Introducing AZT

‘A world of antiretroviral experience’

ANTHONY BRINK

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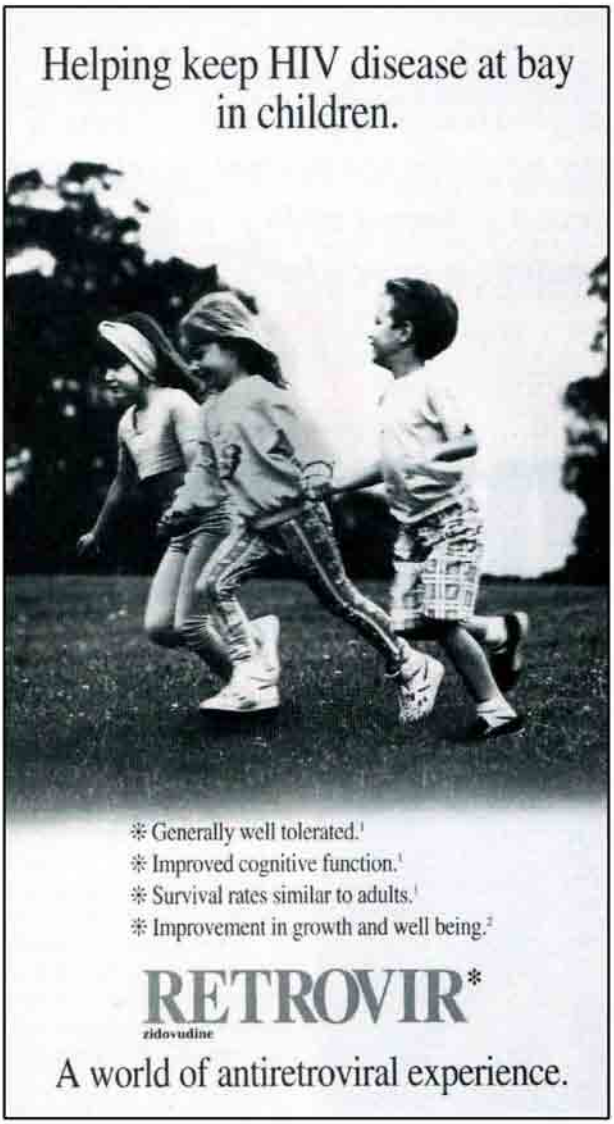
The cover features an advertisement for AZT in *Lancet* in 1991.

The author

Anthony Brink is an advocate of the High Court of South Africa, and the convener and national chairman of the Treatment Information Group (www.tig.org.za). He is also the author of *Debating AZT: Mbeki and the AIDS drug controversy* (2000), *Lying and Thieving: The fraudulent scholarship of Ronald Suresh Roberts in 'Fit to Govern: The Native Intelligence of Thabo Mbeki with reference to chapters 8 and 9 on AIDS: 'A clash of fundamentalisms 1: medical politics' and 'A clash of fundamentalisms 2: racial politics'* (2007), and *The trouble with nevirapine, RUDE LETTERS* and *Poisoning our Children: AZT in pregnancy* (2008). *'Just say yes, Mr President': Mbeki and AIDS*, in preparation, will be a comprehensive history of the AIDS treatment and causation controversies in South Africa, and a multi-disciplinary interrogation and deconstruction of their medical and ideological foundations. His work has been translated into Spanish, French, Russian, Italian, German, and Dutch.



AZT advertised in 1991 in the British medical journal *Lancet* for administration to children

As our patients died on this medicine, no one ever asked who got better on it. We've caused more ravaging disease in these hills and vales with this infernal potion than the plague itself has. I myself have given the poison to thousands, causing them to wither away, and I've personally experienced how audacious murderers are praised.

Faust
Johann Wolfgang von Goethe

The evil that is in the world always comes of ignorance, and good intentions may do as much harm as malevolence, if they lack understanding. On the whole, men are more good than bad; that, however, isn't the real point, but they are more or less ignorant, and it is this that we call vice or virtue, the most incorrigible vice being that of an ignorance that fancies it knows everything and therefore claims for itself the right to kill. There can be no true goodness, nor true love, without the utmost clear-sightedness.

The Plague
Albert Camus

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Preface

As the spark igniting the defining domestic policy controversy of Thabo Mbeki's Presidency – AIDS – the influence and significance of my little book *Debating AZT* can hardly be exaggerated*. Soon after publishing it† I began a sequel reviewing further research papers reporting the exceptionally dangerous toxicity of the drug, a spate of which had appeared in the medical press subsequent to the book's release, combined with a prequel comprising the histories of AZT's invention as an experimental cell-poison and the corrupt manner in which it had been licensed as an AIDS drug. This undertaking was quickly overtaken by another, however: the writing of a comprehensive history and deconstruction of the entire South African AIDS controversy, *'Just say yes, Mr President': Mbeki and AIDS* (currently in the works). My intended sequel cum prequel to *Debating AZT* consequently got relegated to the appendices, along with a brief essay on nevirapine. In time these subsidiary projects swelled to the point where I had to

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* 'Mbeki himself confirmed that the first person to draw his attention to these dissident [scientific critiques of AIDS orthodoxy in late 1999] was a lawyer and part-time jazz musician named Anthony Brink, then practising in the provincial city of Pietermaritzburg. … "That was the first time that I became aware of this alternative viewpoint," Mbeki told me.' – Allister Sparks, *Beyond the Miracle: Inside the New South Africa* (Jonathan Ball Publishers, 2003). '"That," Mbeki told me, "is what sparked it off …"' – Mark Gevisser, *Thabo Mbeki: The Dream Deferred* (Jonathan Ball Publishers, 2007)

† Then in manuscript, subtitled *Questions of safety and utility*, the book was subsequently published as *Debating AZT: Mbeki and the AIDS drug controversy* (Open books, 2001). It's still in print, and is also available as a free download at www.tig.org.za and from many other websites.

excise them and see them to print as independent books in their own right: *The trouble with nevirapine* (Open books, 2008) and this one, *Introducing AZT: 'A world of antiretroviral experience'*.

Introducing AZT is not the comprehensive review of the new research reports that I originally intended. *Debating AZT* was a pretty good summary of the case against the drug based on the toxicity literature published at the time, so I decided against more of the dreary same – its extreme liver toxicity and its propensity to cause bone rot (osteonecrosis), for instance, which I'd thoroughly investigated; instead I opted for a different approach: to sprinkle a collection of research findings, some old, some new, among conflicting statements by proponents and opponents of the drug in such a way as to enable readers to pick their way through fact and conviction and arrive at an informed opinion for themselves.

It would obviously be helpful to read *Debating AZT* to understand properly what was on Mbeki's mind when he warned in the National Council of Provinces on 28 October 1999 that

> There ... exists a large volume of scientific literature alleging that, among other things, the toxicity of this drug is such that it is in fact a danger to health. These are matters of great concern to the Government as it would be irresponsible for us not to heed the dire warnings which medical researchers have been making.

He told DA leader Tony Leon the reason in his letter to him on 1 July 2000 that contrary to his 'extraordinary statement that AZT boosts the immune system',

> Not even the manufacturer of this drug makes this profoundly unscientific claim. The reality is the precise opposite of what you say, this being that AZT is immuno-suppressive. Contrary to the claims you make in promotion of AZT, all responsible medical authorities repeatedly issue serious warnings about the toxicity of antiretroviral drugs, which include AZT.

Why, as biographer Mark Gevisser told BBC News on 7 November 2007, Mbeki considers that he has

> failed on the issue of Aids … He feels even more strongly about the efficacy of anti-retroviral (ARV) medication. He believes that ARV medication is toxic and that it is a project that's been imposed upon particularly vulnerable Africans by the pharmaceutical companies.

And why Gevisser reported in an interview in the *Sunday Times* soon after, on the 18th, that Mbeki 'believes that the damage caused by ARVs is greater than the damage caused by Aids'.

But as a primer *Introducing AZT* will give you a good sense of what's very wrong with AZT and similar ARVs, and how Mbeki's concerns about these drugs stated around the turn of the century have been confirmed again and again, notably by the biggest ARV study conducted to date, published in *Lancet* in August 2006, which found ARV treatment to be useless in terms of real, clinical health outcomes, and that far from saving or extending lives it actually accelerates the death rate of HIV-positive people given it.

Although this book includes some reports on the foetal and neonatal toxicity of AZT, the one to read for an exhaustive review of the literature on this subject and a critical discussion

of official treatment protocols supporting its use is *Poisoning our Children: AZT in pregnancy*.

Inventing AZT in the appendices relates how AZT was purpose-designed as a cell poison, which explains why it's so toxic; *Licensing AZT* tells how it got to be licensed as an AIDS drug on the basis of a fraudulent study ostensibly showing that it saved lives; and *Is AZT antiretroviral?* knocks down the standard lazy rejoinder: 'All drugs are toxic, but AZT fights HIV, so the benefit outweighs the risk.'

Like *Debating AZT*, *Introducing AZT* gives both sides of the argument, with the difference that this book has no author narrative; it lets the proponents and opponents of the drug speak for themselves. To emphasize the contradiction, if it isn't obvious enough, the dupes are quoted in Comic Sans typeface, the now ubiquitous junk font appropriately billed by Microsoft as 'groovy'.

The names index will enable you to look up what your favourite AIDS fighter has to say about how great ARV drugs are. Reading a few citations or quotations appearing above or below your quoted hero will take you past the propaganda into the horrible reality.

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Cape Town
xx xxxxxxxx 2008

Introducing AZT
'A world of antiretroviral experience'

25 mg phial of AZT supplied by Sigma-Aldrich Chemie Gmbh for use in research laboratories, with the label bearing an orange stripe imprinted with a skull and crossbones icon to signify potentially fatal toxic chemical hazard to the handler – spelt out in six languages: 'Toxic Giftig Toxique Toxico Tossico Vergiftig' – and the warning: 'TOXIC Toxic to inhalation, in contact with skin and if swallowed. Target organ(s): Blood Bone marrow. In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). Wear suitable protective clothing.' The latest version of the label also carries a cancer warning.

'You may be looking at a fifteen-year-old label which appeared in a satirical magazine recently.' **Judge Edwin Cameron, Supreme Court of Appeal, on SAfm radio, 18 July 2000**

100 mg capsule of AZT supplied by GlaxoSmithKline for ingestion as an AIDS drug. The package insert recommends: 'A broad range of dosages (between 500mg and 1500 mg/day) have been used.' This is between 20 and 60 times as much AZT that Sigma-Aldrich warns is an exceptionally dangerous toxic chemical hazard upon accidental exposure to it.

'RETROVIR (ZIDOVUDINE) MAY BE ASSOCIATED WITH HEMATOLOGIC TOXICITY INCLUDING GRANULOCYTOPENIA AND SEVERE ANEMIA [*massive destruction of white (immune) and red blood cells respectively*]. … ANTIRETROVIRAL NUCLEOSIDE ANALOGUES, INCLUDING RETROVIR … ARE POTENTIALLY FATAL.' **GlaxoSmithKline: AZT 'Product Information'**

'… for AIDS patients, it is urgently necessary to develop a remedy substituting this toxic substance, AZT.' **Hayakawa et al. *Biochemical and Biophysical Research Communications* 176:87-93 (1991)**

'Clinical manifestations of ANA [*antiretroviral nucleoside analogues, such as AZT*] toxicity: It is self-evident that ANAs, like all drugs, have side-effects. However, the prevalent and at times serious ANA mitochondrial toxic side-effects are par-

ticularly broad ranging with respect to their tissue target and mechanisms of toxicity: Haematological; Myopathy; Cardiotoxicity; Hepatic toxicity; Peripheral neuropathy.' **Lewis and Dalakas,** ***Nature Medicine*** **5:417-22 (1995)**

'The antiretroviral drugs currently licensed in the United Kingdom are zidovudine (azidothymidine), zalcitabine (ddC) and didanosine (ddI). … All are very toxic. Suppression of bone marrow elements can occur with any of the three, as can peripheral neuropathy.' ***Adverse Drug Reaction Bulletin*****, No.178 (1996)**

'I don't see why people who are well should take a drug [*AZT*] which pretty reliably will make them sick.' **Professor Robin Weiss,** ***Positively Healthy News*****, January 1989**

'… there are severe limitations to antiretroviral therapy, including toxic side effects (lipid deposition, increased risk of diabetes and cardiac infarcts, muscular and neurological toxicity). Therefore, it is imperative to launch clinical trials to test additional treatments that are less toxic.' **Dr Robert Gallo and Professor Luc Montagnier,** ***Science*** **298(5599):1730-1 (2002)**

'AZT underwent clinical trials and was introduced as a specific anti-HIV drug many years before there were any data proving that the cells of patients are able to triphosphorylate the parent compound to a level considered sufficient for its putative pharmacological action. Notwithstanding, from the evidence published since 1991 it has become apparent that no such phosphorylation takes place and thus AZT cannot possess an anti-HIV effect. However, the scientific literature does elucidate … a number of biochemical mechanisms which predicate the likelihood of widespread, serious toxicity from

use of this drug. … Based on all these data it is difficult if not impossible to explain why AZT was introduced and still remains the most widely recommended and used anti-HIV drug. [The continued administration of AZT] either alone or in combination … to HIV sero-positive or AIDS patients warrants urgent revision.' **Papadopulos-Eleopulos et al.** ***Current Medical Research and Opinion*** **15, Supplement 1: 'A Critical Analysis of the Pharmacology of AZT and its Use in AIDS' (1999)**

'[AZT-class drugs] are much more toxic than we considered previously. … The layer of fat-storing cells directly beneath the skin, which wastes away … is loaded with mitochondria … other common side effects of [AZT and similar drugs are] nerve and muscle damage, pancreatitis and decreased production of blood cells … all resemble conditions caused by inherited mitochondrial diseases.' **Brinkman et al.** ***Lancet*** **354(9184):1112-5 (1999)**

'[There is] no new evidence in the medical literature in the last year on the adverse effects of AZT.' **Dr Salim Abdool Karim, director of HIV Prevention and Vaccine Research, Medical Research Council, Deputy Vice Chancellor University of KwaZulu-Natal, Professor in Clinical Public Health, Columbia University, USA, and chairman of the Scientific Programme Committee of the 13th International AIDS Conference in Durban 2000,** ***Sunday Independent*****, 14 November 1999**

'Abdool-Karim dismissed the government's objection on the use of the drug [*AZT*] as a "pathetic excuse" [saying] that about 40,000 children could be saved each year if the South African government reversed its opposition to using the anti-AIDS drug … to reduce mother-to-child infection.' ***AIDS Weekly*****, 29 November 1999**

'I've read nothing in the scientific or medical literature that indicates that AZT should not be provided to people.' **Professor William Makgoba, then president of the Medical Research Council, now Vice-Chancellor of the University of KwaZulu-Natal, *Nature* 402(6759): 225 (1999)**

'The drug [*AZT*] being out there is justified.' **Dr Helen Rees, then president of the Medicines Control Council, 9 November 1999**

'[AZT is] harmless.' **Nathan Geffen, TAC national manager; Professor Nicoli Nattrass, economics professor, director of the AIDS and Society Research Unit, University of Cape Town; and Professor Glenda Gray, co-director of the Perinatal HIV Research Unit at Chris Hani Baragwanath Hospital, Soweto, *Nature* 441(7092): 406 (2006)**

'For the past decade in San Francisco we have witnessed the destruction of human life caused by AIDS drugs. We hoped that by exhibiting at the conference, we could warn participants to prevent a similar catastrophe occurring in their countries.' **ACT-UP San Francisco, letter to President Mbeki, after being barred by the organizers from exhibiting at the 13th International AIDS Conference in Durban, read in Parliament by then Deputy President Zuma, 20 April 2000**

'Well, I think the dilemma here is we've got to learn from what has happened here in the last 18 years and try not to repeat it, as we move into Africa … I can't overstate, I think, how severe the problems are with the current therapies. … People are dying from the effects of the therapies themselves in some cases. … People are suffering from severe life-threatening complications of drugs. And a lot of them get to the point where they simply can't use them anymore. So as we

talk about bringing therapy to Africa, even if we can solve the problem and cost and infrastructure and delivery, I have this pang in my heart of are we doing the right thing, you know, with these drugs? Or are we unleashing another kind of epidemic over there of drug side effects as well?' **Martin Delaney, director of the San Francisco-based pro-antiretroviral drug lobby, Project Inform, on Ted Koppel's ABC television show *Nightline*, 6 June 2001**

'These drugs have side effects, but those side effects are not nearly as bad as the package insert leads us to believe they could be.' **Charlene Smith, pro-AZT campaigner on her website, speakout.org.za (accessed mid-1999)**

'… the toxicity of these drugs [*AZT and similar*] is very low indeed.' **Professor Robin Wood, co-director of the Desmond Tutu HIV Centre at the University of Cape Town, *Health-e News*, 13 May 2005**

'Concerned to respond appropriately to [AIDS], many in our country have called on the government to make the drug AZT available in our public health system. … There … exists a large volume of scientific literature alleging that, among other things, the toxicity of this drug is such that it is in fact a danger to health. These are matters of great concern to the government as it would be irresponsible for us not to heed the dire warnings which medical researchers have been making. I have therefore asked the Minister of Health, as a matter of urgency, to go into all these matters so that, to the extent that is possible, we ourselves, including our country's medical authorities, are certain of where the truth lies.' **President Thabo Mbeki, Parliament, 28 October 1999**

'The President has been gravely misinformed about the safety aspects of AZT. … The review ordered by President Mbeki of the anti-AIDS drug is neither necessary nor justified … there is no new data that will raise legitimate concerns about AZT's safety. … GlaxoWellcome are a reputable company. We do not lie to people.' **Peter Moore, medical director of GlaxoWellcome SA (now GlaxoSmithKline), 30 October to 12 December 1999**

'GlaxoWellcome have to be devious to take the position they do now in promoting [AZT], simply because of the weight of evidence against the use of their product.' **Martin Welz, editor and publisher, *noseweek* investigative journal, in the e.tv documentary *The Truth on AZT*, 12 December 1999**

'[AZT is] perfectly acceptable. … It causes slight side effects … but … so do many medicines. … Worries about AZT's safety surfaced in the early 1990s but have long faded.' **Joseph Perriens, director of the Care and Support division of the UN AIDS programme in Geneva, Associated Press report, 3 November 1999**

'AZT is a drug that was developed for use in chemotherapy for cancer patients. It was, however, never used in cancer patients because it was regarded as too toxic to use. Tests have clearly shown that rats that were exposed to high levels of AZT for prolonged periods of time, developed vaginal cancer. This is a very serious finding. Other toxicological data exists with respect to AZT, including damage to nerves, muscles and bone marrow. All of this data needs to be assessed very thoroughly. As the Minister of Health I have a responsibility for ensuring that South Africans get appropriate and affordable healthcare. This responsibility extends to ensuring that no healthcare intervention has a long-term negative effect on

people.' **Dr Manto Tshabalala-Msimang, National Minister of Health, Parliament, 16 November 1999**

'We're making a laughing stock of ourselves. Government is discrediting the drug because it doesn't want to pay for it. But it's backfiring, because there is no evidence … they will find nothing.' **Dr Ruben Sher, head of HIVCare International (a project of the Netcare private hospital group), *Financial Mail*, 9 November 1999**

'AZT is being singled out because government is trying to defend its decision not to provide it for mother-to-child transmission. It's pathetic; the MCC is toadying to the President. There's no medical or scientific reason whatsoever for the MCC to review the material. I'm sure the MCC will come out with a balanced report, but it's nauseating that they're even looking at it. … In Uganda, they're winning the war against the epidemic because they had the political will to do so, not by believing in conspiracy theories.' **Professor Gary Maartens, head of the HIV/AIDS Unit, Groote Schuur Hospital, Cape Town, *Financial Mail*, 9 November 1999**

'I've had a patient coming off AZT in trials because of all the publicity. It's irresponsible, the statements being made. We are losing a lot of the ground we've gained. It means government still doesn't want to take responsibility for the epidemic.' **Dr Ashraf Grimwood, principal medical officer for Cape Town and chairman of the National AIDS Convention of SA (Nacosa), *Financial Mail*, 9 November 1999**

'… published studies have shown that patients on combination therapy with AZT and 3TC have been able to maintain or improve their quality of life.' **Dr Desmond Martin, president of the Southern African HIV Clinicians Society, *Financial Mail*, 9 November 1999**

'AZT is a valuable therapeutic drug. … To combat a fatal disease, it is perfectly acceptable to use drugs slightly more toxic than an aspirin.' **Joseph Perriens, *New York Times*, 25 November 1999**

'[President Mbeki's stated concern about the dangerous toxicity of AZT and other ARVs is] just a red herring to distract attention from the existence of effective treatments. … The government is dragging its feet because it cannot see its way around the cost issues. … With 1,500 new cases every day, the cost of providing an anti-retroviral drugs regimen on that scale is enormous. …This is a very Thatcherite government.' **Zackie Achmat, founder and director of the Treatment Action Campaign (TAC), *Wired*, 22 April 2000**

'I started taking medicine ['stavudine' (d4T), 'lamivudine' (3TC – both drugs chemically similar to AZT) and 'nevirapine'] on 30 August this year for the first time, and so far the only side effect I've experienced has been dizziness in the first few weeks, but since then I've had no real problems.' **Zackie Achmat, 'Let's Talk', SABC 1 television, 30 November 2003**

'The most remarkable thing after I started taking the medicines actually is that in the first three weeks, I became so depressed – I'd never been as depressed in my life.' **Zackie Achmat in *Newsweek*, 24 November 2003**

'[Achmat's] words were bats that flew into each other in the dark. His sentences ended in mid-air. It was as if he looked at you through a dense layer of fog. It was during these times that I wondered what was happening to him. Especially when he cancelled press conferences and public appearances at the eleventh hour. … he talks about his past and the complex interaction between the chemicals in his brain, his genes and the

virus with which he was diagnosed in 1990 … Chances are good this can lead to depression and cognitive reduction and, during the final stages, even to dementia – a condition that usually only afflicts the elderly. … Losing control of his mind is his biggest fear … "As long as I hold on to my dignity." … And then came the physical side effects of the antiretrovirals. Especially peripheral neuropathy – a condition that takes place when the nerve endings are impaired; burning pains are felt in the feet and legs. It was so bad for Achmat, that by the fifth month of antiretroviral treatment he could no longer walk. "I was totally melancholic and dysfunctional at the beginning of the year. I fought with my nearest and dearest, and I did not want to accept that I was experiencing side-effects."' **News24.com, 1 December 2004**

'Today, anti-HIV medication has resulted in a more subtle dementia … At first, patients forget phone numbers and their movements slow. Some worsen until they can't hold a job or perform other activities, but not everyone worsens – and doctors can't predict who will. … many specialists worry [that] nearly all of them may suffer at least some brain symptoms … memory loss and other symptoms of so-called neuroAIDS, which afflicts at least one in five people with HIV and is becoming more common as patients live longer.' **Associated Press, 15 October 2006**

'Things have changed in Zackie Achmat's life. Once readily accessible and always quick with a sound bite, a personal assistant now monitors the cellphone and diary of the chairperson of the Treatment Action Campaign (TAC) and screens visitors before ushering them into Achmat's study. … As much as these changes signify a new level of structure in Achmat's life and the need to manage multiple requests for

interviews, the more profound changes emerge from his first six months of anti-retroviral therapy and how this has forced the charismatic activist to review his life. … a frightening set-back … occurred in February and March … which shook Achmat's self-confidence. … "Going into my fifth month I started feeling a sensation in my feet. At first I dismissed it, thinking I'd done something at the gym. The second week it was clear to me and I thought, 'I can't let Manto win and I can't let Mbeki win', and I kept quiet for three more weeks." When Achmat finally told his doctor about his symptoms, the nerves in his feet were so sensitive that he could barely walk. A change of drugs (from d4T to AZT [*in fact an equally toxic nucleoside analogue drug*]) has arrested the situation and his left foot feels better, but he still can't put any weight on his right foot for any length of time, nor can he walk long distances. … Achmat, who has a clinical history of depression, says that the fact that he was immobile for a week while his doctor tried to bring the side effects under control brought on a terrible depression, the worst he's had in two years.' ***Daily Dispatch*, 28 May 2004**

'[The neurotoxicity of Achmat's ARV treatment caused him] grade 2 peripheral neuropathy [(i.e. painful nerve damage in his limbs), still] being treated … with … neurological pain adjuncts [, as well as CNS (central nervous system) injury (i.e. cytotoxic brain damage)] manifesting in sensory, motor and proprioceptive [disturbances (i.e. impaired ability to feel, see, hear, taste, smell and balance; control his limbs properly; and sense his limb positions and movements)].' **Dr Steven Andrews, affidavit in Cape High Court, Case No. 12156/05**

'Antiretroviral nucleoside analogs used in highly active antiretroviral therapy (HAART) are associated with cardiovascu-

lar and other tissue toxicity associated with mitochondrial DNA depletion. … AZT is a potent inhibitor of thymidine phosphorylation in heart mitochondria.' **McKee et al. *Cardiovascular Toxicology* 4(2):155-67 (2005)**

'We are very concerned about a number of toxicities associated with the long-term use of anti-retroviral drugs. … We are seeing an increasing number of patients with dangerously high levels of cholesterol and triglycerides. … The bad news is that we now must find ways to deal with unanticipated toxicities, including the potential for premature coronary disease.' **Anthony Fauci, director of the National Institute for Allergies and Infectious Diseases, US NIH, press release, 5 February 2001**

'The Treatment Action Campaign's chair, Zackie Achmat, was recovering well after suffering a heart attack just before the start of the Easter weekend, the TAC's electronic newsletter reported on Monday.' **SAPA, 29 March 2005**

'There is no question in the minds of scientists that the government contributes to a climate that raises the possibility that … antiretrovirals are toxic.' **Jerry Coovadia, Head of the Department of Paediatrics and Professor of HIV-AIDS Research, Nelson R Mandela Medical School, University of KwaZulu-Natal, and chairman of the 13th International AIDS Conference in Durban, *Sunday Independent*, 4 June 2000**

'… there is scant medical evidence to support Mbeki's opposition to AZT.' **Mark Schoofs, Pulitzer Prize winner for 'AIDS: The Agony of Africa' in *Village Voice*, 22 December 1999**

'Four years of "hit hard, hit early" HIV treatment may be on the way out in the US, as evidence mounts of the drugs' seri-

ous side effects. AIDS experts in the US are about to complete a humiliating U-turn when the Department of Health and Human Services launches its revised HIV treatment guidelines in January.' ***New Scientist*, 16 December 2000**

James Hayman, before and after a one-month course of 600 mg AZT and 300 mg 3TC daily

'I think the medicine is killing me.' **James Hayman to his lawfirm partner; died 8 June 1998**

'Any doctor, any scientist, medical scientist who has dispensed AZT to an AIDS patient or HIV-positive patient since the Concorde trials [*reported in* Lancet *in April 1994*] has been a party to murder.' **Martin Welz in *The Truth on AZT***

'Before 1986, when zidovudine (formerly called azidothymidine) was introduced, the number of patients with HIV-associated myopathy [*wasting*] was small, and myopathy was

considered a rare complication of HIV infection.' **Dalakas et al.** ***New England Journal of Medicine*** **322(16):1098-105 (1990)**

'A clinically significant myopathy that precedes the development of zidovudine associated mitochondrial myopathy has been a rarity in our experience.' **Coker et al.** ***AIDS*** **5(2):229-31 (1991)**

'… wasting syndrome [occurs] almost exclusively [among AZT-treated patients].' **Poznansky et al.** ***British Medical Journal*** **311:156-158 (1995)**

'… Mbeki took an interest in Aids dissident Anthony Brink's manuscript "Debating AZT". … Mbeki read the manuscript soon after he became president … Brink claimed that the drug AZT, rather than HIV, caused people to "waste away".' **Kerry Cullinan, editor of *Health-e News*, 'Infected by Toxic Ideas', *Financial Mail*, 7 May 2004**

'… as evidence accrues that AZT (zidovudine, *Retrovir*) is associated with lipoatrophy [*wasting*], the guidelines move away from firmly recommending an AZT-containing regimen as part of a nucleoside backbone.' **British HIV Association (BHIVA) draft revised treatment guidelines, 26 April 2005**

'Antiretrovirals [*AZT, 3TC, d4T, ddI*], not features of the host or the immune response to HIV, are overwhelmingly responsible for the development of lipoatrophy, according to studies presented on Monday at the Seventh International Workshop on Adverse Drug Reactions and Lipodystrophy in HIV, in Dublin, Ireland. … Professor William Powderley of University College Dublin, a co-chair of the Workshop, said: "Large numbers of people are being exposed to an avoidable toxicity. The presentations at this meeting show the overwhelming in-

fluence of drug choice on the development of lipoatrophy."' [Hammond et al. *Antiviral Therapy* 10:L4, 2005; Parker et al. *Antiviral Therapy* 10:L5, 2005] **Keith Alcorn, *AIDSmap News*, 15 November 2005**

'It was often difficult [*in AZT clinical trials*] to distinguish adverse events possibly associated with administration of Retrovir [*AZT*] from underlying signs of HIV disease or intercurrent illnesses [i.e. *AZT can cause AIDS-defining illnesses*].' ***Physician's Desk Reference*, Mosby-Year Book Inc., 1996**

'… it is often difficult to differentiate between the manifestations of HIV infection and the manifestations of zidovudine. In addition, very little placebo controlled data is available to assess this difference.' ***USP DI: Drug Information for the Health Care Professional*, 16th edition (United States Pharmacopeial Convention,1996)**

'The side effects of AZT can be indistinguishable from the symptoms of AIDS.' **Professor Anthony Pinching, London consultant immunologist, and early AZT clinical trials overseer, speaking at the 12th International AIDS Conference in Geneva in 1998**

'Patients should be informed that the major toxicities of RETROVIR are neutropenia and/or anemia.' **GlaxoSmithKline, AZT 'Prescribing Information'**

'… neutropenia [means a] decrease in the number of neutrophils in the blood. … It results in an increased susceptibility to infections. … [A] neutrophil [is] a variety of granulocyte (a type of white blood cell) … capable of ingesting and killing

bacteria and provides an important defence against infection.' ***Oxford Concise Medical Dictionary***

'AZT induces significant toxic effects in humans exposed to therapeutic doses. … Cytogenetic observations on H9-AZT cells showed an increase in chromosomal aberrations and nuclear fragmentation when compared with unexposed H9 cells. … The toxicities explored here suggest that the mechanisms of AZT induced cytotoxicity in bone marrow of the patients chronically exposed to the drug in vivo may involve both chromosomal and mitochondrial DNA damage.' **Agarwal and Olivero, *Mutation Research* 390(3):223-231 (1997)**

'[Due to their] potent immunosuppressive properties … profound immunosuppression … often accompanies therapy with nucleoside analog drugs. … they have a number of associated toxicities, some of what may be severe. Of particular concern is immunosuppression which is uniform with standard treatment programs. Each of the nucleoside analogs is associated with a profound lymphocytopenia [*depletion of immune cells*], with a reversal of the CD4/CD8, and opportunistic infections.' **Cheeson, Keating and Plunkett, *Nucleoside Analogs in Cancer Therapy* (New York: Marcel Dekker Inc., 1997)**

'The drug [*AZT*] can inhibit the production of red blood cells and may reduce white blood cell counts to the point where the drug has to be discontinued to avoid infections.' **FDA press release, 5 March 1990**

'What it does, it suppresses the immune system. The very system we want to boost. … I wouldn't take AZT, I would not.' **Dr Tshabalala-Msimang, *The Truth on AZT***

'In your letter to me of June 19, you make the extraordinary statement that AZT boosts the immune system. Not even the manufacturer of this drug makes this profoundly unscientific claim. The reality is the precise opposite of what you say, this being that AZT is immuno-suppressive. Contrary to the claims you make in promotion of AZT, all responsible medical authorities repeatedly issue serious warnings about the toxicity of antiretroviral drugs, which include AZT.' **President Mbeki, letter to DA leader Tony Leon, 1 July 2000**

'It can only be Thabo Mbeki's belief that antiretrovirals like AZT are toxic and destroy the immune system. There is no other explanation for the paranoia that's going on.' **Zackie Achmat, *Saturday Star*, 12 January 2002**

'The estimated probability of developing [*Non-Hodgkin*] lymphoma [*cancerous tumours in lymph nodes*] by 30 months of [*AZT*] therapy was 28.6% and by 36 months, 46.4%.' **Pluda et al. *Annals of Internal Medicine* 113(4):276-282 (1990)**

'Blood transfusion is often necessary in patients with AIDS, especially in those receiving AZT, a drug which produces severe anaemia in a proportion of recipients. Forty nine (36%) of 138 patients treated with AZT required blood transfusion at least once.' **Costello, *Journal of Clinical Pathology* 41:711-715 (1988)**

'Anaemia [during AZT therapy] appears to be due to bone marrow suppression.' **Dainiak et al. *British Journal of Haematology* 69:299-304 (1988)**

'Four patients with the acquired immunodeficiency syndrome … developed severe pancytopenia [*destruction of red and white*

blood cells and clotting platelets] 12 to 17 weeks after the initiation of azidothymidine (AZT) therapy. Partial bone marrow recovery was documented within 4 to 5 weeks [*after discontinuation of AZT*] in three patients, but no marrow recovery has yet occurred in one patient during the more than 6 months since AZT treatment was discontinued.' **Parkash et al. *Annals of Internal Medicine* 107:502-505 (1987)**

'It is worrying that bone marrow changes in patients on zidovudine seem not to be readily reversed when the drug is withdrawn. These findings have serious implications for the use of zidovudine in HIV positive but symptom-free individuals.' **Mir and Costello, *Lancet* 2(8621):1195-6 (1988)**

'AZT appears to be a moderately-strong transplacental carcinogen.' **Olivero et al. *Journal of the Acquired Immunodeficiency Syndrome* 14(4):A29 (1997)**

'The fact is that some of the mice have contracted cancer. It attacks bone marrow. It is very toxic.' **Dr Tshabalala-Msimang in 'Truth and Lies about AZT', *Mail&Guardian*, 1 December 1999**

'Stop giving AZT to the damn mice and start giving it to people.' **Charlene Smith in 'Truth and Lies about AZT'**

'What we are trying to do is to put on the table information so that [if] the citizens of the country … get hold of AZT they do so knowingly, so that tomorrow nobody should say we were not told.' **Dr Tshabalala-Msimang in *The Truth on AZT***

'It's become clear over time that the health minister [*Dr Tshabalala-Msimang*] is not fit to be in her position. How can the government be negotiating over an anti-retroviral treatment plan

when it is being advised by the very man [*Dr Roberto Giraldo, then president of the Group for the Reappraisal of the HIV-AIDS Hypothesis*] who believes that the drugs are poisonous and cause AIDS?' **Jonathan Berger, AIDS Law Project attorney and researcher, and TAC member, 9 March 2002**

'… the government's refusal to introduce a national programme to counter transmission of HIV from pregnant mothers to their infants … as documented in its court papers and in argument on its behalf before the High Court and Constitutional Court, was based in large measure on the alleged toxicity of the drugs – a tenet central to the entire conspiratorialist theory of the AIDS denialists.' **Judge Edwin Cameron, address to the Harvard Law School, published by the *Mail&Guardian* as 'The Dead Hand of Denialism', 17 April 2003**

'If anyone was in doubt that this country's leader remains an Aids dissident, they should read last week's … essay [in] ANC Today [by] President Thabo Mbeki … A hundred flowers under the African sun … This is classic denialist twaddle – the president … still thinks anti-retrovirals are poison. We were not surprised when the Minister of Health Manto Tshabalala-Msimang parroted the self-same conspiracy theory a few days later … These two are, after all, our liabilities in the battle against Aids.' ***Mail&Guardian* editorial, 8 August 2003**

'In a major surprise, the drug AZT – now the standard treatment for children infected by the AIDS virus – proved so ineffective … that federal officials have called off part of a large study involving it. AZT, or zidovudine, also had unexpectedly high rates of adverse side effects in children, like bleeding and biochemical abnormalities, officials said Monday. … Children receiving AZT alone had more rapid rates of disease progression, AIDS-related infections, impaired neurological develop-

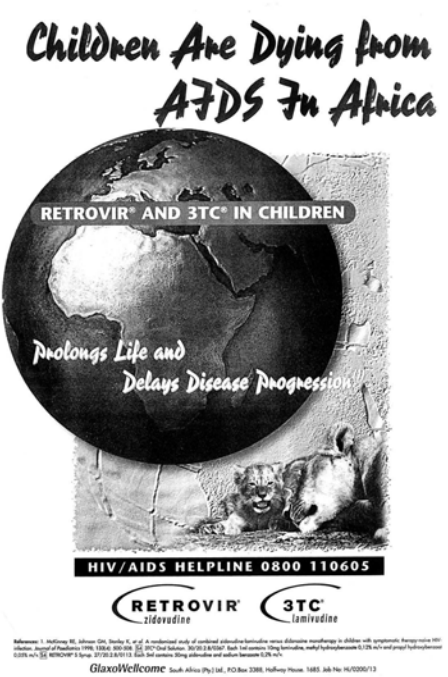
ment and death. The findings clearly caught health officials by surprise. AZT is widely considered the drug of choice in treating HIV-infected children and adults.' **'AIDS Drug AZT Fails Completely',** ***New York Times*****, 14 February 1995**

Xolani Nkosi

Xolani Nkosi: 'I'm taking AZT. I'm taking the cocktail. The bitter one I don't like is AZT. There're other pills. I don't really know the names.' Q: 'Do you ever not take the pills and not tell anyone? XN: 'I used to do that but my mom [*Gail Johnson*] caught me.' **Xolani Nkosi ('Nkosi Johnson'), interviewed by Christine Maggiore in July 2000 for the documentary film *AIDS in Africa*; died 1 June 2001**

'Transfusion was required in 14 [of 21 AZT-treated children] because of low levels of hemoglobin. Dose-limiting neutropenia occurred in most patients who received doses of 1.4 mg per kilogram per hour or more. … The major limitation of the therapy was hematologic toxicity – a decrease in both the hemoglobin concentration and the white-cell count. … Regardless of the starting dose, nearly all patients had a transient

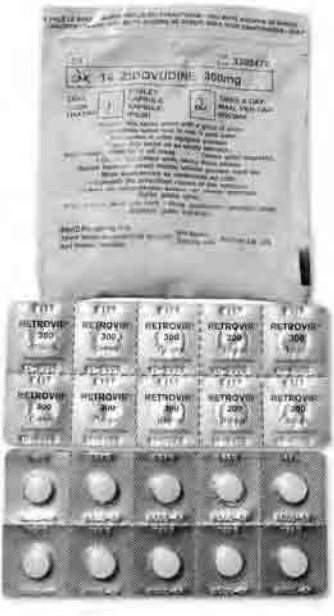
drop in their neutrophil counts within 10 days of the initiation of AZT therapy.' **Pizzo et al.** ***New England Journal of Medicine*** **319(14):889-96 (1988)**



AZT advertised in *Modern Medicine of South Africa* in April 2000. The findings of McKinney et al. in *Journal of Paediatrics* 1998;33(4)500-508 cited in fine print to support the claim that AZT combined with the similar drug 3TC 'Prolongs Life and Delays Disease progression' don't. No non-toxic placebo was used in the trial.

'Transfusion was required in 14 [of 21 AZT-treated children] because of low levels of hemoglobin. Dose-limiting neutropenia occurred in most patients who received doses of 1.4 mg per kilogram per hour or more. … The major limitation of the therapy was hematologic toxicity – a decrease in both the hemoglobin concentration and the white-cell count. … Regardless of the starting dose, nearly all patients had a transient drop in their neutrophil counts within 10 days of the initiation of AZT therapy.' **Pizzo et al.** ***New England Journal of Medicine*** **319(14):889-96 (1988)**

'Thirty-five of thirty-seven [*child*] subjects [*treated with d4T, a nucleoside analogue drug similar to AZT*] experienced serious clinical adverse events, including infection (33 subjects), lymphadenopathy [*damage to lymph nodes*] (19 subjects), hepatosplenomegaly [*abnormal swelling of liver and speen*] (15 subjects), chills and fever (12 subjects), and development of an AIDS-defining condition (4 subjects). …Clinical adverse events of lesser severity that were reported by more than 20% of subjects included rhinitis [*inflamed nasal passages*] (76%), cough (70%), diarrhea (68%), rash (62%), nausea and vomiting (51%), abdominal pain (43%), anorexia [*appetite suppression*] (41%), respiratory disorder (38%), headache (35%), pharyngitis [*inflammation of throat*] (32%), pruritis [*general itching]* (30%), pain (22%), peripheral neurologic symptoms [*loss of sensation and/or pain in hands and feet*] (22%), and nervousness (22%).' **Kline et al.** ***Pediatrics*** **96:247-252 (1995)**



AZT tablets dispensed to HIV-positive pregnant women attending Mowbray Maternity Clinic in Cape Town.

The packet containing the 300 mg tablets prescribes two a day on an empty stomach. This daily dose of 600 mg of AZT exceeds the 500 mg dose that Lenderking et al. reported in the *New England Journal of Medicine* 1994 Mar 17;330(11):738-43 to cause such 'severe side effects' among 'asymptomatic patients' that it was 'life threatening in some cases'.

The packet instructs mothers taking AZT not to nourish their babies naturally by breastfeeding them. This is to prevent babies from being harmed by exposure to traces of toxic AZT in breast milk. But denying babies their mothers' milk and giving them ar-

tificially manufactured formula milk instead creates a massively increased risk of serious disease and retards their mental and physical growth and development.

Mothers are told to 'Complete the prescribed course of this medicine' – in other words keep taking the drug even if it makes them sick.

No information about the dangerous toxicity of AZT for mothers and its harmful and sometimes fatal effects on unborn and newly born babies is provided on or in the packet to enable mothers to make an informed choice about whether to expose themselves and their babies to the risk of being poisoned by the drug.

'AZT FOR PREGNANT WOMEN'
'President Mbeki, AZT/Nevirapine for pregnant women with HIV'
TAC street demonstration placards

'The concentrations of the drug [*AZT*] in the liquor and in the fetal blood [*of 6 aborted human foetuses*] were higher or equalled those found in the maternal blood. … The drug remains contra-indicated in pregnancy.' **Gillet et al. *Journal of Gynecology, Obstetrics, and Biological Reproduction* 19(2):177-180 (1990)**

'In reviewing the frequency of birth defects in this population [*of HIV-positive women treated with AZT during their pregnancies*] we noted eight birth defects (10%) out of 80 live births.' [*In addition, eight women spontaneously aborted following AZT treatment, and eight abortions were 'therapeutically' induced*.] **Kumar**

et al. *Journal of the Acquired Immune Deficiency Syndrome* 7:1034 (1994)

'Prevalence of anomalies [*birth defects*] in the cohort [of '1932 liveborn deliveries from 1993 to 1996 to HIV-infected women in the state of New York (NYS)'] was compared with that of the general NYS population. … Children of study women who were prescribed ZDV had increased adjusted odds of any anomaly … 2.76 times greater than in the general population … Children … in this cohort had a greater prevalence of major anomalies than did the general NYS population.' **Newschaffer et al. *Journal of the Acquired Immune Deficiency Syndrome* 24(3):249-56 (2000)**

'Our findings support the hypothesis of a link between mitochondrial dysfunction [*in babies*] and the perinatal administration of prophylactic nucleoside analogues.' [*Eight children were born with severely impaired energy metabolism and corresponding muscle and other cell damage, manifesting in heart muscle injury and muscle weakness generally. Five children, of whom two died, presented with delayed neurological symptoms – extensive brain damage in the form of massive cortical necrosis, cortical blindness, epilepsy and spastic quadriplegia, and three were described as 'symptom-free' but had 'severe biological or neurological abnormalities'. Four of the children had been exposed in utero to AZT and 3TC combined, and four to AZT alone. None were HIV-positive.*] **Blanche et al. *Lancet* 354(9184):1084-9 (1999)**

'An exhaustive study in a large prospective cohort [of AZT- and 3TC-exposed children found] unexplained symptoms compatible with mitochondrial dysfunction. A total of 2644 of 4392 children were exposed to antiretrovirals … All the children with "established" or "possible" mitochondriopathy di-

agnosed in this study had been exposed to antiretroviral drugs … in the pre, per- and post-partum periods. … The finding that the use of antiretroviral nucleoside analogues in the perinatal period is associated with persistent mitochondrial disease is confirmed … a risk about 30 times higher than that in the general population. … Despite active screening, no similar cases were found in the antiretroviral unexposed group. … by age 18 months … a coherent syndrome is appearing with three main features: neurological symptoms (principally developmental retardation, seizures and behavioral disturbances), significant abnormalities on cerebral MRI (principally lesions of the white matter and brainstem) and often hyperlactataemia either persistent or transient outside the treatment period. First described as a myopathy associated with zidovudine, the issue of mitochondrial toxicity of nucleoside analogues is currently a growing problem. Its clinical expression is highly variable, from peripheral neuropathy to severe lactic acidosis.' **Barret et al.** ***AIDS*** **17(12):1769-1785 (2003)**

'Mitochondrial dysfunction has been reported in HIV-negative children perinatally exposed to zidovudine, a drug often used in HIV-seropositive mothers during pregnancy. The purpose of this study was to determine the incidence of cerebral MR imaging findings in HIV-uninfected children exposed to zidovudine who present with unexplained neurologic symptoms. … Images observed in children with antiretroviral-induced mitochondrial dysfunction are similar to those observed in congenital mitochondrial diseases.' **Tardieu et al.** ***American Journal of Neuroradiology*** **26(4):695-701 (2005)**

'AZT exposure causes a persistent depletion of mtDNA [(*mitochondrial DNA*) in babies exposed to AZT in the womb. Be-

cause] chemically induced tumors take 20 to 30 years to develop … the possibility … exists that exposed children might have an elevated cancer risk that will be manifested later in life. … the results presented here underscore the necessity for long-term follow-up of children of HIV-infected mothers receiving prenatal HAART therapy.' **Poirer et al.** ***Journal of the Acquired Immune Deficiency Syndrome*** **33(2):175-183 (2003)**

'The probability of developing severe disease at 3 years of life was significantly higher in children born to mothers [administered AZT during their pregnancies] than in those born to [untreated] mothers. … The same pattern was observed for severe immune suppression: the probability of developing severe immune suppression was significantly higher in children born to [AZT-treated] mothers … than born to [untreated] mothers. … Finally, survival probability was lower among children [born to AZT-treated mothers] … compared with children born to [untreated] mothers.' **De Martino et al.** ***AIDS*** **13(8):927-33 (1999)**

'Prenatal and perinatal [AZT] exposure were associated with 1.8-fold increased risk of progression to AIDS or death after adjusting simultaneously for all variables associated with disease progression … Restricting the analysis to children born after April 1994 (date of public release of the results of ACTG 076), [AZT] exposure was associated with 2.5-fold increased risk of progression to AIDS or death after adjusting simultaneously for the same variables. … Steady improvements in prognosis of [HIV] infected children unexposed to [AZT] were observed in each successive birth cohort, but infected children exposed to [AZT] lagged behind these temporal changes. Our results are from a well-characterized and prospectively followed cohort of US HIV-infected children and are consistent

with recent results from the Italian Registry for HIV Infection in Children [*reported by de Martino, cited above*].' **Kuhn et al. *Journal of Infectious Diseases* 182(1):104-11 (2000)**

'In this retrospective study, the risk of RPD [*rapid progression of disease*] was five to six times higher among infants born to [AZT] treated compared with untreated mothers. … After adjusting for prematurity and maternal clinical characteristics, RPD was three times more likely to occur in infants born to [AZT] treated compared with findings in untreated mothers.' **De Souza et al. *AIDS* 24(2):154-61 (2000)**

'AZT-exposed [Macaca nemestrina monkey] infants took three times as many sessions (6) as controls (2) to meet criterion on Black-White Learning, a simple discrimination task [and performed] significantly [worse in locating] the reward. … Postnatal weight increase was significantly lower in AZT-exposed infants … Hemoglobin dropped significantly in the AZT-treated animals after treatment began and remained low until the end of the study … The hematological toxicities reported here are consistent with those seen in 500 mg/day AZT-treated humans.' **Ha et al. *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 7(2):154-7 (1994)**

'The AZT animals [*Macaca nemestrina monkeys given AZT during pregnancy*] developed an asymptomatic macrocytic anemia, but hematologic parameters returned to normal when AZT was discontinued. Total leukocyte count decreased during pregnancy and was further affected by AZT administration. AZT-exposed infants were mildly anemic at birth. AZT caused deficits in growth, rooting and snouting reflexes, and the ability to fixate and follow near stimuli visually.' **Ha et al.**

***Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 18:27-38 (1997)**

'In HIV-infected pregnant women treated with two RTIs [*nucleoside analogue reverse transcriptase inhibitors, of which AZT was the most common*] with or without protease inhibitors, one or more adverse events occurred in 29 out of 37 women and in 14 out of 30 babies.' **Lorenzi et al. *AIDS* 12:F241-F247 (1998)**

'[In a major review of data collected between 1986 and April 2004, ARVs were found to cause a] substantially increased risk of severely curtailed pregnancy [*i.e. critical prematurity*] … coupled with a very high neonatal mortality rate.' **Thorne et al. *AIDS* 18(17):2337-2339 (2004)**

'Children born to HIV-positive women who take antiretroviral therapy (ART) during pregnancy are significantly smaller in terms of height, weight and head circumference compared with children born to HIV-positive women not on ART, or who took monotherapy, according the results of a European study examining the effects of ART on uninfected children's growth up to the age of 18 months. ['Does exposure to antiretroviral therapy affect growth in the first 18 months of life in uninfected children born to HIV-infected women?' European Collaborative Study, *JAIDS* 40(3):364-370, 2005] **Edwin Bernard, *AIDSmap News*, 3 November 2005**

'[The administration of AZT and similar 3TC to pregnant African women, and in a later cohort nevirapine as well, was] associated with LBW ['Low Birth Weight']: 'The rate of LBW was 22.3% in the HAART group and 12.4% in the PMTCT group.' **Ekouvi et al. *AIDS* 22(14):1815-20 (2008)**

'Antiretroviral drugs (ARV) as prophylaxis to prevent mother-to-child transmission of HIV results in decreased haematological parameters during and shortly after exposure, with recent data suggesting a more prolonged inhibition of haematopoiesis until at least 18 months [*i.e. ARV drugs given to pregnant women cause persistent bone marrow suppression reducing blood cell production*]. In uninfected children … ARV exposure [before birth was] associated with reduced neutrophil count until at least 8 years of age. … A considerably longer effect of exposure to ARV was shown in uninfected children than previously thought.' **European Collaborative Study, *AIDS* 18(15):2009-17 (2004)**

'The study cohort included 92 HIV-1-infected and 439 uninfected children … Antiretroviral therapy (nonprotease inhibitor) was independently associated with FTT ['Failure to Thrive'] in our cohort … ZDV [*AZT*], in particular, alters mitochondrial metabolism and may have direct nutritional effects.' **Miller TL et al. *Pediatrics* 108(6): 1287-96 (2001)**

'Children exposed to AZT in the womb are not at high risk of "brain damage, neurological disorders, paralysis, spasticity, mental retardation, epilepsy, other serious disorders and early death." The opposite is true. When AZT is used by a pregnant woman to reduce the risk of transmitting HIV to her child, the child is much less likely to contract HIV and much more likely to live a healthier, longer life.' **Professor Robin Wood, affidavit in Case 2807/05, High Court, Cape Town, 17 April 2005**

'I hesitate to call Anthony Brink a liar, but in my reading of the mainstream medical literature I have failed to come across the "hundreds of studies indicating the profound toxicity to all human cells of AZT" and the numerous studies showing that babies exposed to AZT in the womb suffer brain damage, et cetera. …

Why is the "enormous, growing corpus of little-known research literature in the medical/scientific press concerning the serious toxicity of AZT and nevirapine" so little known? Could it be garbage?' **Professor Cecil Karabus, Red Cross Children's Hospital, Cape Town, *Mail&Guardian*, 18 November 2005**

'There is no evidence that has been tabled showing that AZT is toxic to either mother or child.' **Mark Heywood, director of the AIDS Law Project, and national treasurer of the TAC, CNN, 1 April 2000**

'If they're not going to provide us with AZT, then the best thing that the government can do is to ask us to strangle them all at birth.' **Professor Glenda Gray, director of the Paediatric AIDS Unit at Chris Hani-Baragwanath Hospital, *Washington Post*, 16 May 2000**

'There is a critical need to develop effective drug treatments to combat RT dependent viruses such as HIV. Such efforts were recently urged in the United Kingdom-Irish-French Concorde Trial conclusions which reported that the nucleoside analog zidovudine (AZT), a mainstay in the treatment of patients infected with HIV-1, failed to improve the survival or disease progression in asymptomatic patients.' **Procedure to block the replication of reverse transcriptase dependent viruses by the use of inhibitors of deoxynucleotides synthesis: United States Patent 6,046,175. Granted: April 4, 2000. Application No: 245259. Filed: May 17, 1994. Inventors: Lori; Franco (Parma, IT); Cara; Andrea (Rockville, MD); Gao; Wen-Yi (Rockville, MD); Gallo; Robert C. (Bethesda, MD)**

'Extended follow-up of patients in one trial [*of AZT*], the Concorde study, has shown a significantly increased risk of death

among the patients treated early.' **Phillips et al.** ***New England Journal of Medicine*** **336:958-959 (1997)**

'Anti-retroviral drugs can extend life for many years.' **US President George W Bush, State of the Nation address, 27 January 2003**

'Among the top corporate donors at Wednesday's [Republican Party] fund-raiser were GlaxoSmithKline, a multinational drug giant, which gave at least $250,000, according to the Washington Post.' **'Bash Rakes In $30 Million' (at a record-breaking dinner-plate event organised by GlaxoSmith-Kline's president of pharmaceutical operations, Robert Ingram), CBS, 20 June 2002**

'GSK is a leader in bringing HIV/AIDS treatments [*such as AZT*] to patients … and is committed to improving the quality of human life by enabling people to do more, feel better and live longer.' **GlaxoSmithKline marketing mantra**

'People are dying, people whose lives could be extended by getting the right drugs. … Let's stop playing marbles and roll up our sleeves and invoke the spirit that fought apartheid. We did it with apartheid, we can repeat it with AIDS.' **Former Anglican Archbishop Desmond Tutu,** ***Newsmaker*****, SABC2 television, 7 October 2001**

'Yes, our government ought to be providing the drugs that extend people's lives.' **Desmond Tutu, e.tv, 1 December 2001**

'For those who are HIV-positive, we must ensure that they get the proper treatment and drugs which are going to help them resist the pandemic. … We must combine various strategies, firstly giving people the necessary drugs to try and prevent the disease taking the upper hand.' **Former President Nelson**

Mandela addressing schoolchildren in Nyanga community hall, Cape Town, 1 December 2001

'We must find the means to take life-saving treatment to all who need it, regardless of whether they can pay for it, or where they live or whatever reason.' **Nelson Mandela, 14th International AIDS Conference, Barcelona, Spain, 7 July 2002**

'We … learnt with great sadness that Anneline's economic position made her unable to take antiretrovirals earlier. This again emphasises the need for us to make treatment available in the public sector and in places accessible to those who cannot afford otherwise.' **Nelson Mandela on the death of singer Anneline Malebo, *Mercury*, 16 August 2002**

'… there are safe and effective pharmaceuticals available today which can alleviate suffering and extend life. These drugs have proved safe and effective around the world.' **Anglican Archbishop Emeritus Njongonkulu Ndungane, *The World with a Human Face: A Voice from Africa* (Cape Town: David Philip, 2003)**

'With great honesty the TAC has always tried to understand medical science. And this is something with which all South Africans have always struggled. We are scientifically illiterate.' **Zackie Achmat, *Rapport* (translated from Afrikaans), 10 February 2002**

'TAC militants have used songs about fluconazole and Pfizer – this is part of our treatment literacy. We have songs on AZT, nevirapine and soon we will have songs on co-trimoxazole.' **Zackie Achmat, addressing the Context International Conference on HIV/AIDS, University of the Witwatersrand, 7 April 2001**

'… anti-retroviral drugs essential to fighting HIV/AIDS … would save millions of lives … [Mbeki's professed concerns about the] alleged toxicity of anti-retrovirals [are merely] excuses [for not taking] advantage of the space won by the activists.' **Patrick Bond, 'Thabo Mbeki and NEPAD', published in *Thabo Mbeki's World: The Politics and Ideology of Thabo Mbeki*, edited by Sean Jacobs and Richard Calland (Pietermaritzburg: University of Natal Press/Zed Books, 2002)**

'Long-term use of AZT does contain risks, including cancer.' **Peter Moore, in 'Truth and lies about AZT', *Mail&Guardian*, 1 December 1999**

(Voice-over) How does GlaxoWellcome react to new research which claims the drug causes cancer, birth defects and deaths? 'I'm not aware of the data that you've just mentioned to me.' **Peter Moore in *The Truth on AZT*, e.tv, 12 December 1999**

'For more than a decade, AZT has extended and improved the quality of life of millions of people living with HIV/AIDS around the globe, said Dr Peter Moore, Medical Director of Glaxo Wellcome South Africa, adding that hundreds of healthcare workers who have been exposed to the virus in the work situation have also benefited.' **GlaxoWellcome press release, 28 October 1999**

(Voice-over) We asked GlaxoWellcome for proof: how many people have in fact benefited from the drug? 'It is impossible for me to answer that question.' **Peter Moore in *The Truth on AZT***

'AIDS can now be compared with other chronic conditions, which on ['the new combination drug treatments'], and with proper care, can in the long term be subjected to successful medical management.' **Edwin Cameron JA, Jonathan Mann Memorial Lecture:**

'The Deafening Silence of AIDS', at the 13th International AIDS Conference in Durban, 10 July 2000

'The truth is, with the right medication, H.I.V./AIDS is like diabetes – it can be managed.' **Zackie Achmat, *New Yorker*, 19 May 2003**

'The post-1996 AIDS conference hype that "combination therapy including a protease inhibitor will make HIV a chronic, manageable disease just like diabetes" came back to haunt us.' **Carr and Cooper, *Lancet* 352 (S5):16 (1998)**

'[The combination antiretroviral therapy] "dam" is already leaking; there's high danger of it collapsing altogether. Failures are occurring right and left. [Doctors] should expect failure with whatever [antiretroviral drug cocktail they] first use. We should plan on it. We should prepare for it. Clinicians should expect failure. [The patient death rate is rising.] They aren't dying of a traditionally defined AIDS illness. I don't know what they're dying of, but they are dying. They're just wasting and dying. It is sobering; while we are making good guesses, they are just guesses. We don't know what we are doing.' **Professor Michael Saag, University of Alabama, co-editor, *AIDS Therapy* (New York: Churchill Livingston, 1999), interviewed in *Esquire*, April 1999**

'We have seen colonization, we have seen imperialism, we have seen apartheid … and all of them used against us as a people. [Africans have] won their liberation and now they are fighting another war and they are being psychologically terrorized once more because people want to sell [AIDS drugs] and make profits. And there is no benefit in those products. The only thing that can really happen is that once you touch

the antiretrovirals you can go one way.' **Peter Mokaba, the *Star*, 4 April 2002**

'In my heart I believe it is not right to hand them [*AZT and other ARV drugs*] out to my people.' **Dr Tshabalala-Msimang, launching an anti-TB campaign, *c.*15 March 2003**

'Murderer! … Criminal! … Resign! … Manto go to jail! … Manto go home! … You exploit the hunger of our people by talking nutrition. … You should take off your wig and sell it to feed the poor. … I have a sweat because I'm angry. … I'm telling you and Mbeki once and for all….' **Zackie Achmat disrupting the Public Health 2003 conference in Cape Town, objecting to Dr Tshabalala-Msimang delivering the opening address on account of her and President Mbeki's publicly stated concerns about the toxicity of AZT, 25 March 2003**

'The organisers of the conference have only themselves to blame for inviting this criminal.' **Zackie Achmat justifying his conduct immediately afterwards**

'[The TAC is] a pressure group whose salaries are paid by Americans. This is a conglomeration of drug-dealers who serve as marketing agents of toxic drugs.' **ANC Youth League spokesman Khulekani Ntshangase, *Sowetan*, 22 April 2003**

'Data on adverse events to antiretroviral treatment have been recorded in clinical trials, post-marketing analyses, and anecdotal reports. Such data might not be an up-to-date or comprehensive assessment of all possible treatment combinations defined as potent antiretroviral treatment. METHODS: Using a standard clinical and laboratory method, we assessed prevalence of adverse events in 1160 patients who were receiving antiretroviral treatment. We measured the toxic effects

associated with the drug regimen … FINDINGS: 47% (545 of 1160) of patients presented with clinical and 27% (194 of 712) with ['potentially serious'] laboratory adverse events probably or definitely attributed to antiretroviral treatment. Among these, 9% (47 of 545) and 16% (30 of 194), respectively, were graded as serious or severe. … Compound specific associations were identified for zidovudine, lamivudine, stavudine, didanosine, abacavir, ritonavir, saquinavir, indinavir, nelfinavir, efavirenz, and nevirapine. INTERPRETATION: We recorded a high prevalence of toxic effects attributed to antiretroviral treatment for HIV-1.' **Fellay et al. *Lancet*, 358(9290):1322-7 (2001)**

'… as a result of toxicity and side effects among HCP ['healthcare personnel'], a substantial proportion of HCP have been unable to complete a full 4-week course of HIV PEP … Side effects have been reported frequently by persons taking antiretroviral agents as PEP … In multiple instances, a substantial (range: 17%–47%) proportion of HCP taking PEP after occupational exposures to HIV-positive sources did not complete a full 4-week course of therapy because of inability to tolerate the drugs. **Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis, 30 September 2005**

'We don't have routinely collected side-effect data, but we do know that the serious side-effect incidences are less than one percent. Minor side-effects are probably between 10 and 15 percent.' **Dr Fareed Abdullah, Deputy Director General, Western Cape Department of Health, and director of Western Cape AIDS Programme, *Health-e News*, 13 May 2005**

'We have had 400 people on antiretrovirals at university research centres and less than 1% have withdrawn and no one has died from the side effects of the drug[s].' **Dr Salim Abdool Karim, *Sunday Argus*, 8 May 2005**

'The US Food and Drug Administration (FDA) has issued a warning letter to manufacturers of AIDS drugs cautioning them to tone down the optimistic tenor of their antiretroviral … billboard and magazine … drug advertisements. Thomas Abrams, director of the FDA's division of drug marketing, advertising, and communications said that current antiretroviral advertisements directed at consumers are misleading as they fail to depict the limitations of AIDS drugs and also feature healthy looking people … sexy and athletic models in the prime of health who were climbing mountains, sailing boats, and riding bikes. These are pursuits which are quite difficult for people with HIV infection, who have to take drugs several times a day that have debilitating side effects … The advertisements therefore violate the Federal Food and Drug Act.' ***British Medical Journal* 322(7295):1143 (2001)**

'All 4 classes of antiretrovirals (ARVs) and all 19 FDA approved ARVs have been directly or indirectly associated with life-threatening events [*'grade 4' events, particularly 'liver related'*] and death. … Our finding is that the rate of grade 4 events is greater than the rate of AIDS events, and that the risk of death associated with these grade 4 events was very high for many events. … Cardiovascular events [are] associated with the greatest risk of death.' **Reisler et al. *Journal of Acquired Immune Deficiency Syndromes* 34(4):379-86 (2003)**

'I don't want to be pushed or pressurized by a target of three million people on antiretrovirals by 2005. WHO set that target

themselves. They didn't consult us. … It is not about chasing numbers. It is about the quality of health care we provide for our people. … I will also continue to advise people on the side effects of ARVs. I cannot stand on a pedestal and say everything is hunky-dory. … It is absolutely critical that our people know about the side effects, particularly because these are new medicines and not much is known about them. When we were being pressured to use ARVs we did warn about the side effects and, when I get reports about the people on ARVs, nobody presents to me how many people have fallen off the programme or died because of the side effects. I don't know what happens to those who started on antiretrovirals. … There was a time when we were told to give everyone ARVs and we resisted. We were right, I think. … When it comes to talking about the side effects I will always do it. … We must be upright and frank about informing citizens about the use of ARVs. … I'm not happy [with reports of how many people are being treated with them, and will] interrogate [the statistics to establish how many people have died of ARV toxicity]. I will continue to educate the people in this country about the side effects of ARVs … you know me, I tell the truth.' **Dr Tshabalala-Msimang, media briefing at Union Buildings in Pretoria, 5 May 2005**

'I am surprised by the manner she draws up her amazing beliefs … to speak of side effects [*of ARVs*] is contrary to what the scientific evidence suggests. … Her actions could have severe implications for people and the image of the nation. Some form of censure should emerge [for her] careless and dangerous statements.' **Professor Jerry Coovadia, commenting on Dr Tshabalala-Msimang's remarks, *Sunday Independent*, 8 May 2005**

'[It's an] outrageous and dangerous thing to say [that people have died from the toxicity of ARVs].' **Dianne Kohler Barnard MP, Democratic Alliance spokeswoman on Health, *Sunday Independent*, 8 May 2005**

'The Minister is a disgrace [and] should be disciplined by the ANC for her remarks. … Her conduct is undermining and embarrassing the government's own programme and policy.' **Mark Heywood, *Sunday Independent*, 8 May 2005**

'[Although the government appeared to have] crossed the bridge [Dr Tshabalala-Msimang's 'aggressive comments showed the commitment [to ARVs] was not genuine' (per *Sunday Argus* paraphrase)]. The stance on HIV/AIDS is a crime against the nation and history will come back to haunt them.' **Pieter Mulder, Freedom Front leader, *Sunday Argus*, 8 May 2005**

'Mampara of the week: Manto Tshabalala-Msimang. Health Minister Dr Manto Tshabalala-Msimang (First Leningrad Medical Institute 1962-1969) has been trying so hard not to put her foot in it that she has been silent on antiretroviral drugs over the last three months. But the truth will out. … The good doctor said she would continue to warn the public of [ARV] adverse effects. Strange that, for a minister who has okayed R3.4 billion in tenders to dispense them to the public.' **Hogarth, *Sunday Times*, 8 May 2005**

'Manto Tshabalala-Msimang, the health minister, has put her foot in it again. … the minister's nonsensical statements are problematic. She ignores the fact that people are dying because of the slow roll-out … It is worrying that she should issue warnings about the side effects of the very same anti-retrovirals the government is distributing. Why invest millions in an anti-retroviral roll-out and then cast doubt on the drugs? Tshabalala-Msimang's mixed signals … come without a shred of evidence.' ***Sunday***

***Independent* editorial (under the banner, SOUTH AFRICA'S QUALITY SUNDAY NEWSPAPER), 8 May 2005**

'Manto Tshabalala-Msimang, the health minister should go blonde. … Is she dumb or just playing at it? … when the immune system breaks down, medication is essential. … She omitted to mention that anti-retrovirals prolong life. Instead she lamented that they take life. … Right now the challenge is to get the minister off her pedestal. Now and forever.' **Maureen Isaacson, 'Second Take' column, *Sunday Independent*, 8 May 2005**

'There is no single clear intervention that can solely solve the challenges of people living with HIV and AIDS. I think we need to give South Africans options.' **Dr Tshabalala-Msimang opening of the Second National AIDS Conference in Durban, 7 June 2005**

'[Dr Tshabalala-Msimang's comments are] criminal.' **Mark Heywood, *Business Day*, 8 June 2005**

'The TAC's Zackie Achmat said it was regrettable that Tshabalala-Msimang was not taking her oath as a medical professional seriously. Not only had the minister of health consistently failed to support the government's ARV programme, but she was also underperforming in dealing with HIV … "We seriously ask the president to consider seriously whether this minister is appropriate for the job."' ***Cape Times*, 28 June 2005**

'[The absence of a national patient information system makes it impossible to say] how many patients had dropped out of the programme, how many had died … how many had been forced to change drugs because of dangerous side-effects.' **Dr Nomonde Xundu, Chief Director, Department of Health HIV/AIDS Directorate, *Business Day*, 3 March 2006**

'[AZT, 3TC and nevirapine triple-therapy is an] almost miraculous new combination drug treatment. … the new combination drug treatments are not a miracle. But in their physiological and social effects they come very close to being miraculous. … antiretroviral treatment has broken the equation between AIDS and death. … We don't need to suffer all these losses of our fellow countrymen and women. We don't need to suffer because the treatments are available to stop many, if not most, of those deaths. … many, many tens and hundreds of thousands and even millions of people can be saved from a dreadful illness and death by a treatment plan on the part of the government now. … In my own life, it's given me a second chance to live. And it's a wonderful thing. It's so mundane, it's so corny in a way to be alive and yet it's the most wondrous gift that one can have. And I feel deeply grateful for that, and I think it's a gift that should be put in the position, in the hands of so many more people. … For most of the people very ill with AIDS, for most of the people dying from AIDS now, treatment offers a realistic, a pragmatic intervention to save them from death. That's the fact – this isn't a position that I take. The truth is, if those treatments can be made available to them, they need not die of AIDS. It's as simple and as dramatic as that.' **Edwin Cameron JA, *Carte Blanche*, 4 November 2000**

'In contrast with many of my colleagues at SFGH [*San Francisco General Hospital*] in the AIDS program, I am not necessarily a cheerleader for anti-retroviral therapy. I have been one of the people who's questioned, from the beginning, whether or not we're really making an impact with HIV drugs and, if we are making an impact, if it's going in the right direction. … I have a large population of people who have chosen not to take any antiretrovirals since I've been following them – since the very beginning. … They've watched all of their friends go on the antiviral bandwagon and die.' **Dr Donald Abrams,**

Professor of Clinical Medicine, University of California, San Francisco, Assistant Director, AIDS Programme, San Francisco General Hospital, quoted in *Synapse*, October 1996

'For South Africa, the significance of AIDS denialism is momentous. It has to be, since our president, President Thabo Mbeki, has publicly countenanced and officially encouraged it. … The cost in human lives and suffering of denialist-inspired equivocation in national AIDS policy can be described only as horrendous. A leading AIDS activist, Zackie Achmat, has referred to government's policies – with resonant imagery – as "a Holocaust against the poor". Death from AIDS is now avoidable. With carefully administered treatments, and subject to monitoring and with appropriate medical care, AIDS is no longer a fatal disease. I know this from my own life, which without those treatments would have ended three or more years ago. Neither as a person living with AIDS nor as a judge can I stand apart from the struggle for truth and for action about AIDS, and the role lawyers and the legal system are called to play in it. Both Holocaust and AIDS denial remind us of our own terrible weaknesses and vulnerabilities as humans, and of the reluctance we all feel to own them. But the struggle for truth they involve also inspires us to greater thought and action. For truth, classically, is freedom, and from freedom in truth comes the capacity to build and plan and act better. AIDS in Africa calls us with imperative force to unleash that capacity.' **Edwin Cameron JA, 'The Dead Hand of Denialism'**

'For me a miracle happened and I want that miracle to be available to other people where they can be given their lives back, be given a sense of well-being and efficacy and engagement and joy back in their lives. And I believe we can do that, we as South Africans can prevent four to five million deaths through effective

medical care and treatment through the next decades.' **Edwin Cameron JA, SAfm radio, 2 October 2003**

'Some agitate for these extraordinary propositions with a religious fervour born by a degree of fanaticism which is truly frightening.' **President Thabo Mbeki, letter to President Bill Clinton, Prime Minister Tony Blair, Chancellor Gerhard Schroeder, UN Secretary General Kofi Annan and other leaders, 3 April 2000**

'I have the support of my colleagues on the Appeal Court.' **Edwin Cameron JA, SAfm radio, 18 March 2003**

'Furthermore, the fact that the most common current cause of death among people with HIV is liver failure suggests that liver injury may be a major limiting factor in the effectiveness of current HIV treatment.' **Justice et al. paper presentation at the 14th International AIDS Conference, Barcelona, July 2002**

'My tummy is getting a bit larger and people tell me I'm putting on weight. In fact I'm not putting on weight. My liver and some of the other inner organs are growing a bit larger from lipodystrophy … organ thickening … a minimal side effect.' **Edwin Cameron JA, SAfm radio, 18 September 2003**

'"On the 28th of October, 1999, the President gave a speech in which he said AZT was toxic," said Edwin Cameron, the shock of it still fresh. "This signalled the start of an apparent courting of the AIDS denialists. … Of course the drugs are toxic," said Mr. Cameron, almost trembling with exasperation. TAC recently lost three prominent activists whose bodies could not withstand the drugs. But there is no question among credible scientists, he said, that ARVs are the only thing that keep most people with AIDS

alive.' **Edwin Cameron JA, *Globe and Mail* (Canada), 13 Sept 2003**

'I have no doubt that I have natural intellectual gifts.' **Edwin Cameron JA, *Daily Dispatch*, 13 November 2001**

'I talk to them [*ARVs*]. I say, "You're my allies. I want you to enter my virological system and I want you to fight with me against this alien invader."' **Edwin Cameron JA, MNet television show *Carte Blanche*, 4 November 2001**

'There is no doubt that [ARVs] work.' **Professor Jerry Coovadia, *Daily Mail&Guardian*, 10 April 2000**

'About 500 000 people in South Africa are in need of life-saving ARV medicines now, and the number is projected to rise to 1.4 million by 2009.' **Ljumba and others, 'Access to Antiretroviral Therapy', *HealthLink*, Health Systems Trust, 20 July 2004**

'The only intervention that has ever been shown to have a proven impact on mortality is ARV therapy.' **Dr Jim Kim, director of WHO's HIV/AIDS department, *IRIN* (Integrated Regional Information Networks), UN Office for the Coordination of Humanitarian Affairs, December 2004**

'There is overwhelming proof that anti-retrovirals work – in sharp contrast to the fuzzy mumbo-jumbo that constitutes "evidence" about the minister's claims about vitamins and traditional remedies.' **Dianne Kohler Barnard, *Cape Times*, 30 June 2005**

'There is overwhelming and conclusive evidence from local and international clinical trials to support the fact that ARVs improve and indefinitely prolong the lives of patients with Aids.' **Dr Kgosi Letlape, chairman, South African Medical Association, *Pretoria News*, 30 August 2006**

'It costs the government R7000 a year to keep someone alive on ARVs.' **Zackie Achmat, *Mail&Guardian*, 30 November 2006**

'Through this ['CIVIL SOCIETY PARTNERSHIP TO SAVE LIVES'], we want to ensure: … That every one who needs anti-retroviral treatment receives it in time.' **South African Council of Churches statement jointly issued with the TAC and other groups, 1 December 2006**

'The results of this collaborative study, which involved … over 20 000 patients with HIV-1 from Europe and North America, show that the virological response after starting HAART [*Highly Active Antiretroviral Therapy*] has improved steadily since 1996. However, there was no corresponding decrease in the rates of AIDS, or death, up to 1 year of follow-up. Conversely, there was some evidence for an increase in the rate of AIDS in the most recent period. [We noted a] discrepancy between the clear improvement we recorded for virological response and the apparently worsening rates of clinical progression.' **The Antiretroviral Therapy (ART) Cohort Collaborative, *Lancet* 368:451-458 (2006)**

'The major findings are that, despite improved initial HIV virological control … there were no significant improvements in early immunological response as measured by CD4-lymphocyte count, no reduction in all-cause mortality, and a significant increase in combined AIDS/AIDS-related death risk in more recent years.' ***Lancet* covering editorial commenting on 'these somewhat paradoxical trends'**

'Addressing the Cape Town Press Club … [Southern African HIV/AIDS Clinicians Society president Francois] Venter said ARVs were a "modern medical miracle" that gave people 30 to 40 years of health.' ***Cape Argus*, 20 October 2006**

'Investment in ARV prophylaxis will save costs in AIDS-related treatment, as well as countless lives. … We need to massively invest in public delivery systems, combined with a huge increase in uptake of voluntary counselling and testing.' **Dr Douglas Webb of the UN Children Fund's (UNICEF) Africa HIV/AIDS section, *IRIN*, 15 February 2007**

'Antiretroviral treatment restores the health of most people with advanced HIV disease and prolongs life-expectancy substantially (NIH, 2003).' **Nathan Geffen, 'Encouraging Deadly Choices: AIDS Pseudo-Science in the Media', Centre For Social Science Research Working Paper No. 182, February 2007**

'The widespread provision of antiretrovirals in sub-Saharan Africa is one of the most important public health measures of this century.' **Professor Brian Gazzard, founder and past chairman of the British HIV Association (BHIVA) and Research Director of HIV/GUM, St. Stephen's Clinic, Chelsea and Westminster Hospital, London, *Guardian*, 12 September 2008**

'I think AZT can only hasten the demise of the individual. It's an immune disease and AZT only further harms an already decimated immune system.' **Professor Jay Levy, Department of Medicine, University of California at San Francisco, *Newsday*, 12 June 1990**

'The Western Cape report showed that: – Out of a total of 4251 patients enrolled in 3 months, a total of 207 (4.8%) patients died. Out of the total of 2715 patients enrolled in 6 months, a total of 196 (7.2%) patients died. Out of the 914 patients enrolled in 12 months, a total of 114 patients (12.2%) patients died.' [*Plotted on a graph as X and Y values, these data reveal a perfect linear relationship between the death rate of people taking*

ARVs and the duration of their treatment; and they predict that within seven years everyone on ARVs will be dead.] **Maupi Monyemangene, Media Liaison Officer, Department of Health, 6 October 2005**

'United Nations Special Envoy for HIV/AIDS in Africa Stephen Lewis expressed concern on Tuesday over Malawi's rising number of deaths among people receiving HIV/AIDS treatment in the country. Lewis was speaking at the end of his three-day visit to the impoverished southern African country when he was briefed by Malawian government officials that the country was grappling with an 11 percent death rate of people who were receiving free antiretroviral (ARV) drugs in public hospitals. Malawi has managed to increase the number of people receiving free ARVs from about 4,000 two years ago to 70,000 at present.' **'UN concerned about Malawi's rising deaths of AIDS patients on ARVs', China *People's Daily Online*, 1 November 2006**

'South Africa's Ministry of Health has confirmed that close to 6,000 HIV-positive people had died while receiving antiretroviral (ARV) drugs since the government rollout began in 2004 … just below 3 percent of the number of HIV-positive people accessing treatment at government ARV sites during the same period. Health department spokesman Sibani Mngadi said … "The number of people being treated with antiretroviral therapy through our 'Comprehensive Plan on HIV and AIDS' has increased [by] 60,000 in the past year to 235,378 by the end of September 2006."' **'SOUTH AFRICA: Govt AIDS programme on course but people still dying', Reuters Foundation (Source: IRIN), 14 Nov 2006**

'Doctor Henry Sunpath, of McCord Hospital [said] that … the factors encouraging the deaths … "could be … confusing information about the benefits of ARVs, as publicly expressed by the Health Minister Manto Tshabalala-Msimang herself." … Sunpath's sentiments are shared by Dr Francois Venter, an HIV specialist at the University of Witwatersrand in Johannesburg, who charged that "it is conflicting views such as these which … [motivate] scores of people who still turn down or prematurely quit ARV therapy because they are too afraid of the exaggerated side effects."' **'SOUTH AFRICA: Govt AIDS programme on course but people still dying', Reuters Foundation (Source: IRIN), 14 Nov 2006**

'South Africa's strategy for combating AIDS has been shaped by a long-standing antipathy on the part of President Thabo Mbeki and his Health Minister towards antiretroviral therapy. … It is precisely because Mbeki's undermining of the science of HIV treatment costs lives, that his position is so controversial. … Mbeki was portrayed as severely out of step with scientific opinion … and as stupidly pig-headed … The most pernicious legacy of President Mbeki's dissident stance on AIDS has been the erosion of the authority of science and of scientific regulation of medicine in South Africa.' **Nicoli Nattrass, 'AIDS, Science and Governance: The Battle Over Antiretroviral Therapy in Post-Apartheid South Africa', Centre for Social Science Research Working Paper, 19 March 2006**

'Easily the most controversial official in her nation's government, Dr. Tshabalala-Msimang has been a target of AIDS activists and some medical experts since early this decade, when she publicly questioned the safety and effectiveness of conventional AIDS treatments like antiretrovirals for adults and drugs that hinder the transmission of H.I.V. from pregnant women to their unborn children.' ***New York Times*, 23 February 2007**

'Government's new five-year plan to combat HIV/AIDS will cost up to R45bn, according to treasury calculations contained in the latest working draft — significantly more than the R14bn already set aside over the next three years. The biggest slice of the money, up to 40%, is earmarked for AIDS drugs, which government hopes to be able to provide to four-fifths of those in need by 2011, according to the latest working draft, a copy of which has been seen by Business Day.' ***Business Day*, 13 March 2007**

'Our biggest success is that we got government to accept a treatment plan.' **Zackie Achmat, *Mail&Guardian Online*, 30 November 2006**

'[A] distressingly high loss-to-follow up rates [was] reported by some large ART-dispensing facilities … at the 3rd South African AIDS Conference. … For instance, 27% of the first tranche of patients enrolled at King Edward VIII Hospital in Durban starting after April 2004 were "non-persistent" (defined as having failed to return for prescription refills for 90 days or more) within 12 months of starting ART. … Dr Helen Schneider of the Centre for Health Policy at the University of Witwatersrand … concluded about a third of these "drop-outs" were deaths.' **AIDSmap.com, 'Patient retention difficulties for South Africa's public sector' in 'HIV & AIDS Treatment in Practice #90, August 31st, 2007'**

'… Felege Hiwat hospital in Bahir Dar, in the northern Amhara region [Ethiopia] … started over 3600 patients on ART by the end of 2006. However 22% of those patients were lost to follow-up … Home visits and other enquiries were able to locate just 6% of patients, with a further 44% of the LTFUs discovered to be dead, and the remainder still missing. In South

Africa, Klerksdorp Hospital in the North-West province … the loss to follow-up rate … reached 21%. The vast majority of those lost to follow-up defaulted during the first six months of treatment, but an audit of 300 patients lost to follow-up could only identify 126 deaths from local death records. The remainder were still out there somewhere, but, said Dr Ebrahim Variava [*without saying how he knew*], either their address details weren't complete, or they weren't answering their mobile phones.' **AIDSmap.com, 'HIV & AIDS Treatment in Practice #92, September 26th, 2007'**

'… we conducted a systematic search of the English-language published literature, gray literature (project reports available online), and conference abstracts between 2000 and 2007. … We included 32 publications reporting on 33 patient cohorts totaling 74,289 patients in 13 countries in our analysis. … Under the worst-case scenario, 76% of patients would be lost by 2 y [*years*]. The midpoint scenario predicted patient retention of 50% by 2 y. … losing up to half of those who initiate ART within two years is cause for concern. From the data as reported, attrition averaged roughly 22% at 10 mo [*months*] of follow-up. This average comprised mainly deaths (40% of attrition) and losses to follow-up (56%). … we believe that actual attrition is higher than … we report … The midpoint scenario suggests that approximately half of all patients started on ART were no longer on treatment at the end of two years. … A recent attempt to trace lost-to-follow-up patients in Malawi determined that 50% had died, 27% could not be found, and most of the rest had stopped ART … those reporting on these cohorts do not know what ultimately happened to patients categorized as lost to follow-up … our analysis is necessarily limited to publicly available reports and thus poten-

tially subject to publication bias. Researchers may be less inclined to publish long-term outcomes from cohorts that have experienced very high early attrition. … Better information on those who are lost to follow-up is urgently needed.' **Rosen et al. 'Patient retention in antiretroviral therapy programs in sub-Saharan Africa: A systematic review',** ***PLoS Med*** **4(10): e298, October 2007**

'"Embedded" is now a thoroughly filthy word: it signals wholesale journalistic capitulation to … interests that it should be the profession's job to dissect, not embrace.' ***Mail&Guardian*** **editorial deploring media cover of the American invasion of Iraq, 11 November 2003**

'We are proponents of AZT. … Yes [it's objectionable to] cast aspersions on AZT and nevirapine … it's dissident.' ***Mail&Guardian*** **chief operations officer Hoosain Karjeiker to Adv Brink, 9 December 2004**

'The position of the *Mail&Guardian* is that everyone is entitled to treatment. … Our newspaper has been at the forefront of the push for antiretrovirals in this country. Our brand has suffered [from the publication of an article pointing out that 'Hundreds of studies have found that AZT is profoundly toxic to all cells of the human body, and particularly to the blood cells of the immune system' and that 'Numerous studies have found that children exposed to AZT in the womb and after birth suffer brain damage, neurological disorders, paralysis, spasticity, mental retardation, epilepsy, other serious diseases and early death.'] … Publishing [another article referring to 'the side effects of extremely toxic pharmaceutical drugs like AZT and nevirapine'] will continue to damage our brand.' ***Mail&Guardian*** **editor Ferial Haffajee to Adv Brink, 9 December 2004**

'This newspaper has always supported the need for an effective antiretroviral programme and will not in future [publish anything] which dilutes this message or creates confusion in the minds of readers.' **Ferial Haffajee, *Mail&Guardian*, 17 December 2004**

'I do not intend to engage in nonsensical debates on AZT or other AIDS-related matters. I find the issues you raise a total waste of energy but perhaps more exciting for ignorant people in the field. … Remember that I am the scientist and not you.' **Malegapuru Makgoba PhD, then president of the South African Medical Research Council, now Vice-Chancellor and Principal of the University of KwaZulu-Natal, and chairman of the board, *Mail&Guardian*, email to Adv Brink, *c*. 1999**

'[The medical and scientific research findings reviewed in *Debating AZT: Mbeki and the AIDS drug controversy* are] the ravings of [a] drivelling conspiracy-theorist, loony, crackpot, fruitcake. … I'm a professional at spotting weirdos.' **David Beresford *Mail&Guardian*, 22 September 2000**

'The mainstream media … have failed us completely … The subject [*of pharmaceutical drugs*] is just too damned uncomfortable to handle; too complicated, often deliberately, too scientific for the layman. Many hacks who should know better have been lunched, holidayed and bamboozled into silence. Fake nostrums are taken as gospel.' **John le Carré, London *Spectator*, 14 December 2000**

'In South Africa [public perceptions] are informed, mainly, by the media which forms part of the most reactionary forces among those offering consistent ideological resistance to transformation. It is a powerful tool of manipulation, information and propaganda. For example, in the 1995 Media and Market Research of Jocelyn Cooper it was indicated that 70

per cent of the people north of the Parktown Ridge get their information from the newspapers only. They normally do not consult other sources of information.' **Peter Mokaba MP, ANC Election Officer, *Umrabulo* Vol. 10, May 2001**

'If there is to be a way out of the nightmare of history, it will begin with a waking up to the complicity of the corporate mass media in mass murder.' **David Edwards and David Cromwell, *Guardians of Power: The Myth of the Liberal Media* (London: Pluto Press, 2006)**

'TAC has developed an excellent national press strategy and profile. At no additional cost, the organisation has been able to secure regular space and retain its profile … with the organisation relying almost exclusively on the media for its marketing.' **'Treatment Action Campaign (TAC) Evaluation 29 June 2005'**

'It must be said that the role played by the media in forcing government to drop its HIV/AIDS denialism and implement a much more progressive policy has been extraordinary.' **Adjunct Professor Anton Harber, head of journalism and media studies at the University of the Witwatersrand, addressing the Goedgedacht Forum, Western Cape, 22 February 2007**

'Anthony Brink [is] No. 1 [among South Africa's] AIDS DISSIDENTS [and] so dangerous [that] the media [should] deny [his] dissident views publicity … [In making known the research literature on the lethal toxicity of AZT and other ARVs, he merely tries to] hide behind the excuse of promoting scientific debate in order to promote views that are false and dangerous. South Africa cannot let this continue any longer.' **'DEMOCRATIC ALLIANCE PUBLIC HEALTH WARNING!', October 2005**

'Anyone persuaded not to take antiretrovirals … is … dying unnecessarily. … Science and health journalists should talk to the editorial desk and letters editors and vice versa to ensure that AIDS denialist letters are spotted on arrival and spiked, not published.' **John Moore, Professor of Microbiology and Immunology, Weill Medical College, Cornell University, addressing the 'HIV Science and Responsible Journalism' symposium, XVI International AIDS Conference, Toronto, 13 August 2006**

'Brink … has a twisted, perverse anti-science agenda that is based on him trying to "prove" the pre-conceived notion that AIDS is caused by the therapies used to treat it – an utter and manifest nonsense." **Nathan Geffen, *Die Burger*, 2 December 2006**

'Mill's "free market of ideas" needs reinforcement with legislative inhibition on untruth[20]. … [20] Personal correspondence with Edwin Cameron.' **Nathan Geffen, 'Encouraging Deadly Choices: AIDS Pseudo-Science in the Media', Centre For Social Science Research Working Paper No. 182, February 2007**

'Mark Heywood, the deputy chairman of the SA National Aids Council, said that the ANC should "discipline and restrain" the [KwaZulu-Natal Health] MEC and minister [Ms Peggy Nkonyeni and Dr Tshabalala-Msimang for] sending out confusing messages that tell people that the antiretroviral drugs that the government includes in its programme are poisonous and dangerous.'" **Kerry Cullinan and Anna-Maria Lombard, 'Health chiefs back quackery to treat HIV', *Sunday Times*, 18 May 2008**

'The Internet has made it possible for every conspiracy theory to flourish. There are three basic versions of the H.I.V.-denial credo. … The second argues that, even if the virus is harmful, the risks of antiretroviral drugs far outweigh the benefits: AIDS

drugs are poisons, pushed by doctors corrupted by the pharmaceutical industry. The "poison" argument has been proved untrue in hundreds of studies across the globe, among women, men, drug users, homosexuals, and infants.' **Michael Specter, 'The Denialists: The dangerous attacks on the consensus about H.I.V. and AIDS', *The New Yorker*, March 2007**

'We have not been able to discover why doctors prescribe a toxic drug called AZT (Zidovudine) to people who have no other complaint than the presence of antibodies to HIV in their blood. In fact, we cannot understand why humans would take that drug for any reason.' **Kary Mullis PhD, 1993 Chemistry Nobel Laureate, in his foreword to *Inventing the AIDS Virus* by Professor Peter Duesberg (Washington: Regnery, 1996)**

'Look, there's no sociological mystery here … It's just people's income and position being threatened … That's why they're so nasty. In the AIDS field, there is a widespread neurosis among scientists … there's just so much slowly accumulating evidence against them. It's really hard for them to deal with it. They made a really big mistake and they're not ever going to fix it. They're still poisoning people.' **Kary Mullis in 'Out of Control: AIDS and the corruption of medical science' by Celia Farber, *Harper's Magazine*, March 2006**

'Mark Gevisser told the BBC Mr Mbeki thinks he has "failed on the issue of Aids" and regrets dropping the debate. … "He feels even more strongly about the efficacy of anti-retroviral (ARV) medication. He believes that ARV medication is toxic and that it is a project that's been imposed upon particularly vulnerable Africans by the pharmaceutical companies," Mr Gevisser said.' **BBC News, 7 November 2007**

'I think he [*Mbeki*] believes that the damage caused by ARVs is greater than the damage caused by Aids.' **Chris Barron interviewing Mark Gevisser, *Sunday Times*, 18 November 2007**

'Manto Tshabalala-Msimang has been replaced as minister of health by Barbara Anne Hogan – a move hailed by Zackie Achmat of the TAC. … Achmat … has described Hogan's appointment as "the best news that South Africa could have had". He described Hogan as both a good friend and a good person.' **'Achmat hails Manto's replacement', Health24.com, 26 September 2008**

'I think the biggest challenge is HIV/Aids and all the strains that it places on the health system. … I would thoroughly endorse the roll-out of anti-retrovirals and any way we can accelerate that, the better.' **'Q&A with Barbara Hogan', News24.com, 26 September 2008**

'"The public is expecting to see real change. We need to see our health system back on track. There has been some astonishing work done in the Aids programme and in the anti-retroviral roll-out and I am sure we will be making changes from our predecessor's (Aids programme)," said Hogan.' **'Minister promises "real change"', *Weekend Argus*, 27 September 2008**

'According to Professor Nicoli Nattrass of the University of Cape Town, Ms Tshabalala-Msimang created confusion by describing anti-retroviral drugs (ARVs) as toxic.' **'New era for S Africa Aids fight?', BBC News, 6 October 2008**

'We know how to save people's lives. We know the medicine is out there and we know that wealthy countries can afford to do more. That's why it was so frustrating for me to go to South Africa, and see the pain, and see the suffering, and then hear that the country's Minister of Health had promoted the use of beetroot,

sweet potato, and lemon juice as the best way to cure HIV. Thankfully, the South African government eventually repudiated this, but it's impossible to overestimate how important it is for political leaders like this to set a good example for their people. We should never forget that God granted us the power to reason so that we would do His work here on Earth – so that we would use science to cure disease, and heal the sick, and save lives. And one of the miracles to come out of the AIDS pandemic is that scientists have discovered medicine that can give people with HIV a new chance at life. We are called to give them that chance. We have made progress – in South Africa, treatment provided to pregnant women has drastically reduced the incidence of infants born with the infection.' **Senator Barack Obama, speaking on World AIDS Day, 1 December 2006**

'We urge HIV positive mothers to enrol in the Prevention of Mother-to-Child Transmission programme, to make full use of antiretroviral therapy (ART) and to test their children very early so that necessary therapy can be administered in time.' **Deputy President Baleka Mbete, *ANC Today*, 5 December 2008**

'… you are justified in sounding a warning against the long-term therapeutic use of AZT, or its use in pregnant women, because of its demonstrated toxicity and side effects. Unfortunately, the devastating effects of AZT emerged only after the final level of experiments were well underway, that is, the experiments which consisted of giving AZT to large numbers of human patients over a long period of time. Your effort is a worthy one … I hope you succeed in convincing your government not to make AZT available.' **Dr Richard Beltz PhD, Biochemistry Professor Emeritus, Loma Linda University School of Medicine, California, inventor of AZT in autumn 1961, to Adv Brink, 11 May 2000**

Inventing AZT

Charles Mackay's 'catalogue of some of … mankind's … more *outré* enthusiasms', *Extraordinary Popular Delusions and the Madness of Crowds*, first published in 1841, tells how alchemy flourished for centuries, its eminent practitioners tapping sultans and princes for treasure with the promise that they could multiply it, for the pursuit of the philosopher's stone and for the *elixir vitae*. He describes an experiment of the famous Bernard of Treves and his disciples, who 'imagined that there was a marvellous virtue in all excretement, especially human' and who accordingly proceeded to put

> forty-two marks of gold … into a crucible, with a quantity of salt, copperas, aquafortis, egg-shells, mercury, lead, and dung. The alchymists watched this precious mess with intense interest, expecting that it would agglomerate into one lump of pure gold. At the end of three weeks they gave up on the trial, upon some excuse that the crucible was not strong enough, or that some necessary ingredient was wanting. Whether any thief had put his hands into the crucible is not known, but it is alleged that the gold found therein at the close of the experiment was worth only sixteen marks, instead of the forty-two which were put there in the beginning.

The great American war on cancer was just such an affair. In every respect. Biologist Linus Pauling, who notched up not one but two Nobel prizes in his lifetime, wrote it off as worse than folly; he thought it 'essentially a fraud'. Another Nobel laureate, James Watson, the double helix guy, called it, with

ripe historical redolence, 'a lot of shit'. In was in this dead-end pursuit in the early sixties that cancer researcher Dr Richard Beltz, now a biochemistry professor emeritus at the Seventh Day Adventists' Loma Linda University School of Medicine in California, was cooking up new poisons to kill cells with a view to finding that magic bullet to cure cancer that everyone was after. He related to me:

> I synthesized AZT in my laboratory as a NIH Senior Research Fellow (National Cancer Institute) in the autumn of 1961. The AZT was among a group of four new thymidine analogs that I prepared at that time. AZT proved to be the most biologically active of these compounds in preliminary tests. My biological tests showed (1) AZT inhibited the growth of E. coli and S. potsdam [*bacteria*] at very low concentrations, and (2) cultures of E. coli put on agar plates containing AZT showed AZT-resistant clones after a few days of incubation. Subcultures of these clones were entirely resistant to growth inhibition by AZT. Further work showed that AZT had no effect upon the DNA synthesis of T2 bacteriophage [*a virus*] propagated in E. coli cultures. Finally, I prepared 1 gram of crystalline AZT and sent it to a friend at Yale University, Dr. Allen Sartorelli, Professor of Pharmacology, who tested it for anticancer activity. The AZT proved to be inactive against two experimental animal tumors which he was using at that time for screening. This used up the 1 gram of AZT. In my laboratory I found AZT incapable of inhibiting the growth of Jensen sarcoma cells in vitro, at very high concentrations. Thus, AZT showed no activity as a potential anticancer drug when tested by the methods of that era. What I have written here

> summarizes my work with AZT. I did many other experiments within the framework of these findings, but that work consisted of filling in details.

In every account describing the invention of AZT that has been published to date, the credit gone to another cancer researcher, Jerome Horwitz. In *AIDS & HIV in Perspective* (Cambridge University Press, 1994) Professor Barry Schoub, Director of the National Institute of Communicable Diseases in Johannesburg, claims, 'Zidovudine was first synthesised by Horwitz in 1964 together with other nucleoside analogues.' In his excellent examination (from a conventional, orthodox perspective) of the potent social forces that shaped the erection of the HIV-AIDS construct, *Impure Science: AIDS, Activism and the Politics of Knowledge* (University of California Press, 1996), assistant professor of sociology Steven Epstein at the University of California at San Diego, claims similarly:

> In the early 1960s, a researcher named Jerome Horwitz at the Michigan Cancer Institute decided to design a drug that would keep cancer cells from duplicating. With funding from the NCI, and working with such unlikely ingredients as herring sperm, Horwitz and his co-workers designed a group of compounds called dideoxythymidines that were designed to look like nucleosides, the building blocks of DNA. In theory, these nucleoside analogues would substitute themselves for real nucleosides, thereby interfering with formation of DNA molecules. Without more DNA, the cancer cells would simply stop duplicating. In practice the treatment was a complete failure.

Elinor Burkett's searchlight on the corrupt underbelly of AIDS, *The Gravest Show on Earth: America in the Age of AIDS* (Picador, 1996) states:

> Among Wellcome's compounds was a herring and salmon sperm extract developed by Detroit researcher, Jerome Horowitz [*sic*], as a possible cancer treatment. His concoction, AZT, had never made it into human testing. It had been so ineffective against cancer cells, and so toxic that Horowitz didn't even take out a patent.

In *Inventing the AIDS Virus* (Regnery, 1996), cell and molecular biology professor Peter Duesberg of the University of California at Berkeley repeats: 'AZT was invented … in 1964. Jerome Horwitz, heading a lab at the Detroit Cancer Foundation … created a chemically modified form of a DNA building block.' In *Positively False* (IB Taurus, 1998), Joan Shenton says: 'AZT was first developed as a cancer chemotherapy drug in 1964 (to kill unwanted cells)' – tying the discovery of AZT to Horwitz by the year mentioned. In its press release on 20 March 1987, the day AZT was licensed as an AIDS drug, the FDA stated similarly: 'Retrovir was originally developed in 1964 by Dr. Jerome Horowitz [*sic*] of the Michigan Cancer Foundation as a possible treatment for cancer.'

Even the researchers who dredged AZT from medicine's trash can, and whose crummy laboratory studies were the basis for clinical trials on human subjects (without the usual preceding animal efficacy studies), misattribute the invention of AZT to Horwitz. In their letter to the *New York Times* on 28 September 1989 Mitsuya, Weinhold, Yarchoan, Bolognesi, and Broder corrected several lies told by the president of Burroughs Wellcome (now GlaxoSmithKline), T E Haigler Jr,

in his own letter twelve days earlier, stealing the thunder for the invention of AZT and the initial research into its use as an antiretroviral drug. They wrote:

> The company did not perform the first synthesis of AZT. This was done by Dr. Jerome Horowitz [*sic*] at the Michigan Cancer Foundation in 1964, using a Government grant.

Horwitz (not 'Horowitz') got the kudos because he was the first to publish a paper in 1964 in which he described a way of synthesizing AZT and another similar nucleoside analogue. 'However,' as Beltz pointed out to me, 'there was no mention at all in this paper of biological activity or even of potential biological activity'. The popular record has it that Horwitz thereafter tried the drug out on leukaemic mice, without any success, whereafter he just shelved it. That's not quite right, Beltz says:

> I am personally aware that Horwitz went down the same trail of research that I went down after synthesizing AZT. That is, he tested it against experimental animal tumors and found it to be an essentially inactive drug. The results of my tests and of Alan Sartorelli's tests at Yale with AZT on experimental tumors were also uniformly negative. I was struck by the lack of toxicity of AZT toward Jensen tumor cells … the drug was not effective for blocking tumor growth, even at quite high doses.

Beltz explained to me the reason why Horwitz made it to print and not him:

> Let me tell you what happened. I synthesized AZT in the period from June-October, 1961, looking for new

potential anticancer nucleoside analogs. … I delayed publication because my main research focus was to investigate the mechanism of control of DNA synthesis in regenerating liver. I never got around to publishing that early work on AZT. Then in February 1964 my laboratory was destroyed in a fire that burned down the biochemistry department where I was working. I took a 1 year sabbatical leave. The paper by Horwitz describing AZT synthesis was published in the *Journal of Organic Chemistry* in 1964 – Horwitz, J.P., Chua, J. and Noel, M.J. *Organic Chemistry 29: 2076-2078 (1964) Nucleosides. The monomesylates of 1-(2'-Deoxy-beta-D-lyxofuranosyl)thymine*. This was the first published record of AZT synthesis. Accordingly, Dr. Horwitz was properly given credit for being the first to synthesize AZT. I have never disagreed with the historians about this, because it was simply my own fault that I didn't get a paper out on it in 1962 or 1963. By 1964 it was too late. In 1987 the Burroughs-Wellcome Company was making AZT and selling it at what people generally thought was too high a price. To justify the price, David Barry, a Director of Research for the B-W Company, said in a *Wall Street Journal* article that AZT was made by a 7-step synthesis. My synthesis was a 4-step synthesis, so I wrote to Dr. Barry pointing this out and offering my method. There ensued a transfer of information from me to the B-W company, where they proceeded to check out my method. The result was that they wrote back to me after several months and said some complimentary things about the method but decided they would not need to use it because they said they basically already knew most of what I had told

> them. At that point Dr. Barry asked me for historical information about my synthesis of AZT and I replied with a dated, detailed history of the synthesis and testing of AZT in my laboratory. That document is in the files at Burroughs-Wellcome (now Glaxo). I heard nothing more after that, and I have been content to let the matter rest.

I'm pleased to report that the toxicity literature canvassed in an early draft of *Debating AZT*, which I requested Beltz to review, changed his mind about the utility of the drug as a treatment for AIDS, and especially about the wisdom of giving it to pregnant women. On 14 April 1999 Beltz answered an enquiry by my associate David Crowe in Calgary, Canada, concluding that

> we must admit [that AZT] has at least some limited value as an anti-AIDS drug, especially for preventing newborn children from AIDS-infected mothers from acquiring the disease.

But after reading *AZT: A Medicine from Hell* in *Debating AZT* he ditched that opinion. Though understandably put out by my initial imprecision concerning the early history of AZT, gleaned from the texts I cited above, he was happy to disown his creation and lend me his full support, writing on 11 May 2000:

> you are justified in sounding a warning against the long-term therapeutic use of AZT, or its use in pregnant women, because of its demonstrated toxicity and side effects. Unfortunately, the devastating effects of AZT emerged only after the final level of experiments were well underway, that is, the experiments which consisted of giving AZT to large numbers of human

> patients over a long period of time. Your effort is a worthy one … I hope you succeed in convincing your government not to make AZT available.

Possibly embarrassed by GlaxoSmithKline's atrocious misapplication of the cell-poison he'd conceived, Beltz was shy about his paternity, and said he would prefer it kept under the hat. In my opinion, however, his is an important story to tell, because it starkly sets his purpose in making AZT, namely to kill cells, against GlaxoSmithKline's claim that it kills viruses. The record of his invention of the chemical had already been in the public domain since 1972 in any event, albeit hardly ventilated. A student of his, one R Walters, wrote it up in a thesis. It sits on the library shelves of Beltz's university for all to see.

I thank Stuart Thompson for forwarding an email from Beltz, amplifying the history I'd initially got from him. Beltz sent David Crowe the same account of his first synthesis of AZT that he later sent me, but in his correspondence to me Beltz went on to explain how it happened that Horwitz got the credit.

Licensing AZT

Responding to President Mbeki's statement in the National Council of Provinces on 28 October 1999 that there was 'a large volume of scientific literature' showing 'the toxicity of this drug is such that it is in fact a danger to health', and that 'medical researchers' had been issuing 'dire warnings' about it, GlaxoSmithKline's South African medical director Peter Moore claimed he was wrong: 'The President has been gravely misinformed about the safety aspects of AZT.' Why, the drug had been licensed under 'the most stringent regulations'.

This essay looks at the Phase II study, the pivotal AZT licensing trial conducted by Margaret Fischl and others*, on the basis of which the drug was approved in the US and elsewhere; how AZT met 'the most stringent regulations' as it was being licensed by the Food and Drug Administration†.

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* Reported in July 1987 in two concurrent papers in the *New England Journal of Medicine* (……) by Fischl et al.: 'The efficacy of azidothymidine (AZT) in the treatment of AIDS and AIDS related complex', along with 'The Toxicity of Azidothymidine (AZT) in the Treatment of Patients with AIDS' by Richman et al.

† For much of the original sleuthing for this article, all credit to John Lauritsen. His several knockdown critiques in the *New York Native* reappeared in his books *Poison by Prescription: The AZT Story* (Asklepsios, 1990) and *The AIDS War* (Asklepsios, 1993). Lauritsen quotes extensively from FDA director Ellen Cooper's *Medical Officer Review of NDA 19-655*, reporting widespread irregularities in the conduct of the trial found by FDA inspectors, and I cite his excerpts in turn. Professor Peter Duesberg and Dr David Rasnick performed a further useful analysis of the Phase II trial in 'The AIDS dilemma: drug diseases blamed on a passenger virus', published in *Genetica* in September 1998. Celia Farber published a seminal exposé of the FDA approval hearing, 'Sins of Omission: The AZT Scandal', in *Spin*, November 1989. Joan Shenton provided important information in her television docu-

As its name suggests, the Phase II trial was preceded by a preliminary Phase I study, conducted to see whether humans could endure the drug's toxicity. Lauritsen reports that

> 12% died in a time period of only six weeks. The four patients who died were replaced, and all 33 patients continued to take AZT in an 'extended trial', during which an additional 21% died. … a cumulative total of one-third (33%) of the patients died either in the Phase I or in the extended trial.

This appalling death rate was read to mean AZT was not acutely toxic, and was therefore safe to give people every day for six months during a Phase II trial to determine efficacy, i.e. to see whether it actually worked.

The Phase II trial was lavishly sponsored by Burroughs Wellcome (now GlaxoSmithKline) to the tune of $10 000 paid to the principal investigators conducting the study for every patient enrolled at each of the twelve centres at which it was run. It involved a mere two hundred and eighty-nine people, nearly all male, all very sick, half of whom were put on AZT and the other half on placebo. That was how it began anyway, but not for long. The central finding of the study, upon which the FDA based its decision to license AZT, was that the drug could 'decrease mortality'. It was specifically noted that there were no data showing that the drug had any antiviral action in

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mentary *AZT: Cause for Concern*, broadcast on Channel 4 in Britain in February 1992, and in her book *Positively False* (IB Taurus, 1998). I have also relied on Bruce Nussbaum's *Good Intentions: How Big Business and the Medical Establishment are Corrupting the Fight Against AIDS* (Atlantic Monthly Press, 1990); Neville Hodgkinson's *AIDS: The Failure of Contemporary Science* (Fourth Estate, 1996); and Steven Epstein's *Impure Science: AIDS, Activism and the Politics of Knowledge* (University of California Press, 1996).

people (there still aren't), and everyone on the panel knew that what goes on in test tubes is incomparably different from what happens in the infinitely more complex biological systems of the human body. And, as was obvious from the serious ill effects noted on the trial subjects' clinical case records, AZT was extremely poisonous. But the mortality data were most compelling on the face of it: at the point that the trial was stopped, nineteen of the one hundred and thirty-seven-member placebo group had died, against only one of the hundred and forty-five patients given AZT. Unfortunately things weren't as they seemed.

There is nothing to indicate that the test subjects were properly randomised. According to Lauritsen, 'the sicker patients may have been placed in the placebo group to begin with. … The FDA documents indicate that this was indeed the case.' A sharply critical *Statistical Review and Evaluation* of the Phase II trial by the FDA's Lawrence Hauptman reported:

> Two patients died very early in the study. … It is arguable that these patients were sick enough at entry that they should not have been included in the study.

Lauritsen notes: 'Both patients just happened to be in the placebo group.' FDA inspector Patricia Spitzig's seventy-six page report of irregularities objected, inter alia, that 'the sponsor unfairly biases against the placebo group', and 'the sponsor makes the analysis look more favourable to AZT' (quoted by Joan Shenton in *Positively False*). Lauritsen tells that one very ill patient, identified as '1009', had been on AZT before entering the trial. He was put in the placebo group, and his death was counted among the placebo deaths.

The trial rapidly became unblinded. The doctors running the trial weren't supposed to know who was on AZT and who

was on placebo. Nor were the patients. This is the meaning of a 'double-blind' study. But in her *Medical Officer Review of NDA 19-655*, FDA director Ellen Cooper reported that doctors could readily tell who was on AZT and who wasn't from a prominent side effect of the drug as they looked at patients' blood through their microscopes: macrocytosis (sixty-nine per cent of AZT-treated) followed by severe anaemia (twenty-five per cent), i.e., red blood cells swelling up from AZT poisoning before popping off by the ton. Patients themselves quickly cottoned on to who was on AZT and who wasn't. If they didn't get it from their doctors, they were able to find out for themselves easily enough: the drug, reported Cooper, was bitter, the placebo sweet. Or they went off and had their pills analysed – so a chemist approached for the service told investigative reporters in a television exposé of the corruption of the Phase II trial on NBC News on 27 January 1988. Chris Babick of the People with AIDS Coalition corroborated this, telling Shenton how his organisation had referred trial subjects to three laboratories in New York for the analysis of their pills. If the real thing they'd share it; if dud they'd get it from the lucky guys being prescribed it. Or would buy it. All of which jinks were admitted by trial subjects interviewed for the film. Bought? From where? Spitzig reported that supplies of AZT went missing: eighty-seven bottles from the Boston Centre alone – 'undoubtedly [entering] the black market', concluded Lauritsen. Spitzig confirmed that 'some of the Study Drug had been purchased "on the street"'. Some patients got AZT by mistake, or vice versa, with some ostensibly on AZT getting the placebo – a bungle picked up by Spitzig in the case of two patients. Some, discovering they were on placebo, procured other dangerous experimental drugs. According to Cooper's report another FDA investigator made the obvious observa-

tion: 'The fact that the treatment groups unblinded themselves early could have resulted in bias in the workup of patients.' Lauritsen put it absolutely:

> If there is even the slightest doubt that all 'AZT patients' were really getting AZT, and all 'placebo patients' were getting placebos, then the study has fallen apart at its very core.

But Fischl's report in the *New England Journal of Medicine* was silent about this, claiming the trial to have been a 'placebo-controlled double-blind' study. In design yes, but in execution, it's common cause, not by a long shot. Scientists call this scientific fraud. Lawyers would describe GlaxoSmithKline's assertion of the results of a trial like this, in support of their product, as commercial fraud. But plain folks know it as lying. Shamelessly too: years after the trial, Fischl was still denying to Lauritsen, and again later on to Shenton, that the trial became unblinded. But of course it did – obviously so, and for another reason too: for Fischl and her fellow trial overseers to have made the observation that those ostensibly on placebo were dying faster than those on AZT, they had to have known who was on what. Which they weren't supposed to, until the trial was over. But clearly they did.

The trial was designed to run for six months, i.e. twenty-four weeks, but was prematurely terminated at seventeen weeks, i.e. just more than four months – for ethical reasons, the record has it, since the AZT-treated were doing so well. It would have been wrong to withhold the drug from AIDS sufferers another day. In reality, the reason for the early end of the trial was that it was collapsing into chaos. Apart from having become unblinded, 'protocol violations' were being committed all over the place: patients were taking unauthorised concomitant

drugs, thereby skewing the results; 'drug accountability' failures were occurring, i.e. patients took known but unrecorded treatment holidays instead of swallowing the drugs daily as prescribed; patient records were being altered without authority or ostensible reason; and serious adverse effects were not being recorded or were being deleted – all of which was discovered and documented by FDA inspectors in their reports. Cooper reported that the lapses were so widespread that the FDA decided

> to request inspection of all twelve centers which participated in this trial … because one of the early inspections had found significant deviations from FDA regulations regarding the proper conduct of clinical investigations.

But it was a bit late. The panel appointed to consider the data was scheduled to meet a month later. FDA officials met twice to resolve what to do about all the corrupted case reports – so rank at the Boston centre that FDA inspectors recommended that all data from it be canned completely. The fact that dumping the corrupt data would have considerably thinned out the already small database worried one bureaucrat more than the fact that they were junk: 'if exclusion of all patients with protocol violations were strictly applied, quite a few patients would probably be deleted from the database.' Too bad, you might have answered, but you weren't there to insist. So what do you think the FDA resolved to do? Exclude them or include them? Even the completely fouled Boston returns? Take a guess. A really wild one.

Thirty patients in the AZT-treated group (twenty-one per cent) needed repeated blood transfusions to survive the severe anaemia that the drug was causing. Without these repeated

infusions of replacement blood they'd have died during or soon after the study, and their deaths would have raised the death toll in the AZT-treated group from one to thirty-one. That's thirty-one dead in the AZT-treated group versus nineteen in the placebo wing. Add five in the placebo-group who got repeated transfusions as well (we're coming to this), and you get twenty-four. Thirty-one AZT deaths versus twenty-four placebo deaths wouldn't have looked so impressive on the blackboard at the FDA's licensing panel hearing, especially set against the complaints all day about how very poisonous the drug was.

A strange thing about that Phase II trial is that patients in the control group, officially on placebos, also suffered from AZT's toxic effects, with five of them needing multiple blood transfusions too, as mentioned. Whereas thirty-four per cent of AZT-treated patients suffered the loss of more than half their white blood cells from the drug's haematological toxicity, so did six per cent in the placebo group. Sixty-six AZT-treated patients suffered severe nausea. But so did twenty-five in the placebo contingent – three of whose muscles were found to have atrophied, like those of eleven AZT-treated men. Now that we know about the unblinding of the study, the mystery resolves. Many in the placebo group were being poisoned by AZT too. In the terrified hysterical atmosphere, everybody wanted a chance to live, a chance to take the new drug – a sentiment voiced by Pascal de Block, diagnosed HIV-positive, in the BBC Panorama documentary *A Ray of Hope*. De Block said, 'I was desperate to sort of cling on to anything that would bring me life or that would somehow sustain my life.' Such as AZT, advertised as 'a Ray of Hope for us all … Retrovir is a major step forward, our first weapon against this deadly virus.'

Fact is the Phase II trial was a total mess. None other than Martin Delaney, president of the drug industry-funded, ARV-promoting organization Project Inform in San Francisco, flayed the 'multicenter clinical trials of AZT [as] perhaps the sloppiest, most poorly controlled trials ever to serve as the basis for an FDA licensing approval'.

On the strength of the Phase II study Burroughs Wellcome applied to the FDA for a licence to market AZT as an AIDS drug. The FDA appointed a nominally independent panel to review the data. How independent it was you can decide from the fact that some of its members were in the company's pay as consultants involved in the AZT trial whose data were on the table for consideration. The panel sat on 16 January 1987. In 'Sins of Omission: The AZT Scandal' Celia Farber related panel chairman Itzak Brook's account to her of how the day went:

> There was not enough data, not enough followup. Many of the questions we asked the company were answered by, "We have not analyzed the data yet," or "We do not know". I felt that there was some promising data [*the impressive mortality figures*], but I was very worried about the price being paid for it. The side effects were so very severe. It was chemotherapy. Patients were going to need blood transfusions. That's very serious.

Indeed, the toxicity of AZT was so severe, said Cooper at the hearing, that licensing the drug would mean a 'significant and potentially dangerous departure from our normal toxicology requirements', particularly since she'd noted in her review that 'The majority of patients randomized to receive AZT in this trial experienced significant toxicity.' This was an 'under-

statement,' thought Lauritsen, 'considering that many AZT patients were treated with the drug for only a few weeks.' Lauritsen was referring to another critical flaw in the trial: according to Cooper's report, twenty-three of the AZT-treated group were on the drug for less than four weeks, and forty-seven for less than twelve, yet they were counted in among the rest, officially on it for seventeen weeks. Had this bunch, close to half the AZT group, been on the drug for as long as the others, the total mortality tally among the AZT group would certainly have been very much higher.

In no other clinical trial were the wonderful results of Fischl's Phase II study ever reproduced. Not in another big one that followed, reported by Creagh-Kirk et al. in the *Journal of the American Medical Association* in November 1988: 'Survival Experience Among Patients With AIDS Receiving Zidovudine: Follow-up of patients in a compassionate plea program', another mess in which the researchers lost track of fully one quarter of their test subjects – so could hardly comment on how well people did on the drug, being unable to say how many had died out of sight. But the alleged life-saving efficacy of AZT reported in that useless study still turned out nowhere near as terrific as the Phase II trial suggested. In short, the Phase II numbers were too good to be true, something discovered over and over in other trials, such as in a similar one in France at the Claude Bernhard Hospital, discussed in *Debating AZT,* which returned contradictory findings. And 'A controlled trial of early versus late treatment with zidovudine in symptomatic human immunodeficiency virus infection: Results of the Veterans Affairs Cooperative Study', a big one conducted over three years by Hamilton et al. and reported in the *New England Journal of Medicine* in February 1992, found AZT did not have any life extending benefits, and that as

Shenton summarised it, 'those who took it longest got sicker and died quicker'. Hamilton confirmed to her on camera in her documentary *AZT: Cause for Concern*: 'I think it is self-evident that our study does not provide the kind of benefit that everyone wished for.' He dismissed the notion that AZT affords 'quality of life' to those treated with it:

> There has been no formal demonstration of quality of life. … In fact the only study that has been done on this point and published to my knowledge has failed to demonstrate an improvement in quality of life.

Hamilton was referring to the findings of Wu et al. in 'Functional status and well-being in a placebo-controlled trial of zidovudine in early symptomatic HIV infection' reported the *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* in May 1993 that 'patients on AZT had an inferior quality of life compared to those on a placebo in terms of overall health, well-being, energy, mental health and pain' (Shenton's paraphrase). Hamilton was right about Wu's study being the only one reported at the time. A few months later, however, Lenderking et al. backed Wu up in a most important study, to which we'll be returning shortly.

Apart from its superlative efficiency at killing cells, specialist FDA toxicologist Harvey Chernov pointed out in his *Review & Evaluation of Pharmacology and Toxicology Data* report that AZT 'was at least as active … a carcinogen … as the positive control material, methylcholanthrene'. This is to say AZT causes cancer as effectively as a known carcinogen used to induce cancer in research laboratories. Chernov recommended against the licensing of AZT accordingly, adding that 'the full preclinical toxicological profile is far from complete … The available data are insufficient to support FDA approval.' No one but Brook

was paying attention. He told the BBC journalists investigating AZT for their *Ray of Hope* exposé:

> I had serious doubts whether we had all the information we needed about toxicity, about the dose, and even how effective it was. And I felt we needed a few more months to get answers from the company.

Burroughs Wellcome research director David Barry didn't like the sound of that. Based on the impressive mortality data, he'd assumed prompt approval was a foregone conclusion. Brook's suggestion that the panel be circumspect and take more time over the licence application caused his company 'great chagrin,' he said. The cost of preparation for the approval process had been

> a tremendous burden to us. … we have invested more than $80 million … in the program so far. … We would definitely prefer not to continue that program as it is for any significant period of time.

Brook saw through this: 'the implication … was like telling us approve it now or never.' Indeed, put to Barry by the BBC journalists that he was 'consciously putting pressure on the committee for a quick approval', he frankly admitted it: 'Yes, of course.'

As the panel wavered, worrying about the evident extreme toxicity of the drug, and unimpressed by the pressure Barry was applying, Burroughs Wellcome drew a secret ace. Brook told Farber:

> The committee was tending to agree with me that we should wait a little bit, be more cautious. But once the FDA realized we were intending to reject it, they applied political pressure. At about 4 p.m., the head of

> the FDA's Center for Drugs and Biologics asked permission to speak, which is extremely unusual. [*This was Paul Parkman, with whom Barry had co-written a paper while they were office pals in the FDA, before Barry switched jobs for the big salary and stock options*.] Usually they leave us alone. But he said to us, 'Look, if you approve the drug, we can assure you that we will work together with Burroughs Wellcome and make sure the drug is given to the right people.' It was like saying, 'Please do it.'

Brook told Bruce Nussbaum, author of *Good Intentions: How Big Business and the Medical Establishment are Corrupting the Fight Against AIDS* that until that point 'the tide was against approval'. Since the FDA had no inherent interest in seeing any particular drug approved, you can put money down that the manufacturer had placed a couple of calls to the top to engineer the pep talk saving the day. Brook himself drew that conclusion: 'I think that behind the scenes, something definitely happened.' Brook didn't buy Parkman's pitch and voted against approval. But the others all raised their hands, Cooper included. In his book Nussbaum recounts in detail the proceedings of the panel meeting from the minutes kept. It reads like a script from a Marx Brothers movie. Your eyes bulge. Like Harpo's. You can't believe it. Not so much when they were hammering on the toxicity and the missing and conflicting data, which they did all day, especially Cooper, but the quality of the discussion, the level of the debate thereafter.

The decision to approve AZT was a happy one for stock investors. Rapidly rising in anticipation of approval, Burroughs Wellcome share prices thereafter doubled. AZT was formally licensed on 20 March 1987, after a 'review and approval', according to a Public Health Service press release, 'accomplished

within less than four months – one of the shortest approval actions on record'.

Just four weeks later, Lauritsen tells us, ten per cent of the AZT-treated were dead. Duesberg and Rasnick report that by eighteen months the figure had climbed to thirty-two per cent. According to Farber all original test subjects on AZT were dead by the end of 1989. Death was never intended as end-point criterion for the assessment of drug efficacy in the Phase II study, with the result that causes of death were frequently not positively identified and recorded. The reports consequently abounded in speculations and presumptive diagnoses, thereby masking fatal drug intoxication as a cause of death. Nobody thought to biopsy the tissues of the dead to see whether they'd died of muscle rot, an epidemic of which broke out among HIV-positives after AZT was approved, along with neurological damage, resulting in what AIDS experts call AIDS dementia. Neither of which is any coincidence to scientists who've investigated how well AZT poisons off muscle and nerve cells. (Some leading studies are reviewed in *Debating AZT*.)

A week after the licensing trial was terminated an FDA press release reported the approval of a special dispensation allowing 'expanded distribution of the drug to AIDS patients who had been shown to benefit from AZT in the controlled trial'. Eighteen months later, thirty-two per cent of the subjects in the original placebo group now on AZT had joined the original AZT-treated group in Heaven. (The data you can find in 'Prolonged zidovudine therapy in patients with AIDS and AIDS-related complex' by Fischl et al. in the *Journal of the American Medical Association* in November 1989.)

Lauritsen reports that on 17 January 1990, three years after it approved AZT, the FDA announced a new officially recom-

mended AZT treatment dose of 600 mg daily, half of its previous recommendation of 1200 mg, although doses of 1500 mg and 1800 mg were being routinely prescribed too:

> Health and Human Services Secretary Louis Sullivan said in a statement that the change 'means that fewer patients may have to discontinue AZT therapy because of serious side effects.'

(In South Africa they never got the message; the AZT package insert still recommends mediaeval doses of up to 1500 mg of AZT daily.) According to Sullivan the new dose recommendations were based on 'preliminary findings' that half as much was as effective as the former full dose. Nobody got to see them, because they hadn't been published and never were. Lauritsen commented:

> According to those 'preliminary findings', nearly half of those receiving the high dose (1200 milligrams) had side effects that were so serious that they had to discontinue AZT treatment. At the same time, fully a quarter of those receiving the low dose also had to discontinue treatment, for the same reasons.

This then was how AZT was licensed under the most 'stringent regulations' in the US as a treatment for sick people diagnosed with AIDS. In no time at all AZT was being prescribed to HIV-positive people in perfect health too – a treatment trend that began to set in with all the panic almost as soon as AZT came onto the market, but which was officially sanctioned by the FDA on 30 January 1990 when it recommended AZT administration to anyone with a CD4 cell count of less than 500, no matter how healthy.

The study founding the FDA's new treatment indication for AZT, 'Zidovudine in Asymptomatic Human Immuno-defi-

ciency Virus Infection: A Controlled Trial in Persons with Fewer than 500 CD4-Positive Cells per Cubic Millimeter', by Volberding et al., was eventually published in the *New England Journal of Medicine* in April 1990. It was another abortion – in both senses. Lauritsen attended a 'State of the Art Conference on AZT Therapy for Early HIV Infection' in Washington on 3 March 1990, at which Volberding publicly admitted to 'a strong suspicion' that study participants knew who was on the drug and who wasn't. Steven Epstein mentions in *Impure Science: AIDS, Activism and the Politics of Knowledge* that when challenged about the 'non-compliance' problem in the trial – patients not taking AZT daily in terms of the trial design, i.e. taking drug treatment holidays – Volberding's answer was that this actually buttressed the findings since it 'would tend to give results that underestimate the true effect of zidovudine'. He was right about that, but in a sense he didn't think of: the extent of AZT's toxicity would have been masked – and Volberding's claim that AZT was insignificantly toxic was a big selling point to the FDA. When the latter approved it for HIV-positive asymptomatics, thereby expanding the market for AZT tenfold, 'the stock price of parent company Wellcome plc [got an instant lift of] 1.4 billion pounds'.

Poking around the basic flaws of this study, ACGT 019, would be tedious; it's surely enough to point out that the Concorde trial, superior in every respect – in scale, duration, control, completion – refuted the Volberding study outright. And that when William Lenderking of the Harvard School of Public Health put together a team, Volberding included, to reappraise the study, a whole set of different conclusions were arrived at. In *AIDS: The Failure of Contemporary Science* Neville Hodgkinson quotes American AIDS research boss Anthony Fauci, director of the National Institute of Allergy and Infec-

tious Diseases, saying in a press statement in August 1989, after the premature termination of Volberding's ACGT 019 trial:

> This study has clearly demonstrated that early treatment with [AZT] can slow disease progression without significant side effects in HIV-infected persons with fewer than 500 T4 cells who do not yet have symptoms.

But as Hodgkinson noted: 'Four and a half years later, however, a new analysis of the trial data reached a similar conclusion to Concorde: that AZT was essentially useless.' Moreover, as compared with what Volberding and Fauci had claimed about them, a 'very different picture' emerged 'after investigators paid more attention to the drug's side-effects'. Revisiting Volberding's data, Lenderking et al. concluded in 'Evaluation of the Quality of Life Associated with Zidovudine Treatment in Asymptomatic Human Immunodeficiency Virus Infection' published in the *New England Journal of Medicine* in March 1994:

> For asymptomatic patients treated with 500 mg of zidovudine, a reduction in quality of life due to severe side effects of therapy ['life-threatening in some cases'] approximately equals the increase in the quality of life associated with a delay in the progression of HIV disease.

What 'AIDS experts' like these mean by 'quality of life' was clarified by their colleague Andrew Carr in an article he wrote for *Lancet* in the first week of July 2002 (to which we'll later return for a closer look):

> Patients prevented from dying or developing AIDS by HAART [*assuming they are*] can be thought of as having an increased quality of life. The same cannot be said,

> however, for asymptomatic patients at low risk of AIDS. And yet, as with adherence, quality of life was reported in only two of the 23 HAART studies; perhaps not an unexpected figure in view of the fact that only 4% of clinical studies in any medical discipline report data for quality of life [*in the normal sense of the expression*].

Preliminary to his re-analysis and debunk of two more junk trials, the Australian European Collaborative Group Study and the San Francisco Men's Health Study, purporting to show benefits from AZT treatment among HIV-positive asymptomatics with CD4 cell counts above 500/mm^3, Malcolm Zaretsky summarised the Lenderking findings in plainer language in *Genetica* (96(3)) in 1995:

> the harmful effects of AZT on quality of life, concomitants of its toxicity, resulted in no net benefits to these patients [with CD4 cell counts below 500/mm^3 at the start of the trial].

The Concorde trial results published in *Lancet* in April 1994 showed that treating asymptomatic HIV-positives with AZT has no benefits and does not 'delay progression of HIV disease' as Volberding claimed and Lenderking believed. So if we go back to Lenderking's conclusion, and cut out the bad bit, what we're left with is the fact that AZT is completely useless as a medicine, and what's more it's so exceptionally toxic that it can kill you.

No, said GlaxoSmithKline, 'AZT has extended and improved the quality of life of millions of people living with HIV/AIDS around the globe.' It offers you 'A world of antiretroviral experience.'

Is AZT antiretroviral?

GlaxoSmithKline describes AZT's 'Mechanism of Action' in its 2008 'Full Prescribing Information' like this:

> Zidovudine is a synthetic nucleoside analogue. Intracellularly, zidovudine is phosphorylated to its active 5′-triphosphate metabolite, zidovudine triphosphate (ZDV-TP). The principal mode of action of ZDV-TP is inhibition of reverse transcriptase (RT) via DNA chain termination after incorporation of the nucleotide analogue.

What GlaxoSmithKline means by this is that after it's swallowed, AZT gets into our cells and is converted inside them into AZT-TP. In this 'active' form it resembles triphosphylated thymidine (TTP), one of the building blocks of DNA, and this enables it to fake its way into a growing viral DNA chain in its place, terminating it when it does so. This is because AZT lacks the biochemical link that enables further DNA building blocks to join it. So once AZT-TP gets into a DNA chain, it will end it. So the theory goes.

By describing AZT-TP's 'principal mode of action' as 'inhibition of reverse transcriptase', GlaxoSmithKline means to say that it prevents viral RNA changing into DNA by reverse transcription and thus stops the infection of new cells.

Before AZT was rushed to the market as an AIDS drug in 1987, a research team including scientists from the manufacturer's own laboratories investigated the minimum concentration of activated AZT necessary to reduce viral 'retrotranscription' inside our cells by half. The study, reported in November 1986 by Furman et al. in *Proceedings of the National*

Academy of Sciences of the United States of America, found that the inhibition concentration ('IC50') of AZTTP is 0.7 micromolar. This is to say the researchers established the low-water mark for drug efficacy according to the conventions of their business, the minimum level of AZT-TP necessary for it to have a significant antiviral effect. The experiments were performed in petri dishes in entirely artificial conditions, quite unlike what goes on in our bodies, where, for reasons too many and complex to recount here, a very much higher concentration AZT-TP than that would be necessary. But to date, no one has repeated the study in vitro, let alone determined the IC50 of AZTTP in vivo, so 0.7μM remains the only figure we have to go on. Bear in mind though that it's unrealistically low, and by a long shot too.

Not until 1991 did it enter anybody's head to look at the extent to which AZT is triphosphorylated inside our cells – in real life as opposed to in test tubes. Apart from the first botched study, every one of about two dozen studies that followed consistently returned findings revealing that AZT is not triphosphorylated to levels anywhere near the activated drug's IC50 – with the best-designed and executed studies of the lot reporting intracellular AZT-TP concentrations of ten-even 100-fold below it. And even though the dismally low level to which AZT is triphosphorylated in the body had often drawn comment from these researchers, none thought to compare all these AZT-TP in vivo data with the drug's IC50.

In May 1999 a nuclear physicist in the Department of Medical Physics and Engineering at Royal Perth Hospital in Australia, Eleni Papadopulos-Eleopulos, and several co-authors published a monumental review of the literature on the molecular pharmacology of AZT in a special supplement to *Current Medical Research and Opinion*. Analysing the manufac-

turer's claims for AZT, they pointed out that taken as a medicine it cannot possibly be antiretroviral because it's metabolised in the body into its active form to miniscule levels only, way below the minimum concentration necessary for it to act effectively as a viral DNA chain terminator. Which sounds improbable to be sure, since nearly everybody knows that AZT zaps HIV. Why, if it sold about a billion dollars worth in 2000 alone, it must do. Actually it doesn't.

According to AIDS experts, HIV infection levels can be monitored directly over time by measuring levels of what they call viral DNA (viral burden) and viral RNA (viral load). There are a couple of other indices too, but these are the main ones. Papadopulos-Eleopulos noted that every single study (and more have since come in) investigating the effect of AZT administration on pro-viral DNA has found that it hasn't any. Which means that AZT does not terminate it. Similarly, weighed by the criteria for efficacy set by leading American and English AIDS clinicians, AZT has no effect on viral load worth mentioning. And none on any other conventional index of HIV infection levels. From which the authors drew the astounding yet long obvious conclusion:

> A critical analysis of the presently available data ... shows there is neither theoretical nor experimental evidence which proves that AZT, used either alone or in combination with other drugs, has any [anti-HIV] effect.

Remarkably, GlaxoSmithKline admits this frankly in its 'Product Information' advisory on AZT:

> The relationship between in vitro susceptibility of HIV to [AZT] and the inhibition of HIV replication in hu-

> mans or clinical response to therapy has not been established.

Yes indeed. Papadopulos-Eleopulos concluded accordingly:

> Based on all these data it is difficult if not impossible to explain why AZT was introduced and still remains the most widely recommended and used anti-HIV drug.

Aside from not working as claimed, there's another reason. Like arsenic, once universally popular among doctors for injecting into people diagnosed with their useless Wassermann test as infected with syphilis, AZT, triphosphorylated or not, is very poisonous to all cells it reaches, as Papadopulos-Eleopulos noted:

> the scientific literature does elucidate … a number of biochemical mechanisms which predicate the likelihood of widespread, serious toxicity from use of this drug. [The continued administration of AZT] either alone or in combination … to HIV sero-positive or AIDS patients warrants urgent revision.

Indeed, the label on bottles of just 25 milligrams of AZT supplied to research laboratories bears a skull and crossbones set against a bright orange stripe to signify exceptionally dangerous chemical hazard, and reads,

> TOXIC Toxic to inhalation, in contact with skin and if swallowed. Target organ(s) Blood Bone marrow. If you feel unwell, seek medical advice (show the label where possible). Wear suitable protective clothing.

On GlaxoSmithKline's advice, doctors typically dose their patients these days with twenty times as much – along with simi-

lar drugs too – every day until they die. Which, if they stay on them, they invariably do. Is this surprising?

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