injections of live polio vaccine had been used experimentally by doctors in California and New York to treat homosexual men for persistent herpes. Because they had received several shots, these patients would easily have exceeded the 100-organism per dose limit. Clearly implying this was how the American AIDS epidemic started, Kyle called for the results of all United States official tests on polio vaccine stocks to be made public.<sup>5</sup>

Lecatsas and Alexander bounced back into the ring. Responding to Kyle's letter in the same journal, they said it should "generate much-needed discussion on the possibility that HIV's origin lies in poliovaccines, an idea we proposed in 1989 and again at the International Congress of Virology in Berlin, in August 1990."<sup>6</sup>

"We have in our colony a healthy vervet monkey (*Cercopithecus pygerythrus*) which tests seropositive for major HIV-1 antigens by western blot.

"To use this animal's tissue for human vaccine production would be unethical.

"Yet this could have happened many times since monkey kidney tissue was first used in poliovaccine production in the late 1950s. Such cultures could support the growth of retroviruses.

HIV can infect certain CD4 cells, and there is evidence that some mouse and simian fibroblast cultures bear the CD4 antigen, the major HIV receptor."

What this meant was that monkey kidney cultures could contain cells which have the molecular docking point for SIV/HIV. Therefore it was possible that SIV could enter the culture and get into the vaccine.

"The simultaneous appearance in man within the past 30 years of both HIV-1 and HIV-2, which are distantly related in evolutionary terms, suggests contamination since closer relatives to the human strain exist in non-human primates.

"There is circumstantial evidence for a possible poliovirus vaccine origin of AIDS, and to ignore this possibility would be wrong ethically and scientifically," Lecatsas and Alexander concluded.

The argument about the two strains of HIV was of central importance. HIV-1 (identified mainly with the Americo-European and central African epidemic) and HIV-2 (identified mainly with West African cases) both emerged in the medical record in the same period. Both were closer to certain strains of SIV than they were to one another. Lecatsas and Alexander had made a point which was tantamount to saying: you can be knocked over by a car once, but it would be a bit suspicious if you were knocked over twice, by the same car, on the same day. It was an argument for which exponents of the chimp hunter theory had no plausible explanation: it meant that in all the four million years of human-primate predatory interaction the two viral breakthroughs most probably took place in humans in the same geological microsecond. That this also happened to be the age of modern medical technology when human and animal tissues and viruses were being freely mixed, needles and blood exchanged and the products universally disseminated made it seem more than mere coincidence.

\* \* \*

Like a wounded rhinoceros, the medical establishment was goaded into response. First cab off the rank was the august American journal *Science* which reported the *Rolling Stone* article in sneering terms, as soon as it appeared, under the heading "*Rolling Stone Weighs in*".<sup>7</sup>

"Over the years," the article by freelance writer Jon Cohen began, "the origin of AIDS has been the subject of wild speculations, many of them heavy with the odor of conspiracy..."

Having set the scene that, here we are, dealing with yet another wild speculation/conspiracy, Cohen embarked on an

attempted demolition, while feigning objectivity. Conceding that "some researchers contend that the article's hypothesis is not beyond the realm of possibility" he added "most AIDS investigators think the hypothesis is far too speculative to be taken seriously -- since, they argue, there isn't a picogram of evidence for it." Curtis had merely piled "speculation on speculation" he said.

Indeed, Cohen used the word speculate six times, as if this were an utterly disreputable and unheard-of practice in science. He was off-hand about Curtis' scientifically-correct proposal that the theory should be properly tested. *Science* was America's most prestigious general scientific journal and, with *Nature*, the place where many of the world's great research discoveries and advances were announced. Its opinions carried enormous weight.

Cohen also sought comment from Koprowski, who by then had decided -- contrary to what he had told Curtis -- that he had actually grown the vaccine in kidneys from Asian rhesus monkeys imported from the Philippines, which therefore could not have been infected with African SIV.

The *Science* piece then proceeded to shoot the messenger, going to town on Curtis for irresponsible journalism. It had CDC retrovirologist Folks "damning" Curtis for selectively quoting him and for ignoring contrary evidence. It quoted Food and Drug Administration deputy director Gerald Quinnan jr. as saying it is "not possible for SIV to be present in poliovaccines *in any substantial amount*" and it quoted the official CDC line that "the weight of scientific evidence does not support this idea."

Interpreted literally, of course, this scientific doublespeak meant that SIV *could* be present in polio vaccines in small amounts and there was *some* evidence in favour of the idea. The extremely limited Tokyo University trials had suggested HIV/SIV would not grow in pure monkey kidney monolayer, but other eminent virologists pointed out that sometimes these cultures could contain white blood cells, so contamination could not be ruled out. As for the "weight of evidence" cited by America's number one disease watchdog, where was it? Who had ever deeply investigated this issue and published a single substantial finding, as distinct from a pure hunch? It was starting to resemble a scene from *Through the Looking Glass*.

Yet not all of *Science*'s contacts were so unequivocal: SIV researcher Professor Ronald Desrosiers of Harvard Medical School explained that he had never heard a good reason why the polio vaccine theory was not plausible. But Desrosiers then fell into line, "lambasting" *Rolling Stone* as irresponsible -- presumably for

having the effrontery to enhance the idea's plausibility. In the end, *Science* hedged, most of the evidence "seems to be against" the idea that AIDS came from a polio vaccine.

Curtis fought back. In a follow-up letter he invited Cohen to specify which of the other AIDS origin theories had rigorous scientific proof. He also retorted that the *Science* piece was "misleading in many respects" and "flat-out wrong" in printing the assertion that there was not a picogram of evidence. There was a strong -- if circumstantial -- case, he said.<sup>8</sup>

Curtis cited several of the scientists quoted in his article to underline the possibility that HIV was a fast-evolving form of SIV, that it could infect white blood cells and that these could be found in kidney cultures. And he pointed out that he was not the author of the theory as *Science* seemed determined to credit him, but merely its reporter. The theory had been proposed to him by Elswood. This wasn't a point which weighed much with the medical establishment: on television and elsewhere, Curtis was attacked and condemned for not being a scientist yet having the gall to report a scientific hypothesis. It was plainly easier for his critics to sustain this sort of *ad hominem* argument than to give the evidence had had gathered a fair hearing.

Not all of *Science's* readers were as dismissive as their journal. Pathologist Dr Cecil H Fox of New Haven lampooned their headline with the observation that "If *Science* has weighed in on the "origin of AIDS from polio vaccine" debate, it must be in the lightweight category". In a coolly reasoned letter, Fox underlined the lessons from the SV-40 scandal and stated that there was abundant evidence that HIV/SIV could grow in kidney cultures which contained white blood cells.<sup>9</sup>

"The early days of poliovirus vaccine manufacture were not controlled by the U.S. Food and Drug Administration," he pointed out. "Many lots of vaccine were produced by low-bid contractors, who were likely to have been cost-conscious and to have rejected either screening for other viruses or good laboratory practice with their monkey kidney cells cultures. Nor was there much in the way of ethical debate about the testing of vaccines on rural Africans (as was done in the Congo)."

Conceding that it was difficult to test vaccines made so long ago, Fox nevertheless felt that the only ethical thing to do was to use the latest techniques on whatever material survived.

Fox was not the only authoritative figure calling for the Congo vaccines to be tested. Dr Joseph Melnick, one of the original polio pioneers, a figure of unimpeachable scientific repute and a member

of the WHO poliovaccine committee since 1972, also urged testing. "I think all the stocks that were used in human beings at the time in any part of the world should be tested [to] put these questions to rest," he said in the press.<sup>10</sup>

There was one more wild card to be played. In June 1992, a Billi Goldberg wrote to *The Lancet* pointing out that monkey kidneys were not the only type of material used to make the Wistar's polio vaccines. According to papers written by Koprowski's colleague Hayflick, he said, it had also been produced in tissue cultures made from human foetuses.<sup>11</sup>

"Culture of human diploid fibroblasts, on infection with HIV-1, will produce and release infectious virus," Goldberg wrote. "Between August 1958 and April 1960 over 75,000 children under five years of age were immunised in Leopoldville, Belgian Congo, with vaccines prepared at the Wistar Institute. Is there any possibility at all those poliovaccines were developed in the human cell line?"

This was a direct echo of what veterinary microbiologists suspected was the origin of the canine parvovirus pandemic, in which a cat virus may have adapted to its new host, the dog, by being grown in a culture of dog cells, to become a lethal dog disease which spread worldwide in a matter of years.

\* \* \*

Following Curtis's attempt to defend himself in *Science*, Koprowski counterattacked. On 21 August, in the same journal, he made a detailed response to the suggestion that AIDS might have been transmitted to humans in one of his vaccines.

"As a scientist, I did not intend to debate Tom Curtis when he presented his hypothesis about the origin of AIDS in *Rolling Stone*. The publication of his letter in *Science*, however, transferred the debate from the lay press to a highly respected scientific journal. I would now like to state my views, based on facts, in order to counter and thereby repudiate Curtis' hypothesis about the origin of AIDS."<sup>12</sup>

Koprowski began by backgrounding the efforts of researchers to overcome polio epidemics that were raging throughout the world in the late 1940s. He then quoted Curtis's assertion that the vaccination campaign in the Ruzizi valley in 1958 corresponded with one of the areas of highest HIV infection in central Africa, the Kivu district of Zaire.

"This is completely wrong. Ruzizi valley...is located in the northwestern part of the Republic of Burundi, not in the Kivu district of Zaire."



High levels of HIV-positive results in tests on these people could be due to a well-known error -- false positives -- in early tests used to detect antibodies against HIV in blood, Koprowski argued. The researchers who had carried out the tests, he pointed out, had subsequently scaled down their estimates of infection rates in the light of this.

More recent tests, Koprowski stated, showed low rates of HIV infection -- 0.7 per cent for rural Burundi, 1.3 per cent for rural Rwanda and 3.7 per cent for rural Zaire. He accused Curtis of being misleading by suggesting that these areas were heavily infected by AIDS. If the vaccine had been responsible, then surely infection levels would be far higher in the rural areas, he reasoned. Yet it was the cities which had the worst rates -- 25-30 per cent.

Koprowski stated that the same pool of vaccine was administered to children in Poland, yet Poland had one of the lowest AIDS incidences in Europe.

"Even the supposedly early cases of AIDS in Africa were clinically diagnosed several thousand kilometres away from the Kivu region," he claimed. And the British sailor showed symptoms of the disease in 1958, "before any mass vaccination for polio was started."

He then went on to claim that only kidneys from rhesus monkeys "captured in India or the Philippines" were used to produce "all other batches" of vaccine. Despite the Indian embargo on rhesus exports, supplies continued to arrive from the Philippines. In any case, he added, kidney tissue from African green monkeys infected with SIV had been shown not to harbour virus.

He reiterated his dispute with Sabin over the unidentified virus found in CHAT-1, and the negative retest results from his own lab and two others. He contradicted Sabin's statement that he had tested the vaccine itself, claiming the test sample was only from a "seed lot".

Koprowski added that many vaccines made in monkey kidney cultures had been found to contain cell-killing agents and foamy viruses. However, these did not disqualify such vaccines from worldwide use, though it would be better to use human diploid (embryo) cell cultures instead of monkey tissue to make them.

Some 7.2 million Poles, 34,000 Swiss and 1.5 million Croats had received the same vaccines without ill-effect, he argued.

Curtis had failed to distinguish between lots of vaccine and seed lots, Koprowski said. The Wistar had retained no vaccine,

only tissue culture supernatants "that may represent seed lots". Testing these would not settle anything, as "contentious individuals" could still argue that they did not represent the main lot of vaccine used in the Congo.

"The argument for the safety of polio vaccine lies in the absence of any AIDS-related disease among the hundreds of millions of people vaccinated throughout the world; the fact that AIDS is rampant in subequatorial Africa can only be attributed to the polio vaccine by the wildest of lay speculation," Koprowski asserted.

\* \* \*

Meanwhile, within the gothic halls of the Wistar Institute, things were happening. Alarmed at the implications of Curtis's article and the widening coverage of its theories in the American media, the Institute hastily convened an investigation to see if there was any substance to them. Though drawn mainly from other institutions, the committee's six members had much in common: there was no-one from overseas, no experts from fields of science other than microbiology and medical research, no-one from outside the eastern United States and no-one from other professions. It was very much in the family.

The investigative team was headed by Professor Claudio Basilico, chairman of the New York University School of Medicine, and included Professor Ronald Desrosiers of Harvard Medical School, Professor Clayton Buck of the Wistar Institute itself, Professor Frank Lilly of the Albert Einstein College of Medicine, Professor Eckard Wimmer of New York State University Department of Microbiology and Professor David Ho, director of the Aaron Diamond AIDS Research Center. It delivered its report on 18 September 1992.<sup>13</sup>

Responding to the "Curtis hypothesis", they decided to address each possible step in the chain of contamination and infection to see if there were any flaws or weaknesses.

### **1. Was the vaccine contaminated?**

Though SIV and HIV did not grow in kidney cells, the panel concluded that the primary kidney culture could have contained "a low number of lymphocytes and macrophages, known to harbour SIV *in vivo* and to support the replication of SIV in culture."

"Thus the possibility of the presence of a small amount of SIV particles in these culture supernatants cannot be discounted," they agreed. Also, contamination could have taken place at any point in the process of attenuating or growing the vaccine,

including the preparation of "seed" virus, although they felt that this was "quite unlikely". If contamination did occur, it was probably in the grow-out phase, when vaccine was being prepared for the trials, and it "should have been small".

## **2. Where did the monkey kidneys come from?**

The committee regarded it as crucial whether the kidneys came from Asian or African monkeys (despite evidence they can cross-infect). It noted that, around the time of the Belgian Congo trials, the Indian government had an embargo on the export of Asian monkeys, "and thus monkeys of African origin may have been used". It was also important to determine the species, as about 30 per cent of wild green monkeys had been found to harbour SIVs. Unfortunately, no records could be traced, and the source of the kidneys was unlikely ever to be determined, they concluded.

## **3. Could SIV survive vaccine processing?**

The vaccine was subjected to at least two cycles of freezing and thawing, something polio virus withstands readily, but which tends to cause significant loss of infectivity in SIV or HIV. The team also noted that such processing makes retroviruses "labile", meaning subject to change or decay. The CHAT-1 virus was kept deep-frozen for some time at minus 20 celsius and was diluted with saline solution 300-fold to make the final vaccine.

"In summary the possible presence of viral particles in the vaccine preparation cannot be discounted. However, if present, the concentration of SIV particles is likely to have been extremely low."

## **4. Could SIV transfer occur orally?**

While the oral route was not regarded as an efficient way to cause infection with either SIV or HIV, the committee agreed that some of the 300,000 individuals vaccinated could have had sores, wounds or blisters in their mouths that might have provided sites for infection.

Also, as there was good scientific evidence for mothers having transferred HIV to their babies in breast milk, this further strengthened the argument that the virus could be passed either via the mouth or digestive tract. Again, they rated the chance of this happening in a poliovaccine as low, but they agreed that squirting it into children's mouths might produce aerosol particles which could then reach white cells in the respiratory tract and alveoli.

### **5. Could SIV multiply in humans?**

"If SIV or an SIV-like virus did gain access to a susceptible cell in a vaccine recipient, it is possible that it might have multiplied in the human host," the panel decided. SIV had been found to grow in humans cells in culture, and had infected at least one laboratory worker. Yes, it could.

There was an SIV which was close to HIV-2, but no retrovirus had yet been found in monkeys which was closely related to HIV-1, only in chimpanzees. The committee accepted the view of virus experts that the differences in HIV-1 and HIV-2 represented centuries of evolution. It was impossible, in their view, that any *known* (author's italics) SIV could evolve into HIV in the two years between the start of vaccination and the first HIV-positive cases, that is from 1957 to 1959.

They reposed the weight of their concluding argument on the case of British sailor David Carr who, they said, had visited Gibraltar and North Africa between 1955/57 before returning home "by the first half of 1957". This proved he was back in Britain before Koprowski's Congo vaccine trials began, they asserted.

On the strength of this contention alone they concluded: "Therefore it can be stated with almost complete certainty that the large poliovaccine trial begun late in 1957 in Congo (sic) was not the origin of AIDS".

They had erred. Koprowski's own records indicate he began vaccinating in Stanleyville in the 12 months prior to February 24, 1958, that is, from early in 1957, and had vaccinated his chimpanzee keepers at Lindi Camp *earlier still*. Carr's symptoms did not emerge until December 1958, leaving a twenty month window for infection to take place and its signs to appear. In any case, Carr's medical history indicated his visit to Gibraltar took place in the second half of 1957, not long before his discharge from the Royal Navy that November. But this was not the last to be heard of David Carr.

### **6. Could the Wistar vaccine samples be tested?**

The panel adjudged this "not so simple". Testing the seed stocks of vaccine would not be enough, because contamination might have happened when the actual vaccine was prepared, so all lots would have to be tested, if they still could be found and identified as from the ones used in the Congo.

Even if samples still existed, they argued that virus infectivity would certainly have been lost in the past thirty-five years and a negative result from the PCR test would only be seen

as inconclusive, while a positive one would not identify the type of virus. Cloning and sequencing of the viral genes would be needed. Then, if any SIV gene sequences were found which were distantly related to HIV, their relationship would be difficult to determine. It would also be necessary to test other lots of vaccine made in the 1950s, not just CHAT-1.

But what if a significant percentage of polio vaccines used worldwide in the 1950s proved to be contaminated with SIV, the panel wondered (contradicting their earlier insistence that this was likely to have been an event of extremely low probability)? They decided that testing of vaccines would be "laborious, expensive and may be inconclusive".

Placing the disturbing spectre of widespread vaccine contamination with SIV hastily behind them, the Wistar Institute's AIDS/Poliovirus Advisory Committee's reached its final verdict. The panel concluded that:

1. The probability of the AIDS epidemic starting from the poliovirus vaccination campaign in the Congo was "extremely low".

2. Contamination of the vaccine with SIV particles, if any, would have been "extremely small".

3. Transmission of HIV or SIV orally is "extremely rare".

4. The phylogenetic gap between HIV-1 and the known SIVs was too wide to be bridged in a couple of years.

5. The Manchester sailor, David Carr, appeared to have been infected with HIV-1 even before the polio virus trials in the Congo were begun.

Limited testing of Wistar vaccine samples "may be desirable", the panel conceded, but they expressed pessimism that anything conclusive would emerge from it. Of the samples still retained at the Wistar Institute, only one was identified as being "possibly directly relevant" to the Congo trials. It advocated that any tests be performed by the WHO or the United States CDC in Atlanta, and prescribed which tests should be run.

Then came a startling coda.

"In closing, we feel compelled to mention that the current controversy highlights the problems and difficulties associated with using monkey tissues for production of vaccines administered to humans.

"To this day (Sept 18, 1992) live-attenuated poliovirus vaccine is produced in the United States and in most other countries using African green monkey kidney cells.

"Although green monkeys can now be certified free of SIV

for use in vaccine production, specific tests could not have been performed prior to 1985 when SIV was first isolated.

"There may well be other monkey viruses that have not yet been discovered that could possibly contaminate vaccine lots."

The committee called for a serious effort in the United States and other countries to switch to well-characterised cell lines for polio vaccine production, a point that Koprowski himself had raised as far back as 1960. Oddly, it was for raising precisely the same concern that Lecatsas and Alexander had received such savage condemnation from other scientists.

The Wistar exculpation was a remarkable document. It conceded that every aspect of the vaccine theory was biologically and scientifically possible -- except the Manchester sailor, and there it had the dates wrong. The panel had categorised the probability of SIV crossing to humans in the CHAT-1 poliovaccine as extremely low/extremely small/extremely rare, but it had failed to discover a single concrete refutation. In fact, on every scientific ground, it had acknowledged the potential of the polio vaccine theory.

Furthermore, it had recommended that independent tests be run on stored vaccines from the era. And it had concluded by urging the world to take extreme caution in the use of monkey-kidney cultures for making vaccine because of the danger they might be contaminated by unknown viruses.

But in spite of its careful balance, the report had flaws. Its central reasoning was that, as each link in the chain of contamination was improbable, ultimate infection of humans by this chain must be very improbable. Critics such as Louis Pascal noted the weakness in this theory was that improbability would diminish in direct proportion to the number of infected monkeys used to make kidney cultures, the number of contaminated cultures used to grow vaccine, the number of contaminated doses actually made, the number of these administered, the number of infective viral particles per dose and the number of recipients susceptible to infection. What seemed on the surface very improbable might in fact be, statistically, not so unlikely after all. After all, it only required a single infection to start the epidemic.

Nonetheless, *Science* was smug. Under the heading "Panel Nixes Congo Trials as AIDS Source" it reported the Wistar committee's findings, asserting that it had administered "the putative coup de grace" to the polio vaccine theory. The author of the article evidently failed to verify the Carr case and its dates in the scientific literature, and seemed content to take the panel's

word for it.<sup>14</sup>

Curtis pointed out this error in a letter to *Science*, asserting that what the magazine had termed the "putative coup de grace" did not, in fact, debunk the theory -- because by the time Carr's health first began to fail, the polio campaign was well under way and 200,000 people had received the vaccine. He pointed out that the panel had no documentation for its claim that Carr had returned to Britain before the campaign began. He noted that one of the authors of the Wistar report, Desrosiers, had called the use of monkey kidneys for vaccine manufacture "a ticking time-bomb" in the press, and that another, Ho, had admitted that the investigation had not disproved the view that the Congo vaccinations might have sparked the AIDS epidemic.<sup>15</sup>

## Endnotes

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- <sup>1</sup> Curtis T., personal communication, October 25, 1995.
- <sup>2</sup> If this sounds strange, the phenomenon is not unknown in science. Darwin and Wallace, for example for years pursued a similar theory of natural selection. See Desmond A. Moore J., *Darwin*. Penguin 1991.
- <sup>3</sup> Curtis T., The Origin of AIDS: a startling new theory attempts to answer the question 'Was it an Act of God or an Act of Man?', *Rolling Stone*, March 19 1992, pp54-61, 106-109.
- <sup>4</sup> In contrast to the other polio vaccine pioneers, Koprowski never did publish the precise details of how he made the CHAT vaccine or what substrate he used to grow his poliovirus on. See Hooper E. *The River*, Penguin Press, p247.
- <sup>5</sup> Kyle W., Simian retroviruses, poliovaccine, and the origin of AIDS. *The Lancet* 339, March 7 1992, pp 600-601.
- <sup>6</sup> Lecatsas G. & Alexander J.J. Origins of HIV. *The Lancet*, 339, June 6, 1992 p 1427.
- <sup>7</sup> Cohen J., Debate on AIDS Origin: Rolling Stone Weighs In, *Science*, March 20 1992, p1505.
- <sup>8</sup> Curtis T., *Science* 256, 29 May 1992, p 1260.
- <sup>9</sup> Fox C.H., Possible Origin of AIDS. *Science* 256, 29 May 1992, pp1259-1260
- <sup>10</sup> Melnick J., cited in Curtis T., Expert Says Test Vaccine, Backs Check of Polio Stocks for AIDS Virus, *Houston Post* March 22 1992
- <sup>11</sup> Goldberg B., Origin of AIDS. *The Lancet*, 339. June 20 1992, p1548.

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- <sup>12</sup> Koprowski H., AIDS and the Polio Vaccine, *Science* 257, August 21 1992, pp1025-1025.
- <sup>13</sup> Basilico C., Buck C., Desrosiers R., Ho D., Lilly F., Wimmer E., Report from the AIDS/Poliovirus Advisory Committee, September 18. 1992.
- <sup>14</sup> Holden C. edit, Panel Nixes Congo Trials as AIDS Source., *Science* 258, 30 October 1992, p738.
- <sup>15</sup> Curtis T., AIDS Theories, *Science* 259, 1 January 1993, p14.



## Wall of Silence

Koprowski sued. After reading Curtis's response in *Science*, on 16 December 1992 he launched a defamation suit against *Rolling Stone* publisher, Jann Wenner, and Curtis in which his lawyers asserted that they had "destroyed the reputation of Dr Koprowski, in that a reasonable reader could infer Dr Koprowski's polio vaccine infected its recipients with the AIDS virus". The writ further alleged that the article had caused the scientist mental and emotional suffering, as well as humiliation and embarrassment. It claimed that there was "no scientific evidence to support the accusation that Dr Koprowski's polio vaccine introduced AIDS to the human population."

It wasn't the first time Koprowski had reached for the law. Two months earlier he had sued the Associated Press news service over their report on Curtis's article, alleging they had "blackened and injured" his reputation by characterising him as careless and incompetent. *Science* reported the affair in a short piece entitled "Koprowski Sues Rock Mag".<sup>1</sup>

The recourse to law was a development which some in the world scientific community viewed with deep disquiet. In Australia, Brian Martin, who had published Pascal's original paper and was a scholar of the suppression of ideas, wrote to *Nature*: "Whatever one may think of this particular theory, the use of the courts against writers and publishers discussing scientific issues is an unwelcome development. It is likely to have an inhibiting effect on open scientific discussion."

If the same device had been employed against Charles Darwin, against those who opposed nuclear weapons or those with concerns about genetic engineering, he pointed out it would not have been a healthy thing for either science or society.

"Without learning from mistakes, they are bound to be repeated. It would be unfortunate if discussion of possible inadvertent consequences of scientific activity could be inhibited by legal action," Martin wrote.<sup>2</sup>

When news of the lawsuit reached him at Oxford University, evolutionary biologist William Hamilton also felt that such a course was fraught with danger. "I consider the Koprowski lawsuit an attempt to suppress discussion. It was wrong and a very bad precedent to use financial power and law to attack an hypothesis," he commented.<sup>3</sup>

Hamilton was unimpressed by the Wistar panel's "feeble report" and the general "wall of silence" towards manuscripts dealing with the issue. He drew an analogy between the reaction of the medical establishment in its attempts to suppress debate on the polio vaccine theory and the anxiety of the over-powerful Christian Church of mediaeval Europe to suppress heresy.

"Being burned alive as a heretic is admittedly worse than facing financial ruin, but except for the threat being different, we have seen this mode before and also... its belated finale in the Vatican's apology to Bruno and Galileo. Are we starting this all over again with a Medical Establishment now in the robes of a universal Church?" he wondered.

Hamilton also sat down to pen a letter, to the editor-in-chief of *Science*, Dr Daniel Koshland. He argued that Curtis's article had been "good science journalism", being readable, well-researched and attentive to alternative theories. If snags existed with its central contention, then they existed for all competing theories, he pointed out. He cited the *Journal of Medical Ethics* editorial calling Pascal's version of the same theory "important and thoroughly argued". He cited the arguments of Lecatsas and Alexander. He advocated testing of the Wistar vaccine stocks and cited the panel's conclusions. Above all he urged that scientists should be prepared to listen to and investigate with due care all such theories. They should not endeavour to suppress them, by litigation or by any other means.<sup>4</sup> It was a reasonable and reasoned letter from an internationally eminent scientist.

It was rejected. Hamilton received a brief note from *Science* letters editor Christine Gilbert, paradoxically advising him that although *Science* recognised he was "superbly qualified to comment" and appreciated the "merits of his concern", his letter would not appear.

Patiently, he wrote back to Koshland protesting his verdict and urging him to reconsider it in the interests of human safety as well as the conduct of science. He argued that if AIDS had originated in this way, then a very thorough reconsideration of *all ways* by which medicine could transfer new disease was essential: awful though it was, the AIDS pandemic might merely be a warning. Suppose the next pathogen combined the destructiveness of AIDS with the infectiousness of 'flu?

"Even the prospect of nuclear war cannot match the destructive potential of such an event. Thus I think you as editor of *Science* have a grave responsibility to humanity to see that these issues are as fairly discussed as is possible," he urged.<sup>5</sup>

Once aroused, the issue would never go away, Hamilton warned. Sufficient evidence had already emerged for the polio vaccine theory to be taken "very seriously indeed". He rated himself "just a scientist with common sense plus what might be called old-fashioned standards", one of which was that every idea should be assessed on its rational merits and quite independently of "vested interests, power structures, reputations and the like".

He had spoken out, he said, because so many medical scientists felt unable to, for fear of antagonising their colleagues, losing their research grants or of being "oppressed by the hierarchy". This was precisely the fate which had befallen Dr Bernice Eddy, the researcher who had been persecuted for discovering SV-40 contamination of polio vaccine all those years ago, he pointed out.

That such pressures already existed in this case he was personally convinced. "I am finding people far better qualified to investigate the theory than I am, who say to me things like: "Well, I can see the theory may have a case, but I'm afraid I can't touch any of that: our grant comes from the Medical Research Council..." or "Labs that could test what you want in Britain are all in the same boat, they all get their money from the MRC or drug companies. I don't think you are going to find any of them wanting to be testing an old vaccine with a risk of turning up something."

"Surely you must realise," he appealed to Koshland, "that the development of this sort of situation in science is terrible, literally terrible, for all mankind."

Koshland turned him down.

Subsequently, it became clear why. Following its usual practice, *Science* had commissioned an expert American scientist to comment on Hamilton's letter. This reviewer dismissed it on three heads. First it did "not break new ground". Second the reviewer professed himself astonished at Hamilton's astonishment over Koprowski's decision to sue: it was a treasured American freedom "to sue anybody for anything". And third, Hamilton had acknowledged the theory had "serious flaws". The reviewer went on to argue there was a "far better general theory" for the origin of AIDS, though he did not trouble to produce any scientific evidence in support of this claim. Like others before, he held to the view – again without evidence – that SIV transmission from monkeys to humans had been taking place for eons, and it was "changed conditions" in Africa in the postwar era that finally released it into the wider world.

However, after a supercilious opening dismissal even the

*Science* reviewer felt obliged to concede that “no-one can state with any certainty yet that the oral polio vaccine was not the source of HIV-1 introduction into humans”. He went on to admit that monkey kidney culture are often seen under the microscope to contain white blood cells which might harbour the AIDS virus. And he claimed erroneously that “no case of oral sexual transmission of HIV is known”. After some further charges that Hamilton was “emotional...polemical and...pompous”, the reviewer tailed off weakly, saying only that he did “not consider the polio vaccine to be one of the more likely theories of origin”.<sup>6</sup>

It was a characteristic reaction: the lack of scientific evidence, the irrelevancies, the incorrect assertions, the obvious doubts masked by smug comments intended to belittle those who wanted the issue scientifically investigated. But it was enough to satisfy *Science*.

Persistently, Hamilton sent a slightly modified version of his letter to *Nature* editor Sir John Maddox. *Nature* also rejected it, claiming that there was “nothing new” in his arguments. They did, however, encourage him to submit a cut-down version to form part of an article reviewing all theories on the origin of AIDS. Hamilton felt the space constraints thus imposed would force him to prune so severely as to emasculate the argument. He declined.

“I can't say *Nature* was quite as negative as *Science*. Yet it seemed that my pleas were all falling on ears that were semi-deaf with regard to the hypothesis all the same,” he said.

In fact there was plenty that was new in Hamilton's arguments. For example, there was the subtle evolutionary point that when researchers attenuate or weaken a virus by passing it through various animals, they are actually causing a sharp acceleration in its evolution. If a polio virus was thus dramatically weakened, who is to say that a hitch-hiking lentivirus might not become deadly to humans, and more divergent from its origins? Then there was his tongue-in-cheek statistical point that more Africans had probably received polio vaccine than were ever bitten by monkeys. But it made no difference.

Ironically, just two months after Koprowski filed his defamation suit, and almost a year after Curtis's article had appeared in *Rolling Stone*, Elswood and Stricker's paper was finally accepted by the editors of *Research in Virology*. When they had originally submitted it, thirteen months earlier, Luc Montagnier of the Pasteur Institute had written back saying he would recommend it for publication. However, the journal's editorial board finally decided they would accept only a heavily-cut version,

in the form of a letter to the editor. Rather than see the theory buried once more, Elswood and Stricker submitted to this frustrating condition. (Subsequently, it emerged the journal had rejected the full paper after receiving from Koprowski a stinging comment from Sabin, who described the paper as “a most irresponsible communication” but failed to back up his claims.<sup>7</sup>)

In the letter, Elswood and Stricker advanced a concise version of the polio vaccine theory, stating that “a more likely explanation for the AIDS epidemic is a massive population exposure to an HIV-like virus contained in a vaccine”. They cited a colleague of Koprowski's as saying in 1962 that at least eighteen different simian viruses were known to contaminate monkey kidney cells.<sup>8</sup>

The Editorial Board of *Research in Virology* covered itself by running an editorial comment in which it sought to undermine Elswood and Stricker's argument. “It is legitimate to raise questions about the still mysterious origin of the AIDS epidemic and not to exclude the role of medical actions”, the editors said, but then argued – obscurely – that since HIV was not present in Asian rhesus macaques naturally, Koprowski's vaccine could not have been contaminated with it. If the editors knew which monkey kidneys Wistar had used, they were the only ones who did. No-one else has ever been able to find out.

The editors had also argued that since HIV-1 was closest to a chimpanzee SIV, and chimp kidneys had never been used to make vaccine, it was hard to imagine how contamination might have taken place. Finally, they had pointed out that the death of David Carr from AIDS in 1959 indicated the disease was already on the loose at the time of the vaccine campaign, again without verifying the dates.

Why did the scientific press behave so? Was it warned off by the aediles of the medical research establishment? Was it intimidated by the lawsuits? Was it fearful for the public repute of medicine? Was it mugged by its own reviewers? Did it simply not *care* whether AIDS might have been a medical mishap sufficient to kill 70 million people? Or did it prefer not to know?

\* \* \*

For a year or so Koprowski's lawsuit rumbled on, in the process almost destroying Curtis' livelihood as a freelance journalist by forcing him to devote most of his time to the defence of his case.

Although it was never ultimately to go to court, the lawsuit did illuminate the diametrically-opposing views which existed privately among experts on the issue. Dr Robert Gallo, whom

Curtis had interviewed and quoted at the time as conceding poliovaccine transmission was "a theoretical possibility", produced an affidavit stating "the article's hypothesis that Dr Koprowski's vaccine contained HIV-1, or a simian precursor to HIV-1, which infected the recipients of the vaccine in equatorial Africa, is false".<sup>9</sup>

In support of this categorical assertion, he went on: "As far as we know HIV-1 does not survive in the culture of pure monkey cells. As I have been told, the Protocol for the preparation of Dr Koprowski's vaccine called for the preparation of the vaccine in monolayers of monkey kidney cells. CD4+ T cells and macrophages are the target cells for HIV-1 infection. Monolayers of monkey kidney cells do not contain CD4 lymphocytes or macrophage (sic) as far as I know. Therefore HIV-1 could not survive in such a culture." Gallo added he could not remember having conceded to Curtis at the time that such transfer was a theoretical possibility. Pascal, in a privately circulated commentary, drily remarked: "Does not this seem a little too full of lines like "as far as I know" and "as I have been told" and "I do not believe"? Particularly, does this not seem so in view of the certitude expressed in the first sentence?"<sup>10</sup>

If, in spite of these qualifications, Gallo was convinced the polio vaccine idea was false, others were far less certain. Among them was Dr Joseph Melnick, Dean Emeritus at Baylor Medical College and one of the original polio pioneers along with Salk, Sabin and Koprowski, renowned for his meticulous science. "I find this theory to be plausible and one of several possible explanations for the still unsolved mystery of how the modern AIDS epidemic originated," Melnick's affidavit stated.<sup>11</sup>

Melnick directly contradicted Gallo's claim that HIV-1 could not occur in kidney cultures, explaining that these "often contained lymphocytes and macrophages" in which it might survive. (His other points will be dealt with more fully when the wider implications of the lawsuit are considered.)

The contrasting views of Gallo and Melnick threw into sharp relief the range and polarity of expert opinion which existed on the issue, the detail of which has never been fully laid before either the public or the profession of science.

In the upshot, Koprowski's solicitors reached an accommodation with *Rolling Stone* and the matter was settled out of court with the magazine agreeing to print a "clarification" and pay the scientist \$US1. Legal sources indicated it had cost the publishers around \$US500,000 and Koprowski himself some \$US300,000 in lawyers' fees.

In December 1993 *Rolling Stone* published the following statement:

"In our March 19, 1992 issue (RS 626) ROLLING STONE published an article by Tom Curtis entitled "The Origin of AIDS: A Startling New Theory Attempts to Answer the Question 'Was it an Act of God or an Act of Man?'"

"In a nutshell, the article raised the theoretical question of whether the AIDS virus or precursor virus might have been transmitted inadvertently from monkeys to humans during a mass-polio-vaccination campaign that was conducted in the Belgian Congo in 1957 through 1960 using a vaccine developed by Dr Hilary Koprowski. The article did not state that this in fact occurred but only that the possibility that one of his vaccines might have been contaminated with such a virus was one of several disputed and unproven theories.

"The editors of ROLLING STONE wish to clarify that they never intended to suggest in the article that there is any scientific proof, nor do they know of any scientific proof, that Dr Koprowski, an illustrious scientist, was in fact responsible for introducing AIDS to the human population or that he is the father of AIDS. Further, the editors emphasise that the article did not intend to suggest that Dr Koprowski failed to follow accepted procedures; in contrast, it made clear that Dr Koprowski's pioneering work in developing polio vaccines has helped spare suffering and death to hundreds of thousands of potential victims of paralytic poliomyelitis and is perhaps one of his greatest contributions in a lifetime of high and widely-recognized achievements.

"After publication of the article, the Wistar Institute, where the Congo vaccine was made, convened an independent committee of six eminent scientists expressly to examine the theory. After more than six months of consideration of the issue, the Wistar committee concluded that the theoretical possibility of an AIDS virus having been communicated by the Congo vaccine was "extremely low." The committee stated that a seaman in Manchester, England, who had no known contact with the Congo vaccine, died of AIDS in 1959, making him the first confirmed AIDS case. Citing this evidence, the Wistar committee added that "it can be stated with almost complete certainty that the large polio vaccine trial begun in 1957 in the Congo was not the origin of AIDS".

"The article also raised concerns with the production of polio vaccine in primary monkey-kidney cultures which may be inadvertently contaminated with unknown simian viruses. In that regard, Dr Koprowski forthrightly and repeatedly has urged since 1961 the use of well-characterized tissue-culture cell lines instead of primary monkey kidneys for the production of human vaccines. The Wistar committee made the same recommendations. It is significant that the much more appropriate medium of human diploid cell strains for growing polio viruses was first developed under the direction of Dr Koprowski. It is also an important historical fact that the effective use and greater safety of human cell strains for manufacturing polio vaccine were first demonstrated more than 30 years ago by Dr Koprowski.

"Today, all polio vaccines are carefully tested, and there is absolutely no evidence that any vaccines contain the AIDS viruses.

"ROLLING STONE regrets any damage to Dr Koprowski's reputation that may have been caused by the article and believes this clarification sets the record straight."<sup>12</sup>

It was an interesting response. Though framed largely at the insistence of Koprowski's solicitors, it did not state that the clarification was printed as part of a legal settlement, nor did it apologise to Koprowski, though it praised him handsomely. In fact, the statement managed to restate the key points made in the original article. It begged the question: why had so costly a lawsuit been launched to so little effect, when its claims were never tested in court? The answer is unclear but it may be this: in settling out of court, Koprowski left the onus of substantiating the polio vaccine theory on Curtis and the other proponents. Had he gone to court, he would – under America's constitutional protection of the right to free speech and a free press – probably have been obliged to prove that his vaccine was *not* responsible for starting the AIDS epidemic, in order for his lawsuit to succeed.

Nonetheless, *Science* relished the chance to gloat. In a short piece entitled, with lewd innuendo, "*Rolling Stone* Rolls Over for Koprowski", it rehashed its earlier line, stating that "many scientists lambasted the account for piling speculation upon speculation." Technically, this was untrue: the words "lambaste" and "piling speculation upon speculation" were interpretations of the original writer, Cohen, and not attributed to anyone quoted in



the story. Still, worse things happen in journalism than quoting fellow journalists. But there were other inconsistencies which were less easy to excuse. *Science* had been happy to heap scorn on *Rolling Stone*, a rock magazine, for daring to engage in scientific debate, and had dismissed the theory as incredible significantly on the basis of where it had been published. Yet *Science* seemed happy to accept the credibility of a Clarification printed in the same magazine. In other words, *Science* wanted to have its cake and eat it.

Furthermore, and far more gravely, *Science* completely ignored -- if it did not tacitly applaud -- the use of the law in an attempt to squash a scientific hypothesis. However this was all in keeping with the editorial stance the journal seemed determined to maintain on the issue.<sup>13</sup>

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In his meticulous and unremitting fashion, Louis Pascal set about exposing gaping holes in Koprowski's letter attacking Curtis, which had been published in *Science*. Curtis, who by now had learned of the existence of Pascal and his paper, had contacted him and sought his advice. He then prepared a cool and rational, point-by-point reply to Koprowski's charges, in which he corrected various errors and noted Koprowski himself had once warned of the danger of unpleasant "virus surprises" being found in polio vaccine. He mailed it to the editor of *Science*, urging the Wistar vaccines be tested because "we owe to those with AIDS, to ourselves, to preclude (if possible) future "virus surprises" from using monkey tissue, and to the subjects of future experimental vaccine trials in Africa and elsewhere. What we learn may well change how we make vaccines and prompt us to ban future simian-to-human organ transplants."

*Science* clearly felt the issue was getting out of control, and refused to publish Curtis's letter. (See appendix II)

Pascal, meanwhile, took up the cudgels. In a privately circulated paper he advanced a series of cogent criticisms of Koprowski's response. In the first instance, Pascal conceded that Curtis had erred over the locations of Kivu and the Ruzizi valley. They were in fact about fifty kilometres apart, not co-located. However, he said, Koprowski had grossly exaggerated in calling this mis-estimate "completely wrong", and taxed him with attempting to obscure the real proximity of the vaccinations to a key locus of AIDS infection, the Burundi-Rwanda-Kivu region.<sup>14</sup>

Pascal agreed that the authors of the original paper on high HIV seropositivity in the Kivu district (Biggar et al, 1985) had

since watered down their claim, but pointed out that this did not matter, as the area was still one of the most heavily AIDS-infected regions in the world.

The first AIDS case cited by Koprowski, Pascal noted, was "zero kilometres" from the other main vaccination site: Kinshasa (Leopoldville), where 76,000 had received the polio vaccine. This was the African woman who had died in 1962 of Kaposi's sarcoma.

The second AIDS case cited by Koprowski was in Burundi, a tiny country, no part of which was more than 200 kms from the Ruzizi valley, Pascal went on. The third AIDS case was the spouse of the second, and the fourth was from Katanga in the southern Congo, about equidistant from Ruzizi and Kinshasa. This case dated from 1975, well after the epidemic took root. By this time, he pointed out, it had even reached as far afield as Norway. The location of HIV cases 5, 6 and 7 was given only as Zaire.

All the early AIDS cases then, Pascal argued, were traceable either to Burundi or the Congo and within easy travelling distance of a major vaccination site.

Pascal rejected Koprowski's assertion that AIDS levels in Africa were low. The rural rate in Kivu, 3.7 per cent, was ten times that prevailing in the United States, and in any case, WHO had had recognised that African AIDS statistics were notoriously understated because of poor record-keeping. While AIDS rates were higher in urban centres, this was universally true for all sexually transmitted diseases because of the effects of prostitution, he said.

Cheekily, he observed that Sabin and Koprowski were once again at odds, with Koprowski arguing that an AIDS-tainted vaccine would surely have caused high rates of infection, while Sabin had claimed that oral administration of SIV would not have led to any cases at all. "They need to get their stories straight," he jibed.

The number of those infected could have ranged from a single individual, to a few, to many. After all, Pascal said, the monkey bite exponents proposed that the global AIDS pandemic affecting many tens of millions of people began with a single bite.

One of Koprowski's strongest defences was his claim that the same CHAT-1 vaccine batch as was administered in Africa was also given to seven million children in Poland, which has one of the lowest AIDS incidences in Europe. Ignoring Curtis' suggestion that different batches of vaccine were manufactured at different labs (Wyeth and Wistar), Pascal adopted a statistical approach to rebut this.

In the first place he established from information presented by Polish and American researchers at the First International Conference on Live Poliovirus Vaccines, held in Washington in 1959, that the same vaccine lot, CHAT-1 lot 13, was given to 300,000 Africans as was given to 3000 Poles in a pilot trial at Wyszkw and Warsaw.

Secondly, he cited a Polish report stating that the batches used in the larger campaign involving seven million children the following year were CHAT 18 and Wistar CHAT 18 GH and *not* CHAT-1 lot 13. It would have been inconceivable, he pointed out, for either Koprowski or the Polish government to permit the use of CHAT-1 in the large-scale trial -- because by that time Sabin had warned the world through the *British Medical Journal* that it was contaminated by an unknown virus.

So 300,000 people were vaccinated in Africa with CHAT-1 lot 13, and 3000 received the same lot in Poland. Therefore, assuming uniform contamination of the batch, the number of Polish infections should have been one hundredth that of Africa. But Africans and Poles have different sexual mores, which might help explain why the disease rampaged through the more promiscuous central African community but not through Catholic-Communist Poland. If the number of African cases doubled every two years, Pascal reasoned, then a mere fifty initial cases could give rise to 6,500,000 cases by 1992.

Fifty initial African AIDS cases equated with 0.5 of a case in Poland, so maybe no Pole was infected at all, he speculated.

Alternatively, if AIDS cases doubled every three years, then 25 initial Polish HIV infections would credibly give Poland's 1992 rate of 103 cases of full-blown AIDS, plus several hundred cases of HIV infection. "Indeed in a country such as Poland where promiscuity and drug use are very low, it is perfectly possible for initial cases to *decrease*," he added.

Koprowski had neglected other differences between the two campaigns, Pascal claimed. First, in Africa, the virus was squirted, making it possible for viral particles to reach the lungs. In Poland it was administered in milk. Secondly, in Poland, the youngest vaccinees were six months of age (and so had developed immune systems more resistant to infection) whereas in Africa many infants under thirty days old were treated. And thirdly, newborn African babies in Kinshasa received 1,500,000 units of vaccine, seven-and-a-half times more virus than the older Polish infants, who received just 200,000 units.

To the claim that three labs, including Wistar, could not

confirm Sabin's finding of an unidentified virus in CHAT-1, Pascal pointed out that Sabin had retested -- and found it again. In 1960, he even offered Koprowski both his serum and the original sample of vaccine to do the tests for himself. It was unclear whether or not Koprowski took him up.

"This allegedly contaminated lot of vaccine was not used for the main part of the Polish campaign, which did not begin until several months after Koprowski had been informed. Nor was it used in the campaigns in Switzerland or Croatia, which Koprowski illegitimately cites as evidence that the allegedly-contaminated vaccine did not start AIDS.

"No-one has said all of Koprowski's batches were contaminated. No-one has said more than one single batch was contaminated -- the one given to 300,000 Africans and 3000 Poles," Pascal stated.

He also pointed out another discontinuity. Koprowski insisted that he had given Sabin a sample from the "seed lot" of CHAT-1. but Sabin was quite specific that it was from "the large lot" used in the Congo.

Pascal then considered the British sailor, Carr, upon whom Wistar's investigating panel, Koprowski and *Science* all reposed their faith. This was inconclusive evidence, he said, noting that many famous AIDS researchers had inadvertently contaminated their cultures and obtained false positives. He had heard that the sailor's AIDS was not all it was cracked up to be. The PCR test used on Carr's remains was so sensitive a single molecule from a single virus particle could yield a positive result. If HIV were present, its place on the HIV-family tree should easily reveal whether it was an ancestral strain (that is, contracted in the 1950s) or a modern one, the result of a contamination, Pascal suggested.

He also noted that the sailor's AIDS-like symptoms were not manifest "throughout 1958" as Koprowski had claimed but, according to the doctors who treated Carr, had appeared only in December 1958, whereas the Congo vaccinations began around February 1957. Pascal pointed out that the sailor could have become infected in any of several ways, including by a dirty needle if he had been ill and received treatment. Some people develop symptoms even more rapidly than Carr apparently did. In any case, Pascal hinted mysteriously, there was a strong possibility that the HIV did not belong to the sailor at all, but was the result of a modern contamination which probably occurred during testing of his preserved organs, a not-unheard-of occurrence in AIDS laboratories.

There was also a question mark over Koprowski's claim that all his vaccines were produced in kidney tissue obtained from rhesus monkeys "captured in India or the Philippines". India at the time had a ban on their export, and rhesus monkeys do not live in the Philippines, though cynomolgus monkeys do. The species actually used to make the CHAT-1 vaccine remained a mystery.

Pascal dismissed as "absurd" Koprowski's claim that SIV-infected monkeys have no SIV in their kidney tissues. Many scientists had attested that kidney cultures could contain lymphocytes and lymphocytes could harbour SIV/HIV.

He pointed out that eminent AIDS researchers who had emphatically stated that it was impossible for the monkey kidney culture to be contaminated with SIV/HIV had subsequently backed away from their hardline claim or else had covered themselves by making numerous qualifications.

Pascal added that Koprowski appeared not to grasp the nub of the theory -- that it was not everyone who received the vaccine who became infected. "The claim is that a small proportion (probably under one per cent) of those receiving a single batch of Koprowski's vaccine became infected with an SIV that was contaminating it, and these few infected people infected others, who infected others, to form the current worldwide epidemic of AIDS."

In summary, he asserted that Koprowski's letter to *Science* contained "nine provable errors, six of them serious". Moreover, it "did not contain a single significant point that was correct". Some of these errors were so gross, Pascal suggested, that the editors of *Science* ought to be held accountable for having published them, as well as for refusing to publish the letter from Professor Hamilton who had identified 12 similar errors in Koprowski's claims.

The errors pointed out by Hamilton to the editor of *Science* were substantially the same as those identified by Pascal:

1. The proximity of the Ruzizi river and Kivu made it unreasonable of Koprowski to call Curtis's slight inaccuracy "completely wrong".
2. The first AIDS cases cited by Koprowski came from Kinshasa and Burundi, very close to where the vaccine had been used.
3. No two points in Zaire or Burundi relevant to the discussion were "thousands of kilometres apart".
4. The Manchester sailor's symptoms were not present "throughout 1958" but began in December, by which time a quarter of a million Africans had been vaccinated. He was not an impossible case of secondary infection.

5. Rhesus monkeys do not occur in the Philippines
6. Koprowski's own statements on sources of his monkey kidneys had varied.
7. There was no basis to claim SIV-infected monkeys had no SIV in their kidneys.
8. Sabin contradicted Koprowski, saying he tested the large lot of vaccine, not a seed lot.
9. The relevant vaccine was only given to 3000 children in Poland. The nine million vaccinated later in Poland, Croatia and Switzerland were irrelevant to the argument.
10. Follow-up studies in Kinshasa revealed no untoward reactions, but would be unlikely to reveal any for a virus as slow-acting as HIV.
11. Koprowski's letter was very carelessly proofed, as many of its sources were wrongly referenced. (This was corrected three issues later.)
12. Rates of HIV/AIDS infection in rural Zaire, Burundi and elsewhere near the vaccination sites were not low by any world standards other than those of African towns, where normal patterns of venereal disease would explain a more rapid spread.

But these were all matters that the editors of the world scientific press cared not to pursue.

However serious discussion of the AIDS-vaccine theory and its implications had at last begun to germinate on the periphery of the science press. In October 1993, Martin published an article in *BioScience* which had previously been rejected by the *British Medical Journal*. In it, he detailed the stories of Pascal, Curtis and Elswood, using them as a case study to pose some searching questions about the process known as "peer review" which is so fundamental to the publication of scientific findings and ideas.<sup>15</sup>

In essence, a new finding, discovery or theory, when submitted to a scientific journal for publication, is sent out to experts who scrutinise it meticulously and report their views on its suitability for publication. Sometimes (rarely) they approve it as written, but more often they recommend changes or question some of the conclusions drawn by the authors. Often, they recommend that it not be published. It is this process of review by one's international peers which makes science journals superior in character and trustworthiness to all other kinds of magazines and publications.

"On an issue such as AIDS," Martin had written, "where the stakes in human lives are high and there continue to be large unknowns, it makes sense for the scientific community to be open

to a wide range of theories, including ones that are quite unorthodox and indeed outrageous.

"There could be a high cost to pay if one of the theories, ignored because it seemed too unlikely, turns out to be correct. Such an approach of tolerance for a diversity of competing ideas makes a lot of sense whenever the social costs of being wrong are substantial."

Unfortunately, he continued, the scientific system was ill-suited to dealing with unorthodox and challenging views, especially from outsiders. To openly consider them required courage on the part of scientists, reviewers and editors. Without that kind of courage, it was likely that people with challenging ideas, having been rejected by the scientific press, would seek outlets in the popular media. And if, in the end, their ideas proved to be correct, it was the scientific community which would ultimately sustain a loss of credibility and public trust.

Finally Elswood and Stricker hit paydirt as well, with an eight-page article in a journal called *Medical Hypotheses*, the first detailed scientific treatment of the issue to appear in the professional scientific literature. It was accompanied by sixty-five references and sources and was entitled "Polio Vaccines and the Origin of AIDS".

The article appeared in 1994, fifteen years after the first AIDS cases were noticed, nine years after WHO had secretly investigated the possibility of contaminated vaccine, seven years after Snead had first floated the theory, six years after Pascal had first sought publication in the mainstream science press, and three years after Elswood had tipped off Curtis about the "bombshell story".

In their summary Elswood and Stricker said: "Although mass vaccination programs have resulted in the eradication of a number of human infectious diseases, vaccine contamination has been a persistent concern. In particular, it is now known that the early polio vaccines were contaminated with at least one monkey virus, SV40.<sup>16</sup>

"The transfer of monkey viruses to man via contaminated vaccines is particularly relevant to the acquired immunodeficiency syndrome (AIDS), since the causative agent of AIDS, human immunodeficiency virus (HIV), is thought to be derived from a simian precursor virus.

"Furthermore, human infection with this virus appears to be a relatively recent event. We hypothesize that the AIDS pandemic may have originated with a contaminated polio vaccine

that was administered to inhabitants of Equatorial Africa from 1957 to 1959. The mechanism of evolution of HIV from this vaccine remains to be determined."

The paper began with a brief history of vaccines, including some of the more tragic experiments in which human guinea pigs had been killed or made seriously ill. One instance cited was an epidemic of 330,000 cases of hepatitis B in the United States in 1942, which was linked to vaccine given to 50,000 army personnel. Eighty-four people had died.

They reviewed the history of poliovaccine development by Salk and Sabin, including reference to the Cutter incident. They discussed in greater detail the contamination of both polio vaccines with SV-40, and the probable exposure of up to thirty million Americans, besides many in other countries. They recounted all the disturbing diseases which various medical teams had linked to that event including, most recently, a study showing children of mothers vaccinated with SV-40-contaminated vaccine were thirteen times more likely to develop brain cancer than those of unvaccinated mothers.

Elswood and Stricker then went on to recount the history of the human AIDS epidemic and the discovery and naming of HIV. They reported the 1983 finding that Asian monkeys developed AIDS after contact with African monkeys, and the discovery of simian immunodeficiency virus.

"The discovery of a virus related to HIV occurring naturally in the monkey species that was *preferred* for vaccine production caused the World Health Organisation (WHO) to convene two "informal" meetings of experts in 1985," they reported. "At the time, the conclusions issued by WHO seemed reassuring: first, live polio vaccines prepared in African green monkey kidney cultures during the 1970s had been tested for retroviruses...and none had been found; second, WHO had tested vaccine seed stocks as well as 20 batches of vaccine for retroviruses, and again none had been found. In addition, WHO had checked 250 vaccine recipients for HIV antibodies and none were positive. 30 of these recipients were also tested for SIV antibodies, and all were negative. Finally WHO said long-term follow-up of vaccine recipients had shown no sign of adverse effects potentially associated with a retrovirus."

Elswood and Stricker said apprehensions were again revived with the discovery of a new strain of HIV, closely resembling a monkey virus. This was HIV-2. Japanese tests revealed 26 per cent of the green monkeys used for vaccine manufacture in that country had antibodies to SIV. They tested



their vaccine stocks, but found nothing. Nonetheless, they urged that SIV-infected monkeys not be used in vaccine production. More sensitive tests then revealed SIV in virtually all the tissues and organs, including the kidneys, of infected monkeys. "Furthermore an SIV not previously known to infect humans was recovered from the cancer cells of an AIDS patient" who had had no known contact with monkeys.

The discovery of a chimpanzee SIV which was 75-84 per cent identical to human HIV-1 seemed to bridge the phylogenetic gap. Elswood and Stricker took the view that chimps had been so intimately involved in the attenuating, testing and development of polio vaccines that they, too, could be a source of contamination. Even if chimps were not used in the actual vaccine manufacture, they could easily have infected monkeys if housed in the same quarters, in the same way that African monkeys had infected Asian monkeys used in United States labs.

They went on to recount the circumstances of the Belgian Congo vaccine trials, but without mentioning Koprowski by name. He was referred to merely as "the American researcher".

Reciting the literature, Elswood and Stricker then concluded: "It is difficult to believe that the outbreak of HIV infection in Africa at the same time and location as this mass polio vaccine trial is a coincidence..."

"Whether the 1957-59 polio vaccine inoculations in the Belgian Congo were the cause of the cross-species transfer of HIV to man remains to be proven... what we do know is that...it was contaminated."

They then turned their guns on the medical establishment, saying that instead of recognising a possible role of medical science in the origin of AIDS, researchers had been "throwing stones at the first victims" by alleging that African cultural practices were to blame for starting the epidemic.

"But Africans have engaged in these practices for thousands of years, while AIDS is an entirely new disease.

"Whatever the case," they concluded, "as one scientist has written: "The story of AIDS teaches us that animal tissues should not be injected into humans, because the risk of introducing a new virus is too great"."

## Endnotes

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<sup>1</sup> Holden C. edit, Koprowski Sues Rock Mag, *Science* 259, 8

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January 1993, p180.

- <sup>2</sup> Martin B., Stifling the media. *Nature* 363, 1993, p202.
- <sup>3</sup> Hamilton W.D., personal communication, 7 February 1995.
- <sup>4</sup> Hamilton W.D., personal communication, 7 February 1995.
- <sup>5</sup> Hamilton W.D., personal communication, 23 February 1995.
- <sup>6</sup> Anon., Reviewer's comments on letter to *Science* by Hamilton, W.D., presented as evidence in Hilary Koprowski MD v The Associated Press and Bruce Rule, Court of Common Pleas of Philadelphia County, No 4022. May 15, 1997.
- <sup>7</sup> Hooper E., *The River*, Penguin Press, 1999, pp802-803.
- <sup>8</sup> Elswood B.F. and Stricker R.B., Polio vaccines and the origin of AIDS, *Research in Virology* 144, February 2 1993, pp175-177.
- <sup>9</sup> Gallo, R.C., Affidavit to United States District Court for the Eastern District of Pennsylvania, Civil Action No 92-CV-7431, Hilary Koprowski v. Straight Arrow Publishers Inc., Jann S. Wenner and Tom Curtis, 12 May 1993.
- <sup>10</sup> Pascal L., Carelessness with Human Lives: Errors in Hilary Koprowski's Letter to *Science* Concerning the Origin of AIDS and the Refusal by *Science* to Correct Them. 19 September 1994. p15.
- <sup>11</sup> Melnick J., Affidavit to United States District Court for the Eastern District of Pennsylvania, Civil Action No 92-CV-7431, Koprowski v Straight Arrow Publishers, Wenner and Curtis, 21 October 1993.
- <sup>12</sup> Anon. Origin of AIDS Update. *Rolling Stone*, 9 December 1993, p39.
- <sup>13</sup> Holden C. edit, Rolling Stone Rolls Over for Koprowski. *Science* 262, 26 November 1993, p 1369.
- <sup>14</sup> Pascal L., op. cit., September 1994.
- <sup>15</sup> Martin B., "Peer Review and the Origin of AIDS: a case study in Rejected Knowledge". *Bioscience* 43, No. 9, October 1993, pp624-627.
- <sup>16</sup> Elswood B.F and Stricker R.B., Polio Vaccine and the Origin of AIDS. *Medical Hypotheses* 42, 1994 pp 347-354.

## Pandora's Box

ON 28 June 1992, a 35-year-old patient in an American hospital was experimentally implanted with the liver of a baboon. Seventy days later his brain exploded.

The haemorrhage which killed him was the result of a massive fungal infection of his arteries. The doctors who performed the operation, nevertheless, drew encouragement from their results, stating "our experience has shown the feasibility of controlling the rejection of the baboon liver xenograft in a human recipient".<sup>1</sup>

It may perhaps be *another* case of good luck that the agent of the patient's death was not a slow-acting lentivirus like HIV, and he did not arise from his hospital bed, go out into the world, test out his new liver in a singles' bar -- and spawn a second pandemic.

Neither this possibility, nor the failure of the first experiment, was sufficient to deter doctors at the University of Pittsburgh Medical Centre from proceeding with a second baboon-liver xenograft, which they performed in a 62-year-old man on 11 January 1993. The only obvious concern which this action aroused was among animals rights activists, who paraded outside the hospital bearing the slogans "Frankenstein lives in Pittsburgh" and "Stop the Monkey Business". The mainstream international science press passed over the implications of the operation in seeming silence.

The Pittsburgh experiments were by no means the first of their kind: they had been preceded by twelve previous attempts to implant either baboon or chimpanzee kidneys, and two attempts to implant baboon hearts, all of which failed within sixty days. Such experiments were not confined to primates: they included the routine grafting into humans of pig's heart valves, two failed attempts to implant pig's and sheep's hearts into patients, ten cases of the transfer of pig pancreatic tissue and four of pig nerve tissue.

Round the world, experiments involving the use of animal tissues and organs in humans were multiplying. The reason was that demand for organs in western society had become insatiable. In developed countries, it was conservatively estimated, one person in every 10,000 was awaiting a transplant. Most had been waiting six months or more. Some had been in the queue for three years.

The urgency of the situation was compounded by a sharp fall in organ donation in developed countries. During the first six months of 1994, the Eurotransplant Foundation in Holland reported, kidney donations in fifteen Western European countries fell by 15 per cent. Heart and liver donation declined by a similar proportion. Experts blamed the drop on prejudicial media reports about children being kidnapped for their organs, the illicit sale of autopsy tissues and the use of European organs for non-Europeans.<sup>2</sup>

By the second half of the 1990s, the global shortage of human donors for hearts, livers, kidneys, lungs, pancreases, corneas and other transplant organs was driving many researchers to seek substitutes in the animal kingdom, especially among creatures whose general size and internal structure was compatible with humans'. Other research teams were working on the transplantation of animal cells for the treatment of conditions as diverse as diabetes, Alzheimer's disease, Parkinson's disease, Huntington's disease -- and even for the relief of pain.

Several scientific groups were experimenting with the genetic engineering of various animals with human immune system genes, in the hope of overcoming the massive rejection which set in when alien tissues were implanted. Their goal was to equip each implanted organ with a genetic "flag" which fooled the body into accepting the alien tissues. Biotechnology corporations were planning the construction of large industrial farms of "humanised" animals, to satisfy the unrequited hunger for organs. So prodigious were the growth prospects of this industry that investment analysts predicted there would be more than half-a-million animal organs grafted into humans every year by 2010. These would be supplied by some 320 specialised "farms" to a transplant industry turning over \$US5 billion a year, and backed by the largest pharmaceutical houses in the world.

Other teams of researchers were already ahead of the game, trying to implant ordinary animal organs. In cases such as the baboon liver, they simply shotgunned the immune system of the patient with drugs, so that the organ would be accepted.

It had already been recognised that one of the most effective ways to assist a virus to jump species was to put it into a devastated immune system. Of these new experiments, Pascal scathingly commented: "If a mad scientist were trying his best to transfer [deadly animal viruses], how could he possibly do any more...? We already have the clearest possible example of what an animal virus can do to our species."

The American scientists who performed the baboon liver transplants in 1992 and 1993 had been meticulous in screening the donor animal, a fifteen-year-old male baboon, for all the main monkey and human viruses. They checked for SIV, STLV, HTLV-1 and -2, HIV-1 and -2, simian retroviruses 1, 2 and 5 and found nothing. But the baboon tested positive for foamy viruses, and had evidence of previous infection with Epstein-Barr virus, cytomegalovirus, SV-8 and chickenpox. It tested clean for herpes and the deadly herpes B, for hepatitis A, B and C, for Marburg and several other dangerous viruses.

But the researchers had not tested for everything. There was at least one monkey virus of which they had never even heard -- because it was not discovered and reported to the scientific world until April 1994, more than a year after the second baboon liver xenograft took place. It was the simian parvovirus (SPV), a member of the same family as the cat virus that killed millions of dogs in a global pandemic in the late 1970s, after probably jumping species as a result of vaccine experiments. A member of the same virus family also infects humans and is a recognised killer of unborn babies.<sup>3</sup>

This example illustrated that, despite great advances in virology and virus detection since the pioneer days of polio vaccine manufacture, "There are more things in Heaven and Earth, Horatio, than are dream'd of in your philosophy," as Shakespeare put it.

Quite apart from the transplant issue, monkey kidneys were extensively used to grow live polio and other vaccines, and if this was a route for cross-species infection of humans with undiscovered monkey agents, then it still lay open -- though quality control and safety testing were greatly refined since the SV-40 scare of the 1950s. However, many scientists conceded, it was still extremely difficult to test for a virus which no-one had ever heard of. For some organisms, no test at all was available.

A disease caused by a slow agent for which there was for many years no test was the hideously lethal brain disorder Creutzfeld-Jakob disease (CJD), which was transmitted to women in Britain, Australia, France and the United States who were treated for infertility by injecting them with hormones extracted from the brains of corpses. The prime suspect in this disease, a prion, was simpler and more enigmatic even than a virus. A mere chunk of protein, it induced a fatal alteration in the way human cell proteins folded -- and hence the function they performed in the body. It could be transmitted medically by several routes, including poorly-sterilised instruments, injection or transplant of brain

matter and corneal grafts. The agent might lie dormant for twenty or thirty years before emerging to strike down the victim by riddling their brain with tiny holes.

Prions were also implicated in Britain's celebrated "mad cow disease", BSE or bovine spongiform encephalopathy. BSE was another example of a cross-species leap -- in this case a sheep prion which was transferred to cattle and had infected 162,000 cows on 32,000 UK farms between the early 1980s and 1996. The disease was apparently passed to cattle in stockfeed enriched with meatworks protein made from sheep offal, after a change in regulations allowed it to be processed at a lower temperature. Significantly, the agent was able to infect cattle by the oral route. In March 1996, the discovery of a new form of CJD in humans which closely resembled the symptoms of BSE caused a major scare among the British public over meat safety.

Nevertheless, a British government scientific panel resolved not to take any chances and issued a warning about the possibility -- with devastating consequences for the UK's livestock industry. The significance of the BSE episode to the polio vaccine theory was that it demonstrated once more that an unknown slow agent could leap species and ignite an epidemic.

Koprowski had campaigned for thirty years or more against the use of monkey kidneys in tissue culture used to make vaccine, advocating either well-characterised cell lines or use of human foetal cell lines. The Wistar investigating panel had sounded an unambiguous warning that "there may well be other monkey viruses that have not yet been discovered which could possibly contaminate vaccine lots". Panel member Professor Ronald Desrosiers of Harvard Medical School told the media the issue was a "ticking time bomb". Professors Lecatsas and Alexander wrote letters protesting the practice to the international scientific press, and were strongly condemned by other scientists for so doing.

Yet the use of monkey kidneys for making vaccine continued. It continues to this day.

This was acutely ironical. For a decade or more the medico-scientific industry had issued precautionary instructions to humanity intended to halt the spread of AIDS. Yet the same industry appeared loath to apply precautionary principles to its own conduct. It persisted with many practices and was pressing ahead with new experiments which the experts deemed as fraught with hazard. The consequences could be tragic on a dimension unforeseen, South African virologist Jennie Alexander warned in 1995.

"The most awful potential is what we see coming down the line," she said. "We need to look, and see what else might be waiting in the wings."

The fear was not of spectacularly virulent killers like Marburg and Ebola. Rather it was of the sleepers, the slow, clandestine agents which were undetectable or very hard to find using present technology, and capable of lying dormant for years.

"In humans highly virulent viruses with short incubation periods and poor transmissibility, like the haemorrhagic fever viruses, are easily controlled by quarantine, but the greatest threat is posed by slow virus diseases like AIDS and BSE, which can spread silently far and wide before sounding any alarms," Dr John Seale of London's Lister Hospital wrote in *The Journal of the Royal Society of Medicine*.<sup>4</sup>

It was a powerful point. The word "quarantine" dates back to the era of the Black Death. In mediaeval times travellers entering the Italian city of Ragusa were obliged to remain for thirty days in a holding facility on the waterfront until it was clear they were free of plague. This was later extended to forty days (a "quarantina"), to cover the full incubation period of the plague. But for lentiviruses and prions the disease might take twenty years or even longer to manifest itself. During this time, the carrier could still infect many others. Quarantine was impossible. Other means of public health protection such as education were essential. Above all, humanity needed to understand how these plagues began, in order to forestall fresh transmissions.

Seale, a figure known for his controversial views on disease, flatly rejected the notion that SIV could have crossed to humans as a result of some natural transmission event such as a monkey bite or a hunter cutting himself. "HIV-2, which is particularly closely related to SIV<sub>MAC</sub>, seems to have infected humans only recently, probably after virus-containing blood or tissues from another primate species were injected into humans by accident or by design.

"The theory popular amongst many molecular biologists that HIV-1 has been endemic, and largely non-pathogenic, in an isolated group of people in Africa for millennia, is not scientifically credible," he stated. On the contrary, the virus showed signs of having evolved at great speed -- possibly as a result of serial passages in human cell cultures, he speculated.

"It would appear that the AIDS epidemic may be just one of the latest of several mammalian cross-species viral transfers triggered by the techniques of virology in the 20th century, which

subsequently spread out of control in the new host species."

Seale concluded with a warning to his profession: "The attitude that there is no importance in attempting to track down the origins of the AIDS epidemic will be held as highly irresponsible and unacceptable by the public."

Oxford evolutionist William Hamilton, who tried unsuccessfully to publish warnings on this subject in both *Science* and *Nature*, believed that if the contaminated polio vaccine theory were to be substantiated, its implications would be vast both for medicine and for science.

"An immediate stop should be put to experiments involving organ transplants, or other tissue or tissue extract invasions, made from other species into humans," he proposed in 1995.<sup>5</sup>

"Such a ban should continue until it can be proven by the experimenters that the tissues introduced contain *no* viruses. (Actually, this ban ought be already applied: the SV-40 affair, even before its now suggested involvement in asbestosis, should have been enough to warn us of that).

"Live vaccine procedures should be reviewed in the same spirit and most of them discontinued, with alternative intensive work begun on non-live vaccines. Where live vaccines against really serious diseases cannot be avoided, greater effort should be made to switch to culture media that are as phylogenetically remote as possible from humans.

"Raising live vaccines in simian (or, still worse, anthropoid) tissues should always be regarded as inherently extremely dangerous.

"It should be recognised that it is not enough to observe vaccinees or transplantees for a few months or even a few years for effects of possible extraneous viruses."

Hamilton believed it would be of great advantage if medical scientists and doctors were better educated in the facts and theories of neodarwinism. Till now, he said, many had clung to out-of-date concepts about the fixity of host-parasite relationships. This created false confidence that viruses were unable readily to jump species, adapt to new hosts or evolve new strategies against drugs, vaccines and human immunity with breathtaking rapidity. Potentially, such an unjustified overconfidence could lead to disasters like AIDS.

Hamilton considered public health medicine should be compelled to become more open about its procedures. Nations should insist on full disclosure of the details and rationale behind



all public health programs conducted within their borders. He also felt steps should be taken to ensure that medical research did not become dominated by corporations who placed profit ahead of combatting ill health.

"The pressures towards investigation and non-investigation that emanate from huge drug companies and their influence in slanting research in subtle ways should also be examined -- as should the role of journals and peer review in potentially obstructing publications of controversial kinds," he said.

To deal with the ethical issues surrounding the polio vaccine theory, the world science community should establish an international committee "mostly composed of non-medical people" to investigate how a rather obvious and plausible theory came to be scorned and suppressed from publication for so long -- especially when "important consequences concerning mankind's worst epidemic...and others, possibly worse, that may be following, hang in the balance." It would also be interesting to investigate why the theory had to be promoted to science and medicine by outsiders, he suggested.

Hamilton was equally concerned about the growing public anxiety, resentment and fear of science and technology in general, evident in many developed societies. This was emerging as a rising barrier to progress and to the scientific solution of some of the world's most pressing problems. Science, he suggested, may have brought some of this suspicion on its own head.

"In the face of overbearing professional mystique, disregard and now even litigation, the public becomes justified in its growing disillusion with science and in some of its deepest fears," he cautioned.

Hamilton's admonition had fallen on deaf ears in the mainstream scientific community and science press, but in the general media this was not so. In an insightful article published on 21 October 1995, *The Economist* magazine inveighed against the practice of animal tissue transplants for precisely the reasons specified by the Oxford professor and others.

What had roused *The Economist* were the plans of a group of San Francisco and Pittsburgh University researchers to transplant into an AIDS patient the bone marrow of a baboon. Hailed as another cutting-edge advance in xenografting, the rationale behind the operation was that, since baboons seemed immune to HIV, the bone marrow which produces key immune-system cells could be used to prop up or regenerate the flagging immune system of a human AIDS patient. Another option was that baboon

marrow could be used as a temporary support, to keep the patient alive until a suitable human marrow donor was discovered.

Either way, the experiment blithely ignored, or at least discounted, the danger that unknown viruses could cross to the patient along with the baboon marrow. Should the patient be so lucky as to recover, he would then be in a position to pass them to others. In a pointed editorial, entitled "Thanks, but no thanks", *The Economist* demanded that "such operations should, for the moment, be stopped."<sup>6</sup>

"The immediate worry is ...that there exists a danger -- hard to quantify, possibly small but undoubtedly real -- that operations of this kind will enable virulent infections to cross the barrier between animals and people," it said.

"The problem is that, in transplanting the liver or heart of a baboon or pig, infectious agents will surely be transplanted too. If one of these finds the body a congenial home and it then finds a convenient way to transmit itself from one human to another, the blessings of these xeno-transplants may rapidly come to be seen as a curse."

*The Economist* was puzzled why there had been no public outcry over these experiments if the danger was in fact real. It supposed this was because science was simply moving faster than its regulators. It noted the United States Centres for Disease Control was contemplating some rules -- but they were likely to be voluntary. Proponents of xenografts argued that the risks could be minimised if the special animals were bred in disease-free conditions, and all organs were tracked closely after transplant.

*The Economist* was not reassured: if the xenografts worked, they would soon be emulated by doctors in thousands, multiplying the prospects for a species-leap, and minimising the chances of detecting it in time to arrest its spread. "Simple prudence, not alarmism, suggests that it is not yet time to realise the surgeon's dream of an endless supply of organs from beasts," the magazine concluded.

In a feature article which accompanied the editorial *The Economist's* science writer delved further into the issue, pointing out there existed "a heretical explanation" for the origin of the AIDS pandemic: that it had started with a polio vaccine. While acknowledging that few researchers in the field gave this much credence, "the hypothesis has not yet been disproved".<sup>7</sup>

"Whether or not AIDS started this way, the worrying thing is that the idea is plausible in principle. Another simian virus, SV40, is widely thought to have come into the human population

during the polio vaccination campaign..." it said.

*The Economist* had strayed where the scientific press lacked the fortitude to tread. It had highlighted a glaring instance of the importance of the polio vaccine theory: had it received at least some objective consideration in the mainstream scientific press instead of blank-faced incredulity, snide dismissal and emotional rejection, researchers and health policymakers might have been more receptive to the argument about the dangers of xenografts. But once again, because these ideas appeared in a nonscientific journal, they proved easy to ignore.

Now, by the greatest of ironies, the marrow of a baboon was to be medically implanted into a victim of AIDS, a disease which had crossed to humans from primates. This awoke the spectre that efforts to treat a disease which was poised to kill 40 million, might ultimately help to seed a fresh pandemic which would slay millions more.

Such considerations did not deter researchers at the San Francisco General Hospital and the University of Pittsburgh. On 14 December 1995, officials at the heavily-lobbied United States Food and Drug Administration gave them the green light. The doctors immediately went ahead and operated on 38-year-old AIDS patient Jeff Getty, after first knocking down his immune system with a combination of drugs and radiation to make him receptive to the alien material. Medical critics said such an action would be more likely to kill him, but principal investigator Dr Steven Deeks commented "There is a chance here for a real breakthrough". By an irony of history the event was chronicled for the New York Times by its medical writer Lawrence Altman, the journalist who had broken the first story on AIDS to the world, way back in 1981.<sup>8</sup>

The operation itself was a qualified success, from the medical team's point of view. The patient was infused with baboon marrow stem cells and facilitator cells, to help them begin their task of forming more T-cells. The baboon from which the marrow was drawn had been carefully scrutinised for viruses and pronounced unusually free of them, except for baboon endogenous virus, an agent known to infect humans cells in culture. On 4 January 1996, Getty strolled out of hospital smiling, and, in the words of one reporter, "looking strong and healthy" and "ready to go home".

"Wearing jeans and a T-shirt with a button reading "Silence Equals Death", Getty talked briefly to a throng of well-wishers before climbing into a red sports car with a friend and driving off," Associated Press reported. Deeks told the clustered media the

single real surprise was how well it had all gone.<sup>9</sup>

The only wowsery note was sounded by the Humane Society of the United States, which warned that the procedure would expose humans to new animal diseases. The point had not entirely escaped United States health officials and the CDC undertook to follow the patient closely for signs of any new disease. "You can't dismiss out of hand that using animal tissues may be a very effective way to introduce another equivalent infection," CDC epidemiologist Louise Chapman told the press.

*Another equivalent infection?* Did this mean that America's top disease watchdog could not exclude the possibility that the experiments it had sanctioned might kill forty million more people?

Two months after Getty's operation, the concept of xenotransplantation received powerful endorsement from Britain's Nuffield Council on Bioethics, which deemed the practice to be ethical so long as it was strictly regulated. A working party chaired by Professor Mark Walport urged that the technology be allowed to proceed "in the context of a careful regulatory framework", which included rigorous screening for infectious organisms and subsequent monitoring of recipients. Despite such a level of care, the working party rated the risk of transferring a new organism from animals to humans by xenograft as "unquantifiable". The Council concluded: "It is extremely difficult to assess the level of risk that an animal disease will be transmitted to the human population as a result of xenotransplantation. Experts in the field differ widely in their opinions. The conclusion would seem to be that, when considering the possibility of xenografting leading to transmission of disease, the risk is unquantifiable, and it may be extremely small. But it cannot be ruled out."<sup>10</sup>

However, not all scientists were so swift to downplay the risks of xenografts. In an article in *The Ecologist*, Swiss biologist Dr Florianne Koechlin succinctly stated "Xenotransplantation may represent a great hope for prolonging the lives of individual patient groups. Yet it could also endanger the entire population."<sup>11</sup>

The unanswered questions were piling up. Had the baboon marrow procedure been a complete success and become a commonplace operation for millions of AIDS sufferers, what then would be the probability of a new disease entering humans? Who would monitor each recipient, and each recipient's sex partners and *their* sex partners, in every country on earth for decades to come for slow diseases? If a new disease *was* transmitted, would it be detected before the carrier passed it on? Or would it only come to light years after the event, when the next Gaetan Dugas had already

spilt it across a continent?

Without rational acceptance by medical authorities and scientists of at least the *possibility* of the polio vaccine theory, the scale of the threat to humanity was bound to be discounted.

Silence, as Getty's button observed, Equals Death.

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Events surrounding the polio vaccine theory not only carried messages for public health and the practice of science. They also held equally grave implications for liberty, democracy and good government.

One of the strangest aspects of the case was that the Wistar panel had clearly acknowledged that the polio vaccine theory was *possible*, though it had rated the likelihood as very low. It had lent great credence to the risk of vaccine contamination by unknown monkey viruses, strongly advocating the worldwide abandonment of the use of monkey kidneys for making vaccines. Yet Koprowski's lawsuits still went forward.

His suit against *Rolling Stone* yielded him little in the way of salving: for an alleged outlay of some \$US300,000 in legal expenses he obtained just \$1 in recompense, along with an equivocal clarification which both praised him and revisited the polio vaccine theory.

However, one immediate effect was that the media was scared off the issue and dropped it like a hot potato, ignoring even the wider implications of the risks to human safety posed by existing methods of vaccine manufacture and of animal organ transplants. *Rolling Stone*, for one, decided not to publish a second article by Curtis exploring the dangers of transferring viruses through vaccines and xenografts.

The lawsuits' implications affected the whole of society. Tom Curtis's brother, Michael Kent Curtis, was a professor of law at Wake Forest University. While he held no particular opinion on the truth or falsity of the polio vaccine theory, Michael Curtis was troubled by the impact of Koprowski's legal actions on issues such as freedom of speech, scientific practice, civil liberties and the public interest.

It seemed to Professor Curtis that if defamation actions could be used against people exploring complex scientific hypotheses in public, in the same way as if they were a simple slur cast on a person's good name, then the law could easily be employed to suppress the discussion of all sorts of issues which were very much in the public interest. For example, scientists who had obtained laboratory animal evidence that a certain food additive

caused cancer in animals -- and so, by inference, in people -- might be deterred or prevented from publicising the evidence by a lawsuit brought by the manufacturing company, or by the mere menace of one.

"Libel actions thus may have an inhibiting effect on otherwise constitutionally protected free speech," Michael Curtis wrote in a treatise on the legal implications of the case.<sup>12</sup>

The United States Constitution, under the First Amendment, in theory provided protection for the publicising of scientific hypotheses, placing the onus of proving them false on the person doing the suing. In practice, however, the safeguards it offered provided insufficient protection of free speech values, Curtis argued.

"Regardless of the outcome, long and expensive libel suits may have a chilling effect, not only on false ideas, but on those that are true, and on those whose truth is problematic. Critics may be intimidated by the possibility of libel actions."

Professor Curtis pointed out that certain professions, such as doctors and scientists, wielded extraordinary power to shape the lives of ordinary people, and courts should take this into account when evaluating their claims to personal injury. Where the criticism was directed at the area in which they exercised their power, as distinct from at their character, it should be given heightened protection by the courts, he contended.

He identified hypotheses of this sort as being in a special category, which he termed "complex criticisms". Examples included the claim that an apple spray, Alar, was carcinogenic, the issue of the Dalkon contraceptive shield and the behaviour of the asbestos industry towards the issue of mesothelioma. Such claims had value to society and human knowledge, in the end, whether they proved to be true or false, he argued. Complex criticism was not about accusations of wrongdoing, but about protecting society -- and it should not be capable of being defeated by suggestions it was only concerned with wrongdoing.

"Existing legal protections are inadequate for complex criticism because a hypothesis that proves false or a criticism that proves mistaken may still have substantial value in advancing knowledge and political understanding," Curtis contended. "Despite claims of wrongdoing, such stories should be protectable complex criticism because they involve questions of scientific causation, risk allocation, the effect of economic power on political decisions about safety, and the exercise of corporate power."

True or false, the polio vaccine theory had already had one

obviously beneficial impact: it had put renewed scientific and public focus on the question of whether vaccines should be made by safer procedures. But the lawsuit had prevented a second beneficial impact: the publication of an article exploring the dangers of xenografts.

"Free speech and free press rules are designed in part to foster democratic and wise decision making, and that function should be the polestar that guides the courts in their search for free speech rules. We should look at how rules function, not simply at formal considerations," Professor Curtis observed.

Free speech, he reasoned, was an essential tool in the search for truth. As the philosopher, John Stuart Mill, had said:

"The peculiar evil of silencing the expression of an opinion is that it is robbing the human race; posterity as well as the existing generation; those who dissent from the opinion, still more than those who hold it. If the opinion is right, they are deprived of the opportunity of exchanging error for truth: if wrong, they lose, what is almost as great a benefit, the clearer perception and livelier impression of truth, produced with collision with error."

From Galileo to the Scopes Monkey Trial, the law had been brought to bear on innumerable occasions to silence the discussion of scientific hypotheses perceived as threatening to various groups -- to no public benefit and, it might be argued, to considerable public detriment. Was the polio vaccine case any different, Professor Curtis asked? As Thomas Jefferson had once remarked, the only result of such interference with learned debate had been "To make one half the world fools, and the other half hypocrites".

The issue of the truth or falsity of the polio vaccine theory was not one that could be satisfactorily resolved by a court or lay jury, but only by the conscientious application of science.

In an affidavit presented to the litigants in the libel suit, distinguished polio vaccine pioneer Dr Joseph Melnick of Baylor College of Medicine and a member of WHO's polio vaccine committee stated:

"I find this theory both plausible and one of several possible explanations for the still unsolved mystery of how the modern AIDS epidemic originated.

"We in the scientific community simply do not know how

the AIDS virus originated in man. One prevalent hypothesis is that a simian AIDS-like virus, known as Simian Immunodeficiency Virus (SIV) was transmitted from African monkeys to humans, and thereafter evolved into the Human Immunodeficiency Virus (HIV) commonly referred to as AIDS. The question of how this cross-species transfer took place remains an unsolved mystery and has led to several theories.

"In the late 1950s (as well as today), live attenuated polio vaccines were made in monkey kidney tissue cultures. Those tissue cultures often contained small amounts of lymphocytes and macrophages. Such cells are now known to support the replication of SIV in culture and when taken from SIV-infected monkeys to harbour SIV in vivo. Moreover a recent report (Khabbaz et al., *Lancet* 340: 271-273, 1992) has shown that SIV has accidentally infected at least one laboratory worker, consistent with the observation that SIV will grow in human cells.

"It is thus plausible to hypothesize that SIV might have been present in monkey kidney cultures used in the polio vaccines in the Congo and that it might have infected human recipients."

Noting that no test for such a virus existed until at least 1985, Melnick concluded: "I find the hypothesis discussed in the *Rolling Stone* article to be scientifically plausible. So too, I and other virologists concur in the Wistar Committee's recommendation that samples of the polio vaccine used in the Congo should be tested for the possible presence of SIV.

"Finally I am deeply concerned that the mere reporting on a scientific theory by Mr [Tom] Curtis -- who in no manner indicated that Dr Koprowski was negligent or failed to follow accepted procedures -- could become the subject of a libel suit.

"How AIDS originated is a presently unanswerable question, and there are many theories, all of which have strengths and weaknesses, all of which have supporters and detractors. The appropriate forum to debate and test those theories is the laboratory environs, not the courtroom.

"Indeed, I am troubled that if this libel suit were allowed to proceed, then any researcher or scientist could be subjected to litigation simply by setting forth a theory that was unpopular or that might later be proven to be incorrect."<sup>13</sup>

Melnick's scrupulously objective scientific view was



echoed in a second affidavit which carried even greater weight, considering its source. Dr David Ho was the director of the Aaron Diamond AIDS Research Center, a Professor of Medicine and Microbiology at New York University School of Medicine and a scientist of such distinction that he was chosen as *Time* magazine's 1996 Man of the Year. In 1992 he had been a key member of the Wistar Committee which looked into the question of whether the AIDS pandemic could have begun with a contaminated polio vaccine – and concluded it was very unlikely.

A year later, however, it became clear that Ho was having second thoughts about the emphatic quality of the committee's judgement. He agreed to provide an affidavit in the *Rolling Stone* libel suit:

“In sum, I found the hypothesis presented in the (Rolling Stone) Article to be an intriguing, scientifically plausible theory. Indeed, it is a theory that has been independently proposed by others both before and after the publication of the Article. While ultimately the Committee concluded the hypothesis was very unlikely, it concerns me that the mere presentation of a scientific theory – without any indication that the researcher involved, in this case Dr Koprowski, was in any way negligent or somehow failed to follow procedures accepted at the time -could become the subject of a libel suit.

“There is very little in science that can be stated as unequivocal fact. And that is particularly true concerning the origin of AIDS – a question that is presently unanswerable and which is the subject of many conflicting theories. In the highly theoretical, and ever-changing, field of AIDS, I am troubled that a researcher or scientist could be subjected to litigation simply by setting forth a scientific hypothesis later shown to be unsound.”<sup>14</sup>

Equally concerned was Dr Ho's colleague at the Aaron Diamond AIDS Research Center, Dr Preston Marx, who was head of the Center's Animal Models Laboratory and a Professor at New York Medical Center. Although the case of Koprowski against *Rolling Stone* had been settled out of court, Koprowski's original lawsuit, against Associated Press and its reporter Bruce Rule, was still being fought out five years later. Marx agreed to provide the litigants with the views of an expert in the comparative study of disease, especially AIDS, in both animals and humans.

Marx began by making it clear that there was scientific

consensus that HIV was the cause of AIDS, but that science had not yet discovered – and might never discover – how AIDS originated. “It is widely accepted in the scientific community that the modern AIDS epidemic originated in equatorial Africa, which encompasses the countries now known as Zaire (Republic of Congo), Rwanda and Burundi. Most researcher believe that a simian immunodeficiency virus (SIV) that naturally infects one or more species of monkeys or apes in Africa was the source of both types of human immunodeficiency virus (HIV), the virus that causes AIDS. However there is no agreement as to how or when the virus crossed over to humans,” he said.<sup>15</sup>

Marx explained there were many theories about its origin, including Gilks’ suggestion it was transferred to humans in monkey blood during malaria trials. However, in the early 1990s another theory, involving polio vaccine, gained public attention. “This theory argues that certain species of monkeys were infected with SIV, the monkey kidneys were used to propagate polio vaccines in the 1950s, that the use of certain monkeys infected with SIV in the process of manufacturing the vaccines cannot be ruled out, that some stocks of the vaccines may have inadvertently contained SIV, that when the vaccines were introduced in Africa in the 1950s, they transmitted SIV to humans, and that SIV mutated into HIV. This sequence is made more plausible by the apparent coincidence of the administration of the vaccine in Africa in the late 1950s and the epidemic of AIDS in that general area decades later.

“In my opinion,” Marx stated, “at the time the article was written, the Polio Vaccine theory was a plausible explanation for the still unsolved mystery of how the modern AIDS epidemic originated.”

Like Melnick and Ho, Marx concluded by expressing his deep concern that merely making public a scientific theory should generate a libel action: the issue would be far more appropriately resolved in the laboratory, rather than the court.

And it was from the laboratory that vital evidence finally came to light.

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## The White Death

For those who argued that AIDS could not have started in the African polio vaccination campaign, British sailor David Carr was the linchpin. Early in 1995 the linchpin snapped.

Carr, it may be recalled, was the apprentice printer and Royal Navy national serviceman who died in Manchester on 31 August 1959, of a horrific complex of otherwise minor infections. At the time, his death greatly perplexed the doctors who attended him and performed the autopsy on his remains. It was not until two decades later, with the full awareness of the symptoms and significance of the AIDS epidemic, that they decided to re-test Carr's preserved tissues. The results, published in *The Lancet* in 1990 concluded Carr was the earliest known AIDS-case, predating all others reported as occurring in Africa and Norway in the 1960s.

Carr was supposed to have contracted his fatal infection during a brief visit to Tangier, North Africa, late in 1957, shortly before his discharge from the Navy. This was four or five months before the mass trial of polio vaccine commenced in the Ruzizi valley, Belgian Congo -- but some time after initial testing of the vaccine had begun in Stanleyville, in February 1957.

The window of opportunity for an infection to spread from Central Africa to the fleshpots of Tangier in nine months was small, and objectors to the polio vaccine theory had persistently overlooked it. The Wistar panel, in particular, disregarded the infection window, founding its rebuttal of the entire theory on the erroneous claim that Carr must have contracted his HIV *before* the Congo trials began.

Early in 1995 there came a shock development: Professor David Ho of the Aaron Diamond AIDS Research Centre, one of America's most brilliant AIDS researchers and a prominent member of Wistar panel, challenged the authenticity of the Manchester sailor's AIDS.<sup>1</sup>

When Ho and his colleague Dr Tuofu Zhu analysed the processed DNA taken by Corbitt and Williams the only strain of HIV he could find was one which had been prevalent in 1990 -- thirty years after Carr had died. Concerned, he sent the samples to two colleagues, Dr Gerald Myers, director of the Los Alamos National Laboratory's HIV database and a world authority on HIV genetics, and Dr Eddie Holmes of Oxford University, for independent analysis. "Regardless of the region of genome

examined, all phylogenetic analyses showed that the virus in the kidney sample was a member of HIV-1 clade B, the subtype currently prevalent in the United States and Europe," Ho reported.<sup>2</sup>

Myers added that it was inconceivable such a strain could have existed in the 1950s, because of the dramatic speed at which HIV had been mutating. The HIV must have come from some person other than David Carr, most likely a modern person, the scientists concluded.

Ho then decided to repeat the tests run by Corbitt, Bailey and Williams and asked for original samples of Carr's tissues. When these arrived, he probed them exhaustively. They contained neither HIV-1, HIV-2 nor SIV. A final test confirmed the tissue samples had come from a different person to the one who had supplied the HIV, and were of significantly different age. The conclusion was inescapable: whatever had killed David Carr looked very much like AIDS -- but evidently wasn't. "In our opinion, this finding invalidates the conclusion reached in the 1990 *Lancet* report," Ho stated.<sup>3</sup>

The science correspondent for Britain's *The Independent* newspaper, Steve Connor, reported Ho as saying the sailor's AIDS diagnosis was either the result of a mixup or a deliberate switch of experimental materials. Dr George Williams, who attended the sailor back in 1959, and then helped run HIV tests on him thirty years later, declared he was mystified and could not understand the discrepancy. He was absolutely confident of the authenticity of the material.<sup>4</sup> His partners, Gerald Corbitt and Andrew Bailey wrote to *The Lancet* saying that Ho had confirmed their own view that the HIV was a modern strain, but in view of the controversy all samples of Carr's remains should be submitted to a third laboratory for independent testing.<sup>5</sup> Finally, in early 1996, they conceded there must have been an inadvertent laboratory contamination: repeat testing of Carr's tissues had failed to disclose any trace of HIV.<sup>6</sup>

David Carr had been posthumously cleared as the world's first AIDS victim, and the central claim on which the Wistar panel had founded its rebuttal of the polio vaccine theory had been shown to be false - ironically, by one of its own members.

The tests had an important further consequence. They reinforced many researchers in a steadily-growing conviction that HIV/AIDS was a recent human pathogen, which crossed the species barrier only about 35 years earlier -- in other words in the late '50s or early '60s -- and underwent an explosive radiation in the

early 1970s. Dr Myers was one authority who concluded on the strength of the genetic evidence that HIV had entered humankind around 1960.<sup>7</sup> Another was Professor Paul Sharp of Nottingham University, who concurred on the timing, but considered that the HIV-1 family tree pointed to at least two transmission events occurring at about this time.

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In April 1997 science delivered startling new evidence which appeared to reinforce the polio vaccine theory of the origin of AIDS.

During the previous five years Associated Press had defended itself in the libel action brought against it by Koprowski following publication of a media wire service report entitled “Institute will investigate possible link between AIDS and polio vaccine” which was based on Tom Curtis’s original article. The defendants asserted that their report constituted protectable free speech and was, in any case, simply the expression of a scientific hypothesis. Koprowski, on the other hand, was required under the law surrounding the First Amendment to the United States Constitution to prove the polio vaccine theory to be false. This he proceeded to attempt, with the help of opinion from expert witnesses.

Associated Press sought authoritative witnesses of its own. Prominent among these was Richard Middleton, Professor of Microbiology at Rutgers University and adjunct professor at New Jersey University. Middleton spent some time delving around in the scientific literature before unearthing a wealth of material which “in my opinion may not only lend further empirical support for the theory but also has not previously been considered in connection with the theory”.<sup>8</sup>

What Middleton had uncovered was a trove of documented medical evidence pointing to an epidemic outbreak of the rare cancer, Kaposi’s sarcoma or KS, in Central Africa during the late 1950s and 1960s.

KS is a malignancy which usually occurs on the skin and which, until the advent of AIDS, was exceptionally uncommon: only 1200 cases had been reported worldwide between 1872 and 1958, mostly among elderly men of eastern Mediterranean stock. However, KS is 20,000 times more common in patients infected with HIV than among people who are not infected. Indeed, the explosion in cases of KS in New York during the late 1970s and early 1980s was a primary clue leading to the discovery by American doctors of the disease called AIDS.

Middleton's investigation of medical reports on the history of KS revealed there had been a 500 per cent increase in the number of malignant cancers attributable to Kaposi's sarcoma from the very region of Africa in which the polio vaccination program was carried out – the eastern part of the Congo and the border area of Rwanda and Burundi. He also noted a Belgian study which reported 8 cases of KS in children and infants from the same localities – yet KS had not previously been seen among African children.

“A second study, carried out between 1957 and 1970 in the northeast Congo, Rwanda and Burundi revealed that the highest number of human subjects afflicted with Kaposi's sarcoma were located within a 40-mile radius of the Ruzizi Valley,” Middleton stated.

“The significant increase in the percentage of malignant cases attributed to Kaposi's sarcoma is also revealing. A comprehensive study of 500 malignant cases in Africa before 1950 revealed that only 10 out of 500 (2%) were Kaposi's sarcoma. By 1961 the epicentre of Kaposi's sarcoma was in Eastern Zaire – exactly the same area where the polio vaccine trials were conducted – where more than 10% of all malignancies were Kaposi's sarcoma (an apparent 500% jump from 1956-61). Numerous reports have confirmed that, before the discovery of HIV-1 in the early 1980s, the greatest incidence of Kaposi's sarcoma occurred in this area.”

Furthermore, “in 1962 it was reported that more than 12 per cent of all malignant tumors in Zaire were Kaposi's sarcoma, a 600% increase from pre-1957 studies.”

For part of his evidence, Dr Middleton drew on a report by Dr M.S.R.Hutt of St Thomas Hospital Medical School in London, published in the *British Medical Bulletin* in 1984. This contained a map which displayed in graphic terms how heavy was the incidence of KS cancer in the northeastern Congo (9-10.6 per cent of all malignancies), and how rapidly this incidence decreased with distance from the Ruzizi Valley. Countries lying several hundred miles away had rates of only 2-3 per cent, similar to the level originally observed in the Congo before 1950.

“When one compares this illustration with the recent incidence of AIDS emanating from an epicenter in the Ruzizi Valley... one cannot but help reach the conclusion that Kaposi's sarcoma and AIDS are causally related,” Middleton observed.

“One should take into account that the live polio vaccine was administered to thousands of children, including infants less than a month old. If some vaccine contained immuno-suppressive

agents such as SIVs, it would exhibit its greatest adverse effect on children and infants. Numerous studies clearly confirm the fact that the great majority of cases of Kaposi's sarcoma reported from 1957 to 1962 were in children."

In view of the strongly-established links between KS and HIV-1, these studies offered a fresh insight into the plausibility of the polio vaccine theory, Middleton declared.

"The data cannot be lightly dismissed providing, as it does, additional empirical evidence indicating that it is possible that certain doses of polio vaccine administered to human subjects in that region may have inadvertently contained a precursor HIV-1."

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In 1995 a scandal broke which cast a grim sidelight on the way the polio vaccine theory had been greeted by the scientific establishment. This was the revelation of a three-year inquiry by staff of the United States Congress that key elements of the American medical research sector had engaged in a major cover-up over the question of who was first to discover the AIDS virus -- the Americans or the French.

Robert Gallo staked his claim at a press conference hosted by the United States Secretary for Health in 1984. The French had disputed it, alleging, among other things, that the Americans had stolen the French virus to make the United States' lucrative HIV test kit. After years of acrimony, the situation was patched over in 1987 by an agreement which nominated Gallo and Montagnier as "co-discoverers" of the virus.

This failed to appease all parties, however. In July 1994, after continued wrangling, the new director of the United States National Institutes of Health, Dr Harold Varmus, publicly conceded his scientists had made use of the French virus to develop their test kit: the Institute Pasteur was entitled to a higher royalty. This was a direct flow-on from an admission by Gallo in 1991 that he had accidentally used the Pasteur's virus in developing the kit, though an internal inquiry at NIH had subsequently cleared him of any misconduct.

Then, in 1995, an investigation by staff of United States Congressman John Dingell, chair of the House of Representatives Committee responsible for overseeing the NIH, dropped a bombshell: the whole issue had been a cover-up on the part of both NIH and the United States Department of Health and Human



Services, driven by "political and international reputational imperatives" which, it found, "assumed pre-eminence over scientific integrity".<sup>9</sup>

Defending Gallo's claim to be the original discoverer of the AIDS virus had become "tantamount to defending the United States Government itself", the report said. Accused by the French of pirating their virus, the response of United States scientific and health officials had been "to defend at all cost and irrespective of the evidence, the claims of Gallo *et al.*".

The report went on to brand the internal inquiry run by the Health Department "a parody", designed not to find the truth, but rather to fabricate an official record which would support Gallo's claim. In a probe conducted by one of Gallo's superiors "contrary facts and evidence were neither sought nor examined" and the former head of NIH had done all possible to protect the Institute's "superstar senior scientist", the congressional investigators asserted. Even as late as 1993, it alleged, evidence was still being withheld by NIH from the Surgeon General's Board of Enquiry into the matter.

A fierce argument promptly ensued over whether Dingell's report had any status, its critics loudly dismissing it as unofficial and therefore meaningless. Nevertheless, the report's findings illuminated both the ethics and conduct of the United States medical establishment in a disturbing light, raising echoes of its reaction to both the SV-40 and HIV-polio vaccine issues. Scientific evidence and scientific integrity appeared to have taken a back seat to prestige and reputation, not only among senior researchers but also their bosses and even the United States government itself, while efforts had been made to discredit or silence those who raised the matter.

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In spite of all the rhetoric claiming that the origins of the AIDS epidemic were unimportant and a distraction, a handful of scientific teams round the world continued to probe its origins throughout the 1990s, analyzing the genetic makeup of various SIVs and HIVs and trying to place them in a coherent order on a family tree of the immunodeficiency viruses.

Gerald Myers at Los Alamos National laboratory was at the forefront of these, and had already recorded his view that that sequence pointed to an origin around 1960 or just before. Also engaged in the hunt were Beatrice Hahn and Paul Sharp, from Alabama and Nottingham Universities respectively, and a team led by David Ho and Tuofu Zhu at the Rockefeller University.

In February 1998, Ho and Zhu stole the show by publishing in *Nature* a report in which they had analysed the earliest-known sample of HIV, that taken from a blood sample collected from a male Bantu in Kinshasa in 1959. It proved to lie very close to the root of the HIV family tree.

“Our results, the rate of HIV-1 evolution and previously described methods of estimation of evolutionary rates indicate that the major-group viruses that dominate the global AIDS pandemic at present shared a common ancestor in the 1940s or the early 1950s,” they ventured, cautiously.<sup>10</sup>

“The factors that propelled the initial spread of HIV-1 in Central Africa remain unknown: the role of large-scale vaccination campaigns, perhaps with multiple uses of non-sterilized needles, should be carefully examined, although social changes such as easier access to transportation, increasing population density and more frequent sexual contacts may have been important.”

For the first time the subject of vaccination had been broached in a detailed scientific paper, though the authors shied away from the implications. As the Pasteur Institut’s Simon Wain-Hobson observed in a comment piece in the same issue of *Nature*, “we’re in the realm of speculation, meaning the story is not over”.<sup>11</sup>

An intriguing feature of the *Nature* paper by Ho et al is that one of the co-authors was not a scientist, but a British writer called Ed Hooper, who had dedicated the past eight years of his life to tracing the early footprints of AIDS across Africa and the world in a one-man mission to uncover its source. After amassing more evidence than anyone else alive on the topic, Hooper was convinced it was the polio vaccine. The fact that five internationally eminent scientists consented to share the credit for their work with Hooper reflects the impact which his investigations were starting to have on the research community.

However acknowledging the possibility of a polio vaccine origin in private and stating it as a plausible hypothesis before the scientific profession and the world at large were two utterly different things. In January 1999, at least one of the authors, Professor Paul Sharp, put some distance between himself and the hints thrown out in the Ho article. Together with colleagues Beatrice Hahn and Feng Gao he published a paper in *Nature* in which they announced the results of further gene sequencing done on SIVs taken from chimpanzees, which showed one in particular of these chimp SIVs was very similar to the main forms of human HIV-1, groups M, N and O.

The result of this, Hahn and Gao announced to a packed press conference in the US was that they had “discovered the origins of the AIDS virus”, and sourced it to a particular strain of SIV taken from a chimpanzee. The puzzle was now solved, they declared. AIDS had probably originated with a virus from a subspecies of chimpanzee, *Pan troglodytes troglodytes*, which inhabited the western rainforests of Central Africa.

The science behind the gene sequencing was excellent, but the same could not be said of the speculation which Sharp and Hahn then proceeded to indulge in. Without adducing any scientific proof for their views, they argued that the transfer had occurred as a result of hunting practices. In fact, Sharp told the media, transfers of SIVs to humans had probably happened many times in the past and it was recent changes in Africa which had allowed it to escape into the global community. The fact that this flew in the face of all previous history of human sexually-transmitted diseases, in the face of African history, and in the face of the epidemiology of the African AIDS epidemic and the Kaposi’s sarcoma epidemic seemed not to trouble the scientists. Once again, medical research had been discreetly pushed into the background as a possible source and African tribal practices placed under the spotlight – without a shred of hard evidence to back up the claim.

These views were challenged in 1999, when Ed Hooper published his masterwork *The River: a journey back to the source of HIV and AIDS*.<sup>12</sup> More than 1000 pages of detailed research, interviews, scientific citations and incredible human persistence over nine years, *The River* was a powerful attempt to overcome with sheer weight of evidence and argument, international scientific indifference to the OPV/AIDS hypothesis.

Hooper was not a scientist, but he had lived and worked in central Africa during the period when the AIDS epidemic was just starting to emerge. As a BBC correspondent, he reported on its early stages. He had seen many people he knew fall victim to it, and in 1990 published a book entitled *Slim*, which told the story of the East African epidemic. Hooper’s great advantage over all others who had taken strong positions for and against the OPV/AIDS theory was his intimate knowledge of the region, its people and their turbulent and troubled history.

It would be impossible to précis a book such as *The River* here, and those who wish to study the evidence in detail are recommended to read it for themselves. However its outstanding characteristic is the intensity with which Hooper, like those great Victorian-era explorers Speke, Burton, Livingstone and Stanley,

sets out to find the source of the river of AIDS. Every early case from round the world is probed. At the end of this exhaustive investigation Hooper could discover no credible case of AIDS from the 1950s, 60s or early 70s which were not from Central Africa, or directly linked to it. And there was no credible case earlier than the 1959 Kinshasa HIV+ blood sample. “The very earliest cases of AIDS and HIV emerged almost exclusively in the former Belgian colonies of the Congo, Rwanda and Burundi. The major venue for these sporadic early cases was Kinshasa, but they also occurred in Equateur province, Kisangani, Likasi, Uvira, Kigalia and Bujumbura.”<sup>13</sup>

Hooper focused on 38 medically-documented AIDS or likely-AIDS cases from Central Africa between 1959 and 1980. 18 of these are HIV+ blood samples and come from Kinshasa where CHAT vaccine was fed, five from Yambuku 160km from Lisala where the vaccine was used, 16 from Bujumbura, 8 from Rumonge and 3 from Kihanga – all places where CHAT vaccine was used. Two other HIV+ samples come from mountain towns where the vaccine was also fed. Only 10 other HIV+ samples occur in Africa – from Nairobi and Senegal – and as these are from 1981, the virus had had plenty of time to travel.

“Over 87 per cent of all known samples of HIV-1 from Africa from 1980 or earlier come from towns where CHAT was fed. And 100 per cent come from places within one hundred miles of CHAT vaccination sites,” is Hooper’s remarkable conclusion.<sup>14</sup>

But *The River* was remarkable for another aspect – Hooper’s persistence in exploring the origins of the CHAT polio vaccine, how it was made, tested and used. It was here that it was revealed that while the Wistar-made vaccine was used on some 330,000 people at 9 places in the Congo, the Belgian medical authorities went on to vaccinate another 600,000 at 19 further localities, including the city of Kikwit, the mining center of Lubudi in Katanga and along the shores of Lakes Tangyanika and Kivu. The OPV used in this second round of vaccination appears to have been manufactured from Koprowski’s CHAT poliovirus strains in Belgium at the vaccine firm RIT.

For some years medical scientists had dismissed the suggestion that HIV may have begun in a vaccine on the ground that HIV was most closely related genetically to chimpanzee SIV, and chimpanzees had not been used to make vaccine but only to test it. In a remarkable piece of research, Hooper demonstrated that Koprowski and his Belgian collaborator, Dr Ghislain Courtois, had captured and used up some 400 chimpanzees in the testing

program for CHAT vaccine at their research station at Lindi near Kisangani (Stanleyville) – probably the largest chimpanzee farm the world has ever seen. He produced evidence that kidneys from these chimps were cut out and sent back to the US to the Philadelphia Children’s Hospital. The Hospital is near the Wistar Institute and its medical researchers worked hand-in-glove with Wistar scientists. He found that Koprowski had met at least one researcher in the Congo who was growing poliovirus in chimpanzee kidney. But because all records of how the CHAT vaccine was actually made have vanished – “lost in a move” according to Koprowski – there is no definite record of whether chimp kidney was used to make CHAT vaccine or not. Hooper considers it probable, on the grounds that, at that time, researchers were testing many different substrates in the hunt for the most productive, and the one thing readily available to the Wistar team was chimpanzee kidneys from the hundreds of animals sacrificed or which died from stress in captivity at Lindi. Koprowski has given varying accounts of what kidneys he used, but has made no mention of chimpanzee kidney.

Another intriguing aspect of *The River* is Hooper’s linking of the HIV-2 outbreak in West Africa with the use of another poliovaccine between 1957-64 on thousands of people in the towns and rural areas of French West Africa (now Senegal, Guinea Conakry, Ivory Coast, Mali, Niger, Burkina Faso, Benin and Mauretania) and French Equatorial Africa (now Cameroon, Gabon, Central African Republic and Congo Brazzaville). The vaccine was made by the French, using kidneys taken from Guinea baboons and green monkeys. HIV-2 is closest in genetic makeup to SIV from the sooty mangabey, which lives in the western part of West Africa. Hooper thinks it possible SIV could have been passed from sooty mangabeys to the species used to make vaccine either in the wild or in captivity, when they were caged together.

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Adding weight to such a view was the fact that although numerous people, including the distinguished members of the Wistar panel, Melnick, Curtis, Hamilton, Lecatsas, Alexander, Fox, Hooper and Pascal had called for the independent testing of the Wistar vaccine stocks, those early samples had never been tested during the ensuing years -- or, if they had been, then as of 2000 no results had been made public. Furthermore, two independent experts who made offers to conduct tests on the Wistar vaccines had been rebuffed.

Calls for the testing of old Wistar stocks pose certain

difficulties. There is no certainty that samples of the contaminated CHAT-1 batch administered in the Congo still exist, unless Sabin retained his sample. There is no guarantee that the perishable SIV would still survive in it after all these years in cold storage. Cynically, Pascal suggested that any sample turned over to an *American* lab for testing would be found to be negative. Such a view is disrespectful of American science, yet the revelations of the Dingell investigation and the Bernice Eddy affair lent it some credence.

The fictional detective Sherlock Holmes is credited with the aphorism that when you have eliminated the impossible whatever remains, however improbable, must be the truth. This, in a way, is a description of scientific method: set up your theory, making it as strong as you know how, then try everything you conceivably can to knock it over. If, at the end it is still left standing, it is probably fairly close to the truth. Scientific method has yet to be applied to the vaccine theory.

There is one scientific test with the capacity to undermine the Congo vaccine theory. Around the world, stashed away in medical institute freezers and cabinets are thousands of blood and tissue samples collected in Africa during the past half century and more. One example of such a collection is held by the International Red Cross in Amsterdam. If a single blood sample from Africa or America, just one, could be shown to be HIV-positive beyond a shadow of a doubt, and if it came from 1955 or earlier and was clearly an ancestral strain, the Belgian Congo vaccine theory would be undermined. At the most, it would become only one of a number of possible routes for transfer of SIVs to humans

A worldwide repeat, on a larger scale, of the experiment performed by Harvard's Essex and Kanki when they identified the original 1959 Kinshasa HIV+ sample would constitute a first step on such a path. Testing thousands of blood samples using the best available rapid-assay technology and independent scrutiny of the process would go far towards resolving the question of whether polio vaccine transfer may have been an "extremely rare" event, as the Wistar panel hedged -- or a non-event.

If, on the other hand, none of the pre-1955 blood samples reveals a trace of HIV, this would certainly lend weight to a more recent cross-species transmission. It would narrow the time-frame to the era of modern technology.

In that event, exhaustive independent testing of early polio vaccine stocks would certainly be justified. But even that might not cover all eventualities: who is to say, for instance, a dirty needle

used on a Lindi chimp, or any chimp for that matter, was not then used by accident on a human? Or that kidneys from a sacrificed chimpanzee were not then used to prepare vaccine?

It would also justify exhaustive exploration among African monkey populations for possible precursor SIVs for HIV-1 and HIV-2. Although scientists have a number of good candidate viruses – two from chimpanzees for HIV-1 and several from sooty mangabeys for HIV-2 it is by no means clear we have discovered all the SIVs. Even the closest strain of SIV has only 80 per cent similarity in its genetic makeup to HIV-1. Also, as around half of wild African green monkeys are found to be infected with SIVs, yet only 1 per cent of wild chimpanzees, the odds that the HIV precursor is to be found in green monkeys seem high. Yet green monkeys still supply the bulk of the kidneys for polio vaccine manufacture and soon, maybe, for ‘flu vaccine also.

One important reason for researching wild monkey groups is that, through a better understanding of how that monkey group maintains its natural immunity to SIV, an Achilles heel may be discovered which might enable us to disrupt the virus's life-cycle in humans. This point was underlined in an opinion article in *Science* by immunologist William Paul, director of the office of AIDS Research at the United States NIH, who argued the limited progress made in combatting AIDS stemmed from the fact that researchers did not understand its fundamental biology well enough. Primate research should play a central role in learning how the disease developed and how monkeys in turn developed or maintained resistance to it -- since, until recently, there was little unequivocal evidence for acquired human immunity.<sup>15</sup>

The existence of several kinds of HIV -- HIV-1 and its various strains, and HIV-2 -- was seen by some as an argument for treating *all* origin theories twice as seriously. South African virologist Lecatsas, in particular, considered the simultaneous emergence of two or more, quite different, kinds of HIV in the human population in the same time-frame to be powerful evidence of "contamination from some source", rendering the chimp-hunter and other explanations for the transfer highly improbable.

"Monkey viruses like SIV<sub>CPZ</sub> and SIV<sub>MAC</sub> are closer to HIV-1 and HIV-2 respectively (sharing 80-90 per cent of their genetic material) than the two HIVs are to one another (they are only 40 per cent identical in genetic makeup). Logically, one must look at the monkeys in their relationship to man. Simultaneous bites or ritual use of blood leading to infection are extremely unlikely for the obvious reasons," he said.

"Poliovaccines made in a variety of monkey cells have been shown to contain lymphocytes which could carry the virus. Statistically, to use 50 million doses of vaccine per annum for 30 years makes it extremely likely that some contamination has occurred -- just as it did when the monkey virus SV.40 infected millions of people at the start of the polio campaign history. The massive use of the vaccine would select suitable variants which could successfully infect man. The odd monkey bite would almost certainly not succeed," he said.<sup>16</sup>

Oxford Professor William Hamilton believed scientists should devote more effort to unravelling the HIV-1 family tree in an effort to determine the point of origin, especially by sampling and sequencing strains from the localities where polio vaccination was carried out.

South African virologist Alexander said African blood samples from the 1950s and before were still abundant, and urged further testing for the presence of HIV as well as attempts to sequence any which might be found. Searches should also be made for Africans who were "refractory", that is in the process of developing immunity, as these too could indicate populations exposed for the longest time and so, possible points of origin, she suggested.

Without such tests, carried out under rigorous international scrutiny, the polio vaccine theory would *not go away*, she predicted. Scientists might continue to deny it, but in the absence of firm evidence, they would have no case to argue. If the theory was so wrong, then where were the *scientific* papers which refuted it?

Science could reluctantly face up to the issue of a contaminated vaccine in the 1960s, as it did in the case of SV-40, but by the 1990s that was no longer possible, she felt. "Science in the 1960s was gentler, kinder and more honest. There is too much at stake today. There is so much money and politics involved in the whole issue of AIDS.

"It's a great big power-game, with scientists hanging onto their reputations....some are turning into pop-stars.

"Also sections of the medical profession feel threatened by such theories, because they are no good for the image of medicine. It has become a very jittery profession."

As to the persistent refusal of the medical establishment and the mainstream science press to face the necessity of giving the issue objective, rational scientific consideration and investigation, she observed simply: "The silence is deafening...."<sup>17</sup>



Independent testing of old blood stocks will give us a better fix on whether AIDS is truly "an iatrogenic disease", a product of modern medicine. Distasteful and painful though such a suggestion may appear, it is neither wrong nor immoral to entertain it. One of the fundamental Hippocratic injunctions on physicians is encased in the Latin phrase *primum non nocere*: first, to do no harm. A conscientious interpretation of this exhortation demands that medical science make as certain as possible of the truth in a case such as this.

"There is a moral obligation to be intelligent. Ignorance is a vice, and when it results in injury to anyone it becomes a crime, a moral if not a statutory one. To infect another with disease, either directly or indirectly, as a result of ignorance is an immoral act. The purpose of government is to protect its citizens, and a government which fails to shelter its citizens against infections is neither intelligent nor moral." The words are those of Dr Victor Vaughan, president of the American Medical Association in 1915, spoken at the dawn of the modern vaccine era. Contrasted with the "don't want to know" attitude of the medico-scientific majority to the polio vaccine theory of AIDS detailed in this book, they provide an interesting epitaph for the transition of medical ideals in the 20th century.

The WHO has conceded that there exists today a global epidemic of iatrogenic illness and death, although its causes are many and varied. In its publication *World Health*, it said iatrogenic diseases "are rapidly becoming so widespread that they have come to constitute an important category of human pathology". It cited studies conducted at Yale University and Boston Medical school which showed that from eighteen to thirty-five per cent of people in hospital at any one time were suffering a medically-acquired condition -- usually an adverse reaction to a drug.<sup>18</sup> Yet WHO officials had dismissed the polio vaccine theory as being of "no importance".

Disease has constantly reshaped the human destiny, as the second chapter of this book made clear. But disease is not some freakish natural occurrence, some diabolical *deus ex machina* that strikes us down at whim. Epidemic disease is, more often than not, a consequence and a product of human behaviour and technological change. Practices such as travel, trade, war, irrigation, promiscuity, drug-taking, poor hygiene, environmental disturbance, pollution and the like are all primary triggers for epidemic disease. Plagues seldom arise spontaneously: you have to go out and get them. Thus it ought not to be regarded as too incredible that medicine

itself, when founded on an insufficiency of knowledge, might also be a primary cause of epidemic disease.

Considering the trillions upon trillions of live viral particles which have been administered to humans as vaccines, the billions of litres of blood that have been transfused, the tens of thousands of organs transplanted, the billions of unsterilised needles and surgical instruments used under rough conditions, it is truly miraculous that medicine has not caused more epidemics. That at least one pandemic may have established itself as a consequence of medical mischance does not, therefore, seem so implausible. It may have been the price which was forfeit for the millions upon millions of lives which were saved.

Furthermore the altruistic desire which motivates doctors and researchers to save life and reduce suffering will always exist in an equally human context -- a context in which scientists press hard against the frontiers of their knowledge and understanding of the natural world, a context where from time to time they are bound to err or to take decisions in the absence of full knowledge. They will be impelled by many factors -- by ideals, by ambition, by public fears and expectations, by the fascination of discovery, the need for results to satisfy their corporation or funding agency, by pride, nationalism, competitiveness, kindness and pity. Sometimes these imperatives will thrust them harder and faster into the future than they, privately, might wish to go. Very few great discoveries or voyages of exploration are accomplished without sacrifice. Often it is the quality and scale of the sacrifice which endow them with their value in human eyes. The loss of life remains the harshest, yet most cogent measure.

Even were the Congo vaccine theory to be shown as unlikely, there remains Gilks' eminently sensible suggestion that the disease might have been passed in chimpanzee or monkey blood inoculated into humans in malaria experiments. This too, merits far closer scrutiny than it has yet received, as does much other experimentation which seems to have been perpetrated by Western medicine on Africans during the post-WWII period. Finally the chimp hunter/sex rite theories ought not to be discounted because potentially they carry their own lessons for human hygiene and the spread of disease -- and particularly for the practice of primate tissue xenografts.

There has been only one serious attempt to evaluate the polio vaccine theory of AIDS transmission scientifically, and that was by the Wistar investigative panel, composed of six of America's most eminent researchers. They found at every technical

link in the chain of contamination such an event to be possible, though of low probability. Then, they concluded on the strength of the timing of the Carr case, that transmission of HIV in the Congo polio vaccine was virtually impossible. If the panel were to revise its findings in the light of Ho's revelation that Carr did not have AIDS, it could reach only one conclusion: that the polio vaccine theory, at every point, is possible.

Ho himself signalled that he had undergone a change of perspective on this issue as a result of his Carr discovery: a year after the committee of which he was a member found it "very unlikely" he was stating in a legal affidavit that he considered it "an intriguing, scientifically plausible theory".<sup>19</sup>

In 1996, his colleague at the Aaron Diamond AIDS Research Center, Professor Preston Marx stated plainly the implication of Ho's discovery: "While not proving that the polio vaccine theory is true, Dr Ho's findings remove a fundamental underpinning of one of the more important arguments against the theory's plausibility.

"One can only speculate at the conclusion which the Advisory Committee might have reached if the discoveries of Dr Ho, which were published in 1995, had been available when the Advisory Committee issued its report in September 1992."<sup>20</sup>

If six of the world's most eminent microbiologists consider such an event to be possible, then others ought to be more open-minded. Yet medical scientists are constantly making the fallacious claim to members of the public, to the media and to people writing books about AIDS that the polio vaccine theory has been "refuted" or "debunked".

That the public is in danger of being deceived on this issue was evident from the fact that at least three major works emerged in 1995 alone, reciting such claims. And more are being written.

Laurie Garrett in her outstanding work on future epidemics, *The Coming Plague*, dismissed the theory with the catchall sentence: "After careful study it was concluded that the polio vaccines were HIV-free." This created the misleading impression the vaccines had been tested by the Wistar panel and found to be free of SIV. Garrett added the contestable argument that HIV-1 and SIV from African green monkeys were too dissimilar for HIV to have mutated from SIV<sub>AGM</sub> in "less than twenty years".<sup>21</sup>

Then, in *A Summer Plague*, author Tony Gould based his rejection of the theory closely on the Wistar report, asserting "HIV and...SIV do not grow in monkey kidney cells; nor would they be likely to survive the cycles of freezing and thawing the vaccine

went through before it was used. Then there is the question of the time it would take for SIV to mutate into HIV-1, the virus known to have been present in Zaire in 1959." And finally Gould reposed his confidence in the Manchester sailor.<sup>22</sup>

In *Plague's Progress*, another look at future epidemics, Arno Karlen expressed the view that AIDS reached humans "some fifty years ago from African monkeys", and that the timing was recent because the deadliness of the virus suggested it was new. He sided strongly with the view that monkeys eaten for meat, kept as pets or exported for medical experiments were the most probable source of transmission. "The monkey trade was perilous to both hunters and hunted. People were scratched and bitten. Monkeys were crowded in holding pens, cargo planes and lab cages. Primates from all over the world... exchanged pathogens. The result was a crucible of viruses...", he recounted.

Karlen also noted that "throughout history, social and technological change have ushered in new epidemics, from bubonic plague to typhus." But failing to pursue the logic of his own reasoning, he came down in favour of the prehistoric technology of monkey hunting as the most likely means of transmission – despite its lack of scientific evidence - and discredited the polio vaccine theory by including it among a list of conspiracy theories.<sup>23</sup>

Clearly, the establishment consensus has been able to influence the views of first-class medical writers and to shepherd them away from the evidence towards other theories, most of which lack even a fraction of the proof. By such means the myth of a thorough, impartial and conclusive investigation has been perpetuated, and certain researchers feel entitled to claim the theory as "refuted", a word which actually means to *prove completely false*. Anyone encountering this assertion is advised to request the scientific basis for making it.

A second category of dismissal was from those who, like *Science*, preferred to consign the polio vaccine hypothesis to the category of "conspiracy theory". This was a clever manoeuvre, because conspiracy theorists usually harbour a pathological obsession that governments, research establishments and the media should devote all their energies to proving (not investigating, but *proving*) the theorist's claim, no matter how bizarre. To dub something conspiracy theory is therefore tantamount to insisting that officialdom should treat it in the same way they invariably treat crackpot ideas – in other words, they should ignore it.

But where is the alleged conspiracy? The polio vaccine theory was developed by a handful of individuals independently of

one another, all of whom held a personal view that, if HIV was transferred in this way, it was simply a terrible accident. None of the theory's proponents did any more than call for a full and fair investigation in the interests of human welfare. None of them stood to gain from their assertions, or has gained from them -- indeed they all stood to lose, and for some the personal cost has been high.

The Wistar committee reached its conclusions on the basis of experience and judgement, not by experiment and analysis. The polio vaccine theory has *never* been rigorously tested by such means and this remains a crucial scientific oversight. Until it is, the suspicion that AIDS is iatrogenic will never be laid to rest.

Koprowski himself once said, quoting the great Sherlock Holmes: "In solving a problem of this sort, the grand thing is to be able to reason backwards. That is a very useful accomplishment, and a very easy one, but people do not practice it much."<sup>24</sup>

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This book does *not* assert there is conclusive proof that AIDS started in a polio vaccine -- but rather that there exists a strong circumstantial case, which remains to be fully, fairly and scientifically evaluated. It does not contend that the theory is either true or false, but rather that the truth remains to be determined -- and this is best done by science rather than the law.

All notion of blame or discredit should be discarded as inherently unworthy and unscientific sentiments. The practice of careful vaccination must be supported in the strongest terms, as the only means by which humanity can possibly hope to save the lives of the eight million children who perish each year from preventable disease. Nor should it be thought that there is anything wrong with existing polio vaccines -- though the recommendations of the Wistar panel about safer ways to make them ought not to be ignored. That a mistake may occur in one batch of vaccine among thousands is no reason to condemn an entire practice which has saved, and will continue to save, tens of millions of human lives and which will, in all probability, soon bring about the eradication of polio from the human family. That achievement will be due in great measure to the pioneering work, the courage and dedication of Salk, Sabin, Koprowski, Cox, Melnick and their peers.

Nor does any reproach attach to those scientists who doubted and criticised the polio vaccine theory. It is the duty of scientists to be sceptical. Society pays them to have doubts, and science would be a nonsense if they did not. But it is also their responsibility to be open-minded, to test and to revise their

opinions in the light of fresh evidence -- and these requirements have not fairly been served in this case.

However, this book *does* assert there is more evidence favouring the polio vaccine theory than exists for other competing theories, and that this constitutes a powerful argument for it to be received more seriously and investigated more thoroughly. Also, it asserts that rational discussion of the issue has been censored, disparaged and obstructed in various ways.

This book argues we have a need, as well as a right, to know.

The use of the law to forestall debate on such issues is an ominous development for science, for human health and for free speech. For science, it means that legalism has become triumphal over the objective quest for truth -- and there is a grave danger that in future such a principle might be employed by minorities, fundamentalists, corporations and sectional interests anxious to frustrate and impede scientific enquiry and debate. It carries the implication that judges and lay juries may in future be called on to determine scientific fact, rather than scientists.

The lawsuits' practical effect has been to free the scientific community of the necessity to probe into this issue, by chilling the most public form of pressure for its investigation -- the attention of the media. This is an infringement of democratic principles and an assault on free speech.

It is also hostile to the public interest, because the plain implication for human health is that by ignoring it, medical science may be under-rating potential loopholes by which new plagues can enter our species.

\* \* \*

In summary, the evidence favouring the view that AIDS began with a polio vaccine is:

1. The emergence of AIDS and the vaccine campaign in the Belgian Congo coincide closely in time.
2. The emergence of AIDS and its heaviest incidence, in the past and today, coincide closely in geographic location with the Congo vaccination sites.
3. There was an epidemic eruption of the AIDS-linked cancer, Kaposi's sarcoma, in Central Africa from the late 1950s onwards. Its epicentre lay in eastern Congo -- the same region as the vaccine trials.
4. HIV-1 and HIV-2 are evidently descended from different SIVs but appear to have entered the human population and begun to radiate (evolve away) at about the same time, around forty years

ago. This suggests a common mode of transmission in use at that time, but not at other times.

5. The Congo campaign administered live virus to 300,000-plus people, including 149,000 children many of whom were susceptible infants with undeveloped immune systems and who therefore received extra-large doses.

6. The large batch of vaccine used in the Congo was found to be contaminated by at least one unknown virus, and early vaccines were frequently plagued by extraneous monkey viruses.

7. The vaccine was prepared in kidney cell cultures from unknown species of monkeys, many of which were probably infected with SIVs. It may possibly have been passaged in human cells. It was tested, and may have been passaged, in chimpanzees.

8. African monkeys and chimps carry many, varied, strains of SIV two of which are undoubtedly the forerunners of HIV. It is probable that many strains remain to be discovered, and some may never be found owing to the loss of monkey populations. SIVs spread readily among primates in captivity.

9. SIV and HIV infect certain white blood cells and, according to many experts, it is difficult to exclude these from primary tissue cultures. Both viruses infect humans and monkeys.

10. The very rapid mutation rate of HIV, its extreme deadliness, the lack of human protective immunity, and its pattern of evolution all indicate it is a new agent moving through a virgin host population, since around 1960.

11. The SV-40 incident and Cutter incident demonstrate that major mistakes did occur in early polio vaccine manufacture.

12. The SV-40 incident demonstrates that unknown and potentially lethal viruses can be transmitted to humans from monkeys, unintentionally, in vaccines.

13. The canine parvovirus incident demonstrates a species leap can, in a short time, cause a pandemic.

14. There is evidence HIV can be passed orally, either by mothers breast-feeding their babies or by oral sex, making an oral live virus vaccine a credible route for transmission.

15. Since vaccine technology has delivered billions of doses of live and killed viruses to billions of people worldwide over more than forty years, the statistical probability of unwanted viruses slipping through is significant. This contradicts the assertion it was "very low".

16. The popular chimp hunter or monkey bite theory for the transmission of AIDS is unsupported by scientific evidence. To the contrary, the most active primate hunters, the pygmies, were

found to be free of HIV in two studies. It is not known whether HIV can be transferred by biting.

17. No AIDS was seen in 500 years of the African slave trade, emigration or European colonialism. No cases are known prior to 1959.

In fairness, this argument cannot and ought not be viewed as conclusive. Against it, its critics have raised the following points:

1. As things stand, the closest known relative to HIV-1 is an SIV from a chimpanzee, and there is no evidence chimpanzees were directly involved in the vaccine manufacturing process.
2. The closest relative to HIV-2 is an SIV from a sooty mangabey, and there is no evidence these animals were involved in vaccine manufacture.
3. HIV is different from green monkey SIV: it is clearly a substantial mutation. So large a genetic change could not have taken place in so short a space of time, pointing to an earlier cross-species transmission.
4. Tests have shown SIV/HIV cannot multiply or even survive in a monkey kidney tissue culture provided the lymphocytes are carefully excluded.
5. The oral route is an unlikely one for a cross-species transmission to occur.
6. If the same contaminated batch went to Poland and was received by 3000 children, why is Poland not the primary focus for AIDS in Europe?
7. If Carr truly had AIDS, how did he acquire it in such a short time, especially when he may only have been in North Africa?
8. If polio vaccine was the sole source of transmission, why are there two distinctively different strains of HIV apparently originating in different parts of Africa? Why are they of differing virulence?
9. The vaccine theory calls for the conjunction of several unlikely events, making it statistically improbable.
10. Sabin found a contaminating virus in the CHAT vaccine batch, twice, but Koprowski and two other laboratories found no virus. This can be argued to have failed the test of scientific repeatability.
11. How can HIV have spread heterosexually if it was first contracted only by babies?
12. While it is not easy to prove that AIDS existed before the Congo trials, it is much harder to prove that it did not -- making the polio vaccine theory very difficult to substantiate
13. Even the discovery of SIVs in early vaccines would not



necessarily prove they were the source of HIV.

14. There could have been many transmission events taking place undetected over a long time, and this view is supported by the apparent diversity of strains and lesser virulence of HIV-2 in West Africa.

The complexity of many of the claims listed above is such that only a properly constituted international scientific inquiry is capable of resolving the issue. Left to itself and without public pressure, experience indicates that medical science will be reluctant to investigate.

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"Epidemics are not accidents," declared pioneer AIDS researcher Dr Nathan Clumeck, of St Pierre Hospital, Brussels. "A new pathogen will enter a community only when the conditions are ripe for it."<sup>25</sup>

At some moment about forty years ago, those rare conditions came into constellation. The individual requirements for the cross-species transmission of a devastating, sexually-transmitted killer from monkeys into people were fulfilled, and human nature did the rest.

We may never discover the exact point at which SIV passed from primates into humans to become the scourge of AIDS -- but difficulty alone ought not to deter us from attempting to find out. We owe it to our kind to answer the question: *How?*

But there is another, more pressing reason for so doing. Without proof AIDS is iatrogenic, it is possible medical science and industry will, in future, take all conceivable precautions against such a thing ever happening again. But it is not very likely.

Already many experiments are under way which involve the transfer of animal tissues to humans, and old, unsafe vaccine methods continue in use. Until confronted with the sort of hard proof used to substantiate the link between thalidomide and birth defects, it is highly doubtful if the medico-industrial sector will amend its practices. It will continue to incur vast risks for the sake of keeping down its costs, or exploring interesting research possibilities.

At the same time, new diseases are emerging from the ravaged rainforests and savannas to appal us. As the population multiplies, the scope for these agents to cleave great swathes through humanity also magnifies, aided and abetted by such innocent things as air-travel, air-conditioned buildings, child-care centres, eco-tourism and the opening of once-closed frontiers. Humanity is the rich soil in which these primordial creatures must

take root, if they are to survive in a world from which other species are fast vanishing.

If vaccines or xenografts are possible routes for the primary transmission of unknown agents, then methods must change and the lesson be absorbed for the safeguarding of future generations. Finding out whether AIDS is iatrogenic *is* important to human health, to the prevention of future plagues and the saving of lives.

It is also important to our self-knowledge.

It is the philosopher, Louis Pascal, who provides one of the most chilling of insights into the nature of AIDS and its peer-viruses:

"AIDS came to us able to exploit important weaknesses of the human immune system, weaknesses we did not even suspect were there.

"And along with exploitable weaknesses of the human immune system, AIDS has found other exploitable weaknesses in the human mind, character, and society.

"AIDS' talent for exploiting these weaknesses will increase with time. And it will ferret out other weaknesses still unsuspected, and reveal these weaknesses to us through a much starker image than any social critic could possibly sculpt.

"There is a live thing growing within us."<sup>26</sup>

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In 1348, when plague smote Europe, the faces and limbs of its victims became blackened with the blood which erupted from the burst capillaries beneath their skin. From this, the contagion took the name by which it was ever after to be known: The Black Death.

In 1983 a disease was identified which attacks white blood cells. It infected and slew fifty million people over the ensuing four decades and countless more down the years. If, by some grievous mischance, this plague was an unintended gift of white medicine to the people of Africa and the world then, perhaps, the White Death might not be too unfitting a title.

## Endnotes

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## Glossary

**AIDS** - Acquired immune deficiency syndrome. A condition involving depletion of the body's immune defences as a result of a long-running infection by a virus (HIV) and subsequent opportunistic infection by other viruses, bacteria, parasites and fungi.

**Antibody** - a three-lobed chain of proteins able to bind to an antigen (see below) as part of an immune response. This either stops its action or sets it up for destruction by specialised immune system cells. Mostly produced by B lymphocytes in the blood, the presence of antibody is one way of telling if a person has been infected with a particular virus.

**Antigen** - a foreign substance or agent which stimulates an immune response in the body.

**Antisera** - human or animal blood sera containing specific antibodies. Used to test for the presence of particular organisms or to prevent disease after infection has taken place.

**ARV** - AIDS related virus. An early designation of HIV.

**Aspergillus** - a fungus which commonly infects the lungs and other organs of AIDS patients.

**Attenuate** - to dilute or weaken. In the case of vaccines, to subject an organism to strong evolutionary pressure so that its capacity to cause serious disease (virulence) becomes weakened, enabling it to generate a protective immune response in the infected person or animal.

**Black Death** - the Bubonic Plague caused by the bacterium *Yersinia pestis*. 1348-1665. Probably originated in western China or Turkestan, entered Europe through Genoa in Italy and killed 20-30 per cent of the population.

**BSE** - Bovine spongiform encephalopathy. Better known as "Mad Cow Disease". A new agent believed to have crossed into cattle as a result of feeding with infected abattoir meal containing the sheep prion disease scrapie. Causes holes to form in the brain.

**Candida** - a yeastlike fungus which causes candidiasis, usually in the mouth or vagina, but in severe cases can invade other parts of the body.

**Centers for Disease Control** - the US national infectious diseases watchdog, based in Atlanta, Georgia.

**CD4+ lymphocyte** - the white blood cell which carries the CD4 molecule on its outer membrane, to which coat-proteins of the HIV virus bind. Also known as the helper T-cell, it is central to the co-ordination of an immune response. The host cell for HIV.

**CJD** - Creutzfeldt-Jakob disease. A naturally-occurring prion (or viroid) infection in humans which has since been found to transfer medically, causing the brain to become spongiform leading to rapid decline and death. May take from 4-40 years to emerge.

**CPV** - Canine parvovirus. A new and lethal infection of dogs which emerged as a pandemic in the second half of the 1970s and is believed to have crossed from cats.

**Cryptococcus** - a fungus which causes a chronic disseminated disease in humans affecting especially the lungs and nervous system. A characteristic infection of AIDS.

**Cytomegalovirus** - a member of the herpes virus family which causes cells to become greatly enlarged (cytomegalic inclusion disease). Formerly seen only in children, now recognised as characteristic of an undermined immune system. Commonly seen in AIDS cases.

**DNA** - deoxyribosenucleic acid. What your genes are made of. The largest biologically-active molecule known, DNA is responsible for the replication of the key substances of life, nucleic acids and proteins.

**Enteric** - pertaining to the gut.

**Epidemic** - the outbreak and rapid spread of a disease in a community, in which many people are infected at the same time.

**Epidemiology** - the scientific study of epidemics, particularly the

timing, incidence and distribution of the disease.

**Epstein-Barr virus (EBV)** - a member of the herpes virus family which attacks B lymphocytes and causes infectious mononucleosis.

**Etiologic** - related to the cause of a disease.

**FPLV** - Feline panleukopenia virus. A cat virus responsible for cat distemper or enteritis, which is believed to have crossed into dogs to become the lethal agent canine parvovirus.

**Herpes viruses** - a family of DNA viruses responsible for herpes, genital herpes, chickenpox, shingles, mononucleosis and cytomegalic inclusion disease. Herpes simplex is a common co-infection in AIDS cases and may play a role in transferring the HIV virus.

**HIV** - Human immunodeficiency virus. An agent which infects the immune system's helper-T (CD4+) lymphocytes. Regarded by the majority of researchers as the cause of immune system breakdown leading to AIDS.

**HIV-1** - the strain of HIV first discovered and still the most prevalent globally.

**HIV-2** - a strain of HIV with only about 50 per cent genetic similarity to HIV-1. Mainly associated with cases in West Africa.

**HTLV-III** - Human T-cell leukaemia virus III, the name originally applied to HIV by researchers at the US National Institutes of Health.

**Iatrogenic** - (disease) caused by medicine or medical treatment.

**Intracerebrally** - (injected) into the brain.

**Kaposi's sarcoma** - a characteristic brownish-purplish cancer commonly, though not exclusively, associated with AIDS. First appearing on the skin it spreads to the internal organs. Now thought to result from co-infection with herpes virus.

**Lability** - ability to change or adapt, variability.

**LAV** - Lymphadenopathy associated virus. The name originally bestowed by French researchers on HIV.

**Lymphocyte** - a white blood cell produced in the lymph glands. Member of a group of white cells responsible for mounting an immune response to infection. Its two main subgroups are the B lymphocytes which produce antibodies and the T lymphocytes which co-ordinate the immune response and kill infected cells.

**Lymphadenopathy** - infected or swollen lymph nodes or vessels.

**Monolayer** - a tissue culture consisting of a single layer of cells. Used to grow other organisms.

**Oncovirus** - a retrovirus responsible for causing any form of cancer.

**Pandemic** - a universal epidemic.

**Pathogen** - an agent of disease.

**Pathogenicity** - ability to cause disease.

**Phylogenetic** - relating to the evolutionary place of a species or organism.

**Placebo** - an inert substance given to patients in medical trials to compare the effects of a new drug in one group with another group receiving the placebo. Also given to achieve the psychological effect of medication.

**Pneumocystis carinii** - a parasitic micro-organism which produces cysts in the lungs and causes pneumonia. Commonly associated with AIDS.

**Poliovirus** - an enteric virus responsible for causing poliomyelitis, a highly contagious disease which may infect the spinal chord causing paralysis and atrophy of the limbs. Occurs only in humans and is passed in faeces, through poor hygiene.

**Recombination** - the process by which an organism incorporates new genes into its genome and so develops new abilities. A



fundamental mechanism of evolutionary mutation.

**Retrovirus** - a member of a group of viruses whose genetic code consists of ribonucleic acid (RNA) and which use an enzyme, reverse transcriptase, to translate their RNA into DNA for permanent incorporation into the genome of the host cell so that it makes new virus. Includes the lentiviruses and HIV.

**Simian** - relating to monkeys.

**SIV** - Simian immunodeficiency virus. An agent prevalent among African monkeys and apes and believed to be the origin of HIV. There are many different strains of SIV, which can also infect Asian monkeys, causing AIDS, and humans.

**Smallpox** - a severe, contagious viral disease which initially causes fever, cramps and vomiting and subsequently leads to the eruption of pustules throughout the body which leave permanent scars. The disease is restricted to humans.

**Supernatant** - the liquid swimming above a tissue culture or precipitate.

**SPV** - Simian parvovirus. A monkey virus first discovered in captive cynomolgus monkeys in 1994. Causes severe anaemia and may lead to immunosuppression in conjunction with other viruses.

**SV-40** - Simian virus 40. A monkey virus, so called because it was the 40th to be identified. Accidentally administered to millions of humans in poliovaccine in the 1950s.

**Tissue culture** - a growth medium made from particular cells of plants, animals or humans in which other organisms can be cultivated.

**Toxoplasma gondii** - a parasite which invades cells causing toxoplasmosis, a disseminated infection of tissues such as the lungs, nerves, liver, brain, eyes, throat and heart muscle. Sometimes seen in AIDS patients and a cause of AIDS dementia.

**Vaccine** - a preparation of live or killed organisms used to prevent infectious diseases by provoking a protective immune response in the recipient.

**Virion** - a single virus particle.

**Virulence** - the disease-producing capability of an organism. Not to be confused with infectiousness, which refers to its ease of transmission.

**Virus** - a microscopic parasitic organism that can only reproduce inside the cells of other creatures. Viruses normally consist of a length of either DNA or RNA encased in a protein coat and typically measure from 10 to 300 millionths of a millimetre.

**WHO** - the World Health Organisation. Geneva-based United Nations body responsible for co-ordinating international efforts to control disease and improve human health.

**Xenograft** - a transplant of tissue or organs from one species into another, and especially from animals to humans.

**Zoonotic** - pertaining to disease transmitted from animals to humans.