Culture

The rise and fall of AZT: It was the drug that had to work. It brought hope to people with HIV and Aids, and millions for the company that developed it. It had to work. There was nothing else. But for many who used AZT - it didn't

Simon Garfield | Sunday 23 October 2011 02:44 | comments

years later, by the time AZT had been licensed for use, demand for it had grown to gigantic proportions.

By then, Aids patients had grown so desperate that they would sample any of the bootlegged underground therapies, some of which were probably life-threatening. With the arrival of AZT, doctors who had been powerless for so long against a syndrome about which they knew so little, at last had something they could give their patients that had passed stringent official tests.

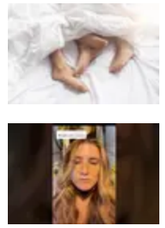
In March 1987, when AZT was available on prescription for the first time, almost everyone with Aids wanted to take it, as did many who had tested positive for HIV. One of these was Michael Cottrell, a gay Englishman. He had tested positive for HIV in 1985 at the age of 22. He took AZT for several months in the late Eighties and suffered severe side-effects from the drug: chronic headaches and nausea, debilitating muscle fatigue. Cottrell felt much worse on AZT than he did off it. But he persevered because it seemed AZT was the only anti-Aids drug there was.

So Cottrell took it early in his infection: after all, if AZT was judged to be effective in treating Aids, then perhaps, it was thought, it would also benefit those who took it before they became ill. AZT spelt hope: psychologically it served to dispel despair. It was never claimed to be a cure, but it did claim to keep you alive longer, and in that extra time it bought, who knew what would happen? Maybe a cure would be found. Maybe a vaccine. Maybe other drugs would be developed to fight the disease, too.

Cottrell still has boxes of AZT capsules at home. He gave up on it after several months, because he couldn't stand how ill he was feeling on the drug; he felt as though his immune system was being damaged rather than strengthened; he believed he had never encountered a drug as toxic as AZT.

Cottrell knew the drug didn't work for him, but he believed he might have been one of the unlucky ones, like people who react badly to penicillin. Then a month ago he woke up to the news that the drug didn't work on HIV at all, and that all his suffering had been avoidable.

Most popular


No woman should ever have to have 'maintenance sex' with her husband

Woman left in tears after being 'shamed' by Alaska Airlines attendant


Sweden vs Canada LIVE: Tokyo 2020 women's football final result


Fauci says US could be in 'trouble' from variant worse than Delta

Popular videos

but, just as important, it looked at how effective the drug was in treating the millions of people with HIV, before they became unwell and showed Aids symptoms. Preliminary results of the trial were published in a letter in the Lancet, and made headlines worldwide. The results suggested that early intervention with AZT - for people who were HIV but had not yet developed any symptoms of Aids - was a waste of time. The study, organised by the British Medical Research Council and the equivalent body in France, reported that it made no difference to either mortality rates or disease progression if one took AZT before the onset of Aids.

In a 'blind' test, AZT was given to 877 people and 872 were given a placebo. As soon as a patient developed any Aids symptoms, he or she (15 per cent were women) would be offered 'open-label' AZT. The mortality rates appeared to be shocking: over the three years of the trial, there were 79 Aids-related deaths in the AZT group, but only 67 in the placebo group. The researchers explained that among so many patients this figure was not statistically significant, but if you were HIV-positive and read of this in the newspapers, you were bound to question all the great claims that had been made for AZT. More people got Aids and died on Concorde than on any previous trial.

There were other causes for concern. Those on AZT developed more side-effects than those on the placebo. The results of the tests also cast doubt on one of the fundamental ways we measure a person's immunity to disease. Those given AZT early increased their 'CD4' or 'T4' cell count; these are the cells attacked by HIV, and their numbers drop as the disease spreads. But the fact that, even with this higher count, patients did not live longer or develop the disease more slowly, struck at one of the basic tenets of Aids research.

Cottrell told the news to his 28-year-old partner Karl Burge, who had been diagnosed as HIV-positive four years ago, and they decided to take action. But what could they do? They had already joined protests against Wellcome plc, the British company that made AZT and had reaped millions in sales and share profits. Wellcome executives had listened to their complaints, and had admitted to certain levels of toxicity in AZT, but claimed that their product still had great beneficial effects. They were

Footage reveals homes and roads destroyed in North Korea flooding

indy100 TRENDING

Prince Harry leaves people in stitches during Meghan's birthday video

Man roasted for complaining about tip after spending £3,500 on dinner

Older man 'persistently hits on' uncomfortable teen in viral TikTok

Brexiteer Tory MP Steve Baker is now calling Brexit a 'fiasco'

People are convinced this homeless man is building a time machine

conversations. indy100 FEATURED

So Cottrell and his friends selected a new target, the Terrence Higgins Trust. This was a strange choice: the trust, Britain's most prominent Aids charity over the past 10 years, is staffed by dedicated professionals and volunteers providing a large range of support and information about all aspects of Aids and HIV; it developed the caring 'buddy' system; it produced information for schools; it sat on many Aids research panels and often met government departments.

So what had it done wrong? It had taken money from Wellcome plc and included positive information about AZT in its many leaflets and documents. Cottrell and his friends felt they were being betrayed by the very organisation that they had believed existed to act in their best interests; they felt that what was once an invaluable institution was acting as a mouthpiece for a multinational pharmaceuticals company.

Last week, Cottrell and Burge were still pitched outside the Terrence Higgins Trust office in central London, four weeks after their protest began. On Wednesday they were arrested and charged with a public order offence after a member of the trust called the police. The protest is growing by the week. They have been joined by John Stevens, diagnosed HIV- positive more than eight years ago, and who also had bad experiences with AZT, and Pierre Hardy, diagnosed HIV-positive four years ago when he was 27 and had felt devastated by its effects. Many other protesters carry placards, collect signatures, hand out leaflets. You will not find a more potent symbol of the complex story of AZT, a story of how the struggle to find a 'magic bullet' to help millions of people has degenerated into a saga of distrust, confusion, and anger. It is a story of health and illness, but it is also a story of scientific ambition, secrecy and political pressure, and of the amounts of money that can be generated when a lethal virus turns into a worldwide epidemic.

IN 1964, Jerome Horwitz was working in his laboratory at the Michigan Cancer Foundation when he had what he hoped was a brilliant idea. At 45, Dr Horwitz was the foundation's director of chemistry, and although not in the scientific premier league, was a respected local researcher with his own lab and assistants. He had spent much of the previous decade

He developed a theoretical solution: what was needed was a chemical that would insert a 'phoney' compound into the DNA 'building block' of a cell to prevent its replication. After years of research, Dr Horwitz came up with

azidothymidine (AZT).

He tried his new compound on leukaemic mice, but it had no effect. Horwitz didn't know why, but AZT didn't work.

Horwitz never became famous. Recently he said AZT 'was a terrible disappointment . . . we dumped it on the junkpile. I didn't keep the notebooks.' The compound remained 'on the shelf', occasionally tried by other researchers but always found to be useless. There was no reason to patent it. But 20 years later, Burroughs Wellcome brought it back to life.

THE WELLCOME group was founded in London by two Americans in 1880. Its first significant achievement was the creation of the tablet - previously most medication had been administered in powder form. In the 1930s the group was split into two distinct parts: the Wellcome Trust, a large charity which devoted its income to scientific research and the maintenance of an institute and library concerned with the history of medicine; and the Wellcome Foundation Ltd, a profit-making pharmaceuticals company that was called Burroughs Wellcome in the United States. In the course of its research, Wellcome employees have won five Nobel prizes.

By 1980, Wellcome had specialised in the treatment of viruses for more than 15 years, and its anti-viral drugs accounted for the bulk of its income. In that year, David Barry, a leading researcher at Burroughs Wellcome in the US, noticed that demand for its drug Septra - a drug that Wellcome had helped to develop a few years earlier to combat a rare form of pneumonia - was suddenly on the increase. Previously this pneumonia, known as PCP, was prevalent only in children with leukaemia, but now many doctors were requesting it for adult males. Most of these men were gay, and living in New York and San Francisco.

two drugs.

Aids (Acquired Immune Deficiency Syndrome) was first classified as a new disease in 1981, but it was not until 1984 that the cause was identified as HIV (Human Immunodeficiency Virus). This cause has since been challenged by several prominent molecular biologists, but it remains the cornerstone of Aids research. And if any company was ideally equipped to conduct research into combating a new virus, it was Wellcome.

It was only natural for Barry to devote much of the company's research resources to fight HIV. No one knew how widespread the virus or Aids was or would become. In 1984, only about 3,000 people had been diagnosed with Aids, but some early forecasts were terrifying: millions of people might already be infected, and hundreds of thousands could die within the next few years. Any scientist could see that Aids was potentially a career-making race to the Nobel prize. Millions might be made from a successful treatment.

After a few years of government inactivity - shameful years in which this new disease was virtually ignored - political ambition added to the desire to find a treatment. Health departments noticed that it wasn't just homosexuals who were being struck down, but also hundreds of haemophiliacs and drug users. A certain amount of official panic took hold: by the time Rock Hudson died in the summer of 1985, it was clear that anyone - even film stars - could be in the frontline.

According to Wellcome's own three-page account, research into HIV began in June 1984. During mass testing of scores of anti-viral

compounds, a substance known at first only as Compound S was found to inhibit viruses in animal cells. Compound S was AZT, a resyn- thesised version of what Horwitz had made 20 years before (Wellcome credits Horwitz in its account, but spells his name wrong).

In November 1984, according to the Wellcome account, the company sent samples of AZT to Duke University in North Carolina, the Food and Drug Administration (FDA) and the National Cancer Institute for

further than Horwitz, but the real test - its effect on humans - was fraught with danger.

But first there is another account of the development of AZT to consider. A US government official named Sam Broder believes he has far more claim to being 'Mr AZT' than anyone at Burroughs Wellcome. Broder, the director of the National Cancer Institute, claims that Burroughs Wellcome showed little interest in developing an anti-Aids drug.

Broder went on a tour of pharmaceuticals companies towards the end of 1984, imploring them to send any possible anti-viral compounds to his lab for testing in safe conditions. 'I went to one prestigious company, hat in hand,' he told the business writer Bruce Nussbaum, whose book, Good Intentions, traces a history of the search for anti-Aids drugs. 'I got about one minute and thirty seconds of a high-ranking officer's time. It was very disappointing for me. It was emblematic of the issue. There was no real interest in it.'

Broder then went to Burroughs Wellcome. He says: 'They made it clear that on the basis of 3,000 patients, there was no way they could practically get involved.' Broder says he then became abrasive. 'As I left, I said, 'You know, we're going to have more than 3,000 cases. It is going to be commercially viable for you . . .' '

Whoever pushed who, the drug came through. When Broder found that the AZT sent to him by Burroughs Wellcome in November 1984 worked against the virus, he assured the company that every effort would be made to get this great new drug to dying patients as soon as possible. The FDA's stringent testing requirements mean that most new drugs take between eight and 10 years to pass from development to the marketplace. AZT was pushed through in just 20 months.

This could have been the early history of almost any drug; the difference is, during what would normally have been an eight-year test period, for six of those years the drug was already on the market. At a time of desperation, this drug looked like the one that would restore hope. The National Cancer Institute had previously tried one other therapy, Suramin, which proved to be toxic in early tests, but AZT appeared to be

the boundless hopes pinned on AZT?

THIS IS how AZT is supposed to work against HIV. HIV enters body cells, usually T4 white blood cells that play a crucial role in the orchestration of the body's immune system. HIV is one of a group of viruses known as retro- viruses, which means that, unlike most living things that store their genetic information as DNA, HIV stores it as RNA. Before HIV can replicate, it must convert its RNA code to DNA by use of a special enzyme. It is during this conversion process that AZT works. When AZT enters the body, it is transformed into a molecule that closely resembles one of the building blocks of DNA. During the process of HIV conversion, this molecule is incorporated mistakenly into the DNA. The addition of this 'phoney' molecule makes the addition of further building blocks impossible and halts replication of the virus. It's a form of chemotherapy. It worked fine under a microscope.

The first human tests were in two phases. The first examined whether AZT could be tolerated in the body at all, and whether it entered the brain, crossing the 'blood-brain barrier'; to know this was important, because a common Aids symptom is dementia. The first Aids patient was injected with AZT in July 1985. This test concluded that the blood-brain barrier was crossed, and that although there were levels of toxicity detected, these were deemed to be safe.

The second phase of the tests, the final hurdle to the granting of a licence for mass production, was a shambles. It was set up six months later to establish whether AZT would combat Aids. This test, overseen by the Food and Drug Administration, involved 282 patients, all of them already ill with Aids or Arc (Aids-related complex). It was to be a placebo test, conducted over 24 months. It was to be a 'double-blind' study in which neither patient nor doctor knew whether the capsules being taken were AZT or starch. (But before the tests could begin, Wellcome had to produce large quantities of AZT, and found it couldn't do it. It had run out of one crucial ingredient: herring sperm. Finally, Wellcome bought it in bulk from another company.)

Mortality rates for people taking AZT were staggeringly lower than those taking the placebo; there had been 19 deaths in the placebo group of 137 people, but only one in the AZT group of 145. Those on AZT also had a decreased number of opportunistic infections and showed improvement in weight gain and T4 cell counts. Wellcome agreed in response to pressure from some sectors of the gay community that if AZT was effective, then dying people should be taken off the placebo at once.

No one claimed it was a cure, but there was huge relief that a breakthrough had been made. There had been much embarrassment when it became known that Rock Hudson had attended the Pasteur Institute in France for treatment; now at last America was showing those foreigners a thing or two. Robert Windom, assistant health secretary, said that 'treatment with AZT prolongs survival of persons with Aids'. The results were 'exciting'.

It was not suitable for everyone, but it was the best thing yet. In fact, it was the only thing. Last year, interviewed in the Wellcome in- house magazine, David Barry said that 'the staff at Wellcome can tell our children, grandchildren and great-grandchildren that we were there, that we made a difference'. When it was shown that AZT worked, 'we . . . first had a frenzied, cheerful celebration, and then a very quiet one. The longer we considered the global implications, the greater the accomplishment we realised Wellcome had made in the control of the HIV epidemic.'

But a few months after AZT was made available, John Lauritsen, a journalist working on the gay newspaper New York Native, obtained test documents through the Freedom of Information Act that suggested that many rules had been broken in the trials. The trial had been 'unblinded' within weeks: some patients claimed they could tell what they were taking by taste; others were so keen to have AZT that they pooled their treatment with other patients to increase their chances of receiving the drug. The documents showed that almost half the AZT patients had received numerous blood transfusions in the course of the trial, because of damage to their bone marrow and immune systems; and that a few had to be taken off AZT altogether.

compared to four more on the placebo. The ratio had switched from 19:1 to 23:3, which suggested AZT might only be effective for a limited time.

If the trial had continued, the ratio might have narrowed even more. The tests would probably still have shown that AZT has some benefits for very ill patients, but with hindsight it is alarming that a new drug was allowed to be

released with so much left to prove. People at Wellcome now put it down to the mood and the severe pressure of the times. Dr Trevor Jones, Director of Research at Wellcome, who has been involved in their development of AZT from the beginning, acknowledged that the trials were subject to extraordinary pressures. 'Much of these accusations (about the breakdown of trial protocol) took place, not at that stage, but later on, when the drug was showing benefit in a less sick population.

'All sorts of things we heard stories about, and some of them I think we can confirm from our data. Patients would go to their doctor, get their treatments, and rather than risk the uncertainty (or receiving the placebo), they'd put the two together, mix them and divide them by half. We know this, because people who were supposed to be on the placebo already had drug levels in them.'

Much of the pressure came from people with HIV and Aids, and their carers, who wanted the drug released immediately. It was unacceptable to administer a placebo, they argued, if AZT worked. And there was no point having a drug released on the market in 10 years - by that time hundreds of thousands would be dead.

Burroughs Wellcome and many other independent research institutions would spend every subsequent year trying to supplement their data on AZT, trying to find out all the things that would normally be known about a drug before it hit the market. In these later years AZT was to become for many people the symbol of all that was wrong with Aids research. Once AZT was shown to have worked, almost all available funds were channelled to support its development and other potential treatments, along with any doubts that HIV was the cause of Aids, were swept aside.

increasing alarmingly, there was no doubt that the financial rewards would be enormous). It suited doctors, because they believed they could help their patients. And it certainly suited people with Aids. Some people had doubts, but hell, if you were ill and dying you wanted to believe. After all the despair and uncertainty, people in authority were saying 'take this, it'll do you good'.

Cottrell was one of the first people to take AZT in Britain. He was prescribed it in 1986, before it was widely available, when he was 23.

'I had recently been diagnosed HIV-positive, and I went into a panic. I thought I was going to die. I remembered something about this drug coming from America and everyone clamouring to get it. I was perfectly healthy. My boyfriend's blood count was quite low, and he was prescribed it by St Stephen's Hospital, and I took it too. Intuitively, I didn't think it was doing me any good. I was prescribed it three times over a period of three years, and I took it out of fear. I was first prescribed 1,200mg a day, and then 500mg, but I still felt bad, even on the lower dose. I had nausea and headaches and muscle fatigue.'

Cottrell took it every four hours, which meant he had to have a bleeper that woke him at three or four o'clock every morning. (People joked that the real Aids money lay in making these bleepers; in New York in the late Eighties, opera performances were punctuated by bleeps.) Cottrell stopped taking AZT after a few weeks, but then he got scared, and began taking it once more. 'I got my drugs every two weeks - a big plastic bagful. I felt that I was carrying my life around in that bag.'

His friend, Pierre Hardy, was diagnosed HIV in 1989, when he was 28. At a specialist clinic he was given a sheet of paper which explained that AZT was the most efficient treatment, but also that it hadn't been around long enough for anyone to know the long-term effects. Like most people in his position, he said he'd try anything, and he was prescribed 500mg a day.

'My T4 count went up along with my general health in the first year, and everything settled down. I had been on AZT for three years, and my T4 count was levelling between 400 and 600 (an average T4 count in healthy adults is between 800 and 1,000). And then last year I started to get sick

count was 90. I thought I was finished.

'When I got home and started to review the whole thing, the whole HIV theory. I threw away all the pills I was taking - I was taking seven every morning and evening. I started to change my diet, and then I went back to my doctor. When I had my new T4 count it was 545. I've had three migraines since January, a little bit of asthma coming back, but basically I feel much better. If I'd continued to believe in the traditional medicine sytem I would have been dead either this year or next year.'

Two weeks ago Hardy met a volunteer with the Terrence Higgins Trust, who told him that he and his boyfriend were taking AZT and it was working like a dream.

'I asked him how long they were on it. He said four months. I said that that was the trap that everyone was falling into. The AZT will work for you for a little while, for the maximum of one year, as it did for me, and afterwards the damage became visible.'

Most people with Aids, and many with asymptomatic HIV, take or have taken AZT. Other drugs have emerged in the past few years that work in a similar way - DDC (produced by the Swiss company Hoffmann-La Roche) and DDI (made by the American company Bristol-Myers Squibb), but AZT is still the market leader. It is hard to think of another product that is so dominant in its field. You read the showbiz autobiographies and those three little letters snap out of the page.

Earvin 'Magic' Johnson, the basketball star who tested HIV-positive in October 1991, was advised to take AZT immediately. He agreed. 'There was a lot of public interest in the fact that I was taking AZT, which was originally used only in the later stages of the illness,' he explained in My Life, his autobiography. 'These days it's used as a preventative, but not everybody knew that. That may be why some people, including a few reporters, concluded that I was sicker than I actually was.' People wrote to Johnson telling him that AZT was not the answer. Somebody advised him to drink all his blood and replace it with new blood. 'Even now I can't go anywhere without somebody coming up and saying, 'I know this friend who knows this doctor who has a cure''

side-effects would hamper him (Nureyev was still dancing at this time). Rudi lost his temper and said: 'I want this medicine.' I replied that there hadn't been long enough to judge the results. But I had to give in and prescribe it - he was so insistent. But he didn't take it regularly. He went off every time with tons of drugs, and every time I went to see him I found unused packets all over the place.'

The film-maker Derek Jarman, who was diagnosed HIV-positive in 1986, has found AZT beneficial. 'It works - it holds everything up. It stops the virus replicating. At the beginning they gave people much too massive doses, which affected us physically. I had no recognisable toxic side-effects from it. I began taking it in September 1990, I think, and I came off it last August.

'I was invited by my doctor to make up my mind whether I took the drug or not, so I rang up various people in America and the general advice was to take it - and this was advice was from quite radical people, not people in with the Wellcome Foundation.

'I came off it because my doctor said that my (T4) count was down. We've never discussed it since. He just suddenly said, 'I think you've had enough AZT, Derek', and I very much trust him, he's a brilliant doctor. The whole thing is so complicated, because I took a lot of other drugs as well. I had to have suppressants for TB, toxoplasmosis and PCP. And then obviously if I got an infection there was fluconazole and all of that area. And then at a certain point they added hydrocortisone and fludrocortisone to keep my energy up.'

Jarman has recently been in hospital. 'At the moment I'm actually on nothing. I've had a skin complaint and they decided it would be very sensible to take me off all my pills, and then go back on the drugs to see if they were causing the skin complaint. They can obviously play around with the drugs.

'My feeling about AZT is that I'm glad I took it, even though I can't prove to you that it did anything. You can say that if it helps someone psychologically then it must be doing some good. I think the doctors generally feel that it does some good. But how do you know?'

have been launched by the company in the past decade, the continued success of AZT is crucial to its growth. The company will be well aware that at the end of last year the World Health Organisation estimated that about 13 million men, women and children have been infected with HIV since the start of the pandemic. (A large proportion of these cases are in sub-Saharan Africa and South and South-east Asia, where AZT and other anti-Aids treatments are unlikely to be available or affordable; the figure for HIV infection in the Americas and Western Europe is estimated at 2.5 million.)

Part of the Wellcome Foundation was floated on the stock market in 1986, the year of the AZT breakthrough. Subsequent rises in share prices have been directly linked to the fortunes of the drug and the results of new trials. In February 1987, the share price jumped 73.5p to 374.5p on the news that AZT would be widely available in the US at dollars 188 for 100 capsules, an extremely high price for a new drug, and one that would yield large profits (this translated to about dollars 10,000 a year for every user). By November 1989 the share price had almost doubled to 724p; year-on-year pre-tax profits were up 28 per cent to pounds 283m. In early 1993, the share price was at 810p; last year's pre-tax profits were pounds 505m.

'In terms of the emotive quality of the demand, there's never been a drug like it,' said

Martin Sherwood, a Wellcome spokesman, shortly after AZT's launch. It was just this emotive demand that led to the picketing of the Wellcome shareholders' meeting in January 1990. Act Up (the Aids Coalition to Unleash Power, co-founded by the playwright Larry Kramer) picketed the AGM at Grosvenor House in London, describing it as 'a gathering of Aids profiteers'. Activists complained about the price of AZT, and what they saw as Wellcome's reluctance to provide all available information on the drug.

Wellcome shareholders were irritated by this intrusion, not least when Act Up members interrupted the meeting and insisted on talking to Sir Alfred Shepperd, the outgoing chairman. But Wellcome executives were

AZT was launched three years earlier? At first Wellcome defended its pricing on

the grounds that AZT took dollars 80m to develop and produce (later revised to dollars 30m), but it soon bowed to pressure (and its economies of scale) and cut the price. The recommended dosage was also reduced for medical reasons, which meant many more people could tolerate its toxicity. Today AZT costs about dollars 3,000 per person per year, or about pounds 2,000.

As would be expected, Wellcome plays up the good news. When, in 1989, two double- blind placebo trials of the effects of AZT on asymptomatic and less seriously ill patients showed that it could delay the progression of the disease, much was made of the results and the share price rose by 30p. But when, four months later, the company admitted that AZT had caused cancer in rodents, it explained that the rats and mice were given 10 times the dose prescribed to humans, and that several other drugs in use by humans had also produced tumours in animals when administered over long periods. Wellcome's share price went down one penny.

Wellcome's PR machine is an impressive force, and much money is spent on convincing the media of AZT's worth. You go and see them and you get a lot of bumph: how AZT works, why it is more effective than other anti- retrovirals. Wellcome house-magazines talk of the extra 400,000 productive years of life it has made possible through the drug, about how many thorough and independent studies have stressed AZT's efficacy.

'The number of people who have shown agression against us concerns us no end,' says Trevor Jones. 'Normally the company tries to distance itself from the patient / physician interaction - it must do. The day-to-day therapy of the patient is not our responsibility. But about three years ago we started to open our labs to people with HIV and their carers, contrary to the advice of my security and other colleagues. You then realise the uncertainty and the frustrations involved in that act of taking a tablet for the very first time. When people with HIV came through the door of the lab I could almost touch their anger. But I realised that the anger was not really about Wellcome or me, but about their mortality. They were

Dr Jones is one of the few pharmaceutical industry representatives on Britain's Medical Controls Agency. Wellcome has clearly selected its spokesman with care. 'People say we're purely acting out of commercial interests, but it is not in our commercial interests to do anything else but get this drug right,' Dr Jones says. 'We wanted to show people that we are working night and day, weekdays and weekends trying to develop better medicines. Otherwise we look like ogres and robber barons all the time. That's the whole history of our business; if you've got a problem with a product, you must, you must, you must tell people. The criticism hurts a lot; our integrity as a scientific body is important to us. I don't take too kindly to people saying, 'Oh, you don't want to listen to Wellcome, because they would say that, wouldn't they?' You can't hide anything in this business, because otherwise who will trust us when we develop another drug, like the new epilepsy drug we've got now? You have to believe that the integrity of science is good.'

Jones has had a bad few weeks. Wellcome's share price was hammered by last month's Concorde trial report, falling 10 per cent to 670p, before rallying to 692p. Five days after the report appeared, Wellcome staged a damage limitation exercise, at which Jones told a press conference that he was unhappy with the way the results were released, without peer review or advice to patients, and saying it had caused panic among those with HIV. He said that the full results had yet to be released, and hoped that a more beneficial picture of early intervention with AZT would emerge at the ninth International Aids Conference in Berlin in June. He also outlined that the protocol of the study had changed from that agreed in 1988. When an American study reported in 1989 that AZT did have beneficial effects on people with asymptomatic HIV, the Concorde officials decided that people on its trial could switch to AZT if they wanted to; this may have led to a diluting of the results.

Last week, Jones reiterated why AZT may still be beneficial, and why doctors should continue to prescribe the drug early. 'We have gathered together 10 studies on asymptomatic patients. Five of these are control studies with placebos, and five are cohort studies, in which we simply give the drug and observe what happens. These studies involved more than 6,500 patients and ranged from one to four years in duration. We

WELLCOME has a presence at all the chief Aids conferences, and will occasionally organise gatherings of its own. In June 1992 it launched Positive Action, 'an international intiative' in support of those with HIV and Aids. For the launch conference in London, journalists flew in from all over Europe to hear Wellcome executives describe how pounds 1m was being distributed to many educational organisations. An emotional climax of sorts was provided by Jerry Breitman, the company's US director of professional relations. He was there to present the 'workplace initiative', and his speech contained a little surprise at the end. Like the wig salesman whose coup de grace is to rip off his own toupee, Breitman declared himself HIV-positive. 'I thought long and hard before deciding to tell my management,' he revealed. 'But . . . when you are part of an enlightened organisation such as Wellcome, I am absolutely convinced that communicating your HIV infection is a positive action . . . It is, truly, one of the best decisions I have made in a very long time.' A few journalists felt distinctly queasy at the theatricality of it all.

One of the initiatives raised was Wellcome's involvement with the Terrence Higgins Trust. This first surfaced in 1991, with the publication of four information leaflets. Two months ago staff at the Trust and volunteers read in their newsletter that the link had been strengthened. The newsletter explained that 'THT, along with the Wellcome Foundation, is about to begin producing an important new medical information series. THT are providing a series of medical updates for all staff and volunteers. We will be providing them on a regular basis every two months in the evening. Costs will be met by the Wellcome Foundation, which also funds our series of general booklets.'

Nick Partridge, chief executive of the trust, is dubbed 'Nick the Sick' on the placards carried by the protesters outside his office. Partridge, in reply, calls them 'New Age flat- earthers who have a naive hope that Holland & Barrett will produce a herbal tea that will be effective against HIV.' Partridge said that the trust actively pursued funding from a wide range of companies and government agencies, and that it was 'quite clear that none of that funding involves an ability by those companies to influence the information we produce. We would be neglecting our duty if we were not in regular contact with Wellcome, Bristol-Myers Squibb

But once they were. In 1991 the trust produced a 24-page booklet on HIV and its treatment; nine pages were devoted to AZT, but only half a page was given to other therapies. The copyright on the leaflet was held by the Wellcome Foundation, which also paid for its printing. 'It was only available for eight months,' Partridge says. 'Information changes quite rapidly. The main fault of that leaflet is that it is too hopeful. By 1991 the hopes around early intervention had probably gone further than we realise, in retrospect, was wise. The desire by many people with HIV to say, 'Yes, we can live with this infection' meant that a lot of hope was invested in the theory of early intervention. For all its faults, our leaflet was still a lot more realistic than the material that Wellcome was putting out on its own. Remember that over the years, there have been many stories of breakthroughs that proved to be wildly optimistic.'

FOR MOST people with HIV, the AZT dream is over. AZT is the future that was; no one believes in the 'magic bullet' any more. It does have benefits for some patients who are seriously ill, but there is now severe doubt over its other uses. This, after the drug has been subjected to more tests, and has been the subject of more post-launch research papers, than perhaps any other modern therapy.

The future for HIV and Aids treatment appears to be in combination treatment - the use of AZT and DDC and DDI and many other compounds used in all manner of variations. Several trials are in progress. Two weeks ago it was announced that Wellcome has joined forces with its competitors Hoffman-La Roche, Bristol-Myers Squibb, Glaxo, SmithKline Beecham and 15 other companies, in an attempt to pool their research knowledge and find an effective treatment.

Wellcome is also developing some other anti-Aids drugs on its own. We won't hear about these for a while; the company doesn't want to raise any hopes.

Jerome Horwitz, the man who created AZT in 1964, is still active in medical research. He's 74 now, but you can still reach him most days at the Meyer L Prentis Cancer Center in Detroit. Occasionally he does a little Aids work, but most of his time involves cancer chemotherapy.

'We were certainly on the cutting edge,' he says of his work in the mid-Sixties. 'When the pharmacologist said, 'Look, Dr Horwitz, your compounds are not effective against leukaemias and I see no future for them', that was like a blow to the solar plexus. We had great hopes. 'I remember one of my students saying at the time that we had a great series ofcompounds just waiting for a disease totreat. It took 25 years before our beliefs were vindicated.'

The first Horwitz heard of AZT's use against HIV was when he read about it in the Wall Street Journal. Burroughs Wellcome established a chair in his name at the Michigan Cancer Foundation, but he has received no financial reward.

'My wife sits across from me at the

breakfast table and reminds me of all the money that Burroughs Wellcome has got out of it and I haven't got a dime. I keep telling her about the legacy I'm leaving. But I wouldn't be being absolutely straight with you if I hadn't thought that I should have gotten something out of it.'-

(Photograph omitted)

More about: Concorde Healthcare HIV Research

Novaya Gazeta