

# POISONING OUR CHILDREN

AZT in pregnancy

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Anthony Brink

**Open books**

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## **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](http://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); The trouble with nevirapine (2008); and RUDE LETTERS and Introducing AZT: 'A world of antiretroviral experience' in press. In recognition of his expertise in ARV pharmacology, he was awarded an honorary co-authorship of a scientific monograph by Papadopoulos-Eleopoulos et al., *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence* (Perth, 2001). His forthcoming book *'Just say yes, Mr President': Mbeki and AIDS* will be a comprehensive history of the AIDS treatment and causation controversies in South Africa, and a multidisciplinary interrogation and deconstruction of their medical and ideological foundations. His work has been translated into Spanish, Portuguese, French, Russian, Italian, German, and Dutch.*

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## Preface

*What do you do if ... university people, professors and scientists ... haven't read ... won't read? What do you do?*

President Thabo Mbeki

*Sunday Times*, 6 February 2000

On 28 October 1999, after reading the manuscript of my book *Debating AZT: Questions of safety and utility*\* and proceeding to re-search the drug further himself, President Thabo Mbeki made an extraordinary announcement in Parliament's National Council of Provinces:

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 ... to go into all these matters so that ... we ourselves, including our country's medical authorities, are certain of where the truth lies.

Since it was – still is – almost universally believed that AZT is a safe and effective drug for preventing African mothers from infecting their babies with HIV (the virus Western medical experts say they get from loving their husbands and/or their boyfriends), and the government had been under pressure to spend billions of rands on buying it for this purpose, Mbeki's statements triggered a local and international furore. 'The President has been gravely misinformed,' claimed AZT manufacturer GlaxoWellcome (now Glaxo-SmithKline), and everyone agreed.

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\* Published as *Debating AZT: Mbeki and the AIDS drug controversy* (Open books, 2001), and online at [www.tig.org.za](http://www.tig.org.za).

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Taking no account of key research papers reporting the serious toxicity of AZT – especially for unborn and newly born children – the Medicines Control Council (MCC) hammed the enquiry Mbeki ordered and suggested that he'd raised a false alarm.

A few months later the call on the government to supply AZT to pregnant women switched to nevirapine instead. Citing the results of HIVNET 012, a single, small-scale study conducted in Uganda, AIDS doctors, activists and journalists claimed that a single magic-bullet dose of nevirapine given to a woman in labour and to her newborn baby could save the child from being infected and killed by HIV. So why, they asked, was the government dragging its heels by running a cautious pilot study to establish whether the drug was safe and effective, and not providing it to all HIV-positive mothers and babies in public hospital maternity wards across the country?

Cheered on by all the media, the Treatment Action Campaign took its demands to court in August 2001 and won an order in December directing the government abandon its UN-AIDS approved pilot study and to supply the drug across the board without further ado.

In early May 2002, on the eve of the government's appeal to the Constitutional Court against this order, the MCC revealed that it was reviewing its special provisional registration of nevirapine as a perinatal anti-HIV prophylactic in view of the fact that its manufacturer Boehringer Ingelheim had a few weeks earlier withdrawn its application to register the drug with the the US Food and Drug Administration for this special indication, after the emergence of what the FDA described as 'potentially quite serious problems' with the conduct of the Ugandan HIVNET 012 nevirapine trial. Unfazed by this development, the learned justices of the Constitutional Court unanimously dismissed the government's appeal in July – never mind that HIVNET 012 had been the lynchpin of the entire case.

A year later, in July 2003, the MCC fell in with the FDA and rejected the corrupt HIVNET 012 trial too, putting Boehringer

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Ingelheim on terms to adduce other clinical trial evidence showing nevirapine to be safe and effective, but allowing its continued administration to women in labour and their babies in the meanwhile, without any evidence that it was.

The time was ripe for an information campaign to counter the TAC's propagandizing, politicking and shilling for the pharmaceutical industry in South Africa. In November 2002, at a convention meeting at a hotel in Johannesburg, I proposed the formation of the Treatment Information Group, and I held a second meeting in Cape Town a few months later, but my professional situation in the law courts in the Eastern Cape at the time was a major practical hindrance, and it was only when I relocated to Cape Town in 2004 that I was really able to get going.

The period afforded Boehringer Ingelheim to justify the continued special registration of nevirapine for perinatal use had long come and gone without any action or decision by the MCC, when in June 2004, as chairman of the TIG, I asked it how it was getting along with its review (the letter is included as Appendix 2 in *The trouble with nevirapine*). The MCC's stupefying response was to issue a public statement on 12 July that it no longer supported the use of nevirapine administered solo, but that it now recommended that pregnant women henceforth be given AZT as well.

Not only was the MCC still countenancing the use of AZT in pregnancy after botching the enquiry Mbeki had requested, it was now actively recommending that it be given to pregnant women in South Africa, mostly black, mostly poor, notwithstanding the subsequent publication of many more research papers reporting the serious harm the drug causes unborn and newly born children.

Here was the MCC ducking the problem that there existed no good clinical trial data to support its continued registration of nevirapine for perinatal use and avoiding the political heat in store for it should it accordingly deregister the drug for this indication. Here was the MCC stepping way outside its statutory jurisdiction to licence pharmaceutical drugs, and proffering a spe-

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cific treatment recommendation in vaunting a particular combination of them.

Noting the MCC's 'pronouncement ... on problems of resistance in the usage of nevirapine as a monotherapy in preventing mother-to-child transmission of HIV' – as if 'resistance' was the real issue – the Cabinet issued a statement on 21 July, recording that

The Department of Health is reviewing the information in order to make a recommendation to Cabinet on the future course of action, taking into account information demonstrating that combined antiretroviral therapy is more effective and less risky. In the meantime, nevirapine monotherapy will be provided in public hospitals as is currently the practice, ensuring that mothers are given all the necessary facts so they can make an informed choice.

My several letters to the MCC canvassing the research literature on how AZT harms unborn and newly born children are collected in this book. The MCC, one of its members confided to Health Minister Dr Tshabalala-Msimang, was 'amazed' by my 'detailed research,' and had been 'unaware' of the data I canvassed in them.

On 22 November 2004, referring to my first two letters only, MCC chairman Professor Peter Eagles wrote to inform me that an 'independent expert' had been engaged to consider them. But the look of it was that faced with the horrible research data brought to their attention in my letters, the small clique of anonymous, secretive, unaccountable pharmaceutical industry sweethearts on the MCC sub-committee who recommended the administration of AZT to African women and their babies would not have the brains, the courage, or the integrity to reverse their blunder, because a public climb-down would be professionally humiliating – and difficult too, considering the pervasive influence of the pharmaceutical industry at medical school campuses, where the MCC's decision-making 'external consultants' teach and make



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fortunes running US government- and drug industry-sponsored drug trials on Africans. And so it turned out.

On 26 November 2004, four days after Eagles's letter, the *Mail&Guardian* ran an invited contribution I submitted for its World AIDS Day supplement, entitled 'Why Should South Africans Continue to be Poisoned by AZT?' The nut of it read:

- Hundreds of studies have found that AZT is profoundly toxic to all cells of the human body, and particularly to the blood cells of our immune system.
- Numerous studies have found that children exposed to AZT in the womb suffer brain damage, neurological disorders, paralysis, spasticity, mental retardation, epilepsy, other serious diseases and early death.

The publication of these unpleasant statements caused a tremendous outcry. Editor Ferial Haffajee promised the following week never to publish anything like them ever again (the amazing saga is recounted in my letter to the newspaper's owner Trevor Ncube, included in *RUDE LETTERS*). The TAC got them banned by the Advertising Standards Authority (the full story is told at [www.tig.org.za](http://www.tig.org.za)). Professor Robin Wood, co-director of the Desmond Tutu HIV Centre at the University of Cape Town, responded in the newspapers and an affidavit in the Cape High Court, claiming that

the toxicity of [AZT and similar drugs] is very low indeed ... 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.

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After reading the contrary medical research findings canvassed in our letters and endnotes, you'll shudder to think this bloke is in charge of teaching medical students. Likewise when you read his UCT colleague Professor Cecil Karabus at the Red Cross Children's Hospital boasting in his letter to the *Mail&Guardian* on 18 November 2005:

In my reading of the mainstream literature I have failed to come across the 'hundreds of studies indicating the profound toxicity to all 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?

Reading the ignorant effusions of white medical experts like these, it will not surprise you to learn that at the University of Cape Town, where medical academics have been particularly vocal in supporting the administration of ARVs to pregnant African women, their dean is on Merck's payroll via a front foundation that it funds: the Enhancing Care Initiative; GlaxoSmithKline has endowed a medical professor's chair; and need I say more about UCT's Boehringer Ingelheim Lung Institute?

On the defensive over its advocacy of nevirapine in the light of Associated Press's revelations in mid-December 2004 concerning the grossly corrupt manner in which HIVNET 012 had been conducted and the suppression of the serious toxicity data (the crime is recounted in *The trouble with nevirapine*), the TAC reaffirmed AZT to be its 'drug of choice' for pregnant women, and Dr Ashraf Coovadia, paediatric HIV clinic chief at Johannesburg's Coronation Mother and Child Hospital, agreed. What 'the Rolls Royce' of AIDS drugs, as he calls AZT, does to unborn and newly born children is the subject of this book.

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After the nevirapine interlude, the pressure on the government to supply AZT to pregnant African women and their babies resumed. On 18 July 2005 the *Cape Times* reported that a study jointly conducted by the US Centers for Disease Control and the South African National Institute of Communicable Diseases found that

About 80% of women with HIV who receive a single dose of nevirapine develop resistance – double what was initially believed. [This] reinforces concerns about the suitability of nevirapine in preventing mother to child transmission

and pumped up the case for using AZT as well.

A couple of months later, the TAC formally resolved at its national congress on 25 September:

Government must introduce ... the better AZT and nevirapine regimen ... for pregnant women [in place of] the single-dose nevirapine regimen currently in use throughout most of the country.

A month after that, on 28 October 2005, nearly a year after Eagles's assurance that an 'independent expert' had been appointed to consider the AZT foetal and neonatal toxicity data I'd brought to his MCC's attention, and six years to the day since Mbeki called attention to the toxicity of AZT in Parliament, Eagles wrote to me again to say: no worries, it's fine.

With the backing of the MCC on this, further litigation by the TAC to compel the government to provide AZT to pregnant women and their babies looked inevitable.

Journalists rallied to the TAC's crusade: 'Government's Aids policy hinders treatment' claimed the title of an article in the *Star* on 25 January 2007, quoting Coovadia complaining to the Wits Aids Research Symposium that

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South Africa has the means to reduce the number of children born infected with HIV to less than 2 percent – but doctors feel ‘hamstrung’ by government policy, which does not conform to international guidelines. ‘What we are providing is sub-standard treatment that is less than what the World Health Organisation (WHO) guidelines stipulate.’ Coovadia explained that the WHO had updated its treatment guidelines to include the use of AZT on top of the nevirapine dose, particularly in countries with adequate resources. ‘By not instituting these new guidelines, doctors are finding themselves in a moral and ethical dilemma because we are offering our patients sub-standard treatment. You cannot believe how frustrating this is,’ he said. ‘Reducing transmission to babies is well within our reach. There is a growing sense of frustration with the lack of haste in changing the policy.’ Coovadia said the government, and particularly the department of health, was well aware of the scientific evidence supporting the introduction of a better regimen for preventing a mother infecting her baby, but had not acted on it.

‘Pretoria Dithers While Babies Are Infected’ wrote Health-e editor Kerry Cullinan at the head of her piece on 29 July 2007. I’ll quote from it at length, because as an epitome of pharmaceutical industry propaganda, it’s an historical testimonial to the splenetically righteous wrong-headedness, the perversity, and the sort of frenetic mythmaking that went down in the Age of AIDS and marshalled public opinion behind AZT:

Despite a number of hospitals being ready to implement ‘dual therapy’ to prevent mother-to-child HIV infection, the national Department of Health has not yet made it national policy.

The Department of Health is stalling the introduction of treatment that can prevent over 90% of pregnant HIV positive women from infecting their babies. Currently, up

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to 30 000 babies are being infected with HIV by their mothers in KwaZulu-Natal alone each year.

A leading paediatrician has described the delay as 'shameful', while the Treatment Action Campaign (TAC) says it is considering court action to force government to expand its programme.

At present, national treatment for the prevention of mother-to-child transmission (PMTCT) consists of one dose of nevirapine to women when they are in labour and one dose to their babies within 72 hours of birth.

However, a year ago the World Health Organisation recommended that pregnant HIV positive women in developing countries should get 'dual therapy' comprising of nevirapine and a short course of AZT to protect their babies from HIV infection.

The Western Cape has been using both nevirapine and AZT since May 2004, and has managed to reduce its mother-to-child HIV infection rate to around 8%.

In KwaZulu-Natal with its nevirapine-only regimen, 22% of HIV positive mothers are infecting their babies with HIV.

'In KwaZulu-Natal alone, 20 000 to 30 000 children are being infected with HIV each year and half of them will need antiretroviral drugs by the age of 12 months,' said a frustrated Professor Nigel Rollins, head of the Centre for Maternal and Child Health at the University of KwaZulu-Natal.

'The delay in introducing dual therapy is shameful. How can women and children be denied the right to treatment when the people on the ground are saying it is possible to implement this?'

South Africa is one of only nine countries in the world where the child mortality rate is increasing instead of decreasing, mainly as a result of children dying of AIDS-related illnesses.

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The Medical Research Council, the National Essential Drugs Committee and the Medicines Control Council have all recommended to government that the country adopt dual therapy.

Last December, many doctors working in government hospitals say they were told to prepare themselves for the imminent introduction of dual therapy.

But the National Health Council – made up of the health minister, provincial health MECs and heads of department – has consistently failed to make dual therapy national policy or even set up a task team to investigate its introduction, even though it has discussed the issue.

Health spokesperson Sibani Mngadi confirmed that the NHC had discussed dual therapy. However, he refused to be drawn on whether the department intended to change its protocol to dual therapy or when this might happen.

‘The National Strategic Plan, adopted by Cabinet, has made room for the introduction of dual therapy,’ said Mngadi.

But when asked if hospitals that were ready could introduce dual therapy, Mngadi said ‘ideally this should not be the case since overarching policies and guidelines stem from the national Department of Health’.

Many hospitals in KwaZulu-Natal and Gauteng are ready to implement the dual therapy. The Northern Cape’s provincial health department has already approved dual therapy, but is waiting for national government’s go-ahead before implementing it.

KwaZulu-Natal health spokesperson Leon Mbangwa said that while his province was preparing to introduce dual therapy, this would not be done ‘until we have received a national directive to do so’ as ‘it is not yet national policy to use dual therapy in South Africa’.

Dr Victor Fredlund confirmed that he had ‘been corresponding with the national and provincial departments

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for the past eight months about the desire of five hospitals in Umkhanyakude [in the far north of KwaZulu-Natal] to implement dual therapy’.

At present, Fredlund’s Mseleni Hospital is offering dual therapy to those patients who can afford to buy AZT.

Gauteng health spokesperson Zanele Mngadi simply said that dual therapy was ‘under review’ and ‘it is envisaged that a decision will be made in this regard soon’.

One Tshwane doctor who asked not to be named said his hospital had already started dual therapy as ‘we think it is better to have to say sorry afterwards than to ask permission’.

TAC spokesperson Nathan Geffen said that his organisation could not understand the delay, as ‘dual therapy will save the lives of babies and reduce the burden on the health system of caring for sick children’.

Geffen added that although it would prefer not to, the TAC was considering court action to compel government to introduce dual therapy. In 2003, the TAC succeeded in getting the courts to compel government to make nevirapine available to pregnant HIV positive women.

This week the Joint Civil Society Monitoring Forum, which represents over 20 health and civil society organisations, wrote to the health department and asked it to immediately allow provinces that were ready to offer dual therapy and to set up a task team to consider how best to implement the WHO recommendations on dual therapy.

‘There is no good public health reason to stall the implementation of dual therapy. It is not difficult to implement. If we are serious about preventing HIV, we must start by preventing babies from getting HIV,’ said Forum spokesperson Fatima Hassan.

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In May, Dr Francois Venter, president of the SA Clinicians Society, wrote to the SA National AIDS Council (SANAC) asking it to investigate the delay.

‘Several doctors and ARV managers working in both rural and urban environments have raised the issue that they have been promised updated guidelines repeatedly, but these have not been forthcoming,’ said Venter in his letter.

The new National HIV/AIDS Strategic Plan aims to reduce the rate of mother to child transmission to 5% by 2011.

Pregnant women with high viral loads and low CD4 counts (measure of immunity in the blood) are most likely to transmit HIV to their babies, but this risk can be substantially reduced by treating them with at least two anti-retroviral drugs to make them less infectious.

‘We will never cut the transmission rate to 5% with one dose of nevirapine. In the US and Europe, mother-to-child transmission has been reduced to around 2% with the use of two to three antiretroviral drugs,’ said Venter.

‘If we fix mother-to-child HIV transmission, we don’t have to expand child HIV treatment.’

On 27 September 2007 the TAC got the AIDS Law Project to hit Dr Tshabalala-Msimang with a letter of demand, reminding her that

at the South African National Aids Council (SANAC) plenary session held on 10 September 2007, the Department of Health committed itself to revising the national treatment guidelines to prevent mother-to-child transmission (PMTCT). The revision would, at the very least, be in line with the World Health Organisation (WHO) guidelines, which recommend administering dual or triple drug regimen, which is significantly more effective in reducing the rate of transmission of HIV from mother to



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child than the currently implemented single-dose regimen of Nevirapine (NVP).

The letter mentioned that

the Department of Health informed the SANAC meeting that the revision of the treatment guidelines would require the approval of the National Health Council (NHC), and that this is due to take place in November 2007.

And that at a

further consultation meeting ... held between various clinicians, paediatricians and obstetricians in South Africa and the Department of Health on 11 September 2007 ... the Department of Health committed itself to revising the treatment guidelines.

Implicitly threatening to force the issue in court, the attorneys demanded a date on which the Department of Health would be implementing the changes, which is to say start dosing pregnant African women and their babies with AZT.

The following month, on the fiftieth anniversary of the commencement of the thalidomide tragedy – October 1957 – I issued a press release about AZT in pregnancy, calling attention to the horrors ahead, but not a single editor or journalist in the country saw fit to pick up the lead – but then the newspapers had consistently promoted the drug from the beginning.

On 18 December, reacting to a Health Department media statement on the 1<sup>st</sup> announcing that 'Dual therapy for Prevention of Mother to Child Transmission of HIV should be implemented from the beginning of next year', I wrote a last-ditch appeal to Dr Tshabalala-Msimang to grant me an audience to present the foetal and neonatal toxicity data on AZT – but too late: I learned afterwards that a decision in principle to supply the drug to pregnant women and their babies had already been taken. Under TAC pressure the government had buckled; in the frenzied moral at-

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mosphere prevailing, it had evidently calculated that it wouldn't have stood a chance trying to hold the line in court against the country's self-billed human rights champions. With the judges all lined up behind them. Including in the Constitutional Court, where the learned justices had stacked one emotive myth on another in the nevirapine case – 'the prospects of the child surviving if infected are so slim ... the nature of the suffering so grave' – and all falling for the perfectly ridiculous idea that a single baptismal shot of nevirapine after birth would miraculously save the allegedly otherwise doomed little babies' lives. The Transvaal Provincial Division of the High Court in which the TAC was set to sue had already crooned its love for AZT on 24 March 2006 in a unanimous full-bench decision in *Costa Gazidis v the Minister of Public Services and Administration and others*:

Counsel for the respondents conceded that the decision not to supply AZT to HIV-positive mothers amounted to a conscious, deliberate and informed policy to sacrifice the life of babies that would contract HIV/AIDS because their mothers were not treated with AZT, in order to save the expense that would have had to be incurred if AZT was to be supplied to mothers suffering from the infection who were on the verge of giving birth. ... It is hardly surprising that some members of the medical profession and of the public at large would describe this policy as a murderous one.

Judges too, who believe one and all that AZT saves African babies from being killed by deadly germs festering in their mothers' vaginas, since that's what they read in the newspapers.

On 28 January 2008 Cullinan's Health-e whooped triumphantly in its headline, 'South Africa: Govt Finally Introduces AZT for HIV+ Mothers':

After years of stalling and much criticism from the HIV/AIDS sector, the Policy Committee of the National

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Health Council on Friday finally adopted new guidelines for the prevention of mother to child transmission (PMTCT). At the heart of the new policy is the addition of second antiretroviral drug, AZT, for pregnant women with HIV and their babies to the current treatment with nevirapine only. The announcement came two days after the Treatment Action Campaign, supported by the HIV Clinicians Society, condemned government inaction and said that over 60 000 infants were being infected each year by HIV, mainly as a result of an outdated drug regimen and an inadequate programme. ... Pregnant women enrolled in the programme will receive AZT from 28 weeks until labour and a single dose nevirapine during labour. Their babies will receive a single dose nevirapine and AZT for seven days. Where a mother has received AZT for less than four weeks of pregnancy, the infant receives AZT for 28 days.

On 5 March Health-e was again thrilled to report, 'DOH Presents Dual Therapy Plan to Parliament':

The extension of government's prevention of mother-to-child HIV transmission is on track, says Dr Nomonde Xundu, although no deadlines have been set. ... Dual therapy will see HIV-positive mothers and their newborn infants getting AZT to boost the efficacy of nevirapine ... 'It is important that we do everything we can to save babies in the meantime (even if not all the provinces are ready),' said [Health Director General Thami] Mseleku. He also disclosed that the guidelines had been updated because there 'is evidence in the world that this (new) policy needs to be implemented to ensure better results'.

It must have pained Mbeki to read his Health Director General talking just like TAC leader Zackie Achmat, claiming that AZT will 'save babies', and that there was 'evidence in the world' that

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when combined with nevirapine AZT gives 'better results' at doing so.

The report went on:

Deputy Director General Dr Nthari Matsau said ... one of the weakest areas of the PMTCT programme had been pharmacovigilance and that money had to be allocated to this area to ensure 'adverse events are recorded'. 'Yes, AZT is toxic, but for now we will give it ... The department has taken on this massive challenge (updated PMTCT programme) in terms of resource requirements and we are driven by the belief that we can reduce transmission if we do this,' Matsau said, adding that a further challenge would be to ensure that HIV negative babies remain negative and are not infected because of poor infant feeding practices.

Imagine Mbeki's further dismay on reading Mseleku's deputy nonchalantly conceding that 'AZT is toxic' to African mothers and their babies and that no adequate measures currently exist in South Africa to ensure 'adverse events are recorded' – such 'adverse events' (reported by Blanche et al. in *Lancet* 1999 Sep 25;354(9184):1084-9) as brain damage in the form of massive cortical necrosis, cortical blindness, epilepsy and spastic quadriplegia, that only became evident several months after birth, along with other 'severe biological or neurological abnormalities' that were picked up only with special testing because they weren't clinically apparent. Nonetheless, believing, as Mseleku does, that AZT 'reduce[s] transmission', Dr Matsau was happy to see African mothers and babies given the drug – adding her fond hope that mothers don't nourish their babies with their breast milk (a 'poor infant feeding practice', she called it), but that they should give them Nestlé formula milk from a bottle instead.

The report added that TAC members would be around to force pregnant African women to continue taking AZT week after

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week, and to give it to their babies no matter how sick it made them:

During her presentation [Health Department HIV/AIDS Unit director Dr Nomonde] Xundu acknowledged the presence of over 20 Treatment Action Campaign activists stating that she hoped the 'TAC will assist us with community based support for drug adherence'. Drug adherence support is an essential component of the updated PMTCT programme as AZT will be administered daily over a period of up to 28 weeks, depending on when a pregnant woman presents to the clinic.

In its statement back on 21 July 2004 the Cabinet expressed its concern that 'mothers are given all the necessary facts so they can make an informed choice' about whether to take AZT during their pregnancies and permit it to be given to their babies. But you can be sure none will be told of the horrible research findings published in the medical research literature and canvassed in my letters to the MCC – much less be informed that AZT is so extraordinarily poisonous that when the chemical company Sigma-Aldrich supplies as little as 25 mg of it for research use (that's one quarter the amount in single 100 mg capsule sold by Glaxo-SmithKline) the label on the bottle bears a skull and crossbones decal embossed on an orange stripe to signify deadly toxic chemical hazard, underscored by the warning 'Toxic' in six different languages, and spelt out:

TOXIC Toxic to inhalation, in contact with skin and if swallowed. Target organs: 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.

It is certain is that new Health Minister Barbara Hogan (appointed by President Kgalema Motlanthe on 25 September 2008) had been aware of this when telling the International AIDS Vac-

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cine Conference 2008 in Cape Town on 13 Oct: 'I want to emphasize that we will scale up mother to child transmission prevention programmes.' And repeating six weeks later on World AIDS Day, 1 December, at Sahara Stadium in Durban: 'We pledge to urgently scale up mother to child ARV treatment.'

And likewise, had Deputy President Baleka Mbete been aware of how harmful AZT and similar drugs are for unborn and newly born children – in South Africa, practically all African – she would never have written in *ANC Today* on 4 December:

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.

AB

Cape Town

15 December 2008

# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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Postnet Suite 273 Private Bag X1 Vlaeberg, Cape Town 8018

26 July 2004

The Registrar: Ms Precious Matsoso  
Medicines Control Council  
2<sup>nd</sup> Floor, Hallmark Building  
Cnr Andries and Vermeulen Streets  
Pretoria

Dear Ms Matsoso

**MCC review of its special registration of nevirapine for  
perinatal administration, and its recent recommendation  
that nevirapine be administered together with AZT**

We record that we have received no response or even acknowledgement of our letter\* to the MCC of the 22<sup>nd</sup> ultimo in the above matter, delivered by courier to your offices at 8h54 on the 24<sup>th</sup>. In the circumstances, we thought fit to make copies available to a wide spectrum of media and interested parties, including hard-copies hand-delivered to President Mbeki and National Minister of Health Dr Tshabalala-Msimang. At the latter's request, we have provided her with further copies of our first letter, together with sufficient copies of the instant one, for distribution to all members of Cabinet and all Provincial Health MECs.

We have taken note of the contents of the MCC's press statement of 12 July concerning the use of nevirapine to prevent mother to child transmission of HIV (pMTCT), following its meeting ten days earlier. (A copy is annexed for easy reference.) Regrettably, we must agree with the criticism of Professor James McIntyre, lead researcher at the Chris Hani-Baragwanath Hospi-

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\* Included in the appendices of *The trouble with nevirapine*.

tal Perinatal HIV Research Unit, that it is ‘confusing and unfortunately badly worded’. Indeed, we find it incoherent and incomprehensible.

It is evident that none of ‘the issues’ listed as having been ‘considered’ by the MCC during its ‘deliberations’, included any of the efficacy and safety questions raised in our letter and traversed in the papers referred to therein. Three of the four ‘issues’ that the MCC ‘considered’ were in fact one: the potential for drug ‘resistance’ emerging among mothers administered a single dose of nevirapine during labour – a matter that must obviously rank second to the primary issues of the efficacy and safety of the drug for babies for the prophylactic purpose intended.

The statement recalls that that ‘the approval of nevirapine’ for pMTCT ‘was conditional upon monitoring of resistance and its impact on efficacy’. In other words, in specially licensing the drug for pMTCT, the MCC accepted that its efficacy and safety had been established by HIVNET 012 (the ‘pivotal study’ as the MCC described it in its resolution of 25 July 2003) – but before granting the drug final approval in the form of unconditional registration for this special indication, the MCC sought assurance from Boehringer Ingelheim, in the form of further research data, that the use of the drug would not lead to the development of drug resistance.

It is evident from point ‘iv’ of the statement, in which the MCC records its ‘view ... that nevirapine monotherapy is less efficacious than combination regimens’, that the MCC’s ‘deliberations’ at its 2 July meeting proceeded from the premise that the efficacy of nevirapine given solo had been demonstrated – notwithstanding its resolution a year earlier to reject the pivotal study that had founded its special registration of nevirapine for pMTCT.

In issuing its ‘Recommendations on ARVs and MTCT prevention 2004’ (7 January 2004 draft, published online, hereinafter referred to as ‘the WHO Recommendations’), to which the MCC referred in point ‘iv’, the World Health Organisation also considered that the ‘efficacy [of] NVP alone in two single-dose regimens



to the mother and the infant ... has been demonstrated'. As authority for this claim, the WHO cites HIVNET 012 – thrown out by the US FDA in March 2002, and by the MCC in July 2003. The WHO also cites the local SAINT trial – expressly dismissed by the MCC in its July 2003 resolution, presumably because it does not meet the basic criteria for a clinical drug trial to be considered a pivotal study. Nowhere in any other drug regulatory jurisdiction is the SAINT trial regarded as up to standard as such.

We mentioned in our first letter that nevirapine is not considered proven safe and effective for administration to American women in labour and their newborn babies, and is not included in the US CDC's current guidelines for pMTCT. We draw your attention to the fact that nevirapine is likewise not recommended for this special indication for British mothers and babies in the United Kingdom, and the drug is not included in the current guidelines for pMTCT published by the British HIV Association (BHIVA) in October 2001. We reiterate: it is only on mothers and babies in the developing world that the US government (at the level of the State Department, no less) and officials of the WHO (under its sway) urge the drug.

The MCC refers in point 'iv' to a 'number of recent studies', including the WHO Recommendations, in support of its view that 'combination regimens' are more 'efficacious' than 'nevirapine monotherapy'. Apart from the latest combination-drug study by Lallemand et al., published in mid-July in the *New England Journal of Medicine*, the 'recent studies' purportedly supporting the use of AZT, 3TC and nevirapine in combination during pregnancy, labour and post-partem are cited in the WHO Recommendations as references 12-19.

We have reviewed these studies, as well as the latest one in the *NEMJ*. All of them share the following basic and fatally destructive methodological defects:

Mothers were incompetently diagnosed as HIV-infected with antibody tests (ELISA and sometimes Western Blot), manufactured and licensed for blood screening only – and not for diag-

nostic use – on account of their well-established non-specificity. No manufacturer of either type of antibody test kit claims that antibody reactivity ipso facto indicates infection with HIV. On the contrary, the medical literature abundantly establishes that it doesn't, but this is perhaps a matter falling less within the MCC's province than the Medical Research Council's – a matter that it has yet to examine.

Babies in the trials cited by the WHO, and the latest one in the *NEMJ*, were diagnosed as having been infected with HIV during pregnancy or birth by means of RNA-based tests utilising PCR technology – in some cases 'qualitative' tests, in others 'quantitative'. But the specificity of such tests is unascertained. Accordingly, in the case of the former, Roche Diagnostic Systems, Inc. explicitly cautions: 'For research use only. Not for use in diagnostic procedures.' And in the case of the latter: 'The Amplicor HIV-1 Monitor test is not intended to be used as a screening test for HIV or as a diagnostic test to confirm the presence of HIV infection.' These express contraindications for the use of the tests as diagnostic instruments have simply been ignored by the researchers who designed and conducted the MTCT studies under discussion – on the assumption, apparently, that RNA-based test readings of the type employed yield definitive diagnostic results, comparable with highly probative DNA matching in forensic applications. In fact this is not the case: such tests are so unreliably non-specific that they are not even permitted by their manufacturers, or the FDA, for commercial blood screening, let alone for making diagnoses in drug trials (or for any other diagnostic purpose).

It is so that in defiance of the manufacturer's explicit contraindication, and the limited, particular non-diagnostic purpose for which the FDA has licensed RNA assays for clinical use (therapeutic treatment response monitoring only), the US CDC inexplicably permits the use of RNA assays for determining HIV infection in babies – but only in the case of possible MTCT of HIV, and not in cases of suspected infection by blood transfusion or in other way, in which case the CDC reverts to its prohibition on the

use of RNA assays to determine whether babies are infected or not. But even this irrational and indefensible exception made by CDC officials does not extend to clinically diagnosing HIV infection among babies: the CDC supports the exceptional use of RNA assays in possible MTCT cases for 'surveillance purposes' only, and not for making a 'clinical diagnosis' of HIV infection.

Notwithstanding this, on the basis of clinical drug trial findings based on these all-but-meaningless test results, babies in the developing world are to be exposed in utero and post-partem on the advice of the WHO to exceedingly toxic chemicals, on the fallacious ground asserted by the MCC, and the WHO, that they have been shown to demonstrate anti-HIV prophylactic activity.

None of the pMTCT studies under discussion were double-blind, placebo-controlled trials of such quality and cogency as to qualify them as pivotal studies for drug licensing purposes in any First World country – or in any Developing World country like ours, in which, it is clear from the US NIH's final *Remonitoring Report* on its admittedly botched HIVNET 012 study, released to the MCC in April 2003, US health officials evidently believe lower standards for demonstrating the safety and efficacy of drugs should apply.

In the case of nevirapine in particular, therefore, we have the incredible situation in South Africa in which, having failed to make the grade as proven safe and effective when used alone perinatally, the drug has now been passed by the MCC for this special and especially dangerous indication provided that it is combined with another extremely toxic drug, AZT. This new treatment protocol 'recommended' by the MCC is clearly based squarely on the WHO Recommendations.

Before we address the disgraceful deficiencies of this grossly partisan, pro-pharmaceutical-cartel document from the WHO, we wish to remind the MCC of the quality of professional expertise emanating from that body, as illuminated by a report in the *New York Times* on 25 November 1999, following President Mbeki's order that the safety of AZT be investigated. "'To combat a fatal

disease, it is perfectly acceptable to use drugs slightly more toxic than an aspirin" ... said Dr. Joseph Perriens, who heads the care and support program of the United Nations AIDS program in Geneva.' Sigma Chemical Co. in the US takes a rather different view of the matter, evident from the labelling of AZT that it manufactures for research use. Alongside a skull and crossbones emblem, with 'Toxic' below it in six different languages, set against a bright orange stripe to signify deadly chemical hazard, the label on bottles containing as little as 25 mg cautions: '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 (show the label where possible). Wear suitable protective clothing.' (See enlarged photograph of AZT bottle annexed hereto. The bottle, in the possession of the writer, is available for inspection.)

The assumptions, methods and interpretation of the sort of MTCT drug studies cited by the WHO have been extensively critiqued by Papadopoulos-Eleopoulos et al. in the monograph\* and PowerPoint slideshow<sup>†</sup> mentioned in our first letter. Even more fundamentally, GlaxoSmithKline's basic claim that AZT acts as a chain terminator of proviral HIV DNA, and thereby works as an antiretroviral agent, was meticulously dismantled and debunked by the same core group of scientists in **A Critical Analysis of the Pharmacology of AZT and its Use in AIDS**, published as a special supplement to *Current Medical Research and Opinion* Vol. 15, 1999<sup>‡</sup>. In short, the drug does not achieve meaningful intracellular levels of its active form (AZT-TP) in vivo, and is therefore incapable of the therapeutic effect that its manufacturer GlaxoSmith-

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\* *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence* (online in 'Quick links' at [www.tig.org.za](http://www.tig.org.za))

<sup>†</sup> *A Critical Analysis of the Evidence Considered Proof that Nevirapine Prevents Mother-To-Child Transmission of HIV* (ditto)

<sup>‡</sup> Also online in 'Quick links' at [www.tig.org.za](http://www.tig.org.za).

## One

Kline claims for it. Nonetheless, AZT remains extremely toxic to all cells. The risk-benefit ratio is accordingly infinite.

With all due respect, it is inconceivable that the MCC's members read and comprehended the purport of these papers before issuing their latest drug combination recommendation for pMTCT, and it raises the problem identified by President Mbeki in an interview in the *Sunday Times* on 6 February 2000: Criticised by *Nature's* local correspondent Dr Michael Cherry for having ordered an enquiry into the safety of AZT the year before, the President responded by forwarding him a copy of Papadopoulos-Eleopoulos's et al. AZT pharmacology analysis to read. Cherry replied by requesting time to consult his colleagues before answering, admitting that he knew very little about the subject. Medical Research Council president (at the time) Dr William Makgoba had also reacted ignorantly to the President's stated concerns about the drug, saying, 'I've read nothing in the medical literature indicating that AZT should not be given to people' – shortly after the publication of the just-mentioned paper, and a host of severe toxicity reports, including gravely crippling and sometimes fatal foetal toxicity, in the preceding months. Remarking on their professional indolence and irresponsibility, President Mbeki asked, 'What do you do if professors won't read articles about subjects they write about? What do you do?' Indeed.

The published literature on the extreme toxicity of AZT, particularly the compound's toxic effects on human, primate and rodent fetuses, is substantial, but a conveniently assembled collection of excerpts from some published papers on this subject, prepared by the writer's associate David Crowe in Calgary, Canada, is annexed hereto\*. Please note that the list is not exhaustive, and there are many more. See also *Debating AZT: Mbeki and the AIDS drug controversy* by the writer, in paperback herewith and saved to the enclosed CD, likewise the writer's essay *Licensing*

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\* Online at <http://aras.ab.ca/azt.html>.

AZT\* describing the fraudulent circumstances in which the drug was licensed in the US and elsewhere.

We wish to highlight that when the effects of exposing babies to AZT in utero is assessed clinically, as opposed to using surrogate markers for drug efficacy, the published research consistently – and predictably – reveals that AZT-exposed babies have a higher mortality rate, higher rate of congenital anomalies, neurological defects, immunological disorders and other serious disease than unexposed babies. It raises the question why this drug is ever given to pregnant women in the first place, other than for commercial reasons. It is difficult to credit that the MCC was aware of this literature in recommending the drug for administration to this class of patient.

An appalling feature of the WHO Recommendations is the manner in which the significance of the human foetal toxicity literature cited is consistently underplayed – where it is mentioned at all, with most of the corpus on this subject omitted from consideration.

The WHO Recommendations allege: ‘Although theoretically ZDV [AZT] may have mutagenic and carcinogenic effects ... no adverse effects have been reported from any trials or studies on ZDV-exposed children.’ This statement is false, contradicted by the findings of Kumar et al. and Newschaffer et al., whose studies are cited in David Crowe’s collection of citations from the medical literature and discussed in numbered paragraph 35 of *Debat-ing AZT*.

Kumar et al., ‘reviewing the frequency of birth defects’ among one hundred and four babies exposed to AZT in utero in India, found eight out of eighty live births grossly malformed, including holes in the chest, abnormal indentations at the base of the spine, misplaced ears, misshapen faces, heart defects, extra digits and albinism. Eight foetuses exposed to the drug died in the womb,

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\* Now included in the appendices of *Introducing AZT: ‘A world of antiretroviral experience’* and online at [www.tig.org.za](http://www.tig.org.za).

and a further eight had to be therapeutically aborted. In their study of 1932 live-births among AZT-treated pregnant women in New York State, Newschaffer et al. found an almost trebled rate of 'major ... congenital anomalies' among AZT-exposed babies.

Furthermore, a small 'study of 195 mother-infant pairs' by Jungmann et al. found that 'exposure to the combination of ART and folate antagonists [e.g. *GlaxoSmithKline's common antibiotic Bactrim (co-trimoxazole)*] was associated with a significantly higher risk of congenital abnormalities. ... Congenital malformations were observed in nine infants (4.6%).' The researchers accordingly wondered in *Sexually Transmitted Infections* 2001 Dec; 77(6):441-3 **Is first trimester exposure to the combination of anti-retroviral therapy and folate antagonists a risk factor for congenital abnormalities?**

Richardson et al. had suggested an affirmative answer a year earlier, reporting in *European Journal of Obstetrics, Gynecology and Reproductive Biology* (2000 Dec;93(2):215-7) two cases of severe **Spinal malformations in the fetuses of HIV infected women receiving combination antiretroviral therapy and co-trimoxazole.**

The WHO Recommendations claim: 'There have been reports of a small number of serious adverse effects possibly associated with exposure to ART in the form of mitochondrial dysfunction (43-45), but an increased rate of serious clinical manifestations has not been confirmed by other studies (46-48).'

On the contrary, and in truth, Barret's et al. findings (cited in reference 44) reported in the self-explanatory title, **Persistent mitochondrial dysfunction in HIV-1 exposed but uninfected infants: clinical screening in a large prospective cohort** provided just this confirmation: '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 ap-

pearing 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 hyperlactaemia 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.'

Blanche et al. (reference 43 in the WHO Recommendations) noted the sort of consequences of 'persistent mitochondrial dysfunction' caused by in utero exposure to AZT (combined in some cases with 3TC, a closely similar drug): eight children in their study 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'.

In view of the MCC's members' manifest failure to have read and considered the papers to which we referred in our first letter, as well as Papadopoulos-Eleopoulos's et al. seminal examination of the molecular pharmacology of AZT published in *CMRO*, we enclose copies for their belated perusal, after which, in acquitting themselves of their obligations to the South African public, particularly to unborn and neonate children most vulnerable to the toxic effects of dangerous chemicals, we trust and expect that they will (a) immediately reconvene to recall their recommendation earlier this month that pregnant women and their babies in South Africa be exposed to AZT and nevirapine, (b) issue an urgent contra-indication directive in this regard, and (c) conclude their review of the special registration of nevirapine for pMTCT



by revoking it, in view of Boehringer Ingelheim's failure to meet the terms set in the MCC's resolution of 25 September 2003.

Having done this, we further expect that the MCC's members will finally address their minds to the AZT triphosphorylation problem identified five years ago by Papadopoulos-Eleopoulos et al. in their epochal AZT biochemistry paper, and will thereafter resolve to deregister the drug before any more South Africans are pointlessly poisoned with it – as millions were crippled and killed by their doctors' mercury and arsenic treatments less than a century ago. Whereas President Mbeki is familiar with and understands this basic and insurmountable biochemical problem with GlaxoSmithKline's claims for its product (he has twice been quoted in the press referring to it), it does not appear that anyone on the MCC is even aware of it. We appreciate that studying Papadopoulos-Eleopoulos's et al. radical investigation of the biochemistry of AZT will require considerable application and effort, because the paper is long and technical, but it is precisely for taking such trouble that the MCC's members are paid their salaries.

We conclude by pointing out that AZT was first synthesized in 1961 by Professor Richard Beltz (not in 1964 by Dr Jerome Horwitz as is generally reported) as an experimental cell-poison (not an anti-viral agent) for possible cancer chemotherapy, under the aegis of the American cancer research programme. (The writer has a detailed history of the process, which Beltz personally recounted to him; see *Inventing AZT*.\*) Reviewing an early draft of the writer's review of the toxicity literature on the drug in *Debating AZT: Mbeki and the AIDS drug controversy*, Beltz remarked approvingly, '... 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 ... devastating effects ... Your effort is a worthy one ... I hope you succeed in convincing your government not to make AZT available.'

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\* Included in the appendices to *Introducing AZT: 'A world of antiretroviral experience* and online at [www.tig.org.za](http://www.tig.org.za).

## One

The MCC, on the other hand, against the vehement advice of the inventor of AZT, considers that South African pregnant women and their babies, mostly black and poor, should be prescribed this poison to ingest as a beneficent medicine – but only when combined with another equally toxic chemical, nevirapine. The WHO Recommendations' concession that 'there is still a lack of information on the effects of short-courses of ARVs to prevent MTCT on the long-term health of the infected mother (and that of her infected infant) ... but research is ongoing' didn't cause the MCC any disquiet, apparently – even though South Africa is ill-equipped to monitor the extent to which mostly African children, 'infected' or otherwise, will be maimed or possibly killed by the experimental toxic treatment.

Yours faithfully

ADV ANTHONY BRINK  
CONVENOR AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

Cc: The South African government, and other interested parties.

### Note

By letter on 2 August 2004 the month of publication of the Barret et al. study was corrected (it was August not December), and this letter has been edited to reflect the fix. A copy of Papadopoulos-Eleopoulos's et al. paper in *Current Medical Research and Opinion* May 1999, **A Critical Analysis of the Pharmacology of AZT and its Use in AIDS** was submitted on the same. It's also online in 'Quick links' at [www.tig.org.za](http://www.tig.org.za).

## **Annexure A**

MCC MEDIA RELEASE: 12 July 2004

### **MCC NO LONGER RECOMMENDS THE USE OF MONOTHERAPY IN PREVENTING MOTHER TO CHILD TRANSMISSION OF HIV**

The South African Medicines Control Council (MCC) reconsidered the merits of nevirapine when used as a monotherapy to reduce the risk of transmission of HIV from mother to child during labour. Council believes that the risk-benefit profile of nevirapine monotherapy has changed and therefore no longer recommends its use for the prevention of mother to child transmission (PMTCT) of HIV.

At a recent meeting of the MCC held on 2 July 2004, Council recommended that nevirapine and zidovudine (AZT), previously approved for monotherapy in PMTCT, only be used in combination therapy.

The approval of nevirapine as monotherapy for this indication, in April 2001, was conditional upon monitoring of resistance and its impact on efficacy.

In its deliberations, the MCC considered the following issues:

- (i) Nevirapine leads to significant resistance in mothers and babies when used as a monotherapy to reduce the risk of transmission of HIV from mother to child compared to a combination therapy;
- (ii) Recent studies conducted in South Africa, using nevirapine as a monotherapy for this purpose, show significant resistance of up to 50%;
- (iii) The clinical significance of these findings needs further investigation as the efficacy of future treatment options in mothers or babies who have nevirapine-resistant HIV may be compromised;

## *One*

(iv) A number of recent studies, including an expert consultation report of the World Health Organisation (February 2004), confirms the view of the MCC that nevirapine monotherapy is less efficacious than combination regimens;

(v) Council's decision applies to all monotherapy interventions when used to reduce the risk of transmission of HIV from mother to child during labour. Council is of the view that combination therapy should be considered for this indication.

The Department of Health has introduced a Comprehensive Plan for Management, Care and Treatment of HIV and AIDS; which introduce ARV's and the opportunity of combination therapy.

# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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24 August 2004

The Registrar: Ms Precious Matsoso  
Medicines Control Council  
2<sup>nd</sup> Floor, Hallmark Building  
Cnr Andries and Vermeulen Streets  
Pretoria

Dear Ms Matsoso

**MCC review of its special registration of nevirapine for  
perinatal administration, and its recent recommendation  
that nevirapine be administered together with AZT**

In this memorandum we will be drawing the MCC's attention to human and animal medical research literature, some of it very recent and some still in press, nearly all omitted from consideration in the World Health Organisation's draft *Antiretroviral drugs and the prevention of mother-to-child transmission of HIV infection in resource-constrained settings: Recommendations for use: 2004 Revision* guidelines (hereinafter referred to as 'the WHO Recommendations'), which has conclusively found and unequivocally predicts that:

- (a) AZT and AZT+3TC treatment of pregnant women in South Africa will kill, mentally or neurologically cripple, and/or otherwise seriously physically harm a number of their babies;
- (b) Most of these babies will sustain 'moderate to severe' mitochondrial damage from in utero and postpartum exposure to these drugs;

- (c) Unlike the case of thalidomide babies, the drug damage caused to babies during gestation and post-partum will not be evident at or soon after birth, and so the toxic cause will therefore be masked, because the harm that AZT and 3TC causes to foetal and neonatal mitochondria only becomes symptomatically evident in children many months after exposure – and, in the case of mostly poor black women and babies in South Africa, long after they have left hospital and have returned traceless to their communities;
- (d) Where the damage caused by AZT and 3TC is less obvious than death, complete or partial paralysis, complete or partial spasticity, blindness, repeated convulsions or mental retardation, it may result in subtler neurological damage giving rise to lifelong neurobehavioural deficits that may easily be mis-attributed to a range of harmful infant challenges, from the ‘very unfavourable psychological and social environments’ attending poverty, through ‘prematurity’, to other serious childhood diseases;
- (e) Apart from brain and other neurological damage, pre-, peri- and postpartum exposure to AZT and AZT+3TC will also result in some cases to permanent bone marrow destruction, with potentially fatal consequences, and to cardiac muscle and other muscle and tissue damage of varying severity, that may be fatal;
- (f) The combination AZT+ 3TC+nevirapine regimen recommended in the WHO Recommendations for administration to pregnant women will cause life-threatening and in some cases fatal diseases in some of them.

We will further substantiate our charge that the WHO Recommendations recommending the administration of AZT+3TC+nevirapine to prevent mother to child transmission of HIV (‘pMTCT’):

## *Two*

- (a) wholly inadequately canvassed the substantial corpus of published human and animal nucleoside analogue (AZT and 3TC) foetal toxicity data published to date of issue (7 January 2004), and disregarded critically important studies;
- (b) trivialised the significance of these studies where it mentioned them at all; and,
- (c) grossly misrepresented the crucial significance of the final report of the French Paediatric HIV Infection Study Group (citation 44 of the WHO Recommendations, and hereinafter referred to as 'the Barret study', after lead author Béatrice Barret).

We will also draw the MCC's attention to the very latest studies on the transplacental mitochondrial toxicity of AZT and 3TC for primate, human and rodent foetuses – reported in January, April and June 2004 respectively – all subsequent to the issue of the WHO Recommendations, and all of which the MCC evidently missed, and consequently failed to take into account, when issuing its new recommendation that in addition to nevirapine HIV-positive pregnant women in South Africa should also be encouraged to take AZT.

It will become obvious to the MCC on reading the new data pointed out in this memorandum that the WHO Recommendations on which it relied in recommending the use of AZT, 3TC and nevirapine during pregnancy have been superannuated, and are now dangerously out of date.

To keep this memorandum within manageable proportions, we have not focussed on d4T, a drug proposed by WHO Recommendations as an alternative to AZT in the AZT+3TC+nevirapine regimen. The literature on d4T is less extensive than on AZT, but like AZT d4T is a nucleoside analogue and has essentially the same severe toxicities – predictably since nucleoside analogue compounds are widely used in cancer chemotherapy to intentionally poison off human cells. We might mention, however, that the WHO Recommendations's sunny estimation of d4T as a drug

good for pregnant women is not shared by the manufacturer itself:

On 2 February 2001 the *New York Times* reported an urgent alert issued by the European Medicines Evaluation Agency [EMEA] after

seven cases of lactic acidosis – three of them fatal – had been reported worldwide in pregnant women taking the two drugs in combination [*d4T (stavudine), sold by Bristol Myers-Squibb as Zerit; and ddI (didanosine), sold by BMS as Videx*]. ... Echoing last month's warning by the US Food and Drug Administration, the EMEA pointed out that lactic acidosis is a known side effect of the class of HIV drugs called nucleoside reverse transcriptase inhibitors (NRTIs). The use of this class of drugs is not recommended during pregnancy unless the potential benefit clearly outweighs the potential risks.

Although the drugs' labels already included strong warnings that lactic acidosis could occur in any patient, the US FDA warned in a special advisory that 'new evidence showed pregnant women have a greater chance of developing the condition' (*per Reuters report*). Bristol-Myers Squibb added this warning to its labelling, and chased the change with a letter sent to fifty thousand AIDS doctors, warning them of the danger.

Reference in the WHO Recommendations to 'reports of a small number of serious adverse effects possibly associated with exposure to ART [antiretroviral therapy] in the form of mitochondrial dysfunction (43-45), but an increased rate of serious clinical manifestations has not been confirmed by other studies (46-48)' creates the falsely misleading impression that:

- (a) the evidence concerning the potentially crippling effect of in utero exposure to AZT or AZT+3TC is doubtful and at best tenuous;



## Two

(b) only three studies suggest 'a possible association' between 'serious adverse effects' of exposure to AZT or AZT+3TC in the womb; and,

(c) subsequent studies disconfirmed tentative earlier ones.

Before we canvass the dire implications of the findings and conclusions reported in the Barret study, which the WHO Recommendations cursorily mentioned, misrepresented and effectively disregarded, it might assist if we recapitulate:

In September 1999 the French Paediatric HIV Infection Study Group published an alert in *Lancet* (citation 43 of the WHO Recommendations, and hereinafter referred to as 'the Blanche alert', after lead author Stéphane Blanche) in which, as the AIDS doctors summarised it in their report of the follow-up and confirmatory Barret study, they 'described eight cases of children presenting principally neurological symptoms compatible with persistent mitochondrial dysfunction. The symptoms and biochemical abnormalities were identified several months after the exposure to antiretroviral drugs.'

But the damage wasn't merely identified several months after the drug exposure: it only became manifest at that time among children who had hitherto appeared normal. That is, there was a time lag of many months between the drug damage and its manifestation in serious symptoms, in some cases ultimately fatal.

The 'neurological symptoms' – which the AIDS doctors might less delicately and more frankly have called massive brain and nerve damage – took the form of extensive cortical necrosis, cortical blindness, epilepsy and spastic quadriplegia in five children. Three further children were described as 'symptom-free' but had 'severe biological or neurological abnormalities' – portending serious health problems and misery in later life. The AIDS doctors also described findings of severely impaired energy metabolism and corresponding muscle and other cell damage, manifesting in heart muscle injury and muscle weakness generally.

The AIDS doctors accordingly concluded in their alert: 'Our findings support the hypothesis of a link between mitochondrial dysfunction [in infants] and the perinatal administration of prophylactic nucleoside analogues.' That is, the appearance of the permanently crippling, and in some cases fatal, mitochondrial disease observed in several children led the AIDS doctors to postulate the discomfiting misgiving that the AZT or AZT+3TC that they had used on the pregnant women in their study, and on most of the children for a few weeks after their births, might be the cause of it.

In a commentary on the Blanche alert in the May-June 2001 issue of the French journal *Therapie* (56(3):261-6), entitled (in translation), **Antiretroviral agents and pregnancy: mitochondrial dysfunction and nucleoside analogs**, Loubeyre-Unique et al. highlighted that the brain-damaging effects of AZT or AZT+3TC will not always be as grotesquely conspicuous as those reported in the Blanche alert, and may take subtler 'neurobehavioral' forms:

An alert was published during 1999 by the French Perinatal Cohort: eight cases of mitochondrial dysfunction were reported among 1754 infants exposed to nucleoside analogues in utero and during the neonatal period. These eight infants were not infected by HIV. Mitochondrial toxicity of nucleoside analogues is clearly described in adult HIV patients receiving NRTI [nucleoside analogue reverse transcriptase inhibitors]. Zidovudine [AZT] (the only and the first NRTI studied) induced mitochondrial DNA dysfunction in animals (monkeys) and neurobehavioural effects in mice at a dose similar to the human dose.

Indeed so: numerous research papers have reported 'neurobehavioural' anomalies in rodents following experimental pre-natal AZT exposure, none of which the WHO Recommendations saw fit to mention in their approbation of AZT and similar chemicals for ingestion by pregnant women in developing countries like

ours. And as we will show, the damaging effect of AZT and 3TC on foetal mitochondrial DNA has been shown in several studies not only in primates, but also in humans.

In 1997 Petyko et al. reported **Learning disturbances in offsprings of zidovudine (AZT) treated rats** in *Neurobiology* (5(1):83-5); in 1998 Applewhite-Black et al. noted **Neurobehavioral and pregnancy effects of prenatal zidovudine exposure in Sprague-Dawley rats: preliminary findings** in *Neurotoxicology and Teratology* (20(3):251-8); in 1999 Rondinini et al., of the Laboratorio di Fisiopatologia di Organo e di Sistema, Istituto Superiore di Sanita, Rome, Italy, described the **Long-term effects of prenatal 3'-azido-3'-deoxythymidine (AZT) exposure on intermale aggressive behaviour of mice** in *Psychopharmacology* (145(3):317-23); in 2000 the same core group of Italian researchers, now led by Venerosi, found **Prolonged perinatal exposure to AZT affects aggressive behaviour of adult CD-1 mice**, reported in *Psychopharmacology* (150(4):404-11); in 2001, in *Teratology* (63(1):26-37), the group, led as before, reported related findings following **Prenatal exposure to anti-HIV drugs: neurobehavioral effects of zidovudine (AZT) + lamivudine (3TC) treatment in mice**; a second paper in 2001 by the group, led by Ricceri, published in *Psychopharmacology*, reported **Prenatal AZT or 3TC and mouse development of locomotor activity and hot-plate responding upon administration of the GABA(A) receptor agonist muscimol**; in 2002 the group, led by Venerosi again, discussed **Animal models of anti-HIV drugs exposure during pregnancy: effects on neurobehavioral development** in the light of the Blanche alert in *Progressive Neuropsychopharmacology and Biological Psychiatry* (26(4):747-61) – mentioning the French report of ‘severe yet few human cases of cardiomyopathy [*heart muscle damage*] and neurological disease likely associated with mitochondrial dysfunction in uninfected infants of seropositive mothers perinatally exposed to AZT’; in the same year, 2002, Melnick et al. made positive findings in their investigation of **The effects of perinatal AZT exposure on the acoustic startle response in adult rats**, reported in

*Neurotoxicology and Teratology* (24(6):773-81); and the most recent study in this subject, by Levin et al., published this year in the January-February issue of *Neurotoxicology and Teratology* (26(1):65-71), returned a **Neurobehavioral assessment of mice after developmental AZT exposure**, in which the researchers recorded their observations of 'subtle neurobehavioral impairments in mice after prenatal AZT exposure at clinically relevant doses'.

Hart et al. propose a mechanism by which AZT mitochondrial toxicity causes neurological damage in their paper, **Acetyl-l-carnitine: a pathogenesis based treatment for HIV-associated antiretroviral toxic neuropathy**, still in press for publication in *AIDS* 2004, 18:1549–1560, but published online by Pubmed on 23 July 2004:

Nucleoside analogue reverse transcriptase inhibitors (NRTI) disrupt neuronal mitochondrial DNA synthesis, impairing energy metabolism and resulting in a distal symmetrical polyneuropathy (DSP), an antiretroviral toxic neuropathy (ATN) that causes significant morbidity

This results from AZT's potent activity as an oxidizing agent, as pointed out in Papadopoulos-Eleopoulos's et al. paper we sent up both in hard-copy and on CD, **A Critical Analysis of the Pharmacology of AZT and its Use in AIDS**, published as a special supplement to the prestigious academic medical journal *Current Medical Research and Opinion* in mid-1999 (archived at [www.theperthgroup.com](http://www.theperthgroup.com))

For those members of the MCC who might have forgotten their biology lessons, and so do not immediately appreciate the significance of mitochondrial damage, it bears emphasizing for the safety of generations of our country's children, black and poor particularly, that mitochondria are intracellular organelles that generate the energy necessary for a wide range of vital cellular processes. When oxidized by a 'mitochondrial toxin' such as AZT (as the drug was described by Lamperth et al. in **Abnormal skeletal and cardiac muscle mitochondria induced by zi-**

**dovudine (AZT) in human muscle in vitro and in an animal model**, published in *Laboratory Investigations*, 1991 Dec;65(6):742-51), mitochondria are unable to produce this essential energy, and several secondary toxic effects follow, including mitochondrial DNA depletion and mutation.

It's relevant to mention here that of all such 'mitochondrial toxin[s]', AZT is the most poisonous: in 1997, in the *Journal of Neurological Science* Benbrick et al. reported a comparative study of the **Cellular and mitochondrial toxicity of zidovudine (AZT), didanosine (ddI) and zalcitabine (ddC) on cultured human muscle cells** (149(1):19-25). Although they found that 'AZT, ddI and ddC all exert cytotoxic [cell-poisoning] effects on human muscle cells and induce functional alterations of mitochondria ... AZT seemed to be the most potent inhibitor of cell proliferation'.

It follows that it would be the most potent inhibitor of foetal cell growth too: in May 1994 Toltzis et al. reported the **Comparative embryonic cytotoxicity of antiretroviral nucleosides** in the *Journal of Infectious Diseases* (169(5):1100-2). The cellular toxicity of ddI, ddC, and d4T, all AIDS drugs in the same chemical class, was compared with that of AZT, which the lead author and other researchers had already found to be 'cytotoxic to early murine embryos both in vivo and in vitro' three years earlier (see citation 38 of the WHO Recommendations). The experiment established that the 'cytotoxicity of all three drugs was significantly less than with zidovudine at equivalent concentration', which is to say that AZT was found best at killing foetal tissue.

Since the term 'mitochondrial toxicity' might have a dry and uninteresting ring to those members of the MCC who've never heard of it before, appended to this memorandum is an excerpt from the Blanche study, describing the earliest-detected eight children worst-affected in the drug experiment on them. It graphically details what we're talking about. (Reading it requires a strong stomach or a hard heart.)

Although the WHO Recommendations claim, 'Short-term ... tolerance of the ARV prophylactic regimens has been demon-

strated', it's legion among doctors in South Africa that for most of them even a few days of AZT treatment following hypodermic needle pricks is unbearable, due to the extremely unpleasant subjective experience of the drug's toxicity. Yet the WHO Recommendations suggest that pregnant women should take it for six months of their pregnancies – even right throughout them:

For pregnant women it may be desirable to initiate ARV treatment after the first trimester of pregnancy, that is after the period of major organ development in the fetus, although for pregnant women who require treatment or who are severely ill, the benefit of early therapy [during the first semester] would likely outweigh any potential fetal risks and therapy should be initiated in such cases.

Notwithstanding GlaxoSmithKline's childish pretensions in its marketing motto, 'Our global quest is to improve the quality of human life by enabling people to do more, feel better and live longer', rather than making a killing in the business sense, irrespective of the human cost, the toxic ill-effects of AZT and similar drugs are unendurable for most people – as was found in an investigation to quantify this problem by Fellay et al., written up as the **Prevalence of adverse events associated with potent antiretroviral treatment: Swiss HIV Cohort Study** published on 20 October 2001 in *Lancet* (358(9290):1322-7).

The researchers reported 'a high prevalence of toxic effects' in a cohort of 1160 patients on AZT and related drugs, more than two thirds of whom suffered side effects severe enough to affect treatment adherence – in other words prevent them from continuing to take the drugs as prescribed. Forty-seven per cent reported clinical problems like vomiting, diarrhoea, nausea, abnormal fat growth, mood swings, insomnia and fatigue. Blood tests revealed 'potentially serious' abnormalities among twenty-seven per cent. The researchers classed a 'significant proportion' of these adverse events as 'serious or severe'. Kidney dysfunction

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and severe fatigue that were ‘probably or definitely’ due to the drugs led to some patients winding up in hospital.

And just by the way: rather than ‘enabling people ... to live longer’, AZT helps them to live shorter – as Andrew Phillips at the Royal Free Hospital School of Medicine in London and George Smith at the University of Bristol reminded their medical colleagues in a letter to the *New England Journal of Medicine* on 27 March 1997: ‘Extended follow-up of patients in one [AZT] trial, the [*well-conducted, large-scale, double-blind*] Concorde study [*which found AZT to be useless as an AIDS drug*], has shown a significantly increased risk of death among the patients treated early.’ Needless to say, you don’t see this mentioned in GlaxoSmithKline’s package insert.

As might be expected, pregnant women find the drugs as hard to take as Fellay et al. found people generally do. In 1998 in *AIDS* (12:F241-247) Lorenzi et al. reported **Antiretroviral therapies in pregnancy: maternal fetal and neonatal effects**: ‘... 29 out of 37 women and ... 14 out of 30 babies [suffered] one or more adverse events.’ Reuters Health synopsisized the trouble:

Following combination antiretroviral therapy administered during pregnancy, most HIV-positive mothers and about half of their children developed one or more adverse events. Of thirty babies, ‘the most common adverse event was prematurity (ten infants), followed by anemia (eight infants). The investigators also noted 2 cases of cutaneous angioma [*blood vessel malformation presenting as spotty tumours*], 2 cases of cryptorchidism [*testicles retained within the abdominal cavity*], and 1 case of transient hepatitis. Two infants ... developed ... intracerebral hemorrhage [*bleeding on the brain*]’ and one ‘extrahepatic biliary atresia [*potentially fatal constriction of bile duct*].

In contradistinction to the WHO Recommendations’s allegation that AZT is readily tolerated by pregnant women, the Blanche study cited three contrary investigations – published in *J Acquir*

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*Defic Syndr Hum Retrovir* 1995;9:401-07; *Lancet* 1994;344: 207-09 (the latter paper appositely entitled **Zidovudine for mother, fetus and child: hope or poison?**) and *Drug Saf* 1995;12:274-82 – in support of its note that ‘Tolerance of this treatment has been a concern.’ Actually, a bit more than a concern: in *Teratology*. 2000 Aug;62(2):93-9, Patterson et al. pointed out that ‘many pregnant women are unable to tolerate AZT because of toxicity’. So who’s not telling the truth?

When AZT and similar drugs make pregnant women in the Developing World desperately sick, just as all the literature and the skull and crossbones on Sigma Chemical Co.’s label predicts, the WHO Recommendations advise that they be forced to stay the course:

Adherence to ARV drugs for prevention of MTCT or treatment is of critical importance, and should be promoted from the time ARV is started, and reinforced throughout prophylaxis and/or treatment, ideally at the family and community level. Guidance should include discussion with women about the known potential adverse effects of the ARV regimen they have been prescribed and importance of adherence, so they can anticipate and know how to manage minor and/or transient side effects and do not inappropriately stop therapy. After starting ARV treatment or prophylaxis, women should be seen frequently to reinforce the need for adherence to the regimen and to assess and manage any side effects of the drug. ... When ARVs are used as prophylaxis to prevent MTCT, side effects such as ARV-associated nausea, which may compound the pregnancy-associated sickness, or fears that ARV drugs might harm the foetus, should not be considered to be a contra-indication or a reason for stopping ARV treatment.

Four years after the publication of the Blanche alert, the Barret study, which followed up a ‘large ... cohort’ of ‘2644 of 4392 chil-



dren ... exposed to antiretrovirals' conclusively 'confirmed ... a preliminary report' (the Blanche alert) that 'Children exposed to nucleoside analogues during the perinatal period are at risk of a neurological syndrome associated with persistent mitochondrial dysfunction ... a risk about 30 times higher than that in the general population.'

The WHO Recommendations, however, gave these very serious and conclusive findings just a passing mention, dishonestly representing their purport in doing so: 'There have been reports of a small number of serious adverse effects possibly associated with exposure to ART in the form of mitochondrial dysfunction (43-45)'. (The Barret study is citation 44, the Blanche alert 43, and another definitive study by Poirer et al., discussed below, is 45.)

Reading the WHO Recommendations, ignorant of the data reported in these three studies, one would think that the safety of AZT during and after pregnancy was a sure thing: 'The safety of ARV's used for a limited period of time in pregnancy for the purpose of prevention of peri-partum MTCT has been demonstrated. ... The potential short-term toxicity in exposed infants, if any, is expected to be very small.'

Perhaps the WHO Recommendations's author needs glasses, because as the Blanche alert reported, far from being 'short-term', the effect of foetal and neonatal exposure to AZT and 3TC is 'persistent mitochondrial dysfunction ... months or years after the end of antiretroviral treatment', sometimes causing brain damage that shows up in Magnetic Resonance Imaging (MRI) scans, and other serious tissue damage, fatal in some cases.

As for the WHO Recommendations's allegation that the incidence of these ill-effects was 'very small', it is apparent from the Barret study that its '30 times higher than that in the general population' assessment of the risk of serious mitochondrial damage and consequent brain, neurological, muscle and organ tissue injury – high enough as it is – was actually conservatively computed; and we submit that the risk of serious harm that the MCC threatens South African children, mostly black, mostly poor, by

advocating their exposure to AZT or AZT+3TC before and after birth is very much higher indeed. In fact the AIDS doctors admitted as much:

The true incidence [of the risk] could be higher because additional children in the cohort have similar symptomology, and several arguments strongly suggest a mitochondrial origin for these cases.

The number of children reported injured in the Barret study was parsimoniously arrived at in a process employing 'restrictive criteria', in which the majority of suspected cases of '196 children presenting with at least one major sign or two minor signs [of] mitochondrial dysfunction' of the 2644 drug-exposed were eliminated, leaving a remainder of just twenty-nine cases of mitochondrial dysfunction that the AIDS doctors considered 'established'.

Ninety-one children, including eleven who died, were thrown off the roll of 'possible' injury cases, notwithstanding their exhibition of 'at least one major sign or two minor signs on two different occasions as defined in the screening procedure', for the reason that the AIDS doctors identified 'another cause that could account for the symptoms and/or resulted in no suspicion of mitochondrial dysfunction for 91 children'. (The defective logic of these people leaps off the page. But then they're AIDS doctors.)

It's noteworthy that 'This group of 91 cases included 11 children who died during the study period.' Nobody thought of exhuming their remains for autopsies to determine what killed them, more especially in view of the fact that AZT poisoning frequently leaves pathologists with clear biochemical clues.

In the case of '61 children, the symptoms identified in the database, which were confirmed by the investigator, disappeared spontaneously: various investigations during the symptomatic period were not conclusive.' Because they were not 'conclusive', they were eliminated – not monitored for the possible reappearance of their symptoms, or other ones. Without explanation, the

AIDS doctors figured: 'Complementary investigation after clearance of the symptoms was not considered justified.' Just like that.

One would have thought that in a properly conducted investigation, no effort and no expense would have been spared in conducting the most thorough examination of every drug-exposed child possible, employing every diagnostic tool, assay, psychometric and psychomotor test available to medicine and to toxic neurophysiology and toxic neuropsychology. But the children weren't deemed worth it – probably because, as appears from the Blanche alert, most of them were black. (As are most victims of foetal AZT poisoning in the US and European inner-cities.)

Since 'For 15 children, complementary evaluation was not possible (child lost to follow-up, parental refusal)', there is no way of knowing how many of them were hurt or killed. For eight more, 'results from complementary investigations are not yet fully available and conclusions not yet possible'. What we do know is that those eight children would have exhibited 'at least one major, or two minor signs' of "'possible" mitochondrial dysfunction' to warrant the 'complementary investigations'.

As they excluded the children exhibiting 'at least one major, or two minor signs' of "'possible" mitochondrial dysfunction' the AIDS doctors admitted: 'The diagnosis of mitochondrial disease in children is sometimes considered to be very difficult and even arbitrary. ... Only cases of "established" mitochondrial dysfunction are presented here.' Their use of inverted commas around "possible and "established" were used to indicate the arbitrariness of the body count, and that only the most severely injured were included in the tally. This implies that many more could have been.

That the AIDS doctors weren't at all sure about the extent of the harm they had caused, and that they may have missed many injured children, was suggested in their report:

In some children, the symptoms [of 'toxic-induced mitochondrial dysfunction'] are very strongly expressed. In

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others, the symptoms are mild and only a specific and adapted program of complementary examinations can diagnose or suggest the existence of mitochondrial toxicity. ... The symptoms in the children in our study were not specific, and may therefore not have been identified as toxic effects of treatment.

The AIDS doctors also employed a surprisingly crude and imprecise method for gathering information about the harm that they had caused the children by supervising their exposure to AZT or AZT+3TC before and after they were born:

The attending clinician was allowed to decide the extent of these investigations: consequently the investigations performed varied with the severity of the symptoms and the clinician's evaluation of the pertinence of the mitochondrial hypothesis.

In other words, things depended on how clever or stupid the particular doctor was.

How many drug injury cases on the less-severe end of the spectrum were missed and therefore unaccounted for, because of this ridiculous procedure, is anyone's guess. Presumably the 'attending physician' had also administered or prescribed the toxic medicine, and, if so, would naturally have been less than astute to expose as many of his medical disasters to the world as possible.

The most extreme forms of injury to the chemically-crippled children were noted in the Barret study as 'motor abnormality' (typically involving muscular impairment such as trouble walking, talking and with hand-control), 'repeated seizures' (i.e. epilepsy), 'major cognitive delay' (i.e. mental retardation), 'tetraplegia' (total limb paralysis), 'hemiplegia' (left or right side paralysis) 'retardation of language acquisition' (evidencing brain damage), 'cardiomyopathy' (damaged heart muscle, predicting early death), 'nystagmus' (uncontrollable rapid movement of the eyes, evidencing brain damage) and 'severe malaise' (non-specific per-

sistent ill-health and weakness, consistent with toxic chemical poisoning).

In the case of twelve children in the Barret study, cerebral MRI scans revealed brain tissue atrophy (wasting), necrosis (tissue death) and other serious abnormalities. It is noteworthy, however, that in arriving at this figure, the AIDS doctors applied a remarkably restrictive protocol for interpreting MRI brain scans of children who appeared to have sustained brain damage through pre-, peri- and postnatal AZT and AZT+3TC exposure:

All the cerebral MRI data underwent two independent expert analyses. In cases of divergent interpretations, the 'least severe' interpretation was used for the final analysis of the results: an MRI that was judged to be normal by one party and to be abnormal by the other was considered to be normal, regardless of the number and severity of the abnormalities observed. If the MRI findings were considered to be abnormal by both parties, only the abnormalities observed by both were included in the analysis.

Obviously, had the AIDS doctors designed a more sensitive protocol for a higher vigilance and detection level, many more cases of visible drug-damage to brain tissue would have been recorded.

Even so, it's important to keep in mind that it's trite in neurology that even profound, clinically apparent neurological damage or deterioration, whatever the cause, is not necessarily manifest in any observable brain tissue anomaly. Advanced Alzheimer's disease, for example, as discussed in the modern standard reference, the *Oxford Textbook of Medicine*, is a case in point.

As they reported the iatrogenic horror that they had wreaked on the babies upon whom they had earlier been experimenting with their poisonous chemicals, one can only wonder how much greater the scale of the harm that would have been ascertained and reported had an independent panel of scientists been con-

vened to audit the scale of the disaster. The conservative reporting bias corrupting the integrity of the Barret study findings, as bad as they were, was inevitable, given that the self-same group of AIDS doctors who had caused the carnage with its reckless medical experiments was in charge of ascertaining its extent and human cost.

The Barret study confirming the transplacental mitochondrial toxicity of AZT for human fetuses and neonates was preceded by another one by the same group of AIDS doctors, this time led by Laurent Mandelbrot, published in the *Journal of the American Medical Association* on 25 April 2001 (285(16)2083-93): **Lamivudine-zidovudine combination for prevention of maternal-infant transmission of HIV-1** (citation 26 of the WHO Recommendations).

Yet again, of babies born to 445 AZT+3TC treated mothers enrolled in the study, 151 children suffered 'moderate to severe hematologic adverse events' resulting from their exposure to the drugs, including such 'frequent serious adverse events' as 'neutropenia and anemia, requiring blood transfusion in nine children and premature treatment discontinuation in nineteen. Two uninfected children died at age 1 year from neurologic complications related to mitochondrial dysfunction.' The AIDS doctors concluded that

Lamivudine-zidovudine may be effective in preventing maternal-infant HIV transmission. However, severe adverse effects ... occurred. Thus, the role of this combination therapy in this setting is as yet unclear, and further research involving a variety of strategies is needed to definitively ascertain its utility for preventing maternal-infant HIV transmission.

That is another way of saying that however excited they were by their scintillating laboratory test results, the AIDS doctors' enthusiasm was chilled by the deaths of the children they had killed with their drugs, or poisoned – some so severely that they needed

blood transfusions (an inevitably fatal procedure in many cases). These disagreeable real-world outcomes understandably made the AIDS doctors reticent about recommending to others the drug combo they had just tried on their pregnant patients and their babies.

But in pressing the administration of AZT mixed with 3TC and nevirapine on poor women and their babies in Third World countries, the AIDS doctors hired by the WHO had no such qualms:

ZDV [AZT], 3TC and NVP are the drugs of first choice to be used to prevent peripartum MTCT. ... All three drugs can be taken twice daily and infant formulations are available. To further simplify the treatment, ZDV and 3TC are available in a co-formulation, thus reducing the number of pills to be taken. ... Where available a highly potent ARV prophylactic regimen for these women would be the triple cocktail of ZDV+3TC+NVP from 32 weeks of gestation through delivery and for three days post-partum.

We pause to mention here that a few days after the draft WHO Recommendations were published on 7 January 2004, insouciantly selling the above-mentioned drugs to pregnant women in the Developing World to be taken during most of their pregnancies, nevirapine manufacturer Boehringer Ingelheim issued a special safety alert in the US concerning the use of its drug in pregnancy. The English online news service *AIDSmap* captured it in a report on the 30<sup>th</sup>:

Boehringer Ingelheim, the manufacturer of the non-nucleoside reverse transcriptase inhibitor (NNRTI) nevirapine (Viramune) has issued important new safety information in a letter to doctors in the US about the drug's potentially fatal liver toxicities. Safety information contained in packets of the drug will now caution that women with CD4 cell counts above 250 cells/mm<sup>3</sup>, including pregnant women, who are taking nevirapine for

chronic HIV infection, have a twelve-fold greater risk of serious liver side-effects, and that these have sometimes been fatal. Liver events present the greatest risk of fatality if they occur in the first six weeks of nevirapine treatment, and are often associated with a rash. However, the risk continues after this time and Boehringer Ingelheim is cautioning doctors to closely monitor patients for the first 18 weeks of nevirapine therapy. Even when nevirapine treatment is discontinued, the manufacturer is warning that in some instances hepatic injury has continued to progress. Boehringer Ingelheim also uses its letter to remind healthcare providers that any patient taking nevirapine can experience hepatic toxicities. Because of this some doctors recommend that nevirapine-treated individuals should be monitored more often than once a month. In particular, it is recommended by some experts that liver function be monitored before nevirapine treatment is started, at the time of nevirapine dose escalation and two weeks later.

In other words, a higher CD4 cell count – read by AIDS doctors (but not by informed immunologists) like the fall of a diviner's bones and shells as an optimistic indication of how healthy you are – predisposes you to dying of liver failure if you take nevirapine. This phosphorescent wisdom has been adopted by AIDS doctors as their latest new doctrine.

Although the WHO Recommendations punted nevirapine together with AZT and 3TC as a 'first-line' treatment combination to be administered during pregnancy and to babies after their births, American AIDS doctors were jolted a few months later into having different ideas. A paper about fatal and other serious **Maternal Toxicity With Continuous Nevirapine in Pregnancy: Results From PACTG 1022** by Hitti et al. had bitter pills to report on 1 July 2004 in the *Journal of Acquired Immune Deficiency Syndromes* (36(3):772-776).



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The AIDS doctors had teed off with the 'OBJECTIVE: To compare the safety of nelfinavir and nevirapine-based antiretroviral treatment in HIV-1-infected pregnant women', giving seventeen of thirty-eight pregnant women 'nevirapine with zidovudine plus lamivudine', and the rest the latter two drugs with nelfinavir in place of nevirapine. Within two to twenty-six weeks of treatment, drug toxicity caused five women in the AZT+3TC+nevirapine group – twenty-nine per cent of them – to abandon the drugs. But it was too late for an ailing African-American woman (who had been admitted perfectly healthy into the study) after her baby was cut from her: '1 subject developed fulminant hepatic failure and died, and another developed Stevens-Johnson syndrome.'

With these disappointments, the study was smartly aborted. But instead of fingering the drugs on the strength of all that had been published about their toxicities, underscored by the CDC's ban, on the advice of the FDA, of even short-term nevirapine prophylaxis for doctors and nurses suffering needlestick injuries, the AIDS doctors brilliantly blamed the fatality and life-threatening adverse effect on the alleged unique allergic predisposition to nevirapine toxicity mentioned above:

Continuous nevirapine may be associated with increased toxicity among HIV-1-infected pregnant women with CD4 cell counts greater than 250 cells/microL, as has been observed in non-pregnant women.

A month after publication of the Barret study, AIDS doctors from the same study group, this time led by Le Chenadec, reported further unpleasant findings under the title, **Perinatal anti-retroviral treatment and hematopoiesis in HIV-uninfected infants** (*AIDS*. 2003 Sep 26;17(14):2053-61): In utero AZT exposure may lead to 'persistent inhibition of hematopoietic stem cells [causing a] significant and durable effect on hematopoiesis up to the age of 18 months'. And as might have been expected, the authors found: 'Combinations of antiretroviral treatments were as-

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sociated with larger decreases [of hematopoietic stem cells] than monotherapy up to 15 months of age.'

Expressed in lay terms, the French AIDS doctors found that AZT and 3TC poisons off babies' bone marrow – old hat to Sigma Chemical Co., whose AZT label has always told us: 'TOXIC Toxic to inhalation, in contact with skin and if swallowed. Target organ(s) Blood Bone marrow. ... Wear suitable protective clothing.'

This ought not to have hit the AIDS doctors as any big surprise in any event: the potent stem-cell and general haematological toxicity of AZT reported everywhere in the medical and scientific press is surely too notorious to need labouring in this memorandum, but for any members of the MCC ignorant of it, or who could use a refresher in this subject, some of the published research on this score is summed up (as at 15 November 2000) in paragraphs 10 to 13 of *Debating AZT: Mbeki and the AIDS drug controversy* (appended hereto as an excerpt for easy reference), and in David Crowe's collection of citations annexed to our second letter.

That antiretroviral drugs reach and can destroy foetal bone marrow was already known to doctors (who read their journals) by 1998: in the May issue of *Pediatric Infectious Diseases Journal* (17(5):435-436), Watson et al. had reported **Profound anemia in a newborn infant of a mother receiving antiretroviral therapy**. The HIV-negative baby, born to a positive mother who had been treated with a cocktail of AZT, 3TC and a protease inhibitor, was found to be suffering 'high output congestive heart failure secondary to profound anemia'. The paediatricians excluded 'infection, nutritional deficiencies, congenital leukemia and congenital red blood cell aplasia in the child' and naturally considered the 'cause of the life-threatening anemia in our infant ... to be in utero erythroid marrow suppression by one or more of the antiretroviral agents administered to the mother'.

The WHO Recommendations mentioned Le Chenadec's et al. findings about persistent anaemia in children exposed to AZT or AZT+3TC in utero and after birth (citation 37bis), but cavalierly

dismissed them with the comment that their 'clinical significance' is 'unknown'. In reality, it is elementary in paediatric medicine that persistent anaemia in an infant is a very serious condition indeed. It means, practically, that no matter how much he breathes, the child is unable to get enough oxygen, becomes breathless after any exertion, is constantly tired, and has poor resistance to infections. He's chronically very pale and unwell.

And far from being of 'unknown clinical significance', in May 1999 Mocroft et al. reported their finding in *AIDS* 3(8):943-50 that **Anaemia is an independent predictive marker for clinical prognosis in HIV-infected patients from across Europe**, confirming that 'low haemoglobin levels were found to be 'a strong independent prognostic marker for death'. Which is to say that the 'clinical significance' of persistent anaemia is that it's 'a strong independent prognostic marker' for dying young. (No prizes for guessing that Mocroft et al. also 'found that 78.2% of the patients with mild or severe anaemia at baseline had received zidovudine'.)

What the WHO Recommendations scandalously neglected to mention is that the Barret study specifically addressed the likely reasons why 'other studies' (in the words of the WHO), which preceded their report, had not found the 'serious clinical manifestations' (ibid) of nucleoside analogue foetal toxicity that they had. Barret and colleagues explained the reason:

In a preliminary report we described eight cases of children presenting principally neurological symptoms compatible with persistent mitochondrial dysfunction ... The symptoms and biochemical abnormalities were identified several months after the exposure to antiretroviral drugs. Subsequently, a review of five different US cohorts failed to identify mortality specifically linked to mitochondrial disorder, but it is important to note that the review did not address possible symptomatology in living HIV-uninfected children. ... Children born to HIV-infected

mothers, even when they themselves are not infected, may show symptoms of various types. These symptoms are often associated with easily identifiable causes, but in some cases are not readily explained. Investigators of the French paediatric study have for some years been interested in a series of symptoms, mostly neurological, of children born to HIV-infected women. The neurological symptoms include cognitive delay, behavioural disorders, motor abnormalities and convulsions. Demonstration of drug toxicity during pregnancy is not easy when the suspected event is rare and the symptoms non-specific.

Contrary to the deceptive suggestion in the WHO Recommendations that there is any lingering uncertainty about the issue, there is no question at all that exposing babies to AZT in utero will cause them some degree of permanent mitochondrial damage, from sub-clinical to fatal; and there is a wealth of research data, including some very recent papers, establishing this:

Two months before the publication of the Barret study, Poirer et al., all staff scientists at the US National Cancer Institute (hereinafter referred to as 'the NCI group'), published a study reported in the June 2003 issue of the *Journal of Acquired Immune Deficiency Syndromes* (33(2):175-83 – citation 45 of the WHO Recommendations): **Long-Term Mitochondrial Toxicity in HIV-Uninfected Infants Born to HIV-Infected Mothers**, in which they stated their findings concerning drug-caused mitochondrial DNA damage categorically and unequivocally: 'AZT exposure causes a persistent depletion of mtDNA [mitochondrial DNA]' among babies exposed to AZT in the womb.

Interviewed about these findings by Reuters Health on 8 July 2003, Miriam Poirer remarked: 'We were stunned. We thought there might be some subtle changes, but we did not expect anything so striking.' She also mentioned that in her group's preceding primate studies, in which monkey foetuses had been exposed to human-equivalent doses of AZT+3TC,

we found major morphological damage in mitochondria of umbilical cords, and depletion of mitochondrial DNA in the brain, the heart, and the skeleton.

The primate studies to which Poirer was referring were all published in 2000, and all returned findings with the gravest negative implications for the continued use of nucleoside analogue drugs during human pregnancy. The WHO Recommendations, however, completely ignored them.

In May 2000, led by Gerschenson, the NCI group noted findings starkly conveyed in the title of their paper **Fetal mitochondrial heart and skeletal muscle damage in *Erythrocebus patas* monkeys exposed in utero to 3'-azido-3'-deoxythymidine**, published in *AIDS Research and Human Retroviruses* (16(7):635-44). Human-equivalent doses of AZT were given to pregnant monkeys during the second half of their gestational terms. Their babies were killed at birth, after which their 'cardiac and skeletal muscle' tissues were structurally examined by electron microscopy and with oxidative phosphorylation enzyme assays. It was found that

At the human-equivalent dose of AZT (6 mg of AZT/kg bw), there was an approximately 85% decrease in the specific activity of NADH dehydrogenase (complex I) and three- to sixfold increases in specific activities of succinate dehydrogenase (complex II) and cytochrome-c oxidase (complex IV).

The NCI group reported that 'a dose-dependent depletion of mitochondrial DNA levels was observed in both tissues', and concluded: 'The data demonstrate that transplacental AZT exposure causes cardiac and skeletal muscle mitochondrial myopathy in the patas monkey fetus.'

The heart damage and partial and complete human paralysis in children exposed to AZT and AZT+3TC in utero, observed and described in both the Blanche alert and the Barret study, is consistent with the NCI group's 'cardiac and muscle mitochondrial

myopathy' finding in their primate study, and indeed with the vast mass of AZT-induced human and animal mitochondrial myopathy research data, both clinical and biological, reported in the medical and scientific press – briefly overviewed (as at 15 November 2000) in *Debating AZT: Mbeki and the AIDS drug controversy* and in Crowe's collected AZT citations.

In June 2000, led by Ewings, the NCI group reported its research into the transplacental mitochondrial toxicity of AZT for foetal monkey brains, and again announced appalling findings in the title to their paper, **Genotoxic and functional consequences of transplacental zidovudine exposure in fetal monkey brain mitochondria**, published in the *Journal of Acquired Immune Deficiency Syndromes* (24(2):100-5). Performing the same EM and enzyme assay investigations as before, this time of neonatal brain tissue, the NCI group found that

in fetal patas monkeys given a human equivalent daily dose of AZT during the last half of pregnancy, mitochondria in the fetal cerebrum appear to sustain moderate damage.

Since the cerebrum controls and coordinates all voluntary activity in the body and governs the lower parts of the nervous system, these findings explain the crippling physical manifestations of brain damage among babies and children reported and described in the Blanche alert and in the Barret study.

In November 2000 two of the NCI group, Gerschenson and Poirer, published a further primate study of the mitochondrial toxicity of AZT for monkey foetuses, exposed to human-equivalent doses of the drug during the second halves of their mothers' pregnancies, in the *Annals of the New York Academy of Sciences* (918:269-81) – again bluntly entitled **Fetal patas monkeys sustain mitochondrial toxicity as a result of in utero zidovudine exposure**. 'The fetal tissues examined include heart and skeletal muscle, which have high energy requirements, and placenta, which is less dependent on mitochondrial integrity.' Their study

demonstrate[d] that mitochondrial toxicity, evidenced by depletion in mtDNA and OXPHOS enzyme abnormalities, is manifested similarly in heart, skeletal muscle, and placenta of AZT-exposed monkey fetuses.

In January this year, in *AIDS* (20(1):91-100), the NCI group, led by Gerschenson, reported their investigation of the foetal mitochondrial toxicity of AZT when combined with 3TC, in a paper entitled **Mitochondrial toxicity in fetal *Erythrocebus patas* monkeys exposed transplacentally to zidovudine plus lamivudine**. Electron microscopy examination of 'drug-exposed fetal cardiac and skeletal muscle cells showed mitochondrial membrane compromise, mitochondrial proliferation, and damaged sarcomeres, while mitochondria in brain cerebrum and cerebellum were morphologically normal'. The drugs were found to have resulted in massive mitochondrial DNA depletion –

(>50%) in heart, skeletal muscle, cerebellum, and cerebrum from drug-exposed fetuses compared to unexposed controls. Overall, the data indicate that significant mitochondrial damage was observed at birth in monkey fetuses exposed in utero to AZT plus 3TC in a human-equivalent dosing protocol.

These research findings were published in the same month as the WHO Recommendations, and like those of the NCI group's preceding findings, their baleful implications were not considered in them.

That children exposed to even a so-called 'short course' of AZT in utero and after birth are liable to suffer serious permanent harm is predictable from the massive corpus of published literature on the mitochondrial toxicity of AZT resulting from adult and paediatric ingestion – a toxicity with multiple pathways, both short- and long-term, as investigated and discussed by Massini et al. in **Zidovudine-induced experimental myopathy: dual**

**mechanism of mitochondrial damage**, published in July 1999 in the *Journal of Neurological Science* (166(2):131-40).

Exacerbating the danger of foetal toxicity is the fact that following maternal ingestion, nucleoside analogues have been found in numerous human and animal studies to readily cross the placenta, accumulating in foetal blood and foetal tissues to concentrations equal to or much higher than maternal levels:

Hankins et al., in a study of the **Transplacental transfer of zidovudine in the near-term pregnant baboon** reported in the *American Journal of Obstetrics and Gynecology* in September 1990 (163(3):728-32), found 'higher fetal concentrations of the medication and its metabolite' 5'-glucuronide azidothymidine than in maternal blood.

In a **Preliminary study on the transport of AZT (Retrovir-zidovudine) through the placenta** (translated from French) reported in the same year in the *Journal of Gynecology Obstetrics and Biological Reproduction* 1990;19(2):177-80, Gillet et al. described a human study on six pregnant volunteers about to undergo elective abortions. All agreed to take AZT before the procedure. Following their abortions, levels of the drug found in their aborted foetuses were measured. The study found that 'The concentrations of the drug in the liquor and in the fetal blood were higher or equalled those found in the maternal blood.'

Pons et al. reported alike the following year, 1991, in the *European Journal of Obstetrics, Gynecology and Reproductive Biology* (40(3):229-31) in their paper, **Placental passage of azathiothymidine (AZT) during the second trimester of pregnancy: study by direct fetal blood sampling under ultrasound:**

AZT-therapy during pregnancy is actually contraindicated. Two HIV-positive pregnant women, who were due to have an induced abortion in the second trimester of pregnancy, were treated with AZT. Blood samples from mothers and fetuses and amniotic fluid samples were taken simultaneously. AZT crossed the placental barrier



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in the two patients. AZT and GAZT concentrations from the two fetuses were close to those obtained in the two women and in six non-pregnant volunteers.

As the Barret study summed up what is now well established:

Transplacental passage of nucleoside analogues such as zidovudine or lamivudine is high and fetuses and newborns exposed, sometimes for several months, to the drugs must therefore also be exposed to their effects.

Indeed so: numerous studies have confirmed high levels of AZT in foetal tissues after maternal treatment with the drug, but it would seem futile to recite them all here in view of the latest lunatic fad among AIDS doctors. The old medical concern, expressed in 1991 by Pons et al., cited above, that especially vulnerable unborn (and newborn) babies should not be exposed to harmful chemicals with transplacental permeability has gone out of fashion in the age of American AIDS medicine, with many AIDS doctors now urging unblinkingly that AZT be administered directly to newborn babies for the first few weeks of their lives.

Actually, babies do well to go on AZT for a good solid six weeks after birth, enthuse American AIDS doctors in the **Recommendations of the US Public Health service task force on the use of zidovudine to reduce perinatal transmission of human immunodeficiency virus**. *MMWR Morb Mortal Wkly Rep* 1994;43 (RR-11):1-20.

The WHO Recommendations similarly vaunt an 'antepartum + intrapartum + postpartum ZDV+3TC regimen' as proven most 'effective', citing studies claiming pMTCT benefits of 'Long (4 weeks)' and '(6 weeks)' and 'Short (1week) ... Post-partum infant' treatment with AZT or AZT+3TC, but finally settle, whimsically and without any cited authority, on the prescription of 'ZDV+3TC for three days after delivery'.

Why AIDS doctors should still be pressing AZT on newborn babies, when it has officially been found too poisonous for older

children is one of the many dazzling wonders of the AIDS epoch. In a study in the US, designed by Dr Janet Englwood, and sponsored by both the National Institute of Allergy and Infectious Diseases and the National Institute of Child Health and Human Development, 839 HIV-positive children were divided into three groups and treated with AZT, ddI and a combination of both. The 'AZT alone' wing of the study had to be called off abruptly in February 1995 due to the 'more rapid rates of ... bleeding and biochemical abnormalities' exhibited by the children in this group.

On 14 February 1995 the *New York Times* reported Englwood's et al. findings without mincing words: *AIDS drug AZT fails completely*:

In a major surprise, the drug AZT – now the standard treatment for children infected by the AIDS virus – proved so ineffective in halting disease progression 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 development 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.

Another clinical trial involving the closely similar drug d4T, **A phase I/II evaluation of Stavudine (d4T) in children with human immunodeficiency virus infection**, ended just as dismally – as Kline et al. reported the following year in *Pediatrics* (96:247-252):

Thirty-five of thirty-seven [*child*] subjects experienced serious clinical adverse events, including infection (33 subjects), lymphadenopathy [*damage to lymph nodes*] (19 sub-

jects), hepatosplenomegaly [*abnormal swelling of liver and spleen*] (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%).

Notwithstanding these findings, GlaxoSmithKline and Bristol Myers-Squibb continue to indicate AZT and d4T for children in their package inserts, without a word about these clinical trial disasters.

The speed with which AZT reaches the foetus after maternal ingestion has been reported in many studies: Little et al. began investigating this in rodent models, and published their findings concerning the **Pharmacokinetics of azidothymidine during late pregnancy in Long-Evans rats** in September 1989 in the *American Journal of Obstetrics and Gynecology* (161(3):732-4):

The drug crosses the placenta to reach concentrations in the placenta and fetus that are comparable to 75% and 58%, respectively, of those in the maternal serum by 2 hours after administration. By 4 to 6 hours after administration azidothymidine concentrations in the placenta and fetal liver significantly exceed maternal concentrations.

Boal et al., reporting **Pharmacokinetic and toxicity studies of AZT (zidovudine) following perfusion of human term placenta for 14 hours** in *Toxicology and Applied Pharmacology* in March 1997 (143(1):13-21) found 'AZT readily crossed the placenta into the

fetal compartment reaching equilibrium with maternal levels within 60-90 min after addition of each administration of AZT'.

The following month, reporting their study of **Transplacental pharmacokinetics and fetal distribution of azidothymidine, its glucuronide, and phosphorylated metabolites in late-term rhesus macaques after maternal infusion** in April 1997 in *Drug Metabolism and Disposition* (25(4):453-9), Patterson et al. noted that 'AZT-monophosphate was detected in almost all fetal tissues examined'.

The NCI group, led by Olivero et al., investigated **3'-azido-3'-deoxythymidine [AZT] transplacental perfusion kinetics and DNA incorporation in normal human placentas in similar terms perfused with AZT** and reported these findings in July 1999 in *Mutation Research* (428(1-2):41-7). Concerned because

transplacental exposure studies demonstrated that AZT is a moderate to strong transplacental carcinogen in mice [and] the consequences of transplacental AZT exposure to the [human] fetus remain unknown

the NCI group investigated 'the extent and kinetics of AZT transfer across the human placenta'. They reported their findings with the following warning:

Since AZT crosses the human placenta and becomes rapidly incorporated [*within 2 hours of AZT perfusion*] into DNA of placental tissue in a dose-dependent fashion, [this suggests] that even short exposures to this drug might induce [*human*] fetal genotoxicity.

We should mention that we respectfully disagree with the NCI group's finding that AZT is incorporated into foetal DNA; and that whatever the drug's danger to human foetuses, we don't consider the danger of incorporation into foetal DNA to be one of them. So as not to burden this memorandum with a technical discussion of the inappropriate assay that we contend was employed by the NCI group in arriving at their erroneous conclu-

sion here, let alone the basic AZT triphosphorylation problem (which AIDS doctors haven't ever heard about), we will provide the reasons for our dissension from the NCI group on this aspect separately, if requested. We point out, though, that it is generally accepted in medicine that AZT is incorporated into human foetal DNA after maternal ingestion/infusion (e.g. as stated in the Blanche alert); and we mention that the NCI group have published two further papers making this claim in relation both to apes and humans: **Incorporation of 3'-azido-3'-deoxythymidine (AZT) into fetal DNA and fetal tissue distribution of drug after infusion of pregnant late-term rhesus macaques with a human-equivalent AZT dose.** *J Acquir Immune Defic Syndr.* 1999 Dec 15;22(5):477-83; and **Incorporation of zidovudine into cord blood DNA of infants and peripheral blood DNA of their HIV-1-positive mothers.** *Ann N Y Acad Sci.* 2000 Nov;918:262-8.

Although the worst cases of AZT-induced mitochondrial disease in children exposed to the drug in the womb have proved fatal, or have resulted in conspicuously obvious permanent brain damage, or other serious injury – described in the Blanche alert as 'symptom-free ... severe biological or neurological abnormalities' – the absence of a narrow, distinct set of symptoms of mitochondrial poisoning makes it difficult to identify and diagnose – all the more so in a developing country like ours without a widely available First World medical infrastructure to monitor the time-bombing mess.

**In A comparison of genetic mitochondrial disease and nucleoside analogue toxicity. Does fetal nucleoside toxicity underlie reports of mitochondrial disease in infants born to women treated for HIV infection?** in *Annals of the New York Academy of Sciences* in November 2000 (918:247-61) Haas et al. made the same point:

Recent reports of mitochondrial disease in infants whose mothers were treated in pregnancy with nucleoside analogues are of concern. Chronic nucleoside analogue

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treatment of adults has long been known to cause mitochondrial DNA depletion with the risk of multisystem disease. Combination nucleoside analogue treatment regimens [e.g. AZT+3TC] may have the greatest risk of toxicity.

In other words, mitochondrial poisoning in utero can result in a wide array of disease conditions among children. Again the point was made in the report of the Barret study, noting that the

clinical expression ... of the mitochondrial toxicity of nucleoside analogues ... is highly variable, from peripheral neuropathy to severe lactic acidosis.

As Le Chenadec et al. were also to discover in 2003 (their study discussed above), Haas's et al. observation that the combination of nucleoside analogues such as AZT together with 3TC during pregnancy 'may have the greatest risk of toxicity' has been repeatedly confirmed:

The NCI group, led by Olivero, reporting the **Transplacental genotoxicity of combined antiretroviral nucleoside analogue therapy in Erythrocebus patas monkeys** in *Journal of Acquired Immune Deficiency Syndromes* on 1 April 2002 (29(4):323-9), found exactly that – noting that 'the total DNA damage sustained by fetuses exposed to both drugs [AZT and 3TC] was at least double that observed in fetuses exposed to ZDV [AZT] alone'.

Walker et al. found similarly, reporting in *AIDS* (16:2165-2173) in the same year, with the title of their paper pointing up their finding of **Increased long-term mitochondrial toxicity in combinations of nucleoside analogue reverse transcriptase inhibitors**.

Naturally the authors of the WHO Recommendations didn't think fit to mention any of this when recommending that pregnant women in the Developing World, and their unborn and newly born babies, be given AZT and 3TC mixed.

It is crucially important to appreciate that the frequency and severity of mitochondrial damage caused to children exposed to

AZT in utero is not always immediately clinically obvious, even when it is severe, and that it may be initially clinically asymptomatic, as the Blanche alert noted – where the crippling, sometimes fatal, effects of AZT and AZT+3TC exposure in utero only became manifest among children several months after exposure.

Recent research on the subject of mitochondrial toxicity of nucleoside analogue drugs for human foetuses by the NCI group, led by Divi, which the scientists described as a ‘pilot study’, was published a few months ago in April 2004 in *AIDS* (18(7):1013-21) – subsequent to the publication of the WHO Recommendations – under the title, **Mitochondrial damage and DNA depletion in cord blood and umbilical cord from infants exposed in utero to Combivir** (i.e.AZT and 3TC). The NCI group found that a

cohort of HIV-1-uninfected Combivir-exposed infants with no clinical symptoms showed morphological and molecular evidence of mitochondrial damage. ... In umbilical cords from six of nine infants born to HIV-1-infected mothers taking Combivir moderate to severe mitochondrial morphological damage was observed ... while none of seven unexposed infants showed similar damage.

Having regard to all the data on the mitochondrial toxicity of AZT published to date, along with findings made about the rapid transport of AZT across the placenta and its accumulation in foetal blood to equivalent or higher than maternal levels, there is no reason to doubt that the findings of Divi’s et al. pilot investigation – that two thirds of babies exposed to nucleoside analogue drugs in utero will suffer ‘moderate to severe’ mitochondrial damage – will in time be confirmed by a future large scale study.

The most recent research on transplacental nucleoside analogue foetal mitochondrial toxicity, conducted by Bishop et al., was reported online on 30 June 2004 by Pubmed, in advance of print publication in *Toxicological Science*, under the title **Mitochondrial Damage Revealed by Morphometric and Semiquantitative**

## **Analysis of Mouse Pup Cardiomyocytes Following in Utero and Postnatal Exposure to Zidovudine and Lamivudine:**

That myopathy and cardiomyopathy, related to mitochondrial damage, develop in some adults chronically treated with ZDV has long been known; recently, reports have suggested that similar adverse effects may occur in some infants exposed perinatally. Using a mouse model of human neonatal exposure, we treated pregnant CD-1 mice twice daily with doses of 75 mg/kg ZDV plus 37.5 mg/kg lamivudine throughout gestation and lactation; pups were exposed by direct gavage beginning postnatal day (PND) 4 and sacrificed on PND 28. Hearts were removed rapidly, and ventricles were processed for electron microscopy. Morphometric and semiquantitative morphological analyses were performed on 3 micrographs from each of 3 blocks from each of 3 females and 3 males from the control and treated groups. Treated mice showed significant increases in the mean area and decreases in the mean number of cardiomyocytic mitochondria compared to controls. We observed clusters of damaged mitochondria more frequently in treated animals than in controls; damage included fragmentation and loss of cristae. These results, demonstrating alterations in cardiomyocytic mitochondria of mice exposed in utero and postnatally, may model cardiac damage reported in human infants similarly exposed to ZDV.

Even before it was licensed by the FDA as an AIDS drug in 1987, AZT had been found to be carcinogenic by FDA toxicologist Harvey Chernov in a review of numerous studies entitled *Review & Evaluation of Pharmacology & Toxicology Data* that he sent up in December 1986 for consideration by the licensing panel. Since local GlaxoSmithKline medical director Peter Moore is on record candidly warning much the same – ‘Long-term use of AZT [‘for more than six months’] does contain risks, including cancer’



(*Mail&Guardian*, 1 December 1999) – we won't lumber this memorandum with all the published studies.

But as far back as 1997, the NCI group, particularly concerned about the potentially carcinogenic consequences of exposing human foetuses to AZT, conducted animal investigations into this, and found positively, as indicated in the title of their paper published in November that year in the *Journal of the National Cancer Institute* (89(21):1602-8), **Transplacental effects of 3'-azido-2',3'-dideoxythymidine (AZT): tumorigenicity in mice and genotoxicity in mice and monkeys.**

Pregnant mice and monkeys were given AZT in the second halves of their gestational terms. By one year of age, the mice exposed to AZT in utero 'exhibited statistically significant, dose-dependent increases in tumor incidence and tumor multiplicity in the lungs, liver, and female reproductive organs'. 'AZT,' the NCI group accordingly noted, 'is genotoxic in fetal mice and monkeys and is a moderately strong transplacental carcinogen in mice examined at 1 year of age.' They advised accordingly: 'Careful long-term follow-up of AZT-exposed children would seem to be appropriate.'

Having established that

AZT is unequivocally a transplacental genotoxin and carcinogen [and] given transplacentally to mice, benzo[a]pyrene [*a known carcinogen employed in research laboratories to induce cancers*] produced lung and liver tumour multiplicities similar to those observed

with AZT, the NCI group recorded their concern that

the current practice of treating HIV-positive women and their infants with high doses of AZT could increase cancer risk in the drug-exposed children when they reach young adulthood or middle age.

Only GlaxoSmithKline's lawyers took note: on 4 March 1998, to hedge the company against damages actions arising from the de-

velopment of cancers in people exposed to AZT before they were born, the 'PRECAUTIONS: Information for Patients: Carcinogenesis, Mutagenesis, Impairment of Fertility' section of AZT's 'PRODUCT INFORMATION' was amplified: to the sentence, 'The long-term consequences of in utero and infant exposure to Retrovir [AZT] are unknown', was added the phrase, 'including the possible risk of cancer'.

The subsequent appearance of cancers in children exposed to AZT in utero, just as the NCI group's animal studies predicted, hasn't caused any alarm among AIDS doctors who promote the drug as a perinatal anti-HIV prophylactic – due, it appears, to a typical medical mindset problem, particularly among those whose professional reputations are deeply invested in this asinine treatment. In a private note to the writer, praising the 'good comprehensive review of the literature you performed' in *Debating AZT: Mbeki and the AIDS drug controversy*, Ofelia Olivero of the NCI group remarked upon this phenomenon: 'During my research I noticed a lot of resistance from many different people to believe our data. In general there is resistance to the "bad news".'

This 'resistance to the "bad news"' is well illustrated in the case of Ellen Cooper, one of the US FDA panellists who approved the licensing of AZT as an AIDS drug in February 1987 (see the fraud spilled in *Licensing AZT*) and Principal Investigator of the Women and Infants Transmission Study (ACTG076, sponsored, like the original licensing trial, by the drug's manufacturer) on the basis of which AZT, previously strenuously contraindicated in pregnancy by numerous authorities, is today used in pregnancy – a study meticulously analysed and completely debunked by Papadopoulos-Eleopoulos et al. in their exhaustive, 130 000-word *Mother to child transmission of HIV and its prevention with AZT and zidovudine* monograph, which we sent you in hard-copy last month. (It's archived online at [www.theperthgroup.com](http://www.theperthgroup.com).)

Cooper was quoted in the September/October 1998 issue of *Mothering* magazine:

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We don't know what the long-term effects of AZT use during pregnancy might be, but so far we have seen virtually no adverse effects in the short term. ... Not one single tumor. Not one. ... I mean [the children] have cancers, lymphomas, and other problems like that ... but there's no reason to link those cancers to AZT.

But given Olivero's findings that AZT has exhibited transplacental carcinogenicity in animal models, and Pluda's et al. discovery of the **Development of non-Hodgkin lymphoma in a cohort of patients with severe human immunodeficiency virus (HIV) infection on long-term antiretroviral therapy**, published in *Annals of Internal Medicine*, in August 1990 (113(4):276-82) – just under half of them within three years, an incidence of the disease about fifty times higher than normal – there would seem to be every reason in common sense to 'link those cancers to AZT'.

Whether in decades to come, the 'unequivocally' established 'transplacental genotoxi[city] and carcinogen[icity]' of AZT in animal models likewise manifests among human adults exposed to AZT in their mother's wombs, like thousands of DES victims in the First World today, remains to be seen.

The transplacental carcinogenicity of DES had been well-established in many animal studies, but all were ignored by medical experts and doctors lauding the drug. To quote Nora Cody speaking in July 1999 at the National DES Research Conference in Bethesda in the US:

30 years ago today DES was still being prescribed to pregnant women in this country and, indeed, around the world. By 1969 scientists had studied this scientific substance for over three decades. Over and over, they had found cancer in laboratory animals.

For those girls lucky enough not to be born with deformed, virilised genitals, only when they reached adulthood did the harm the drug had caused become apparent in the form of ordinarily

rare carcinomas in their vaginas and cervixes (among other problems).

It's significant in this regard that the murine studies of the NCI group led by Olivero, reported in 1997 (discussed above), found that mice exposed to AZT in utero 'exhibited statistically significant, dose-dependent increases in tumor incidence and tumor multiplicity in the lungs, liver, and female reproductive organs'.

The NCI group, led by Diwan, published further findings of **Multiorgan transplacental and neonatal carcinogenicity of 3'-azido-3'-deoxythymidine in mice** in *Toxicology and Applied Pharmacology* in November 1999 (161(1):82-99). Following up on their 1997 study of one-year-old mice exposed in utero to AZT,

Findings for all remaining offspring up to 2 years old are reported here. AZT effects were most prominent in female offspring, with a significant threefold increase in lung tumors, a reduction in lymphoblastic and follicle center cell lymphomas, and a significant increase in histiocytic sarcomas (0 in controls, 3% after low-dose AZT, and 8% after high-dose AZT,  $p = 0.022$ ). Dose-dependent incidences of mammary gland, ovarian, and seminal vesicle tumors were low but significant: 0/106 controls, 3/105 low-dose, and 8/105 high-dose mice presented one of these neoplasms ( $p = 0.0025$ ). Incidences of females showing any clearly AZT-related neoplasm, in lung, liver, ovary, or mammary gland or histiocytic sarcoma, in the second year, were 12/32 after the low dose and 14/27 after the high dose vs 3/23 controls ( $p = 0.0045$ ). Also, the sensitivity of neonatal mice was assessed by administration of 25, 50, 100, or 200 mg/kg AZT on postnatal days 1 through 8. The effects at 2 years were similar to those seen after transplacental exposure, with significant increases in lung, liver, and mammary tumors in females. The results confirm that AZT is a moderately effec-

tive perinatal carcinogen in mice, targeting several tissue types.

Another study by the NCI group, led by Bialkowska, **Oxidative DNA damage in fetal tissues after transplacental exposure to 3'-azido-3'-deoxythymidine (AZT)**, was published the following year in the May 2000 issue of *Carcinogenesis* (21(5):1059-62). Noting that 'AZT has been found to be a perinatal carcinogen in mice' the NCI researchers investigated possible mechanisms for this in further studies with pregnant mice and monkeys. In the case of mice they found that exposing mice foetuses to AZT ('the transplacental carcinogenesis regimen'!) led to

Significant increases in 8-oxo-2'-deoxyguano-sine (8-oxo-dG) ... in the livers, a target tissue for transplacental carcinogenesis, and in the kidneys. ... Tissues were also obtained from fetal patas monkeys (*Erythrocebus patas*), whose mothers had received 10 mg AZT/day during the last half of gestation. Although limited numbers of samples were available, possible increases in 8-oxo-dG were noted, relative to controls, for placenta and for fetal lung and brain ( $P = 0.055$  for treatment-related increases in these tissues). These results suggest that an increase in reactive oxygen species could contribute to the mechanism of transplacental carcinogenesis by AZT in mice, and that this may also occur in primates.

Presuming that the MCC is even aware of the AZT transplacental carcinogenicity data canvassed in this memorandum, which we doubt, it's hard to imagine that its members will be happy to take a wait-and-see position in regard to whether South African babies, born to mostly poor African mothers, develop cancers in childhood and adulthood, thanks to the AZT they have just recommended their mothers ingest while carrying them. Surely not any African members.

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The administration of AZT to pregnant women and their newborn babies is justified, one reads over and over like a stuck gramophone, on the basis that it saves babies' lives. As Blanche et al. were blanching over their sinking suspicion confessed in their 'Early report' in *Lancet* in 1999 that they had crippled and in some cases killed children in the most terrible way with their strong drugs, they defended themselves saying, 'Prophylaxis of mother-to-child transmission of HIV-1 infection has saved thousands of children from death.'

But in a paper that was otherwise thoroughly referenced, there was no reference put up to support this show-stopping claim. That's because there isn't one to cite. Just as there isn't one for leading American AIDS expert Lynne Mofenson's foundational claim in September 2000 in the *New England Journal of Medicine* (343(11):803-805) in an editorial, **Perinatal Exposure to Zidovudine – Benefits and Risks**: 'Mother-to-child transmission of the human immunodeficiency virus (HIV) causes a chronic and ultimately fatal pediatric infection.' There's no reference supporting that either – but the French AIDS doctors who published the Blanche alert and Barret study bought it anyway, citing the Mofenson editorial in their AZT+3TC paper discussed above (Mandelbrot et al. in *JAMA* 285(16)2083-93.)

There is no good evidence that children privileged enough to get AZT while in their mothers' wombs, and immediately after birth for a while, do better and go on to live happier, healthier lives than children sadly deprived of it. On the contrary, when AIDS doctors are finished playing in their laboratories with all their little tests, and return to the real world in which their AZT-burned infant patients have to make their way, and they look at how the drug-treated babies have turned out, as against untreated children, they consistently find that AZT-exposed babies are very much worse off. Which is to be expected by anybody with even a fleeting familiarity with the toxic pharmacology of the drug.

That exposure to AZT in the womb and after birth leads to a higher death and serious disease rate among drug-exposed babies than untreated ones has been apparent for several years, but in the contemporary AIDS craze this has simply been disregarded:

1. In **Rapid disease progression in HIV-1 perinatally infected children born to mothers receiving zidovudine monotherapy during pregnancy**, reported in May 1999 in *AIDS*, (13:927-33) de Martino et al. reported that

Comparison of HIV-1-infected children whose mothers were treated with ZDV with children whose mothers were not treated showed that the former group had a higher probability of developing severe disease (57.3% ... versus 37.2%) ... or severe immune suppression (53.9% ... versus 37.5% ...) and a lower survival [rate] (72.2% ... versus 81.0% ...).

2. In June 2000, De Souza et al. published consistent findings in *Journal of Acquired Immune Deficiency Syndromes* (1;24(2):154-61) concerning the **Effect of prenatal zidovudine on disease progression in perinatally HIV-1-infected infants**. Their objective was to

determine the influence of prenatal zidovudine (ZDV) prophylaxis on the course of HIV-1 infection in children by comparing the clinical outcome of infants born to HIV-1-seropositive mothers who did versus those who did not receive ZDV during pregnancy. ... The main outcome measure was rapid disease progression (RPD) in the infant, defined as occurrence of a category C disease or AIDS-related death before 18 months of age. ... Among infected infants, the RPD rate was 29.4% in the no ZDV group compared with 70.6% in the ZDV group ... The rate of RPD was five to six times higher among infants born to treated compared with untreated mothers

3. In July 2000, in the *Journal of Infectious Diseases* (182(1):104-11), Kuhn et al. reported likewise in their study of 325 HIV-positive children born between 1986 and 1997 until death or diagnosis with AIDS, under the title, **Disease progression and early viral dynamics in human immunodeficiency virus-infected children exposed to zidovudine during prenatal and perinatal periods.** Their findings were summarised in a report by Reuters Health:

Among infected children who did not receive ART before AIDS diagnosis, 44% developed AIDS or died before age 12 months when they were exposed to prenatal or perinatal zidovudine. However, among HIV-infected infants not exposed to zidovudine prophylaxis, rate of death or progression to AIDS was only 24% ... Zidovudine exposure before birth or perinatally appears to accelerate disease progression in HIV-infected infants.

4. In **Timing of perinatal human immunodeficiency virus type 1 infection and rate of neurodevelopment**, reported in *Pediatric Infectious Diseases Journal* in September 2000 (19(9):862-71) Smith et al. reported late-presenting evidence of neurological and brain damage caused by exposure to AZT in utero and after birth. As the Blanche alert had noted a year previously – subsequently confirmed by the Barret study in mid-2003 – the stultifying drug injury to the brain took time to become symptomatically evident, and, in the study in point, only became apparent when the children were specially tested for cognitive function and performance:

Infants with early positive HIV-1 cultures demonstrated a notable decrement in neurodevelopmental functioning within the first 30 months of life. They achieved motor developmental scores that were increasingly and significantly discrepant both from the average and from scores achieved by late HIV-1-positive children over the course of the study period. Those children with early HIV-1-



positive cultures also demonstrated a trend toward a similar decline in mental functioning over time ... The mothers of infants with early [HIV] positive cultures were more likely to receive ZDV [AZT] treatment during pregnancy, and their infants were more likely to receive ZDV treatment prophylactically during the first 6 weeks of life.

5. Concerning the WHO Recommendations's advocacy of a return to long-course AZT for pregnant African women, rather than the short-course treatment that has become the fashion among AIDS doctors in recent years, the data entered in Table 3 in **A trial of shortened zidovudine regimens to prevent mother-to-child transmission of human immunodeficiency virus type 1** by Lalemant et al., published in the *New England Journal of Medicine* on 5 October 2000 (343(14):982-91), reaffirmed the harm this causes children: a 7% congenital abnormality rate following long-course exposure versus 1% after short-course exposure; likewise a 7% neutropenia and leukopenia rate versus 2%; infections or other 'HIV-related' events were 43% versus 33%; and neonatal or other obstetrical events occurred in 22% versus 14% of cases. Mothers on long course AZT treatment had a higher rate of stillbirth (8% vs. 4%), severe anaemia (7% vs 4%), infection or other HIV events (20% vs 17%), and events related to pregnancy or delivery (24% vs 17%) than mothers who received the short course. Which is not to say that short-course foetal exposure to AZT is safe:

6. In support of the suggestion that AZT may safely be taken in pregnancy – 'There have been reports of a small number of serious adverse effects possibly associated with exposure to ART [antiretroviral therapy] in the form of mitochondrial dysfunction (43-45), but an increased rate of serious clinical manifestations has not been confirmed by other studies (46-48)' – the WHO Guidelines cite a study (citation 47) by Chotpitayasunondh et al., including staffers of the US CDC, **Safety of late in utero exposure to zidovudine in infants born to human immunodeficiency virus-infected mothers: Bangkok**, published in *Pediatrics* in Janu-

ary 2001 (107:E5). The happy title notwithstanding, the researchers reported a five times higher febrile convulsion rate and an 11% higher incidence of serious disease among the short-course AZT-exposed babies as compared with the unexposed. This the AIDS doctors dismissed as

a slightly higher risk for disease progression among ZDV-exposed, HIV-infected children during the 18-month follow-up period, although this difference was not statistically significant.

And as for the dishonest suggestion in the WHO Guidelines that this study was at variance with others that reported mitochondrial dysfunction among AZT-exposed babies – in the sense of disconfirming them – Chotpitayasunondh et al. specifically conceded that

our sample size was chosen to determine the efficacy of short-course ZDV and to identify adverse events that occur with high frequency; it was not large enough to detect an increased rate of adverse events that occur rarely. Also, the number of infected children is too small and follow-up too short to draw conclusions about disease progression related to ZDV exposure. Second, our review of clinical conditions potentially associated with mitochondrial dysfunction was retrospective and could not evaluate the incidence of subtle clinical findings or laboratory abnormalities that might suggest mitochondrial dysfunction. Third, as in other studies to date, our follow-up period of 18 months is too short to enable us to evaluate the incidence of conditions, such as cancer, that may take many years to develop.

7. But the striking ‘incidence of conditions, such as’ infant death following the treatment of babies and children with AZT and a similar drug, ddI, was revealed by Chotpitayasunondh himself in

an interview he gave Karen Emmons for her article in the *San Francisco Examiner* on 31 May 1999:

Of the children who were born HIV-positive in Bangkok in the past four years and received the combination drug treatment, Chotpitayasunondh said that one-fourth died in their first year, about 33 percent by their second year, 40 percent by age 3, and then the mortality tapered off.

To repeat: forty per cent of the AZT-treated babies were dead before their third birthday. But to the wide-eyed American reporter, this was evidence that **Thailand wins a round in fight against HIV**, as she called her piece, rather than 'An iatrogenic disaster in Thailand'.

8. The conclusion that this appalling death rate was the result of AZT (and ddI) poisoning is supported by a similar fatality tally among AZT-exposed children reported by Lipshultz et al. in *Circulation* on 26 September 2000 in their paper **Cardiac Dysfunction and Mortality in HIV-Infected Children** (102(13):1542-8): 'Other factors associated with lower cumulative survival included ... a history of zidovudine therapy.' Table 1 in the published report reflected that 37.5% of children given AZT died, as against 22.8% of the untreated children – which is to say that treatment with AZT almost doubled their death rate.

Yet even as they reported these brute facts, many of the AIDS doctors who conducted these studies were telling us what great stuff AZT is, and that its use in pregnancy should unquestionably be continued. They weren't put out by their own data showing that AZT-exposed infants get sick and die at a much higher rate than unexposed ones. That AZT causes AIDS one might say. As Heresi et al. did, more or less, in September 1997 in their report in *Clinical Infectious Diseases* (25(3):739-40), describing **Pneumocystis carinii pneumonia in infants who were exposed to human immunodeficiency virus but were not infected: an exception to the AIDS surveillance case definition**: 'We present two cases of se-

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vere PCP [*pneumocystis carinii pneumonia, a classic and original AIDS-defining disease*] in infants who were perinatally exposed to HIV [and AZT] but who were uninfected with HIV.’ An unremarkable turn for the worse in the babies’ health, really, since as the *The Physician’s Desk Reference* revealingly notes,

It was often difficult [in AZT clinical trials] to distinguish adverse events possibly associated with administration of Retrovir from underlying signs of HIV disease or inter-current illnesses.

And likewise, in company with De Martino, de Souza, Kuhn and fellow AIDS doctors, having just confirmed that indeed, as they had feared, AZT and 3TC cripples and in some cases kills children exposed to it before and after birth, the French AIDS doctors in the Barret study tried slapping down any worries by asserting emotively, again without authority in the shape of any controlled study,

It is clear that the number of children worldwide who suffer because that have not received antiretroviral treatments is inestimably larger than the number of children who suffer due to the toxicity of these treatments.

It was the same spiel in the Blanche alert: ‘We are aware that the suggestion that antiretroviral drugs are toxic raises delicate issues.’ Which the doctors tried stilling by immediately laying their earnest claim on us that ‘Prophylaxis of mother-to-child transmission of HIV-1 infection has saved thousands of children from death.’ Except that, when clinical outcomes are considered – and not meaningless, unvalidated, non-specific blood tests (about as scientific as an apartheid Race Classification Board inspector’s pencil test) – the ‘children who suffer’ turn out to be the beneficiaries of American medicine.

The sort of canards professed by the French AIDS doctors in excusing the atrocities they had perpetrated are known in a religious context as articles of faith; and, in the high purpose that the

doctors proclaim in their healing mission against the sex-virus (especially prevalent among blacks, such AIDS doctors say), they are used to justify the violence they deploy against women and children, well knowing that it will injure many of them, as we see. Implying, though, that strong measures are called for. That a firm approach is needed with these people.

Indeed, against what US Secretary of State Colin Powell described to Larry King on 11 July 2003 as a 'weapon of mass destruction', formally declared 'a threat to US national security' by former US President Bill Clinton on 29 April 2000 (bringing the NSC and the CIA with all its internationally-situated spooks and goons into the game), 'aggressive, effective action' is what's needed – so insisted former US ambassador Cameron Hume at Rhodes University on 21 October 2002.

The Barret study confirms and predicts with absolute, incontestable certainty that children exposed to AZT before birth will be injured, and in some cases killed. We wonder whether the MCC joins in the view expressed by the Americans, and by those white AIDS doctors in France, that the killing and maiming of mostly black, mostly poor children by 'aggressive, effective action' in the holy war on AIDS is acceptable collateral damage. Because we think it's criminal and we think it's obscene.

Especially since, as you will have read by now, the vacancy of the entire pMTCT project (just like the 'weapons of mass destruction' ruse for the Americans' other neo-colonial business further north) was revealed as Papadopoulos-Eleopoulos et al. demolished it brick by brick in their *Mother to child transmission of HIV and its prevention with AZT and nevirapine* monograph.

To be honest, we think that any member of the MCC who, after having read that paper, still subscribes to any of this MTCT mythology – this new American idea that mothers, mostly black, mostly poor, can kill their babies by bearing them, giving birth to them and by breastfeeding them, and that they do well from transplacental exposure to carcinogenic, mutagenic cell-poisons – really needs new batteries.

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Way back in 1991 Hayakawa et al. made an alarm call, **Massive Conversion Of Guanosine To 8-Hydroxy-Guanosine In Mouse Liver Mitochondrial DNA By Administration Of Azido-thymidine** in *Biochemical and Biophysical Research Communications* (176, 87-93), warning, in the light of their findings, that 'it is urgently necessary to develop a remedy substituting this toxic substance, AZT'.

In their monumental 25 000-word examination and explosion of GlaxoSmithKline's core claims in biochemistry for AZT as a medicine, **A Critical Analysis of the Pharmacology of AZT and its Use in AIDS**, Papadopoulos-Eleopoulos et al. took the same view:

A critical analysis of the presently available data which claim that AZT has anti-HIV effects shows there is neither theoretical nor experimental evidence which proves that AZT, used either alone or in combination with other drugs, has any such effect. The recommendation that AZT, either alone or in combination, is administered to HIV seropositive or AIDS patients warrants urgent revision.

Particularly because, as they point out,

the scientific literature ... elucidate[s] a number of biochemical mechanisms which predicate the likelihood of widespread, serious toxicity from use of this drug.

The French AIDS doctors conducting the Barret study grudgingly conceded that it's high time that AZT in maternity hospitals – like bloodletting, arsenic and mercury as earlier standards of medical care – should be ditched: 'Many antiretroviral molecules of different therapeutic classes are now available and it is very plausible that certain molecules or combinations of molecules be better tolerated than others by the fetus and newborn.' Better tolerated.

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The WHO Guidelines, it should be noted, spring directly from the germ-chemotherapy paradigm of AIDS promoted by the pharmaceutical cartel, and by all those busy bees in the research industry and in academia that it supports, flying them around and lavishing grants upon them, and who in turn faithfully serve it; and they take no account of alternatives to the aggressive use of highly toxic chemicals on mothers and their unborn and newborn babies in the Developing World.

And more's the pity that the French AIDS doctors didn't share Hayakawa, Papadopulos-Eleopulos and their colleagues' sense of urgency as they surveyed the wasteland after waging their noble battle in maternity wards in what the WHO Recommendations calls the 'fight' against 'the HIV/AIDS epidemic' – a 'fight' joined by a sprinkling of loyal natives such as William Makgoba (to whom we'll return) and Kgosi Letlape, who heads the South African Medical Association, against an epidemic strangely invisible to most other Africans, other than in the drearily familiar form of diseases of poverty, which have afflicted them ever since they lost their lands. But which big-time local AIDS expert Professor Jerry Coovadia attributes, as all non-African AIDS doctors do, to the 'unbridled sexuality' of 'newly independent people' – by which he means the unique, fantastic promiscuity of the servants.

Admittedly it would have taken a lot of courage for the French AIDS doctors reporting the Barret study to have publicly repudiated their deadly medicines; and as they demonstrated, none of them were man enough for it. The question is: is the MCC? Alexander Pope once gave the problem an encouraging spin, however: 'A man should never be ashamed to admit that he has been in the wrong, which is but saying, in other words, that he is wiser today than he was yesterday.' Generations of affected South Africans, mostly black, mostly poor, will be looking back and asking: how could this have been allowed to happen? Wasn't there anyone there to protect us?

After the lessons supposed to have been learned in the precedent thalidomide disaster, well they might wonder. But a brief

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review of that tragedy in the 3<sup>rd</sup> edition of the *Oxford Illustrated Companion to Medicine* explains things in terms of the characteristic constipation of the medical mind:

It was then widely believed that the human placenta was impervious to poisons except in such doses as killed the mother. Yet there was already widespread evidence that this was untrue and that fetuses could be deformed by external influences, including poisoning and therapeutic drugs ... but most of it had been ignored because this suited the contemporary mind-set or *Denkstil*. ... Why did the medical profession ignore the extensive existing evidence that teratogenic substances (causing developmental abnormalities in the fetus) could cross the placenta? It is useful to look at the question as part of a mind-set or a shared view of reality that controls, organizes, and limits perception and understanding. We all tend to ignore what does not fit the theories and beliefs with which we live.

As disaster-porn, the brain damage and other crippling harm that AZT causes during pregnancy and after birth does not make such salaciously spectacular copy for the newspapers as that caused by thalidomide – whipping up public interest and sympathy, and therefore good for circulation and profits – but for the victims, their parents, their siblings and others close to them, the consequences, kicking in several months after drug-exposure, are just as horrible, just as tragic. Every minute, every hour, every day, for a lifetime.

We do understand that it is embarrassing for doctors, AIDS experts especially, to admit that they have been mistaken – doubly so when their medicaments, ladled down with the best intentions, to gratifying public acclaim, turn out to have been harmful and sometimes deadly; but the history of Western medicine is one of grand errors, usually lasting centuries and sometimes millennia, and scarcely credible afterwards.



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We trust that in the light of the data presented in this memorandum, however, the MCC will act robustly, and not faff around in the manner of Supreme Court of Appeal Judge Edwin Cameron, who, when confronted with the AZT toxicity data for unborn babies set before him by President Mbeki in mid-March 2000, in a fifteen-page reply to the former's appeal for the provision of this elixir to pregnant women, told reporters that his 'heart sank' as he read it 'with a sense of fear and dismay' – not because the data appalled him as it had the President when he read an early draft of *Debating AZT: Questions of safety and utility*, causing him to change his mind radically about the drug, but because, it appears, he winced at owning to what a fool he had made of himself in publicly advocating the drug.

We must confess, to be frank, that, although he likes publicly to declaim that 'I have no doubt that I have natural intellectual gifts', we find little evidence of them in his prosecution of his pet cause. Despite being presented with the case against the use of AZT in pregnancy thrice in 2000 – by President Mbeki, African historian Professor Charles Gesheker of UC California at Chico, and this writer – he has failed to weigh it, much less apologise to President Mbeki for aspersing him repeatedly from local and foreign podia on account of his well-founded concern over this drug – perhaps in the sort of terms in which the English novelist John le Carré framed a complimentary review of *Debating AZT: Mbeki and the AIDS drug controversy*:

I agree with (the alas late) Donald Woods: [AZT] needs much more serious debate than Big Pharma and the usual club of fringe beneficiaries are permitting. There is simply too big a case to answer, and it's not being answered. Having said that, I suppose I look a bit of a fool because I'm one of the numberless well-intentioned people who have been championing cheapo antiretrovirals for the Third World's afflicted etc.

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We hope that unlike his lordship, the MCC will react rather more responsibly, and will move quickly to revoke its latest recommendations, however awkward this might be. After which, some resignations might be in order, if, in this country, ordinary principles apply to failure in public office – evidenced by the MCC's disgraceful ignorance of the published literature in its field.

The MCC really wouldn't be acting out of turn in grasping the nettle and doing the right thing by making this radical move. After all, the Americans are allowed to fundamentally change their minds about AIDS treatment every five minutes. As with AZT for AIDS cases *in extremis* only (what the FDA licensed it for). Then for people told they're HIV-positive – when their cell counts are down, even if they're feeling just fine. As with warning against exposing foetuses to AZT. Then urging it as a good thing. As with the 'hit early, hit hard' approach in the mid-nineties – you gobble bracing doses of AZT and other drugs the moment you light up the test. Since AZT turned out to be no good alone. Then the big official U-turn in early 2001, recommending that it's better to leave the virus alone for as long as possible, before going on the poisonous drugs, so that the patient can live longer. These are the experts, kids.

Although we are still to receive any formal acknowledgement from the MCC of any of our correspondence, we have learned that individual members have been telephoning Dr Tshabalala-Msimang, telling her that they were 'amazed' by the 'detailed research' in our preceding letters, and that they had been 'unaware' of it. It is obvious that the MCC has been equally unaware of most, if not all, of the research findings reported in this memorandum. But it certainly knows of them now.

We also know from a confidential disclosure made by one of the MCC's members that it is running scared of being sued by the TAC – a not unjustified apprehension, to be fair, in view of the resolution the TAC passed in August 2002 to sue if the MCC disturbs its victory over the government in the courts, and the fact

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that the South African judiciary, in its loftiest reaches, holds the TAC in such high esteem. Why it even enjoined the government to hold hands with it in the battle against AIDS. Because gee we must all fight this together.

But the question we think everyone needs to start asking is: for how much longer are our new democracy, our people and the MCC going to be held hostage to the pharmaceutical cartel by a neurotic, clinically depressed, scientifically illiterate, American-financed drug industry pimp, posing as a human rights crusader against our national liberation movement – appropriately qualified for his controlled, loyal opposition role in the drug business with the experience he derived from his work as male prostitute, and a Standard Six. (It should be conceded, though, that the Treatment Action Campaign's foreign millions are generously shared: unemployed black people from the peri-urban ghettos called out to dance on demand for the cameras get a free summer tee-shirt and R100 'for transport and refreshments'.)

As far as deregistering nevirapine for perinatal use is concerned – what we started out asking about, and now long overdue – we don't think you need lose much sleep over the prospect of being over-ruled and reversed if attacked in the courts by this dreadful person, in the light of a new paper in the pipe, **Low efficacy of nevirapine (HIVNET012) in preventing perinatal HIV-1 transmission in a real-life situation**, by Quaghebeur et al, still in press for publication in *AIDS* 2004 Sep 3;18:1854-1856 but posted online by Pubmed already.

The researchers found that when 'in a real-life situation in Kenya' they tried the HIVNET 012 regimen (a hit of nevirapine each for mother and child), it was an unmitigated flop: 'The perinatal HIV-1 transmission rate at 14 weeks was 18.1%, similar to the 21.7% before the intervention. These data call for further evaluation of the simple nevirapine regimen in field conditions, and underline the need for alternative strategies.' Game over, so to say.

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The authors lamented that ‘despite the lack of validated efficacy data outside research settings’ doctors everywhere went dilly for this ludicrous medical gimmick – just as our clever judges did in prescribing nevirapine for heaving women and their newborn babies in South Africa, one of whom found the good they were all doing so terribly moving that he burst into tears afterwards.\*

And as for retracting your recommendations over AZT use in pregnancy, and then doing whatever it takes, either by way of deregistration, or the issue of a special urgent alert like the FDA and EMEA do from time to time, to ensure pregnant women and babies don’t come anywhere near this poison, we can’t see that in litigation launched by the TAC a judge with any brains will interfere with your moves after he’s seen the information contained in this memorandum.

In conclusion might we raise what could seem a rather tangential point? Actually it goes right to the heart of things.

In 1794, writing from a prison cell in Paris for speaking too plainly, the English radical Thomas Paine persisted irrepressibly in *The Age of Reason*:

As the object of the Church, as is the case in all national establishments of Churches, was the power and the revenue, and terror the means it used, it is consistent to suppose that the most miraculous and wonderful things they had collected stood the best chance of being voted. ... The resurrection and ascension, supposing them to have taken place, admitted of public and ocular demonstration, like that of the ascension of a balloon, or the sun at noonday, to all Jerusalem at least. A thing which everybody is required to believe requires that the proof and evidence of it should be equal to all, and universal. ... Instead of this a small number of persons, not more than eight or nine, are

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\* Related in *The trouble with nevirapine*.

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introduced as proxies for the whole world, to say they saw it, and all the rest of the world are called upon to believe it.

So taking Tom Paine's cue, if it isn't too impertinent of us to ask: could we also be shown this virus, about which such a fuss is made, on which so much public money is spent, and high-mindedly fighting which, to the great benefit of the pharmaceutical business, so many South African children, mostly black, mostly poor, are in jeopardy of being really messed up, even killed?

At the second meeting of the International AIDS Advisory Panel in Johannesburg in July 2000, this writer was personally witness to a solemn pact clinched, on behalf of the believers, by Professor Barry Shoub, Director of the National Institute for Communicable Diseases, and Professor William Makgoba, then Director of the MRC, and now VC of the University of KwaZulu-Natal. With his very own eyes this writer saw them pledging to conduct an experiment in which they'd have a go at isolating this terrifying virus in the standard, accepted manner (no short-cuts) from the blood of a person declared infected because his blood had lit up one of these antibody tests used to tell hundreds of South Africans daily, to their great dismay, that they've got the virus in them. But we're all still waiting, because as the gents concerned have shown, they're not good for their promises; and like bankrupt hucksters they just duck and dive and make all sorts of excuses whenever reminded.

Could the MCC maybe give them a friendly call, and ask them what's holding up the show? It could explain, very properly, that it needs to know, because the continued registration of a whole lot of extremely poisonous big-ticket drugs is on the line. And could you let us know whether it's because they quietly fret that if the experiment is carried out as agreed they could just come up empty-handed? It's a simple request we pose; and if indeed no virus is found – just a few biologically ambiguous traces – it

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could save the public purse an awful lot of waste, money that could then be much better spent, and spare many people, big and small, but mostly black, mostly poor, unnecessary poisoning and unnecessary suffering. But then again, we reckon that this might be the very impediment, for if no virus is found, and regular folk discover that they've all been taken for one hell of a ride, it will be the end of the money for the experts, and guys like Messrs Shoub and Makgoba might have to exchange their white vestments for blue overalls and go out looking for new jobs on the railways. With everyone laughing.

We do appreciate that our wonder about 'HIV' sounds rather off-the-wall. Just as it would have been to question the experts a couple of centuries ago with their doctorates in divinity, devilry and demonology, who were telling us that the Devil was corrupting the realm, and that he did so by way of obsession (possession) or by affording ungodly people with maleficent, preternatural powers; whose learned tomes on the subject filled library shelves at the University of Cambridge; and whose evidence in court got the accused (invariably from the working classes) hanged and burned in their umpteen thousands – in England, right up to 1736. (Lynching of accused witches continued in rural parts for well over a century.)

They claimed to know the certain tests: the hidden mole in the armpit, black cats, failure to sink when swum in ponds – dropped in to see, with left thumb tied to right big toe and vice versa – even introspective loneliness among the old, and insufferable insolence among the young. Since hey they were the experts. And some professional witchfinders, like the renowned Mathew Hopkins Esquire, whose evidence saw many people off, went about making a real good living out of it. As luminaries in the AIDS oligarchy do today.

But as you might have understood after reading that all-important Appendix XI to *Mother to child transmission of HIV and its prevention with AZT and nevirapine*, namely, *A critical examina-*

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*tion of the evidence for the existence of HIV\**, our request is maybe not so foolish after all. (If you found the detail and all those two hundred odd references a taxing read, there's a simplified version in press for imminent publication in the journal *Medical Hypotheses*.

This is our final friendly request for a formal response from you on the pressing issues we have raised in our correspondence to date. We know you are listening. And you know everyone's watching. We appreciate that you are sweating in fear of being attacked by the TAC. After all, they do have fans in high places – noisy some of them too, hectoring like a fishwife all the time. We don't mean to rush you unreasonably. We know that many of the matters raised in this letter will be new: nobody has critiqued the Barret study before, for instance, or lined up all the very latest foetal toxicity studies to demonstrate just how truly crazy it is to give AZT and 3TC and nevirapine to pregnant women and their babies.

Yours faithfully

ADV ANTHONY BRINK  
CONVENOR AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

Cc: The South African Government, all Provincial Health MECs, media and other interested parties.

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\* Online in 'Quick links' at [www.tig.org.za](http://www.tig.org.za).

## Annexure A

Eight drug-injured children, two fatally, described by Blanche et al. in 'Persistent mitochondrial dysfunction and perinatal exposure to antiretroviral nucleoside analogues', *Lancet* 1999 Sep 25;354(9184):1084-9

At age 4.5 months, the first patient presented with visual impairment. Cerebral nuclear magnetic resonance imaging showed initially (at age 5.0 months) demyelinating lesions of the brainstem that became more severe and secondarily associated (at 11.0 months) with sustentorial lesions. From age 4.5 months to 11.0 months, the growth was abnormal and associated with vomiting. There were no important hepatic, pancreatic muscle enzyme, or haematological abnormalities, but blood and cerebrospinal fluid lactate concentrations were high (2.5 mmol/L [normal <1.5 mmol/L] and 4.5 mmol/L [<2.0 mmol/L], respectively). The child died aged 13 months because of respiratory and cardiac-rhythm disorders. The symptoms were compatible with Leigh's syndrome and mitochondrial investigations were done at age 12 months.

The second patient, from age 4 months until death at 11 months, had refractory epilepsy and deterioration of cognitive and psychomotor abilities. Cerebral imaging showed diffuse demyelinating lesions associated with massive cortical necrosis (figure). There were no substantial biological abnormalities for liver, pancreas, muscle, or haematological markers. The blood lactate concentration was high (2.5 mmol/L) but cerebrospinal fluid lactate was normal. Several disorders were excluded because of normal results from the following diagnostic procedures: or-



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ganic-acid chromatography (urine), aminoacid chromatography (serum, urine, cerebrospinal fluid), serum cholesterol, triglycerides, vitamins A and E, pyruvate dehydrogenase activity in lymphocytes, fatty-acid oxidation and biotinidase activities (lymphocytes), very long-chain fatty acids (serum), lysosomal enzymes (galactosidase, galactosylceramidase, arylsulfatase A, mannosidase, GM1 and GM ganglioside), copper and ceruloplasmin (serum), and oligosaccharide excretion (urine). These symptoms were consistent with ALPERS syndrome, and led to mitochondrial investigations between ages 5 months and 7 months.

At age 8 months, during a febrile episode, patient three had a seizure and was thought to be hypotonic. At age 15 months, the child showed symptoms of hypokinetic hypertrophic cardiomyopathy. Blood hepatic and pancreatic enzyme concentrations were normal but the child had neutropenia neutrophils  $0.931 \text{ } 09/\text{L}$  [normal  $> 1.531 \text{ } 09/\text{L}$ ], high concentrations of muscle creatine phosphokinase in blood ( $350 \text{ IU/L}$  [ $<250 \text{ IU/L}$ ]), and persistently high blood lactate concentrations ( $4\text{mmol/L}$ ), although cerebrospinal lactate was normal. Endomyocardial biopsy showed intracytoplasmic vacuolisation in myocytes, but without inflammation. The cardiomyopathy progressively improved and symptoms of peripheral myopathy were seen at age 2.5 years. At age 4.0 years, the child's cardiac function was normal, but moderate muscular deficit persisted; lactate and muscle creatine phosphokinase concentrations in blood remained high. Electroretinography showed macular and peripheral abnormalities. Cerebral nuclear magnetic resonance imaging was normal.

In the fourth patient, early development was normal. Between ages 14 months and 27 months, the child had four episodes of febrile seizures. Neurological assessment at

age 27 months showed mild spastic diplegia. Haematological and biochemical findings, including lactate concentrations in blood and cerebrospinal fluid, were normal. Cerebral nuclear magnetic resonance imaging showed moderate hypersignal of the white matter in T2-weighted images, with no evidence of necrosis (figure).

From age 7 months until 15 months, patient five had repeated seizures. Cognitive development and neurological assessments between episodes were normal until age 15 months. The child developed status epilepticus for 4 h, which led to severe neurological dysfunction with cortical blindness and spastic tetraparesis. Biological tests at 15 months showed only high blood hepatic enzyme concentrations (aspartate and alanine aminotransferases 200 IU/L [ $<40$  IU/L]), which progressively returned to normal. Blood and cerebrospinal fluid lactate concentrations were measured only at the time of mitochondrial assessment and were not retrospectively available. Nuclear magnetic resonance imaging at age 16 months showed large necrotic lesions of the white matter and cortical grey matter. At age 3.5 years the child had severe sequelae and microcephaly.

Patient six was symptom-free until age 14 months, but persistent biochemical abnormalities were seen on standard follow-up of the epidemiological survey (which included lactate assays). The child had had high concentrations of blood lactate (4 mmol/L), hepatic aspartate aminotransferase (50 IU/L), and pancreatic lipase (200 IU/L [ $<150$  IU/L]) since birth that persisted until age 14 months. Cerebrospinal fluid lactate was normal. These biological abnormalities led to specific mitochondrial investigation, including cerebral nuclear magnetic resonance imaging that showed delayed myelinisation, which is difficult to interpret at that age.

## *Two*

Patient seven was symptom-free until age 4 months, at which time he became hypotonic with apnoea. The child regained normal breathing and consciousness after resuscitation, with no apparent sequelae. There were no biological abnormalities during routine biological follow-up, but blood lactate concentrations (routinely assayed in this institution) were continuously high ( $>4$  mmol/L) from the first test at 4 weeks to 7 months. Cerebral nuclear magnetic resonance imaging was normal. Near-miss syndromes and lactataemia justified mitochondrial investigations.

The eighth child was symptom-free. Persistent hepatic and pancreatic abnormalities (alanine aminotransferase 80 IU/L and lipase 180 IU/L) were seen from birth in the routine prospective biological follow-up. Blood lactate concentrations that were systematically added to the normal screening in the institution were normal, as were cerebrospinal fluid concentrations. At age 20 months, biological abnormalities persisted unchanged; a specific mitochondrial investigation was therefore done, including electroretinography, which was abnormal, and cerebral nuclear magnetic resonance imaging that showed abnormalities of the periventricular white matter.

No child was infected with HIV-1, and all were HIV-1 seronegative at age 15 months, or at death before this age for patients one and two. For all children, repeated tests for HIV-1 by PCR and by culture were negative.

## Annexure B

*Debating AZT: Mbeki and the AIDS drug controversy: paras 10-13*

[10] In his answer to my essay, Martin admits that AZT destroys bone marrow, but then hedges: HIV 'may' be the real culprit. This is a tired old tale rehashed. Mercury and arsenic salts – doctors' favourites for ages – poisoned the patient, whose death was then blamed on unbalanced humours or germs. That AZT destroys bone marrow is frankly declared by its manufacturer. So let's not fudge. In 1987 in *Annals of Internal Medicine*, Gill *et al* reported *Azidothymidine Associated with Bone Marrow Failure in the Acquired Immunodeficiency Syndrome (AIDS)*: 'Four patients with [AIDS], and a history of *Pneumocystis carinii* pneumonia developed severe pancytopenia [marked decrease in all types of blood cells] ... 12 to 17 weeks after the initiation of azidothymidine therapy ... Partial bone marrow recovery was documented within 4 to 5 weeks in three patients, but no marrow recovery has yet occurred in one patient during the more than 6 months since AZT treatment was discontinued.' In the same year in the *New England Journal of Medicine* Richman *et al* reported *The Toxicity of Azidothymidine (AZT) in the Treatment of Patients with AIDS and AIDS-Related Complex*: 'Anemia ... developed in 24% of AZT recipients and 4% of placebo recipients ( $P < 0.001$ ). 21% of AZT recipients and 4% of placebo recipients required multiple red-cell transfusions ( $P < 0.001$ ). Neutropenia ( $< 500$  cells per cubic millimeter) occurred in 16% of AZT recipients, as compared with 2% of placebo recipients ( $P < 0.001$ ).' The next year, Walker *et al* followed up in *Annals of Internal Medicine* reporting *Anemia and erythropoiesis in patients with the acquired immunodeficiency syndrome (AIDS) and Kaposi sarcoma treated with zidovudine*: 'In the current study, transfusion-dependent anemia occurred in 6 of 15 patients with AIDS and Kaposi sarcoma who were receiving zidovudine therapy. All 6 affected patients required their first blood transfusion between 3 and 9 weeks after starting zidvoudine therapy, and each re-

quired 4 to 14 units of packed erythrocytes to maintain a hemoglobin level above 100 g/L over a 12-week study.’ Consistent with this, Costello reported in the same year, in the *Journal of Clinical Pathology* that, ‘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.’ For AIDS doctors slow to the point, Harrison’s *Principles of Internal Medicine* spells it out: ‘[AZT], used for treating [HIV], often causes severe megaloblastic anemia ... caused by impaired DNA synthesis.’ Even in the modern age where AZT dosing levels are now hugely reduced, in 1998, in the *New England Journal of Medicine*, Hymes *et al* investigated and reported *The Effect of Azidothymidine on HIV-related Thrombocytopenia*, and found again: ‘The hematocrit [red blood cell count] decreased in the same patients ... with three of eight patients requiring red-cell transfusion by the fourth week of treatment.’ So did Mocroft *et al* in their paper in *AIDS* in 1999: *Anaemia is an independent predictive marker for clinical prognosis of HIV-infected patients from across Europe*: ‘We found that 78.2% of the [HIV-infected] patients with mild or severe anaemia at baseline had received zidovudine’.

[11] In their 1988 paper in the *British Journal of Haematology*, entitled, *3’-Azido-3’-deoxythymidine inhibits proliferation in vitro of human haematopoietic progenitor cells*, Dainiak *et al* reported their investigation of ‘the mechanism by which cytopenias develop [*i.e.* cell depletion, which is] ... a serious, dose limiting toxicity of AZT therapy.’ Observing that ‘Anaemia [during AZT therapy] appears to be due to bone marrow suppression [and] nearly one half of patients treated with AZT for [HIV]-associated disease develop transfusion-dependent anaemia due to bone marrow depression’, they concluded from their study that ‘AZT is a potent inhibitor of haematopoiesis *in vitro*, and that erythroid progenitors are particularly sensitive to its action. These results may explain the

marrow hypoplasia that occurs during AZT administration *in vivo*.'

[12] AZT reaches and can destroy foetal bone marrow too. In the May 1998 issue of the *Pediatric Infectious Diseases Journal*, Watson *et al* at the University of Rochester Medical Center in New York reported the case of an HIV-negative baby born to a positive mother who had been treated with a HAART cocktail of AZT, 3TC and a protease inhibitor, suffering 'high output congestive heart failure secondary to profound anemia.' The paediatricians excluded 'infection, nutritional deficiencies, congenital leukemia and congenital red blood cell aplasia in the child' and considered the 'cause of the life-threatening anemia in our infant ... to be in utero erythroid marrow suppression by one or more of the anti-retroviral agents administered to the mother.'

[13] Martin alleges that 'toxicity in most cases is reversible.' This optimistic jive was flatly contradicted by Mir and Costello just a year after AZT was approved. They reported their concern in the *Lancet* in 1988 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.'



# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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30 September 2004

The Registrar: Ms Precious Matsoso  
Medicines Control Council  
2<sup>nd</sup> Floor, Hallmark Building  
Cnr Andries and Vermeulen Streets  
Pretoria

Dear Ms Matsoso

**MCC review of its special registration of nevirapine for perinatal administration, and its recent recommendation that nevirapine be administered together with AZT**

Subsequent to dispatching our last letter to you in the above matter, we located a copy of the finalised version of the draft *Antiretroviral drugs and the prevention of mother-to-child transmission of HIV infection in resource-constrained settings Recommendations for use 2004 Revision* (the 'WHO Recommendations'), which we critiqued in our previous letters, now entitled *ANTIRETROVIRAL DRUGS FOR TREATING PREGNANT WOMEN AND PREVENTING HIV INFECTION IN INFANTS: GUIDELINES ON CARE, TREATMENT AND SUPPORT FOR WOMEN LIVING WITH HIV/AIDS AND THEIR CHILDREN IN RESOURCE-CONSTRAINED SETTINGS* (hereinafter referred to as 'the WHO Guidelines').

The finalised WHO Guidelines are undated, but according to the WHO's website were published on 14 July 2004 – that is, twelve days after the MCC's meeting at which it decided to disavow nevirapine for solo use to prevent mother to child transmission of HIV in favour of combining it with nucleoside analogue drugs such as AZT.



### Three

It is revealed on the 'Acknowledgements' page of the WHO Guidelines that the anonymously produced preceding draft WHO Recommendations were written by long-time collaborators Francois Dabis of the *Institut de Santé Publique, Epidémiologie et Développement (ISPED) Université Victor Segalen Bordeaux 2* in France, and Marie-Louis Newell of the Centre for Paediatric Epidemiology and Biostatistics, Institute of Child Health in London, UK.

Both Dabis and Newell are leading members of the 'IAS Ghent Group' – more fully named 'The Ghent IAS Working Group on HIV in Women and Children'.

'IAS' is the acronym of the International AIDS Society.

The 'Acknowledgements' page of the WHO Guidelines records that a meeting took place 'in Geneva, Switzerland on 5-6 February 2004 convened by the WHO to review the draft recommendations and [make] suggestions on its revision', and that South Africa's James McIntyre attended it.

It is apparent upon a perusal of the finalised WHO Guidelines, however, that there is no substantial difference between their contents and those of the draft WHO Recommendations, and that the former are essentially the latter reframed. It is plain therefore that nothing new or original of any substance was contributed by any of the consultants invited to 'review the draft recommendations and [make] suggestions on its revision', and that Dabis and Newell must accordingly be credited as the principal authors of the finalized WHO Guidelines and of the treatment prescriptions they proffer.

Although winsomely sub-titled *GUIDELINES ON CARE, TREATMENT AND SUPPORT FOR WOMEN LIVING WITH HIV/AIDS AND THEIR CHILDREN IN RESOURCE-CONSTRAINED SETTINGS*, the WHO Guidelines have nothing to say about care and support in the ordinary sense of these expressions and everything to say about what antiretroviral drugs pregnant women and their babies should be put on as soon as possible.

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This is because to Dabis and Newell, and AIDS doctors in general, 'care' has acquired the peculiar meaning conceived by the marketing arm of the pharmaceutical industry, namely, the administration of antiretroviral drugs: at a satellite meeting held on 12 July 2004 at the Bangkok AIDS Conference to discuss their about-to-be-released WHO Guidelines, they claimed them to be 'expert consensus documents ... developed over the past six months in partnership with the Ghent IAS Group using available evidence and in the context of increasing access to care of women and children'. By this they mean in the context of the WHO's 'Treat 3 million by 2005' with antiretroviral drugs programme, whose motto is emblazoned on the cover of their WHO Guidelines.

This programme dovetails with the long-term marketing strategy of nevirapine manufacturer Boehringer Ingelheim: its summer 2004 edition of *VIRAMUNE-Access Update*, puffed by a front-page colour photograph of a pair of happy natives, explains the company's business development plan:

Boehringer Ingelheim is in its fifth year since it announced the VIRAMUNE [nevirapine] Donation Programme, one of its contributions to the alleviation of HIV/AIDS around the world. Since then, VIRAMUNE has been provided free of charge for the Prevention of Mother to Child Transmission of HIV. Boehringer Ingelheim and WHO recognise the potential for PMTCT sites to serve as natural entry points for providing access to chronic treatment within the '3X5' strategy. This means that the healthcare infrastructure that has been built up through PMTCT programmes will be leveraged to eventually lead to greater access to chronic treatment in these communities.

Boehringer Ingelheim has even established a caring charity:

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The Boehringer Ingelheim Cares Foundation, Inc. is an independent, not-for-profit tax-exempt organization established in 2001 by the Boehringer Ingelheim Corporation in Ridgefield, CT [Connecticut, US]. The Foundation's mission is to improve lives through innovative philanthropic contributions and donations of healthcare products and resources.

None of the literature concerning the foetal and neonatal toxicity of antiretroviral drugs that was published concurrently with or subsequent to the release of the draft WHO Recommendations on 7 January 2004, which we canvassed in our last letter to the MCC, was mentioned in the final WHO Guidelines – much less were its grave implications for the use of antiretroviral drugs in pregnancy discussed.

It is evident therefore that neither Dabis nor Newell checked whether any relevant new toxicity research had been reported between the date that their draft WHO Recommendations were released and the publication of the finalised WHO Guidelines more than six months later.

And from their failure to draw these authors' attention to this latest reported research at the Geneva meeting, it is equally plain that none of the people hired to discuss and comment on the draft WHO Recommendations – South Africa's James McIntyre included – had bothered themselves with keeping abreast of the current toxicity literature either.

Dabis and Newell's new WHO Guidelines are accordingly situated solidly within the currently hegemonic chemotherapeutic approach to AIDS, sold to clinicians and academics by the pharmaceutical cartel, a medical paradigm to which the International AIDS Society is entirely beholden – as is plain from the prominent advertisement of the industry's AIDS drugs on the website of the IAS journal *AIDS*, hard copies of which are thick with AIDS drug advertisements.

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Although the IAS styles itself altruistically as ‘Scientists and Healthcare Workers Committed to HIV/AIDS’, in reality what the IAS is ‘committed to’ is the movement of pharmaceutical industry merchandise. A leading member of Dabis and Newell’s IAS Ghent Group, and a prominent consultant on their WHO Guidelines, is Joep Lange, just-retired president of the IAS, and current chairman of PharmAccess International, an AIDS drug lobby group, whose name unambiguously proclaims its mission in developing countries on behalf of the drug industry cartel.

With the cartel breathing heavily behind them, there’s naturally not a mention in the WHO Guidelines of caring in the form of nutritional support for ‘children in resource-constrained settings’, notwithstanding plenty of reports like Beisel’s in October 1996 in the *Journal of Nutrition* (126(10 Suppl):2611S-2615S), **Nutrition in pediatric HIV infection: setting the research agenda: Nutrition and immune function: overview:**

Malnutrition can have adverse, even devastating effects on the antigen-specific arms of the immune system and on generalized host defensive mechanisms. ... Immunological dysfunctions associated with malnutrition have been termed Nutritionally Acquired Immune Deficiency Syndromes (NAIDS). Infants and small children are at great risk because they possess only immature, inexperienced immune systems and very small protein reserves. The combination of NAIDS and common childhood infections is the leading cause of human mortality. NAIDS can generally be corrected by appropriate nutritional rehabilitation, but from a viewpoint highly important to this Workshop, AIDS and NAIDS are intensely synergistic. AIDS-induced malnutrition can lead to the secondary development of NAIDS, with its much broader array of additional immunological dysfunctions. The complex and far reaching insults to the immune system caused by NAIDS, and the synergistic combination of NAIDS and

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AIDS, thereby hasten the demise of many victims of AIDS. Aggressive nutritional support for children with HIV infections could delay, or lessen, the development of NAIDS and avoidance of NAIDS would improve both quality and length of life.

Dabis and Newell's endearing reference in their WHO Guidelines's subtitle to 'women ... and their children in resource-constrained settings' is European code for Africans: 'In 2003 an estimated 700 000 children were newly infected with HIV, about 90% of these infections occurred in sub-Saharan Africa.' AIDS drug experiments on pregnant African women and their babies are mentioned throughout the WHO Guidelines. In reference to a clinical trial conducted in Thailand, Dabis and Newell mark the principal intended territory for the application of their WHO Guidelines: 'Although these trial data are reassuring, it is not known whether ZDV from 28 weeks in Africa will result in serious anaemia in programmes where anaemia is common and women are not screened.' And in a recent statement by Newell, discussed below, she urges that 'we cannot ignore the AIDS epidemic taking place today in Africa today' and that 'It is our duty to disseminate the results of this study, and other research taking place across Europe.'

Dabis and Newell's claim that their WHO Guidelines represent the 'expert consensus' springs from the simple expedient of having consulted very narrowly – specifically, only those clinicians known to share their medical thinking.

In the all-important matter of drug safety, Dabis and Newell failed to solicit the advice of any scientist or clinician who has contributed to the foetal toxicity literature. None of the participants in the 'Technical Consultation on Antiretroviral Drugs and the Prevention of Mother-To-Child Transmission of HIV Infection in Resource-limited Settings' – the meeting mentioned above – 'to review the draft recommendations and for making comments and suggestions on its revision', nor any other persons listed who

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were approached for ‘comment ... on [Dabis and Newell’s] first draft’, nor any of the ‘WHO staff [who] contributed to writing these guidelines’ have any specific expertise in the subject of toxic pharmacology, both demonstrated in numerous clinical and experimental studies, and potential, having regard to all that is known about the toxicity of AIDS drugs – nucleoside analogues in particular, described by Brinkman et al. in September 1999 in *Lancet* (354 (9184):1112-5) as ‘much more toxic than we considered previously’.

On the contrary: another of Dabis and Newell’s senior consultants was UNAIDS’s HIV/AIDS Programme chief Joseph Perriens (mentioned in our second letter), famously on record in the *New York Times* describing AZT as ‘slightly more toxic than an aspirin’. (Like Cape Town University Medical School Dean Professor Nicky Padayachee, a loyal AIDS drug pusher too, Perriens is in the pay of the pharmaceutical drug industry and the American government. Both Perriens and Padayachee are members of another ARV drug promoting outfit, ECI (Enhancing Care Initiative), ‘a multidisciplinary, multinational program that aims to enhance the care of people living with HIV/AIDS in resource scarce countries’, co-funded by AIDS drug manufacturer Merck and the US Department of Health and Human Services.)

Another consultant who approved Dabis and Newell’s draft was the FDA’s thoughtful Ellen Cooper, whom we quoted in our last letter:

We don’t know what the long-term effects of AZT use during pregnancy might be, but so far we have seen virtually no adverse effects in the short term. ... Not one single tumor. Not one. ... I mean [the children] have cancers, lymphomas, and other problems like that ... but there’s no reason to link those cancers to AZT.

Local consultant James McIntyre is a GlaxoSmithKline asset, who sang AZT’s praises (‘the *muthi*’, he calls it) from the pulpit of the company temple in the centre of the exhibition hall at the 13<sup>th</sup>

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International AIDS Conference in Durban in July 2000. His colleague at the Chris Hani-Baragwanath Hospital Paediatric AIDS Unit is Glenda Gray, who responded to President Mbeki and Dr Tshabalala-Msimang's stated concerns about the toxicity of AZT in 1999 by pouting in the *Washington Post* on 16 May 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.'

This was the luminous quality of the intelligence that Dabis and Newell had at their disposal during the review of their draft WHO Recommendations in Geneva.

Concerning the safety of nevirapine taken during pregnancy, Dabis, Newell and their consultants seem to have short memories. The transplacental cytotoxicity of nevirapine was established in murine studies even before the drug was provisionally licensed in the US in 1996, and thereafter elsewhere in the world, with Boehringer Ingelheim cautioning in its license application to the FDA: 'In rats ... a significant decrease in fetal weight occurred at doses producing systemic concentrations approximately 50% higher than human therapeutic exposure.'

Yet the lesson of thalidomide is that humans are much more susceptible to injury by transplacental toxins than animals. In pregnancy safety studies duly conducted by the manufacturer, rodent foetuses experimentally exposed to thalidomide were not born deformed as humans later were (see photograph annexed), which is how and why the directors of thalidomide manufacturer Chemie Grünenthal got off the hook at their prosecution in Aachen, West Germany in the sixties.

And when on 5 January 2001 the US CDC issued a special contraindication advisory against even four-week use of nevirapine by health professionals following needlestick injuries, the Health Systems Trust published a reassuring note a week later in *Health-Link Bulletin* that:

The South African pilot studies to reduce mother-to-child transmission of HIV through the administration of nevi-

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rapine will not be delayed by recent reports of drug toxicity. However the women participating in the program will be closely monitored, according to recent press reports. The CDC in the US recently issued a warning on the toxic side effects of nevirapine when administered over several weeks. ... These included severe liver damage, when used to treat health care workers accidentally exposed to HIV by needle sticks. However, vertical transmission prevention requires only one dose of the drug. ... The reports on the toxicity of Nevirapine will have no impact on the Democratic Alliance's proposal to provide the medicine free to HIV-positive pregnant women in the party's controlled municipalities. Party spokesman Sandy Kalyan said reports of Nevirapine being potentially harmful concerned multiple doses of the drug. ... The South African Medicines Control Council last year registered nevirapine and approved its use for trials after UNAIDS and WHO endorsed the drug as a safe treatment for *one-off* use in the recommended dosage, saying the benefits outweighed the potential adverse effects. [Our emphasis]

In embracing Dabis and Newell's WHO Guidelines, the MCC has abandoned its former caution, having regard to the CDC's warning three years ago that 'healthy persons taking abbreviated 4-week NVP regimens for PEP are at risk for serious adverse events' such as 'Severe, life-threatening, and fatal cases of hepatotoxicity and skin reactions. ... The median onset of these symptoms was 14 days after beginning NVP for PEP (range: 3 – 36 days).'

Irrespective of this, the WHO Guidelines propose that African women endure the acute, severe toxicity of nevirapine throughout their pregnancies, with their unborn babies exposed transplacentally all the while, no matter that rodent studies conducted by



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Boehringer Ingelheim found 'significant decrease in fetal weight' resulting from exposure in utero.

Even single-dose nevirapine treatment after birth has again been shown recently to be very toxic for a high proportion of treated babies: a study by Taha et al., **Nevirapine and zidovudine at birth to reduce perinatal transmission of HIV in an African setting: a randomized controlled trial**, was published in *Journal of the American Medical Association* (292(2):202-9) on the same day as the WHO Guidelines – which mentioned the study (citation 33) as a paper still in press that 'showed no benefit of adding ZDV for one week to neonatal single-dose NVP when the mother had received intrapartum NVP'.

What Dabis and Newell neglected to mention in their WHO Guidelines is that the study also found an incidence of 'Grades 3 and 4 adverse events' at a rate of '4.9% ... and 5.4% ... in infants receiving NVP only and NVP plus ZDV, respectively'. That is, one in twenty African babies suffered serious toxic reactions to the drugs. But then the AIDS doctors who reported the study weren't troubled by this either, noting simply: 'The safety of the regimen containing neonatal ZDV was similar to that of a standard NVP regimen.'

Dabis and Newell's failure to consult broadly goes some way to explaining why they gave the 'available evidence' concerning the foetal toxicity of antiretroviral drugs such short shrift in their draft WHO Recommendations and finalised WHO Guidelines.

A further reason accounting for the dangerously inadequate two-page treatment they accorded the all important issue of maternal, foetal and neonatal safety in their fifty page WHO Guidelines is the fact that both of them are epidemiologists, a medical speciality concerned with tracking the occurrence of disease in given populations – a distant remove from clinical medicine, molecular biology, molecular pharmacology, medical toxicology and pathology. (This also explains their shared ignorance and their fundamental misapprehensions as to the (very limited, *non-diagnostic*) clinical meanings of antibody and genetic 'HIV' test

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results, on the fallacious basis of which they have erected their careers in purportedly preventing African mothers from infecting their babies with HIV.)

In writing their WHO Guidelines, notwithstanding their professional interest in disease incidence, neither Dabis nor Newell had any regard to the appearance of *clinical* disease among the babies in the studies they cited; instead their preoccupation was with laboratory testing outcomes, on the corrupt assumptions that HIV-antibody-positive, or a certain 'viral load' measure, equates with disease (HIV-infected), and the inexorable development of disease (AIDS). Which is flat wrong on all scores. We've dealt with the tests before; in March 2002 Morgan et al. reported in *AIDS* (16:597-603) that untreated 'HIV infected' Ugandans are surviving 'considerably longer than has been expected'. Just as all the predictions once made for supposedly deadly Hepatitis C Virus have likewise flopped.

Like all AIDS doctors propounding the use of the pharmaceutical industry's wares in pregnancy, Dabis, Newell and their consultants also appear to be unaware of the European Collaborative Study's finding reported in *Lancet* in November 1988 (2(8619):1039-43) that without any drug intervention most babies spontaneously sero-revert to HIV-negative in any event. Which is to say – proceeding from AIDS doctors' universal fallacy that HIV-positive means HIV-infected – that most HIV-positive babies spontaneously cure themselves of HIV infection without the intervention of AIDS doctors and their pills.

And as we pointed out in our last letter, several studies in which the clinical effect of treating pregnant women with AZT has been investigated have found that babies exposed to the drug in utero suffer substantially higher death, serious disease and other health impairments than unexposed babies. And the HIV-NET 012 single dose nevirapine regimen has been found to have no clinical health benefit when the mortality rate of treated children is compared with that of untreated ones.

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Despite the fact that the HIVNET 012 study was a hopeless mess, Dabis and Newell persist in citing it in their WHO Guidelines in support of the single-dose perinatal nevirapine regimen tried in the study (citations 7 and 8).

Boehringer Ingelheim's main German website also still pretends that nothing's remiss:

Viramune® may be used alone as a single oral dose to the mother during labour and a single oral dose to the infant within 24 hours after birth for the prevention of mother-to-child transmission of HIV-1 pregnant women who are not taking antiretroviral therapy at time of labour.

But the company hastens immediately thereafter to make clear that this special drug indication is intended for dun-hued mothers and babies, not fair ones:

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We recognise that the Internet serves a global community. The pharmaceutical industry, however, is subject to country specific regulatory considerations, which affect the information we can provide on our products. In addition the registration status of pharmaceutical products may not be the same in different regions of the world and the approved product labels may also differ according to country specific requirements.

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Ignorant of the toxic pharmacology of antiretroviral drugs at a molecular level, epidemiologists Dabis and Newell reassure us about the safety of the drugs they indicate by citing some favourably low adverse event reporting data – failing to appreciate,

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as Null et al. note in their comprehensive review of contemporary iatrogenesis in the US, **Death by Medicine**, published online in December 2003, that 'As few as 5% and only up to 20% of iatrogenic acts are ever reported' – in support of which observation the researchers cite several authoritative investigations, to wit, by Leape LL. **Error in medicine**. *JAMA*. 1994 Dec 21;272(23):1851-7; Vincent C, Stanhope N, Crowley-Murphy M. **Reasons for not reporting adverse incidents: an empirical study**. *J Eval Clin Pract*. 1999 Feb;5(1):13-21; Wald, H and Shojania, K. **Incident Reporting in Making Health Care Safer: A Critical Analysis of Patient Safety Practices**, Agency for Healthcare Research and Quality (AHRQ), 2001; Dickinson JG. **Dickinson's FDA Review**. March 2000; 7 (3):13-14; and Cohen JS. *Overdose: The Case Against the Drug Companies*. 2001, Tarcher-Putnum, New York.

The case of thalidomide neuropathy is also instructive concerning the limits to safety conclusions that can be drawn from toxic injury reports. Although well-known as a foetal teratogen, little known is that thalidomide is a potent neurotoxin, which caused many thousands of adult Europeans ingesting the drug to suffer permanent neuropathy at an incidence of about one in five exposures. Yet not a single report of neuropathy among lepers given the drug in the Developing World has been published in the medical literature.

The perfect harmony between the commercial aims of the pharmaceutical drug industry, those of Dabis and Newell's IAS, and those of the WHO, are naturally and inevitably manifest in the WHO Guidelines.

Dabis's professional commitment to the administration of synthetic pharmaceutical drugs as the perfect solution to what he declaims dramatically in the preface to the WHO Guidelines as 'the greatest health crisis the world faces today', to the exclusion of all alternative nutritional and natural treatment modalities, is evident from his discouragement of breastfeeding by HIV-positive mothers in his WHO Guidelines and from other platforms, and his bid (in *Lancet* 1998 Aug 22;352(9128):653-5) to dis-

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credit research published by the Harvard School of Public Health that has shown that vitamin supplementation is effective in reducing mother to child transmission of HIV according to the usual surrogate indices.

Dabis and Newell's professional bias in favour of the use of antiretroviral drugs during pregnancy and after birth, the blithe manner in which they discount the toxicity literature, where they treat it at all, and their disregard of alternative non-toxic interventions, arise from the following:

Both have long championed the administration of AZT to pregnant women in the Developing World, and cite their own research work, its interpretation and the conclusions they draw from it, in support of the recommendations they make in the WHO Guidelines. Indeed, an ardent proponent of AZT use in pregnancy, on which he has built his career and reputation, Dabis cites his own experiments on African mothers and their children in Côte d'Ivoire and Burkina Faso in support of his antiretroviral drug treatment recommendations expressed in the WHO Guidelines no less than five times – citations 11, 16, 23, 24, 38 – more than any other researcher's.

Dabis's conflict of interest arising from his own professional investment in the administration of AZT to Africans naturally disqualifies him from (a) giving impartial consideration to 'the available evidence' where it militates against the medical treatment he has made his name advocating, i.e., the latest research reports concerning the harm it causes children, (b) from according these findings due weight, and (c) from considering the possibility that the relatively recent (only decade-old) medical practice of exposing mostly non-white unborn and newly born babies to such potent transplacental cytotoxins as AZT, 3TC and nevirapine has been a grave mistake, a terrible wrong turn in contemporary medical practice.

Newell's professional incompetence in assessing the significance of the latest published evidence that AZT and 3TC have seriously harmful toxicity for unborn and newly born babies, and

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consequently should never be used during pregnancy and post partum, is revealed by the fact that two months after the French Paediatric HIV Infection Study Group published its final report in August last (the Barret study referred to in our previous letters) concerning the serious, sometimes fatal, foetal and neonatal toxic effects of AZT or AZT+3TC, she wrote (with Thorne) in **Antenatal and neonatal antiretroviral therapy in HIV-infected women and their infants: a review of safety issues**, published in the October-December issue of the Polish paediatrics journal *Medycyna wieku rozwojowego* (7(4 Pt 1):425-36), that

Concerns regarding mitochondrial dysfunction in children with foetal/neonatal exposure to zidovudine have arisen following a report from France of eight uninfected children with mitochondrial dysfunction, of whom two died. However, there is limited additional evidence of clinically evident mitochondrial disease in children exposed to antiretroviral therapy in utero or neonatally, and the absence of any excess mortality in large observational cohort studies of children born to HIV infected women and exposed to antiretroviral drugs is reassuring.

Newell's reference was to what the French Paediatric HIV Infection Study Group called their 'Preliminary report' (the Blanche report) four years earlier. She'd apparently missed its final one (the Barret study) in August.

That only a few children were reported killed by AZT and 3TC in the 'Preliminary report' Newell considered 'reassuring'. That other children were reported gravely neurologically crippled, she evidently thought to be of no account. And passing her by was the obviously defective methodology in other studies that counted drug deaths only and thereby missed further such grave injury cases – as discussed in the Barret study. Even less did it enter Newell's head that very many more cases of subclinical neurological harm would have gone unrecorded in 'observational cohort studies' as coarse as corpse counts.

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In this latter regard, we wish to emphasize that it is not only gross and sometimes fatal neurological damage caused by the use of antiretroviral drugs in pregnancy that ought to be of concern to the MCC, but also subclinical irreversible neurological injury – the sort of damage that would not be immediately apparent upon clinical examination and so would not attract closer attention and investigation, as was the case in the drug-exposed children investigated by French Paediatric HIV Infection Study Group (the Blanche alert, the Barret study), where electrophysiological investigation of every drug-exposed child, including the recording of sensory nerve action potentials (SNAPs), would doubtlessly have detected wide-scale subclinical neuropathy. The French Group researchers' failure to appreciate this would certainly have led to countless damaged children going unrecorded, since the only children investigated were those who exhibited gross clinical manifestations of drug injury.

Of all human organs, the brain and nervous system is the most sensitive to toxic chemical damage, especially during foetal and neonatal development. Significant permanent chemical harm to the nervous system may go undetected without specialised testing, and yet will substantially diminish a child's and later adult's quality of life.

It's revealing that in common with Dabis and all other AIDS doctors, Newell also disdains natural childbirth and breastfeeding by African women diagnosed HIV-positive in favour of surgeons' knives and formula milk. This is despite the absence of any clinical evidence whatsoever that African babies delivered by medically imposed Caesarean section have better clinical health outcomes than babies born naturally. And, as might be expected by any informed person with any common sense, there is equally no clinical evidence whatsoever that babies denied their mothers' breast milk at the instance of AIDS doctors are healthier than babies fed factory-produced formula milk – whatever the mothers' 'HIV status'. But the abstract to Newell's article in *Med Wieku Rozwoj* nonetheless commenced brightly:

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Specific interventions to prevent mother-to-child transmission (MTCT) include antiretroviral therapy, elective caesarean section and avoidance of breastfeeding. Rates of MTCT below 1-2% are now achievable in developed country settings.

A recent press release by her University College, London, on 14 September 2004, quoted Newell making the same claim:

HIV infected pregnant women who choose an elective caesarean can reduce by half the risk of infection to their child, while breastfeeding increases the risk of transmission. Although with the application of a number of interventions, the rate of mother-to-child infection has been successfully reduced to 1% in Europe, we cannot ignore the AIDS epidemic taking place today in Africa today. It is our duty to disseminate the results of this study, and other research taking place across Europe.

Ghent IAS Group member Ruth Nduati expressed this perverted medical antipathy – standard among AIDS doctors, yet contrary to reams of literature reporting the benefits of breastfeeding for every aspect of physical and intellectual development and long term health, and the harmful deficiencies of substitute factory-made milk – in her opening address at an IAS meeting on 16 July 2003 to discuss and promote the use of AIDS drugs during pregnancy, in which she alleged that ‘breastfeeding continues to diminish the efficacy of protocols to administer’ AIDS drugs to pregnant women, because, she said, ‘about 44% of the transmission is through breastfeeding’.

(This orthodox medical stupidity is currently being imparted by South African AIDS doctors to African women at antenatal clinics and hospitals: David Coetzee told the IAS meeting that ‘96 per cent of the women [attending antenatal clinics in the poor shack settlement of Khayelitsha, Cape Town] said they did not breast-feed at all ... in order to prevent transmission to their child’.)



### *Three*

Clearly ignorant of the latest published toxicity research canvassed in our last letter, and dull to the dire significance of the toxicity reports that she glossed over in her WHO Guidelines, Newell again (in this latter document) shared with us that she found it 'reassuring' that

MTCT prophylaxis with short-course ZDV was not associated with short-term clinical or laboratory toxicity among pregnant women in several controlled trials and long-term follow-up. Trials from Thailand suggest that serious anaemia in women receiving ZDV from 28 weeks of pregnancy is rare and no increase in serious haematological toxicity was observed with ZDV started at 36 weeks in trials in Africa. Although these trial data are reassuring, it is not known whether ZDV from 28 weeks in Africa will result in serious anaemia in programmes where anaemia is common and women are not screened.

In other words, although it's 'not known whether ZDV from 28 weeks in Africa will result in serious anaemia' – that is, potentially fatal destruction of infant (and maternal) bone marrow and red blood cells – Dabis and Newell suggest that the drug be prescribed to African women throughout their pregnancies regardless:

Although there are concerns relating to potential effects of ARV drugs on the developing fetus, suspending treatment during the first trimester is generally not recommended. ... For eligible women, ARV treatment should be started as soon as possible during pregnancy. ... ZDV [AZT] should be included in the regimen whenever possible. ... A regimen consisting of ZDV starting from week 28 of pregnancy, single dose NVP and ZDV during labour plus ZDV for one week given to the infant is highly efficacious.

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It's worth mentioning, as a vignette showcasing the quality of thinking expressed in their WHO Guidelines, that Dabis and Newell cite Bardeguez et al. (in *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 2003, 32(2): 170–181) noting that 'HIV-related disease progression does not appear to be altered by receiving ZDV prophylaxis'. That is to say, taking antiretroviral drugs does not make sick pregnant women better, or prevent healthy pregnant women getting sick on the drugs – a finding they elsewhere contradict in their WHO Guidelines: 'Potent combination treatment has substantial benefits for the woman's health.'

This latter claim – right out of a drug industry advertisement – is contradicted by numerous clinical studies, most recently by Reisler et al. in *Journal of Acquired Immune Deficiency Syndromes* (2003 Dec 1;34(4):379-86); and by Brown et al., who presented similar, albeit obfuscated findings at the 15<sup>th</sup> International AIDS Conference in July 2004 in Bangkok: **Non-AIDS serious adverse events are as important as AIDS events in patients with advanced multi-drug resistant HIV disease.**

Upon an analysis of

serious or life-threatening events that are not AIDS defining, AIDS events, and death among patients treated with highly active antiretroviral therapy (HAART) in the setting of 5 large multicenter randomized treatment trials conducted in the United States

Reisler et al. discovered, as they reported both in their conclusion and in the title to their paper, that **Grade 4 events are as important as AIDS events in the era of HAART**, i.e. that people given 'potent combination therapy' have an approximately equal chance of being dangerously poisoned or killed by AIDS drugs as they do of developing AIDS defining diseases. Which, in as many words, GlaxoSmithKline long ago admitted that AIDS drugs can cause in its entry under 'Retrovir' (AZT) in the *Physician's Desk Reference*: '... it was often difficult to distinguish adverse events

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possibly associated with administration of Retrovir from underlying signs of HIV disease or intercurrent illnesses.’ And all of which would lead most ordinary guys to wonder what the point of taking the drugs is, in pregnancy especially.

By their silence as to the critical matter of drug dosing levels, Dabis and Newell imply in their WHO Guidelines that the prophylactic doses of AZT, 3TC and nevirapine combinations given to pregnant African women and their newborn babies should be the same as therapeutic ones – the ones good at causing life-threatening Grade 4 events.

This reading is supported by the US Department of Health and Human Services’s publication *A Guide to the Clinical Care of Women with HIV* (2000), which echoes the US CDC’s still current recommendation in *Morbidity and Mortality Weekly Report* 1998; 47[RR-2] that ‘pregnant women should be treated according to standard guidelines for antiretroviral therapy in adults’. In other words, American AIDS doctors don’t see any need to reduce the usual dose to protect the foetus.

These dose recommendations, however, were made during the ‘hit early, hit hard’ HIV treatment era in full swing, with high-dose, multi-drug combinations being the medical convention, before the reported human toll on AIDS patients – described by AIDS treatment expert Professor Michael Saag of the University of Alabama in *Esquire* on 1 March 1999: ‘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.’ – led the US Department of Health and Human Services to renounce this brutal mediaeval treatment orthodoxy in favour of delaying initiation of antiretroviral treatment for as long as possible:

On 5 February 2001 the US National Institutes of Health released their *HIV Treatment Guidelines Updated for Adults and Adolescents* – summed up by US government’s top AIDS don, National Institute of Allergy and Infectious Diseases (NIAID) director Anthony Fauci the day before in the *New York Times*: ‘We are adopting a significantly more conservative recommendation pro-

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file’ – the idea being, as the reporter paraphrased him, to allow ‘the virus to remain in the body longer in return for sparing the patient the drug toxicities’.

This official U-turn in AIDS treatment policy, abruptly and somewhat embarrassingly ending AIDS doctors’ ‘hit early, hit hard’ craze, was followed by another officially endorsed reversal: patients put on antiretroviral drugs should be given treatment holidays to ‘reduce toxicity’:

**Short-cycle structured intermittent treatment of chronic HIV infection with highly active antiretroviral therapy: effects on virologic, immunologic, and toxicity parameters** by Dybul et al. – including Fauci – was published in December the same year in *Proceedings of the National Academy of Sciences* (98(26):15161-6), reporting that by all conventional surrogate markers patients did no worse from having treatment holidays: a week on, a week off. This paper thus debunked the ‘resistance’ argument with which AIDS doctors had terrorised their suffering patients to ‘adhere’ to their drug prescriptions or die.

Since ‘Adherence to such a regimen may be problematic for certain patients’, i.e. even alternate weeks will be unendurable, the same principal authors (Fauci included again) have recently come up with another idea: **A proof-of-concept study of short-cycle intermittent antiretroviral therapy with a once-daily regimen of didanosine, lamivudine, and efavirenz for the treatment of chronic HIV infection**, published in June this year in the *Journal of Infectious Diseases* (189(11):1974-82), found that it did no harm to reduce drug combination intake to one dose a day.

But paying no heed to these huge, successive retreats from formerly aggressive AIDS treatment convention, Dabis and Newell’s WHO Guidelines offer no such medical mercy for pregnant African women and their babies, and instead move in precisely the opposite direction. Whereas in 1998 UNAIDS, the WHO and UNICEF endorsed short-course AZT treatment of pregnant women to reduce mother to child transmission of HIV, Dabis and Newell’s current WHO Guidelines urge aggressive triple combi-

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nations of AZT, 3TC and nevirapine, administered without respite throughout pregnancy or started after a month into it.

The look of it is that as AIDS drugs are being progressively retired in the North, with the mounting toxicity data threatening to block out the sun (as was the case with mercury and arsenic salts in their dying days in the early 20<sup>th</sup> century), the pharmaceutical industry is manoeuvring to dump them in the South.

This is what happened after the thalidomide disaster: in 1965, as German prosecutors were preparing the indictment of Chemie Grünenthal's directors for their criminal prosecution, the company resumed production of the drug to take up the slack in its vast production capacity. Since thalidomide had been invented as a cell-poison in 1953, and had initially been marketed for a couple of years from 1956 onward as an antibiotic for respiratory infections (it was notoriously repackaged as mother's little helper between 1957 and 1962), Chemie Grünenthal began marketing the drug in the Third World as a treatment for out-of-sight lepers. The 'inevitable result', the *Oxford Companion to Medicine* tells us, is that "'thalidomide babies" are once again being born', notably all over South America.

Incredibly, in 1998 the WHO approved this new treatment indication for thalidomide. Four years later the WHO quietly revoked its imprimatur on this diabolical abuse, but without any concessions as to the harm it had caused and the magnitude of the organisation's failure to the most vulnerable of the Developing World's poor. Thalidomide continues to be manufactured and hawked in South America, where it is still deforming children on that continent today.

The WHO's support, until recently, for the use of thalidomide in the Developing World, right after it had been banned in the first, presents a vivid illustration of how the WHO has been hijacked by the pharmaceutical cartel and by the faithful clergy it directly and indirectly retains in medical orders worldwide; and it explodes any illusion that the WHO functions as an impartial international body applying the best available science, and be-

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yond the dictates of the cartel's utterly ruthless commercial programme.

We suggest that the integrity, authority and reliability of the WHO Guidelines should be assessed in the light of the organisation's colossal betrayal of the people of the Developing World in the recent thalidomide fiasco.

Dabis and Newell make their violent treatment proposals despite a mass of foetal toxicity and multi-drug toxic synergy reports that have been published subsequent to the adoption of the AZT short-course policy in 1998.

Any informed and thoughtful doctor would have been impelled to greater caution by these studies, but instead, for unborn (and newly born) African babies, Dabis and Newell recklessly extend the duration and variety of drug exposure. And without thinking, the MCC goes along.

The WHO Guidelines effectively codify best clinical practice regarding the prescription of AIDS drugs to HIV-positive women and their babies in the Developing World; and after the brief single-dose nevirapine interregnum, they mark the return of AZT with a vengeance.

Having been synthesized as an experimental cell poison in 1961 (see *Inventing AZT*), AZT was licensed by the FDA in 1987 as an AIDS drug not because it had any demonstrated antiviral activity (it was pertinently noted by the FDA licensing panel that none had been shown – and still hasn't, as you will have read in Papadopoulos-Eleopoulos's et al. mammoth analysis of the molecular pharmacology of the drug that we sent up to you), but because it appeared, on a superficial look at the mortality data in the Phase II AZT trial, to extend lives (but see the writer's exposé of the trial, *Licensing AZT*).

AZT and 3TC are nucleoside analogues, a class of drug employed in cancer chemotherapy purposely to kill human cells, as discussed in a leading textbook in this subject by Cheson et al, *Nucleoside Analogs in Cancer Therapy* (Marcel Dekker Inc. New York, 1997).

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And don't go believing GlaxoSmithKline's lies that AZT is somehow specific for HIV and doesn't kill human cells like all other nucleoside analogue drugs in its chemical class ('Competition by zidovudine-TP for HIV reverse transcriptase is approximately 100-fold greater than for cellular DNA polymerase alpha'), because Gill et al. reported great success slaughtering blood cells with AZT in a study reported in June 1995 in the *New England Journal of Medicine* (332(26):1744-8): **Treatment of adult T-cell leukaemia-lymphoma with a combination of interferon alfa and zidovudine**. As did Hermine et al. simultaneously in the same journal: **Treatment of Adult T-Cell Leukemia-Lymphoma with Zidovudine and Interferon Alfa**.

Other researchers too: Matutes et al. published effective results using **Interferon alpha and zidovudine therapy in adult T-cell leukaemia lymphoma: response and outcome in 15 patients** in the *British Journal of Haematology* in June 2001(113(3):779-84).

For killing blood cells, AZT's as good as ever: Aouba et al. have recently published a study consistent with those preceding: **Hemophagocytic syndrome as a presenting sign of transformation of smoldering to acute adult T-cell leukemia/lymphoma: efficacy of anti-retroviral and interferon therapy** in June 2004 in the *American Journal of Hematology* (76(2):187-9). But then the bottle – labelled by Sigma Chemical Company more honestly than GlaxoSmithKline – does say: 'Toxic Toxic to inhalation, in contact with skin and if swallowed. Target organs: Blood Bone marrow ... Wear suitable protective clothing.'

AZT's not only deadly poisonous to blood cells; it's been used with great effect to deliberately kill other human tissues too. In January 1999, in the *Journal of the American Academy of Dermatology* (40(1):116-21), Chan et al. reported A novel chemotherapeutic regimen (interferon alfa, zidovudine, and etretinate) for adult T-cell lymphoma resulting in rapid tumor destruction.

The dangers of exposing a growing foetus to nucleoside analogues are accordingly well-recognised in cancer chemotherapy.

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Citing, inter alia, *The Chemotherapy Source Book* (3<sup>rd</sup> edition). Ed. Perry, Lippincott Williams and Wilkins, 2001; *Martindale: the complete drug reference* (33<sup>rd</sup> edition). Eds. Sweetman et al. Pharmaceutical Press, 2002; and the *British National Formulary* (46<sup>th</sup> edition) British Medical Association and Royal Pharmaceutical Society of Great Britain, September 2003, CancerBACUP, 'Europe's leading cancer information service' warns:

It is not advisable to become pregnant or father a child while taking fludarabine [a nucleoside analogue drug] as it may harm the developing foetus. It is important to use effective contraception whilst taking this drug, and for at least a few months afterwards.

Another cancer treatment information service, CancerHelp UK, warns alike concerning the use of the drug. Because it

stop[s] cells making and repairing DNA ... This drug may have a harmful effect on a baby that is developing in your womb. It is not advisable to become pregnant or father a child if you are having this drug. You should talk about contraception with your doctor before having the treatment.

The American Cancer Society similarly warns under 'Pregnancy':

Although pregnancy may be possible during chemotherapy, it is not advisable because some chemotherapy may cause birth defects. Doctors advise women of childbearing age, from the teens through the end of menopause, to use birth control throughout their treatment.

If a woman is pregnant when her cancer is discovered, it may be possible to delay chemotherapy until after the baby is born.



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For a woman who needs treatment sooner, the doctor may suggest starting chemotherapy after the 12th week of pregnancy when the fetus is beyond the stage of greatest risk.

In some cases, termination of the pregnancy may be considered.

If you or your partner is considering pregnancy after completing chemotherapy, discuss the matter with your physician.

But for unborn African babies, AIDS doctors such as Dabis and Newell propose that a lesser safety standard be applied than for white ones in the First World, throwing to the wind the well-settled medical convention that growing human foetuses should not be exposed to cytotoxic nucleoside analogue drugs generally, and not during the first term in particular – especially since chemotherapeutic drugs in pregnancy have been shown in animal studies to cause cancer in offspring: in the case of AZT specifically, in the studies we surveyed in our last letter, and chemotherapeutic drugs generally, as Llombart found way back in September 1976, reporting in *Das Osterreichische Kneipp-Magazin* (3(3):72-7) **Tumoral drugs as possible blastogenic agents: the problem of anti-blastic medication.**

Llombart made 'careful note ... of the possible appearance of tumors throughout the lives' of 1264 rats born to mothers treated with double the usual kg/day human dose of a range of standard chemotherapy drugs. In an incidence of tumour development of up to 37.42 % following transplacental foetal drug exposure,

The benign forms predominated in all the tumors produced, but with some of the drugs the malignant varieties produced were made as 39.3% of the tumors. The location and type of tumors were variable; there being cutaneous, glandular, mammary, hepatic, renal, and tumors of the

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nervous system; there were also tumors of epithelial, connective and nervous variety.

That chemotherapeutic drugs similar to AZT and 3TC cause permanent *late-onset* brain and neurological damage even among adults with fully formed brains and nervous systems has been reported in a string of recent papers.

Van Dam et al. began by reporting **Impairment of cognitive function in women receiving adjuvant treatment for high-risk breast cancer: high-dose versus standard-dose chemotherapy** in February 1998 in the *Journal of the National Cancer Institute* (90(3):182-3). Their paper in *Cancer* a year later, **Cognitive deficits after postoperative adjuvant chemotherapy for breast carcinoma** (90(3):182-3), reported the 'late effects on neuropsychologic functioning of CMF adjuvant chemotherapy' years after cessation of treatment, and found objective evidence of

Impairment in cognitive function ... in 28% of the patients treated with chemotherapy compared with 12% of the patients in the control group ... Cognitive impairment following chemotherapy was noticed in a broad domain of functioning, including attention, mental flexibility, speed of information processing, visual memory, and motor function.

Other confirmatory studies have followed, most recently by Wefel et al. in June this year in *Cancer* (100(11):2292-9). The title of their report augurs grimly: **The cognitive sequelae of standard-dose adjuvant chemotherapy in women with breast carcinoma: results of a prospective, randomized, longitudinal trial.**

All these findings are consistent with those of the French Paediatric AIDS Study Group, which reported crippling, sometimes fatal, neurological injuries to babies exposed to AZT and 3TC in utero and post partum – findings to be expected in the light of Busidan's et al. report in the *Journal of Pharmacological Science* in

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December 2001 (90(12):1964-71) concerning **AZT distribution in the fetal and postnatal rat central nervous system:**

The distribution of 3'-azido-3'-deoxythymidine (AZT, zidovudine), an antiviral drug used in the treatment of human immunodeficiency virus, was investigated in gestation day-20 (G-20) fetuses and in postnatal day-20 (PND-20) rats. At both ages, a single dose of 150 mg/kg (1.78 mmol/kg) AZT was administered orally along with tracer amounts of <sup>14</sup>C-AZT, and rats were randomly killed at 15, 30, 60, 120, or 240 min after dosing. The fetuses, brains, and spinal cords were processed for autoradiography. ... In the G-20 rats, the brain showed higher levels of AZT than spinal cord only at the 30-min sample time, whereas in the PND-20 rats, greater radioactivity was found in the spinal cord up to the 240-min sample time. This pattern of AZT distribution in the central nervous system may hypothetically be attributed to the postnatal development of an organic anion carrier system believed to be responsible for transporting AZT from the brain to the blood, resulting in relatively greater overall exposure of the spinal cord to AZT than observed in the brain.

It's really no coincidence that the CDC should have added 'AIDS dementia' to its list of AIDS defining illnesses in the same year, 1987, that AZT was licensed in the US as an AIDS drug, in the light of Bacellar's et al. report in the October 1994 issue of *Neurology* (44(10):1892-900) that

the risk of developing HIV dementia among those reporting any antiretroviral use (AZT, ddI, ddC, or d4T) was 97% higher than among those not using this antiretroviral therapy. ... In addition, the findings of our analysis seem to confirm previous observation of a neurotoxic effect of antiretroviral agents ... linked ... to the development of

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toxic sensory neuropathies, usually in a dose-response fashion.

The neurological injury of children reported by the French Paediatric HIV Infection Study Group in 1999 and 2003 was consistent with this finding.

Relying blindly on the incompetents responsible for producing the WHO Guidelines, the MCC's recent recommendation that HIV-positive pregnant women be given AZT has put thousands of South Africans, mostly black, mostly poor, at risk of suffering the same iatrogenic tragedy.

The MCC's demonstrated fealty to the pharmaceutical cartel at the expense of the welfare of our South African people, mostly black, mostly poor, underscores the urgent need for a radical overhaul of its composition. In this regard, we think an observation made by KwaZulu-Natal Health MEC Dr Zweli Mkhize a few years ago rather apposite: 'There is in this country a long history of whites telling us what do with our bodies ... There has always been this debate about Africans determining what is right for Africans, not whites.'

It's a curious coincidence that the IAS Ghent Group's caring mission into Africa on behalf of GlaxoSmithKline and Boehringer Ingelheim should sue out from Belgium – as does *Médecins Sans Frontières* on the same drug-dealing trip. Of all Europe's colonial projects in nineteenth and twentieth century Africa, Belgium's Congo was the most callously murderous, killing, according to the best scholarly estimates, about ten million Africans.

As he raped the country, Leopold II (honorary president of the British Aborigines Protection Society) sold his depredations to the believing world as a Christian crusade to secure the 'abolition of the traffic in slaves', an involvement motivated by 'the noble aim of rendering lasting and disinterested services to the cause of progress'.

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Some might see the same criminal energy pumping behind it, the same metaphysical corruption driving it. We do. *Plus ça change, plus c'est la meme chose.* The horror, the horror.

Yours faithfully

ADV ANTHONY BRINK  
CONVENER AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

Cc: The South African government, all provincial Health MECs, media and other interested parties.

#### IMPORTANT POSTSCRIPT:

After gross irregularities both in the conduct of the HIVNET 012 nevirapine trial in Uganda and the US National Institutes of Health's subsequent attempt to whitewash them in its 'Remonitoring Report' were brought to the attention of the Oversight and Investigations Subcommittee of the Energy and Commerce Committee of the US House of Representatives in March this year, the committee ordered the National Institutes of Health to submit to an independent investigation of both the trial irregularities and the cover-up. The Institute of Medicine, a branch of the National Academy of Sciences of the United States of America, was tasked to carry it out in about June. Its website currently notes:

At the request of the National Institutes of Health (NIH), the Institute of Medicine (IOM) is conducting an independent review of the HIVNET 012 perinatal HIV prevention trial. ... The NIH has asked the IOM to review methodological and data interpretation issues related to protocol design, data collection, recordkeeping, quality control, and analysis. The committee will assess the impact of

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these issues on the validity of overall findings and conclusions of the trial.

On 21 September 2004 the National Whistleblower Center ('NWC') in Washington wrote to the IOM, raising rampant conflict of interest in the IOM panel, and other serious matters compromising the enquiry. A copy of its letter is annexed. (Two members of the panel reacted by resigning; the other issues remain to be resolved.)

The pressing local relevance of these developments in the US – even though the MCC has rejected both the HIVNET 012 study and the NIH's subsequent defence of it – arises from reference in the NWC's letter to a plethora of 'unreported adverse that were not recorded, as the principal investigators admitted to the Westat auditor' and the fact that 'the study physicians evaluated adverse events often on the basis of third hand descriptions from non-physicians and without personally examining all patients'.

HIVNET 012 is the study on the basis of which the MCC specially registered nevirapine as both safe and effective for administration to women in labour and their newborn babies in South Africa, and it was the lynchpin of the Treatment Action Campaign's successful case against our government in the High and Constitutional Courts, forcing it to supply the drug for this indication.

After subsequently rejecting HIVNET 012, as well as the NIH's attempt to save the study in its 'Remonitoring Report', the MCC put Boehringer Ingelheim on terms to come up with other evidence of safety and efficacy to warrant the continued special registration of the drug. The time allowed the company has long come and gone. In our first letter in June we asked what the MCC was doing about this. We're still waiting to hear.

The HIVNET 012 trial overseers' admission that numerous adverse events went unrecorded, and that those adverse events that were recorded were often based on hearsay only, underscores the urgency of the need for the MCC to determine its review of its

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continued registration of nevirapine for even single-dose perinatal use. The safety data reported in HIVNET 012, on the basis of which the MCC specially registered nevirapine for perinatal use in South Africa, bad as they were, have turned out to be utterly corrupt.

The continued registration of the drug for perinatal use is indefensible. In the circumstances, why has the MCC not revoked the special conditional license it granted Boehringer Ingelheim to market nevirapine for administration to women in labour and their newborn babies?

Has everyone gone fishing?

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Thalidomide victim

‘Distavel [*thalidomide*] can be given with complete safety to pregnant women and nursing mothers without adverse effect on mother or child. ... Outstandingly safe, Distavel has been prescribed for nearly three years in this country [UK]. ... there is no case on record in which even gross overdosage with Distaval has had harmful results. Put your mind at rest. Depend on the safety of DISTAVAL ... a harmless, safe and effective sedative with no side effects. ... Harmless even over a long period of use ... completely harmless even for infants.’

**British Distillers (Biochemicals) plc c.1961**

‘The piperidinedione hypnotic thalidomide was responsible for thousands of children with disastrous defects such as absence of limbs. This occurred especially in Germany. Pregnant women ingesting a single hypnotic dose of the drug between the twenty-fourth and thirty-sixth day of their pregnancy have delivered severely deformed babies.’

***Medical Pharmacology, Andres Goth, 9<sup>th</sup> edition, 1984***



# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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20 October 2004

The Registrar: Ms Precious Matsoso  
Medicines Control Council  
2<sup>nd</sup> Floor, Hallmark Building  
Cnr Andries and Vermeulen Streets  
Pretoria

Dear Ms Matsoso

**MCC review of its special registration of nevirapine for  
perinatal administration, and its recent recommendation  
that nevirapine be administered together with AZT**

I refer to our meeting at your offices in a different connection last Thursday, at which I enquired whether there was any prospect of the MCC ever responding to our letters. You answered that a reply had been prepared and was awaiting signature. I informed you that as our seventh letter, sent up to you by courier on the Friday before (8 October 2004), contained crucial additional research data and other information pertinent to the matters in question, we hoped that the MCC would consider it before arriving at any conclusions. I record that I handed you an extra copy.

This is to confirm that you agreed to see to it that the MCC considers our seventh letter before issuing its response.

As we mentioned in our seventh letter we intend commencing proceedings to have the MCC publicly called to account for its failure to discharge its official function to the people of South Africa, namely to protect them from the marketing of harmful products by the pharmaceutical industry. In anticipation of a con-

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sidered response from the MCC to our correspondence, however, we'll put our approach to the Public Protector on hold for one month.

This month five years ago, on 28 October 1999, after reading my survey of the medical literature published to date on the exceptionally dangerous toxicity of AZT in *Debating AZT: Questions of Safety and Utility*, President Mbeki called attention to the threat to public health posed by AZT in his address to the National Council of Provinces and directed that an enquiry be conducted into the issues raised in the subtitle. (The manuscript was updated and published a year later as *Debating AZT: Mbeki and the AIDS drug controversy*.)

What emerged at the time from public statements made by several leading AIDS experts was that President Mbeki was much better informed in the subject than they were. Then MRC president William Makgoba boasted of being a total ignoramus: 'I've read nothing in the scientific or medical literature indicating that AZT should not be given to people.' So did his similarly bone idle AIDS research chief at the MRC, Salim Abdool Karim: There is 'no new evidence in the medical literature in the last year on the adverse effects of AZT'.

As the MCC proceeded to disgrace itself by botching the enquiry that President Mbeki had entrusted it to conduct, its then chairperson, Helen Rees, let on that its members were no less uninformed and clueless than their medical eminences aforementioned: 'The drug being out there is justified,' she announced, delivering the MCC's all-clear verdict – as if President Mbeki had been carrying on about nothing like Henny Penny.

Indeed, that the MCC hadn't taken President Mbeki's formally raised concerns seriously emerged from a patronising statement that Rees made to *Newsday* on 11 July 2000:

most researchers ... concluded long ago that the HIV-fighting value of antiretroviral drugs (such as AZT) were worth the awful side-effects they can trigger ... case

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closed. So what gives with South Africa? You can't just view this matter as a health issue, South Africans wearily explain. You also must see it as a political issue. It's all wrapped up in the South African liberation movement, observed Dr. Helen Rees, who chairs South Africa's Medicines Control Council. Today, nothing is beyond debate – and that is a heady thing for this long-repressed nation. 'I don't have a problem with someone who says, "Go back and look at this again,"' Rees said, 'because people need room to learn and grow.'

The pity of it was that the English immigrant – who presumed to understand and elucidate the troubled psychological dynamics behind the liberation politics of the President's intervention, and who wearily indulged his 'need' for 'room to learn and grow' – felt above taking her own advice.

Shortly after President Mbeki alerted the people of South Africa to the fact 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', Dr Tshabalala-Msimang made a number of public statements, both in Parliament and to the media, that were supportive of his concerns, particularly in regard to the use of AZT during pregnancy. The MCC might find it instructive to reconsider them in the light of research findings published since.

*'There is no substantial data that AZT stops the transmission of HIV from mother to child. There is too much conflicting data to make concrete policy.'* Any of the MCC's members who have actually troubled themselves to read Papadopoulos-Eleopoulos's et al. exhaustive examination of the subject published in October 2001 that we sent up to you, *Mother to Child Transmission of HIV and its Prevention with AZT and Nevirapine: A Critical Analysis of the Evidence*, will have seen the fallacy identified by Dr Tshabalala-Msimang in her first sentence meticulously and comprehensively taken to

#### Four

pieces. The monograph closely discusses the 'conflicting data' alluded to in her second sentence, and lays it hopelessly bare.

*'I want to dispel this myth [that the only proper approach to AIDS is to supply AZT] because it is absolutely not true. The pharmaceutical industry and those who have a vested interest in the drug industry fuel this propaganda.'* Our last letter unveiled the pervasive influence of the 'drug industry' over WHO policy-making, as well as of 'those who have a vested interest in it'.

*'There is a lack of information on how the drugs affect these children over time.'* Since Dr Tshabalala-Msimang made that statement in late 1999, a profusion of published research data, set out in our letters, have provided new 'information on how the drugs affect these children over time'. Horribly.

*'We have to be very cautious ... so that we do not look back 10 to 15 years down the line and find that we had exposed ... our people to a dangerous drug. ... We have to be very cautious, very sensitive.'* Numerous studies published in the five years since this statement was made have unequivocally confirmed Dr Tshabalala-Msimang's worst apprehensions: AZT is an extremely 'dangerous drug', especially when used in pregnancy. But insensitive to these new findings, the MCC has thrown all caution to the wind in recommending AZT for administration to pregnant women, mostly black, mostly poor.

*'Could you with a clear conscience introduce those toxic drugs to a woman and her child? I say no.'* The MCC's members, in recommending AZT to mostly black, mostly poor South African pregnant women and their newborn babies, have demonstrated that they subscribe to an entirely distinct set of moral values from those of our President and Health Minister.

*'Until we are convinced that the drug AZT is safe, as a responsible government we will not move in that direction.'* Research findings reported in the five years since this statement was made have con-

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sistently shown, as Brinkman et al. had just noted in *Lancet* two months earlier (1999 Sep 25;354(9184):1112-5), that AZT is 'much more toxic than we considered previously'. And yet ten years ago Lenderking et al. had already reported in the *New England Journal of Medicine* (1994 Mar 17;330(11):738-43) that just 500 mg of AZT given daily to 'asymptomatic patients' causes 'severe side effects' that are 'life threatening in some cases'. But the cartel's stooges advising the WHO and the MCC propose that asymptomatic pregnant African women, mostly black, mostly poor – who have been declared HIV-infected by AIDS doctors on the strength of a useless antibody *blood screening* test that reacts positively to *past pregnancy* among about seventy other documented cross-reacting conditions and diseases – be fed not just 'life-threatening' AZT during their pregnancies, but equally toxic 3TC and nevirapine as well. To their newborn babies too. Since they're the experts.

*'AZT is a confirmed carcinogen. ... The fact is that some of the mice [given AZT] have contracted cancer. It attacks bone marrow. It is very toxic.'* Five years on, notwithstanding the accumulation of further consistent research reports in this regard that we canvassed in our letters, the MCC's members have disregarded them all and have chosen to accord themselves with the position taken by famed AZT advocate Charlene Smith in her glittering retort to Dr Tshabalala-Msimang's above-cited warning: 'Stop giving AZT to the damn mice and start giving it to people.'

With such dumb blondes as Glenda Gray, Helen Rees and Charlene Smith calling the AIDS drug policy shots in South Africa, maybe Michael Moore should fly in and document their performance as his next project and call it Stupid White Women. (He'd find no shortage of them in the virology faculties of our country's medical schools either.) But seriously, having regard to the corpus of published AZT toxicity data drawn to the MCC's attention in our correspondence, we propose that any of its members still recommending the prescription of AZT to pregnant women and

*Four*

their newborn babies, mostly black, mostly poor, are equally ignorant, lazy, simple, corrupt or depraved.

Dr Miklos Nyiszli, a Jewish pathologist interned at Auschwitz and forced to conduct autopsies on other prisoners killed by Dr Josef Mengele in the course of his Nazi medical experiments, described the sort: 'Among all criminals and murderers, the most dangerous type is the criminal physician.' Since AZT has been shown to kill children exposed to it in the womb, and neurologically and otherwise seriously harm others, those intransigent members of the MCC, who, notwithstanding notice of the dreadful research data traversed in our correspondence, persist in putting the commercial interests of the pharmaceutical cartel and their own face above the safety of the African people of our country, might reflect on whether this cap fits them too.

Yours faithfully

ADV ANTHONY BRINK  
CONVENER AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

Cc: The South African government, all provincial Health MECs, media and other interested parties

# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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8 December 2004

The Chairperson: Medicines Control Council  
Professor Peter Eagles  
School of Pharmacy  
University of the Western Cape  
Private Bag X17  
Bellville

Dear Professor Eagles

**MCC review of its special registration of nevirapine for  
perinatal administration, and its recent recommendation  
that nevirapine be administered together with AZT**

Thanks for your letter of acknowledgement in this matter, just in, dated 22 November 2004 – five months to the day since our first letter. But we were most put out to see reference to our first two letters only. In fact we sent up six more plus an addendum, as well as two substantial scientific papers in lever-arch files, which closely examine the pharmacology of AZT and nevirapine, and a PowerPoint slideshow on CD concerning the latter drug. All our submissions were hand-delivered by courier. Your people seem to have lost them. Would you make enquiries about this? Our sixth and seventh letters\*, which extensively analysed the AZT foetal toxicity literature, are particularly crucial to the proper determination of the safety issues we raise. The addendum amplified our sixth letter, citing more AZT foetal toxicity studies.

Assuming the worst, we enclose another complete set of our letters for you to read, as well as bound copies of the big scientific

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\* Letters Two and Three herein.

## *Five*

papers that we sent up, and ten CDs onto which all materials sent up to the MCC have been saved. Would you personally see to it that all members of the MCC's sub-committee responsible for the registration and recommendation of nevirapine and AZT as perinatal anti-HIV prophylactics get a copy? We obviously can't count on your staff in Pretoria to do this.

We note with concern your statement that 'An independent external opinion on the scientific and clinical conclusions made in your letters has been sought by the MCC and is awaited.' Who's this guy? Has he filed a sworn conflict of interest declaration?

Aren't the MCC's members sufficiently independent? Aren't they able to weigh the issues and make up their own minds as their appointments require? It seems that the MCC has abdicated its statutory responsibility to apply its collective mind to the drug safety issues raised in our submissions, and has unlawfully asked someone else to do its job for them. We'll be taking this point formally if needs be.

We note your mention of plans to establish a Pharmacovigilance Centre at the University of the Free State. MEDUNSA has the same idea. This sounds all very soothing, but given the findings already made abroad about the horrible effects of AZT on unborn and newly born babies, we think the MCC should act immediately to pull this drug, and not wait and see how many more children, mostly black, mostly poor, are killed or maimed in South Africa too, before doing so. Did we need a new research institute in this country to find out how many babies were being born deformed here before dumping thalidomide? Or did South Africa heed the early evidence overseas?

In conclusion, two recent developments have taken place that afford the MCC a face-saving exit from the bog it waded into in recommending on 12 July that pregnant women continue taking nevirapine – in combination with AZT.

First: Associated Press is about to blow the whistle on the deliberate suppression by top US NIH officials of two reports concerning serious toxic side effects and unreported deaths in the



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HIVNET 012 nevirapine trial, which the NIH had financed, so as not to upset President Bush's \$500 million mission to fight AIDS in Africa, centring on the provision of nevirapine. Which he proceeded to announce on 19 June 2002, having been kept in the dark about the dangers of the drug:

This major commitment of my government to prevent mother-to-child HIV transmission is the first of this scale by any government, anywhere. We will support programs that administer a single dose of nevirapine to the mother at the time of delivery, and at least one dose to the infant shortly after birth. This therapy reduces the chances of infection by nearly 50 percent.

I have a copy of the draft AP article, for which I was interviewed, and was informed that it will be the first of an intended series on the drug, the next major drug scandal.

Now that the MCC has been alerted to this deadly fraud on us by the Americans, we suggest that it direct some enquiries about it to the NIH. We were impressed by its rejection of the NIH's attempt to dupe it into accepting HIVNET 012 by way of its 'Re-monitoring Report' snowjob, and trust that it will be as impervious to the dissembling of these crooks a second time round. The issues are identified in a letter written by the National Whistleblowers Center in Washington, annexed to our seventh letter.

If the MCC doesn't take this up with the NIH, we will see to it that it is very publicly asked later on why it turned a blind eye to this critical information provided to it about the hazards of the HIVNET 012 nevirapine regimen for South African women and their babies, mostly black, mostly poor.

Second: In a major review of data collected between 1986 and April 2004, the European Collaborative Study has just reported that AIDS drugs cause a 'substantially increased risk of severely curtailed pregnancy [*i.e. critical prematurity*] ... coupled with a very high neonatal mortality rate'. (Thorne et al. **Increased risk of adverse pregnancy outcomes in HIV-infected women treated**

**with highly active antiretroviral therapy in Europe.** *AIDS* 18: 2337-2339, 2004.)

In the light of these findings, on top of all the others we've reviewed, we think that only a moron or a really malevolent racist would continue recommending that pregnant women in South Africa, mostly black, mostly poor, be given AZT combined with nevirapine during their pregnancies. What do you reckon?

The *Mail&Guardian* isn't likely to share this view, though. You might have seen our full-page piece on the back of its World AIDS Day supplement, which the paper had invited us to place, asking 'Why should South Africans continue to be poisoned with AZT?', and 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 our immune system.

Numerous studies have found that children exposed to AZT in the womb suffer brain damage, neurological disorders, paralysis, spasticity, epilepsy, other serious diseases and early death.

M&G editor Ferial Haffajee's response to a slew of angry letters about this, three of which protested that the statement of such unspeakable facts would actually 'kill people', was that our piece 'should not have been carried' and such writing 'will not be carried in the *Mail&Guardian* in future'.

After agreeing with this writer to publish a reply, she spiked it minutes before going to press. When we phoned to enquire about this change of tune, we got M&G Chief Operations Officer Hoosain Karjeiker on the line. He explained that what was objectionable in our reply was our reference to 'the side effects of extremely toxic pharmaceutical drugs like AZT and nevirapine'. 'We are proponents of AZT,' he said. 'Once again the ad casts aspersions on AZT and nevirapine.' 'Do you mean it's unacceptable to state that AZT is toxic?' we asked incredulously. 'Yes,' he replied; it's 'dissident'.

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Editor Haffejee phoned about an hour later with more of the same:

Our newspaper has been at the forefront of the push for antiretrovirals in this country. Our brand has suffered because of your ad two weeks ago. The new ad contains the same message, albeit not as strong. Publishing it will continue to damage our brand.

Run by such people do you think this could be why black intellectuals and politicians here generally refer to the *Mail&Guardian* as the 'Mail and Garbage'?

Can we expect a better show from the MCC now that it's been given all the facts?

Yours faithfully

ADV ANTHONY BRINK  
CONVENOR AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

Cc: The South African government and other interested parties;  
the Registrar: MCC



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18 January 2005

The Chairperson: Medicines Control Council  
Professor Peter Eagles  
School of Pharmacy  
University of the Western Cape  
Private Bag X17  
Bellville

Dear Professor Eagles

**MCC review of its special registration of nevirapine for  
perinatal administration, and its recent recommendation  
that nevirapine be administered together with AZT**

I write to draw the MCC's attention to the latest findings of brain damage among children exposed to AZT and 3TC in utero, reported by Poblano et al. at the end of last year. Enclosed are both the Pubmed abstract of their paper, and the full text, which the authors kindly sent me.

Please pass the information on to the responsible sub-committee.

Yours sincerely

ADV ANTHONY BRINK  
CONVENER AND NATIONAL CHAIRMAN  
TREATMENT INFORMATION GROUP

**Excerpt: Effects of prenatal exposure to Zidovudine and Lamivudine on brainstem auditory evoked potentials in infants**

**from HIV-infected women.** Poblano et al. *Proc West Pharmacol Soc.* 2004;47:46-9:

The purpose of this study was to determine whether there were differences in Brainstem Auditory Evoked Potential (BAEP) waves and interval interwaves in a group of Zidovudine (AZT) alone or AZT plus Lamivudine (3TC) prenatally exposed infants ... compared with a group of infants not exposed to antiretroviral drugs. Results could provide an index of neurotoxicity in newborns. ... Infants were included in the study if they were exposed prenatally to AZT alone or AZT plus 3TC. ... Comparison of wave latencies showed significant delay of wave I and I-III interwave interval in the AZT-3TC-treated group. DISCUSSION ... Infants with AZT/3TC exposure displayed less-well-developed BAEP within lower brainstem regions, suggesting subclinical dysfunction in these auditory centers within the brainstem. To our knowledge this is the first study to recognise brainstem toxicity of antiretroviral treatment in perinatally exposed newborns. One possible explanation of this fact is that AZT/3TC cause mitochondrial damage in cochlear hair cells [19] and in brainstem neurons, such as that observed in adult patients. Our data suggested that antiretroviral therapy has a preferential effect in the lower brainstem neurons and in auditory nerve and thus may represent the targets of drug damage. The results presented here suggested the possibility of antiretroviral neurotoxicity during a critical period of auditory system development.

Reference 19 is to Marra's et al. positive finding concerning **Hearing loss and antiretroviral therapy in patients infected with HIV-1**, reported in *Archives of Neurology* (1997 Apr;54(4):407-10): 'Hearing loss is common among HIV-infected individuals and is associated with antiretroviral therapy in those aged 35 years or older.'

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*He was exceptionally knowledgeable about medicine. From the scientific point of view, he was the only SS officer there of quality. For me, he was very worth talking with. He was an ideologue, body and soul. Never any emotion; he showed no hate or fanaticism ... and as the Jews were going to die anyway, he saw no reason not to use them first for medical experiments.*

Hans Münch, acquitted at the Auschwitz doctors trial in Cracow, Poland, on 22 December 1947, speaking of his fugitive colleague Josef Mengele

On 24 February 2005 the US Public Health Service released its updated Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV-1 Transmission in the United States. The Recommendations were drawn by a bunch of AIDS doctors (all MDs), whose 'Executive Secretary', and probable principal author, was Lynne Mofenson, a prominent apologist for the administration of AZT to pregnant women. The Recommendations essentially echo the WHO Guidelines – indeed, Mofenson was a consultant in their formulation. To read them is to recall Münch speaking about Mengele: one is struck by the AIDS doctors' single-mindedness, their relentlessness, their absolute determination to do what they believe must be done for these people with the bad blood. Mostly people of colour. And irrespective of the human cost.

The Recommendations assert that 'pregnancy is not a reason to defer standard therapy' (AZT and similar drugs), notwithstanding that AZT remains classified by the FDA as a 'C' class drug, meaning that the potentially harmful effects of the drug on the unborn child remain unknown, as the Recommendations explicitly concede: 'Data to address many of these considerations ['the

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potential for adverse short or long-term effects on the fetus and newborns'] are not yet available.' Except that in the last few years ample evidence has been reported that AZT may be profoundly harmful, sometimes fatally, to unborn and newly born children. To this the AIDS doctors pay lip service in their Recommendations, warning that

Information included in these guidelines may not represent approval by the Food and Drug Administration (FDA) or approved labelling for the particular product or indications in question. Specifically, the terms 'safe' and 'effective' may not be synonymous with the FDA-defined legal standards for product approval.

In view of this, the Recommendations say,

offering antiretroviral therapy to HIV-1 infected women during pregnancy ... should be accompanied by a discussion of the known and unknown short- and long-term ... risks of such therapy to infected women and their infants.

In other words, AIDS doctors should explain to worried mothers bearing babies inside them that they're swallowing extremely toxic chemotherapy that could kill, seriously injure or neurologically damage their children for life in a manner that won't necessarily be clinically obvious. Of course they never do explain this.

A striking illustration of the dismal quality of the expertise of the doctors who drew the Recommendations lies in the fact that they proceeded from a decade-old fallacy, thoroughly debunked in the scientific press, concerning 'the pathogenesis of HIV-1', and they entirely ignore the official reversal of the 'hit early, hit hard' treatment approach announced by the US Department of Health and Human Services on 5 January 2001.

So we have the Recommendations claiming

substantial advances have been made in the understanding of the pathogenesis of HIV-1 infection and in the



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treatment and monitoring of persons with HIV-1 disease. These advances have resulted in changes in standard antiretroviral therapy for HIV-1. More aggressive combination drug regimens that maximally suppress viral replication are now recommended.

These statements refer to Ho, Wei and Shaw's novel model of HIV pathogenesis, proposed in the mid-nineties, that HIV isn't a slow virus (a lentivirus) as had been supposed for the preceding ten years, but is instead a rapidly proliferating one best defeated by 'aggressive' ARV drug treatment. The new 'understanding' was almost immediately exposed by the AIDS experts themselves as nonsense (leaving a theoretical vacuum in its place), although it took another five years for the 'aggressive' treatment approach based upon it to be officially reassessed and abandoned.

The Recommendations note on their front cover that 'It is emphasized that concepts relevant to HIV management evolve rapidly.' Indeed so, but they are evolving in the opposite direction from what the AIDS doctors suggest in their Recommendations. The latest development in this reverse direction appears in the British HIV Association's draft revised guidelines published on 26 April 2005. Written by leading UK AIDS doctor Professor Brian Gazzard, the BHIVA guidelines warn that

as evidence accrues that AZT (zidovudine, Retrovir) is associated with lipoatrophy [*wasting, due to the drug's mitochondrial toxicity*], the guidelines move away from firmly recommending an AZT-containing regimen as part of a nucleoside backbone.

Tardieu et al. of the French Pediatric HIV Infection Study Group (Blanche, Barret et al.) reported in the same month in the *American Journal of Neuroradiology* (26(4):695-701) that

Mitochondrial dysfunction has been reported in HIV-negative children perinatally exposed to zidovudine, a drug often used in HIV-seropositive mothers during

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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.

As Brinkman explained years ago in *Lancet* (1999 Sep 25; 354(9184):1112-5), AZT and related 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 [*intracellular organelles crucial to energy metabolism*] ... other common side effects of [AZT and related drugs are] nerve and muscle damage, pancreatitis and decreased production of blood cells ... all resemble conditions caused by inherited mitochondrial diseases.

Despite this, the American AIDS doctors firmly recommend in their new Recommendations that in 'resource-constrained settings' such as South Africa 'to prevent perinatal transmission, ZDV [AZT] chemoprophylaxis should be incorporated into the antiretroviral regimen'. Which is to say pregnant women should swallow it regardless of how it has been shown to poison them and their babies.

On 28 October 2005 we finally received MCC chairman Professor Peter Eagles's response (dated five weeks earlier) to all our correspondence. Absolutely nothing to worry about, he said,

your documentation has not shown that the potential risks of adverse effects of the antiretroviral agents in question are greater, more serious, or on a larger scale than the risks of complications from HIV-infection and its adverse effect on the lives of babies and children. Information which has become available subsequent to the

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Medicines Control Council (MCC) resolution of 02 July 2004 has also not changed the overall assessment of the risk of HIV-1 infection compared to the adverse effects of antiretroviral agents in PMTCT. (For example, we refer you to the frequently updated guidelines on the 'Aidsinfo' website: [www.aidsinfo.nih.gov](http://www.aidsinfo.nih.gov).)

These are the Recommendations discussed above. The MCC's anonymous 'expert' appointed to consider our 'documentation' had disposed of the matter by simply referring to the Americans.

A few days later, on 3 November, *AIDSmap* summed up the latest paper regarding the harm AIDS drugs do to unborn children, **Does exposure to antiretroviral therapy affect growth in the first 18 months of life in uninfected children born to HIV-infected women?** reported by the European Collaborative Study in the *Journal of Acquired Immune Deficiency Syndromes* (40 (3): 364-370):

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 to the results of a European study examining the effects of ART on uninfected children's growth up to the age of 18 months.

Having trouble thinking straight, like all AIDS doctors believing they're going about a higher purpose in saving babies from their mothers' germs (just as Nazi doctors went about theirs in the same mystical thrall, although not paid the same grant millions for doing so), the European Collaborative Study group were unable to acknowledge that they were actually doing something terrible: first they said the stunted growth was 'unlikely to be clinically relevant at this age' (eighteen months); then they pre-

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tended that it may be, but they weren't sure: 'the subsequent clinical implications of this finding are unclear'.

But they are clear. 'Growth faltering, particularly stunting, may adversely affect a child's quality of life, especially once they reach adolescence,' noted Newell et al. in *Pediatrics* in January 2003 (111(1):e52-60), claiming in their paper that AIDS drugs don't actually stunt growth – no, the cell-killing chemicals help children grow!

Which is not what Miller et al. found and reported in the same journal two years earlier (108(6):1287-96) under the title, **Maternal and infant factors associated with failure to thrive in children with vertically transmitted Human Immunodeficiency Virus-1 infection: the prospective, P2C2 Human Immunodeficiency Virus Multicenter study:**

The study cohort included 92 HIV-1-infected and 439 uninfected children ... Antiretroviral therapy ... was independently associated with FTT [*Failure to Thrive*] in our cohort ... ZDV [AZT], in particular, alters mitochondrial metabolism and may have direct nutritional effects.

Moye et al. had reported consistently in the *Journal of Pediatrics* (128: 58-67) in 1996 regarding the effect of treating HIV-positive babies with AZT:

In contrast with anecdotal clinical observations and other studies indicating that zidovudine favorably influences weight-growth rates, our analysis suggests the opposite ... our findings suggest that the widely held view that antiretroviral treatment improves growth in children with HIV disease needs further study.

The trouble the European Collaborative Study's AIDS doctors have seeing what they're doing is underscored by their previous report on 21 October 2004 in *AIDS* (18(15):2009-17):

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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. ARVs given to pregnant women cause persistent, probably permanent, bone marrow suppression, thus reducing blood cell production*]. In uninfected children ... ARV exposure [before birth was] associated with reduced neutrophil count until at least 8 years of age. ... CONCLUSION: A considerably longer effect of exposure to ARV was shown in uninfected children than previously thought.

Again the AIDS doctors administering the toxic drugs claim that 'the clinical implications are not clear', yet it's basic to immunologists that 'a decrease in the number of neutrophils in the blood ... results in an increased susceptibility to infections' as the *Oxford Concise Medical Dictionary* puts it – explaining that 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'. Could this be why babies poisoned by AZT in the womb, and immediately after birth in some cases too, have been reported in numerous studies to suffer much higher rates of serious disease and early death than unexposed babies?

Don't ask an AIDS doctor though. He'll tell you it's the HIV infection coming on, which his toxic drugs just weren't strong enough to stop. Just as doctors used to blame that stubbornly resilient syphilis spirochaete for the slobbering and shambling seen among what they called G.P.I. cases (General Paralysis of the Insane), for whom repeated injections of neurotoxic arsenic (Salvarsan) just weren't strong enough from 1910 right up until the fifties. And given to pregnant women, not strong enough to prevent stillbirth, blindness, deafness, mental retardation, facial and limb deformity and no end of other birth defects and illnesses.

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In August 2006 the WHO issued new recommendations for the treatment of HIV-positive pregnant women with a 'more efficacious' regimen for preventing mother to child transmission of HIV 'in resource-constrained settings' than one dose of nevirapine each to mother and baby, namely

AZT from 28 weeks of pregnancy (or as soon as possible thereafter); during labour – AZT/3TC plus sd [*single dose*]-NVP); and postpartum – AZT/3TC for seven days for women and sd-NVP and AZT for one week for infants.

The most telling recent data concerning the deadly effect of this 'more efficacious' treatment came from neighbouring Botswana the following month. **Botswana PMTCT programme highly successful – except for the excess mortality** read the dumbfounding title of an article published on 12 September 2006 by *AIDSmap*, a drug industry shill that pumps out a

regular electronic newsletter for health care workers and community-based organisations on HIV treatment in resource-limited settings ... supported by ... GlaxoSmith-Kline's Positive Action Programme (a founding sponsor), ... Abbott, Boehringer Ingelheim, ... Merck, Roche and Tibotec.

The article began by noting that this 'excess mortality' among AZT- and AZT+nevirapine-exposed babies was taking place in a

country that has been the continent's flagship HIV control programme ... going all out since 1999 ... identifying and providing free PMTCT services to a much higher percentage (~85%) of pregnant mothers with HIV than any other country [with] virtually universal ... formula feeding ... in Botswana (~98% of infants in the HIV-transmission study were formula fed). ... But the bottom line is, that despite the low HIV transmission data ... Botswana's own mortality data shows that something isn't working.

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... data show that infant mortality is still on the increase.

In short, following the implementation of a wide-scale perinatal AZT and AZT+nevirapine programme in Botswana, the infant death rate is rising. Which is to say that with the benefit of the treatment more young African children are dying than ever before. In the words of Ernest Hemingway: 'It was a brilliant cure, but we lost the patient.'

A report on 1 May 2007 by Feiterna-Sperling et al. in the *Journal of Acquired Immune Deficiency Syndromes* 45(1):43-51 helped explain why. In a

prospective observational study to investigate hematologic alterations during the first 3 months of life in HIV-exposed uninfected infants subjected to antiretroviral medication before and after birth ... Two hundred twenty-one consecutive uninfected infants born to HIV-positive mothers on antiretroviral medication during pregnancy were included. Perinatal transmission prophylaxis comprised zidovudine (ZDV) administered intravenously intrapartum and 10 days after birth. ... Median hemoglobin was significantly lower in HAART-exposed newborns from birth ... until day 28. During follow-up, 119 (53.8%) infants had anemia grade 2 or higher on at least 1 occasion; 16 (7.2%) received red blood cell transfusion at 23 (range: 1-56) days of age. Neutropenia grade 2 or higher occurred in 106 (48.0%) infants at least once; 8 infants had staphylococcal infections, and 2 infections were severe. ... Antiretroviral transmission prophylaxis is associated with significant anemia and neutropenia in HIV-uninfected infants during the first 3 months of life. Anemia was more profound in HAART-exposed infants.

And in the same month, explaining how in the face of all the evidence against the drug the WHO could be recommending that pregnant women and their babies in the Developing World be

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given AZT, Associated Press wired a report on the 7<sup>th</sup> under the heading 'WHO Criticized for Neglecting Evidence':

When developing 'evidence-based' guidelines, the World Health Organization routinely forgets one key ingredient: evidence. That is the verdict from a study published in *The Lancet* [by Oxman et al.] online Tuesday. ... 'This is a pretty seismic event,' said *Lancet* editor Dr. Richard Horton, who was not involved in the research for the article. 'It undermines the very purpose of WHO.' ... WHO's Director of Research Policy Dr. Tikki Pang said that some of his WHO colleagues were shocked by *The Lancet's* study, but he acknowledged the criticism had merit, and explained that time pressures and a lack of both information and money sometimes compromised WHO work. 'We know our credibility is at stake,' Pang said, 'and we are now going to get our act together.' WHO officials also noted that, in many cases, evidence simply did not exist. 'People are well-intended at WHO,' Oxman said. 'The problem is that good intentions and plausible theories aren't sufficient.'

On 12 September 2008 Ekouvi et al. (including Francois Dabis and Stephane Blanche) reported in *AIDS* (22(14):1815-20) that the administration of AZT and similar 3TC to African women given during their pregnancies, 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,' they found. Seven percent of the babies in the study died in their first year, but unlike many other reported findings, the researchers did not see any connection between toxic drug exposure in the womb and infant mortality. Nor were they bothered by the clinical implications of being born underweight, in other words stunted, thanks to antenatal exposure to a cell-poisoning drug – summed up in June by Hernández and Mericq in *Best Practice & Research Clinical Endocrinology & Metabolism* (22(3):463-76): 'Child-



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ren born small for gestational age (SGA) are at higher risk for perinatal morbidity, mortality and chronic diseases in later life.' In the same issue of the journal (pp 477-88), in **Effects of being born small for gestational age on long-term intellectual performance**, Lundgren and Tuvemo added:

Size at birth has been associated repeatedly with increased risk of cardiovascular morbidity and mortality later in life. However, there is accumulating evidence to suggest an association between being born small for gestational age (SGA) and increased risk of lower intelligence, poor academic performance, low social competence and behavioural problems, compared with individuals born appropriate for gestational age.

On 6 October 2008 Professor Luc Montagnier of the Pasteur Institute in Paris won the Nobel Prize for Medicine for his claim in *Science* in 1983 to have discovered 'HIV'. In the year he was pronounced the world's most hallowed AIDS expert, he published his book *Les combats de la vie: Mieux que guérir, prévenir* (Fighting for Life: Prevention is Better than Cure) in which he warned that AZT is harmful to unborn and newly born babies (I translate):

an aspect that has been completely hidden by specialized medicine, on which medical teaching should start serious work [is the fact that] antiviral treatments for AIDS ... also have an effect on mitochondrial DNA polymerase ... It is the unwanted effect of antiretroviral treatments and of chemotherapy in general, of any treatment, that has an effect on the cellular or mitochondrial DNA. The same can be said of anti-cancer drugs. The heavy chemotherapies of cancer or AIDS consistently bring about oxidative stress.

Exposing babies to AZT before and after birth was a medical practice belonging to the past, he argued:

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Until the end of the nineties we treated the mother with AZT before and during labour to prevent the mother to child transmission of AIDS. This treatment was also administered to the baby just after birth. Nowadays we use other products. But at that time, as a member of the National AIDS Council, I raised this question by warning my colleagues about this problem of AZT interfering with mitochondrial DNA and its potential long-term effects on babies. Let's imagine that these babies later have daughters (the mitochondria are transmitted by the mother): will these daughters' mitochondrial stock be normal? We don't know. The effects of this kind of treatment could very well leap generations, just as diethylstilbestrol later caused ovary cancers, infertility and malformations among the daughters of the mothers treated with it. Chemotherapy with AZT is not innocuous, and I raised this with the people who monitor these babies all their lives. Normally it would be necessary to monitor the following generation as well... Is this guideline that I was able to get adopted still followed? I'm afraid not.

But the ill effects of AZT's mitochondrial toxicity mentioned by Montagnier weren't just potential in the next generation, they were immediate.

In the September 2008 issue of the *Journal of Neurologic Physical Therapy* (32(3):118-21) Nicole Baillieu, a researcher in the Department of Physiotherapy in the Health Sciences faculty at the University of the Witwatersrand, and Dr Joanne Potterton, a lecturer there, reported **The extent of delay of language, motor, and cognitive development in HIV-positive infants**. '97.5% of the sample' were found to be

functioning below expected motor and cognitive age ... Eighty-five percent ... demonstrated gross motor delay, which was the most adversely affected skill. Language

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was descriptively analysed, revealing global language delay in 82.5% of the children.

The sample comprised

Forty HIV-positive, antiretrovirus-naïve children aged 18 to 30 months attending the Harriet Shezi Pediatric HIV Clinic at Chris hani Baragwanath Hospital, Johannesburg

The authors didn't report whether the mothers of the 'antiretrovirus-naïve children' had been given AZT during their pregnancies. But given that the brain damage in evidence matched precisely that reported by Blanche, Barret and others, who determined that it was unequivocally caused by AZT (with or without similar 3TC), it's a certainty that they were.

Indeed, at the Fourth South African AIDS Conference in Durban in April 2009, Potterton presented an abstract of her findings on the limited benefits of a 'basic home stimulation programme' in Soweto for 'motor and cognitive development in HIV-positive children under 30 months'. In reporting how these African children were suffering

developmental delay, failure to achieve development milestones ... deterioration of intellectual abilities ... spastic quadriparesis (a spastic rigidity of the limbs often accompanied by difficulty in swallowing and seizures), dystonic posturing (abnormal or 'locked in' movements) and regression in motor milestones

she could have been describing the HIV-negative children investigated by Blanche, Barret and their colleagues, who, they unequivocally found, had been brain-damaged by AZT or AZT+3TC (see Appendix 1).

Naturally Potterton blamed the virus instead of the medicine: 'South African children who are infected with HIV are at risk of severe cognitive and motor delay.' So did the authors of six studies reviewed by Abubaker et al. three months earlier. In **Pedia-**

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**tric HIV and neurodevelopment in sub-Saharan Africa: a systematic review** published in *Tropical Medicine and International Health* (13(7): 880-7) they found:

In infancy a consistent delay in motor development was observed ... a severe degree of impairment. Mental delay showed a moderate delay at 18 months ... Language delay did not appear until 24 months.

Their 'CONCLUSION'?

Although HIV has been shown to affect all domains of child functioning, motor development is the most apparent in terms of severity, early onset, and persistence across all age groups.

Oblivious to the research literature identifying AZT and similar drugs as the 'confirmed' cause of permanent brain damage, mental retardation and crippling physical injury, among other grave ills, it didn't occur to any of the authors to implicate the toxic drugs in the neurological injuries they reported.

Back in South Africa it was much the same myopia at a workshop 'The HIV-Exposed but Uninfected Infant' held at the University of Stellenbosch between 3 and 5 November 2009 by the Peter Wall Institute for Advanced Studies at the University of British Columbia, Canada, in collaboration with the Stellenbosch Institute for Advanced Study. The subtitle of the conference pointed up the problem: 'How to explain excess Morbidity and Mortality? "Bad News after Good News"'. The object of the experts gathered was accordingly to devise a study to determine why

babies exposed to HIV but uninfected (HEU) by their mothers are at enhanced risk of poor health and development during the first year of life [and] to identify why HEU babies suffer so much illness during the first year of life.

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But not just 'babies exposed to HIV', babies exposed to ARVs:

babies in South Africa ... born to mothers who are infected with HIV [who had been on] effective mother to child prevention of transmission programs.

The workshop promised to

discuss the multiple dimensions of this problem in an attempt to plan a study to explain this peculiar phenomenon. Potential contributing factors include poverty, malnutrition, lack of access to health care and exposure to adverse environmental factors and/or transmissible infectious diseases.

No expert attending the workshop raised the possibility that the severe toxicological insult caused babies in utero and after birth by AZT and similar ARV exposure might be indicated as the cause of 'why HEU babies suffer so much illness during the first year of life'. Not even prompted by the clue in the workshop 'Introduction':

It is clear that susceptibility to disease of any type is multifaceted, involving, among other factors, genetics, environmental exposures (toxins, pollution, microbes), nutrition and psychosocial conditions. Many studies have been performed in the developed world to identify the factors that put children at risk for suffering from HIV-related illnesses, but none has identified [the factors implicated in] severe disease in those babies who are not infected (HEU).

And as far as 'exposure' to 'toxins' go, it's hard to imagine one more obviously dangerous and harmful to babies than a cell poison originally purpose-designed and synthesized to kill human cells, which comes packaged for research use in minute 25 mg quantities with a skull and crossbones on a bright orange stripe to signify deadly toxic chemical hazard, and spelt out:

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TOXIC Toxic to inhalation, in contact with skin and if swallowed. Target organs: 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.

One of the workshop participants was Louise Kuhn, who in July 2000 had reported a ten-year study in the *Journal of Infectious Diseases* (182(1):104-11), **Disease progression and early viral dynamics in human immunodeficiency virus-infected children exposed to zidovudine during prenatal and perinatal periods**, in which she found (as Reuters Health summarised):

Among infected children who did not receive ART before AIDS diagnosis, 44% developed AIDS or died before age 12 months when they were exposed to prenatal or perinatal zidovudine. However, among HIV-infected infants not exposed to zidovudine prophylaxis, rate of death or progression to AIDS was only 24% ... Zidovudine exposure before birth or perinatally appears to accelerate disease progression in HIV-infected infants.

Precisely as other researchers working independently reported too. But by the time the workshop in Stellenbosch was held, Kuhn appeared to have forgotten.

Maybe it was the wine. Or maybe it's just that if you've built your career researching and promoting a particular medical intervention, it's hard to face the reality that the particular medical intervention you've built your career researching and promoting is actually monstrously harmful, when all along you've imagined that you've been on the side of the angels, saving little babies lives. It's only natural.

That AZT and similar drugs, being extraordinarily toxic, make babies very sick is the ultimate elephant in the room, a plain fact in plain sight, but unnoticed by the experts because it's too horrible to take on board.

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Consider the glaring findings of Sutthent et al. published in July 2002 in the *Journal of Clinical Virology* (25(1):47-56) regarding the **Effect of perinatal short-course zidovudine on the clinical and virological manifestations of HIV-1 subtype E infection in infants:**

OBJECTIVES: To investigate the effects of short-course regimen of oral ZDV for prophylaxis of HIV-1 subtype E vertical transmission among 'break-through' HIV-1 infected infants. STUDY DESIGN: The study analyzed clinical and virological outcomes of 80 infants, whose mothers received ZDV prophylaxis starting at 36 weeks gestation (group Z) and 37 infants whose mothers never received anti-retroviral drugs (group C), at the ages of 1-2, 4-6, and 12 months. RESULTS: Of the 12 HIV-1 infected infants, 5/7 (71.4%) from group Z and 1/5 (20%) from group C progressed to a symptomatic clinical stage by the age 4-6 months. ... CONCLUSION: Our results preliminary suggested that infected infants who were perinatally exposed to ZDV may have a more rapid early disease progression with unfavorable viral manifestations than those without exposure to antiretroviral drug.

Now why would that be?

On 1 June 2009, in **Immune reconstitution inflammatory syndrome among HIV-infected South African infants initiating antiretroviral therapy**, published in *AIDS* 23(9):1097-107, Smith et al. – Kuhn included – described how of

169 HIV-infected children ['less than 24 months of age'] initiating HAART ... (21%) children developed IRIS at a median of 16 days ... Bacille Calmette-Guérin reaction was most common occurring in 24/34 (71%) children, primarily injection site lesions and/or ipsilateral axillary lymphadenitis with abscess. Other IRIS conditions (not mutually exclusive) included *Mycobacterium tuberculo-*

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sis (n = 12), cytomegalovirus pneumonia (n = 1), Streptococcus pneumonia sepsis (n = 1), and severe seborrheic dermatitis (n = 1). ... CONCLUSION: Infants and young children with advanced HIV disease initiating HAART are at high risk for developing IRIS, leading to additional morbidity and possibly impairing virologic response to antiretroviral treatment.

Which is to say babies given ARVs are wont to get seriously ill and die on them, as one might reasonably expect considering how toxic they are, only you really mustn't say this or next they'll be calling you an AIDS denialist.



**Blanche et al. describe eight children severely harmed by AZT exposure in the womb and postnatally, two fatally, in 'Persistent mitochondrial dysfunction and perinatal exposure to anti-retroviral nucleoside analogues', *Lancet* 1999 Sep 25; 354 (9184): 1084-9.**

Note that in all cases the crippling injuries caused by AZT during gestation and after birth were not immediately evident, but only became apparent several months later. And in common with the others cited above, the researchers do not consider and report the likelihood of widespread subclinical, undiagnosable, permanent neurological and mental/psychological impairment resulting from AZT exposure in utero and after birth.

'At age 4.5 months, the first patient presented with visual impairment. Cerebral nuclear magnetic resonance imaging showed initially (at age 5.0 months) demyelinating lesions of the brain-stem that became more severe and secondarily associated (at 11.0 months) with sustentorial lesions. From age 4.5 months to 11.0 months, the growth was abnormal and associated with vomiting. There were no important hepatic, pancreatic, muscle enzyme, or haematological abnormalities, but blood and cerebrospinal fluid lactate concentrations were high (2.5 mmol/L [normal <1.5 mmol/L] and 4.5 mmol/L [<2.0 mmol/L], respectively). The child died aged 13 months because of respiratory and cardiac-rhythm disorders. The symptoms were compatible with Leigh's syndrome and mitochondrial investigations were done at age 12 months.

'The second patient, from age 4 months until death at 11 months, had refractory epilepsy and deterioration of cognitive and psychomotor abilities. Cerebral imaging showed diffuse demyelinating lesions associated with massive cortical necrosis (figure). There were no substantial biological abnormalities for liver, pancreas, muscle, or haematological markers. The blood lactate con-

*Appendix 1: AZT and brain damage: eight reported cases*

centration was high (2.5 mmol/L) but cerebrospinal fluid lactate was normal. Several disorders were excluded because of normal results from the following diagnostic procedures: organic-acid chromatography (urine), aminoacid chromatography (serum, urine, cerebrospinal fluid), serum cholesterol, triglycerides, vitamins A and E, pyruvate dehydrogenase activity in lymphocytes, fatty-acid oxidation and biotinidase activities (lymphocytes), very long-chain fatty acids (serum), lysosomal enzymes (galactosidase, galactosylceramidase, arylsulphatase A, mannosidase, GM1 and GM ganglioside), copper and ceruloplasmin (serum), and oligosaccharide excretion (urine). These symptoms were consistent with ALPERS syndrome, and led to mitochondrial investigations between ages 5 months and 7 months.

'At age 8 months, during a febrile episode, patient three had a seizure and was thought to be hypotonic. At age 15 months, the child showed symptoms of hypokinetic hypertrophic cardiomyopathy. Blood hepatic and pancreatic enzyme concentrations were normal but the child had neutropenia neutrophils 0.931 09/L [normal > 1.531 09/L), high concentrations of muscle creatine phosphokinase in blood (350 IU/L [<250 IU/L]), and persistently high blood lactate concentrations (4mmol/L), although cerebrospinal lactate was normal. Endomyocardiac biopsy showed intracytoplasmic vacuolisation in myocytes, but without inflammation. The cardiomyopathy progressively improved and symptoms of peripheral myopathy were seen at age 2.5 years. At age 4.0 years, the child's cardiac function was normal, but moderate muscular deficit persisted; lactate and muscle creatine phosphokinase concentrations in blood remained high. Electroretinography showed macular and peripheral abnormalities. Cerebral nuclear magnetic resonance imaging was normal.

'In the fourth patient, early development was normal. Between ages 14 months and 27 months, the child had four episodes of

### *Appendix 1: AZT and brain damage: eight reported cases*

febrile seizures. Neurological assessment at age 27 months showed mild spastic diplegia. Haematological and biochemical findings, including lactate concentrations in blood and cerebrospinal fluid, were normal. Cerebral nuclear magnetic resonance imaging showed moderate hypersignal of the white matter in T2-weighted images, with no evidence of necrosis (figure).

‘From age 7 months until 15 months, patient five had repeated seizures. Cognitive development and neurological assessments between episodes were normal until age 15 months. The child developed status epilepticus for 4 h, which led to severe neurological dysfunction with cortical blindness and spastic tetraparesis. Biological tests at 15 months showed only high blood hepatic enzyme concentrations (aspartate and alanine aminotransferases 200 IU/L [ $<40$  IU/L]), which progressively returned to normal. Blood and cerebrospinal fluid lactate concentrations were measured only at the time of mitochondrial assessment and were not retrospectively available. Nuclear magnetic resonance imaging at age 16 months showed large necrotic lesions of the white matter and cortical grey matter. At age 3.5 years the child had severe sequelae and microcephaly.

‘Patient six was symptom-free until age 14 months, but persistent biochemical abnormalities were seen on standard follow-up of the epidemiological survey (which included lactate assays). The child had had high concentrations of blood lactate (4 mmol/L), hepatic aspartate aminotransferase (50 IU/L), and pancreatic lipase (200 IU/L [ $<150$  IU/L]) since birth that persisted until age 14 months. Cerebrospinal fluid lactate was normal. These biological abnormalities led to specific mitochondrial investigation, including cerebral nuclear magnetic resonance imaging that showed delayed myelinisation, which is difficult to interpret at that age.

‘Patient seven was symptom-free until age 4 months, at which time he became hypotonic with apnoea. The child regained nor-

*Appendix 1: AZT and brain damage: eight reported cases*

mal breathing and consciousness after resuscitation, with no apparent sequelae. There were no biological abnormalities during routine biological follow-up, but blood lactate concentrations (routinely assayed in this institution) were continuously high ( $>4$  mmol/L) from the first test at 4 weeks to 7 months. Cerebral nuclear magnetic resonance imaging was normal. Near-miss syndromes and lactataemia justified mitochondrial investigations.

‘The eighth child was symptom-free. Persistent hepatic and pancreatic abnormalities (alanine aminotransferase 80 IU/L and lipase 180 IU/L) were seen from birth in the routine prospective biological follow-up. Blood lactate concentrations that were systematically added to the normal screening in the institution were normal, as were cerebrospinal fluid concentrations. At age 20 months, biological abnormalities persisted unchanged; a specific mitochondrial investigation was therefore done, including electroretinography, which was abnormal, and cerebral nuclear magnetic resonance imaging that showed abnormalities of the periventricular white matter.

‘No child was infected with HIV-1, and all were HIV-1 seronegative at age 15 months, or at death before this age for patients one and two. For all children, repeated tests for HIV-1 by PCR and by culture were negative.’

# TREATMENT INFORMATION GROUP

*thinking about AIDS drugs*

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TIG PRESS STATEMENT: 31 OCTOBER 2007

OCTOBER 1957: THALIDOMIDE AND PREGNANCY

OCTOBER 2007: AZT AND PREGNANCY

ANOTHER TRAGEDY OF COUNTLESS CHILDREN KILLED  
AND MAIMED FORETOLD

Fifty years ago this month, the German pharmaceutical manufacturer Chemie Grünenthal began marketing thalidomide for use by pregnant women as a sedative and antiemetic, and the resulting tragedy of thousands of children killed in the womb or born with missing or grotesquely stunted limbs and/or internal organ deformities is well-known.

Little known is that thousands more suffered neurological injuries such as deafness and nerve-damage causing life-long pain, and even more were injured sub-clinically, permanently damaging their health and reducing their quality of life.

Little known too is that thalidomide was a best-seller, both on its own and combined with other drugs, whose alleged safety in pregnancy was extolled as a selling point by its manufacturer; and concerned, well-meaning doctors recommended it to pregnant women accordingly.

Although millions of prescriptions were written for thalidomide before it was withdrawn in the West in 1962, only about 10 000 children were visibly crippled by it. So it's arguable from these figures that thalidomide is safe for a woman to take during pregnancy, because the risk of her baby being harmed by it is minute. But it's unthinkable in Western countries today to give a

## *Appendix 2: Press Statement*

pregnant woman any drug known to potentially damage the child she's bearing. And certainly not if she's white.

Because many of the injuries that thalidomide caused unborn babies were hideously conspicuous, and therefore readily reportable by newspaper and television journalists, the thalidomide episode is generally thought the worst drug disaster in the modern era. It isn't; an incomparably greater one immediately preceded it. From 1910 until the late fifties, doctors repeatedly injected Salvarsan (arsenic) into people diagnosed with syphilis by means of the Wassermann test (now universally accepted to have been entirely non-specific and completely worthless) – a treatment formally approved by the Health Organization of the League of Nations in 1934. This included pregnant women to prevent mother to child transmission of the disease. Already known then to be extremely toxic, arsenic is now officially rated the deadliest poison known to man, weighted for risk of exposure, by the US Agency for Toxic Substances and Disease Registry.

For fifty years, babies killed in the womb, born with cancer, blind, deaf, paralysed, mentally retarded, otherwise brain-damaged, malformed, and/or very sick and soon dead, were said by doctors to have contracted 'congenital syphilis' from their mothers – a once common disease that practically disappeared with the abandonment of arsenic as a treatment for pregnant women.

Although the enormous medical blunder and human tragedy that resulted from the administration of arsenic by concerned, well-meaning doctors for half a century as an intended curative and preventative treatment for syphilis vastly exceeds the scale of the thalidomide tragedy, it's quite unknown to journalists, and it's consequently quite unknown to the general public today.

On the 1<sup>st</sup> of this month, the same day fifty years ago that the thalidomide horror began (it continues in the Developing World, in Latin America particularly), the Treatment Action Campaign

## *Appendix 2: Press Statement*

put the South African government on terms to provide AZT to HIV-positive pregnant women, mostly African, mostly poor.

It's very little known among journalists, and therefore very little known by the general public, that AZT is a cell-poison, purpose-designed by Dr Richard Beltz in 1961 to kill blood cells for potential use as a cancer chemotherapy in the treatment of leukaemia.<sup>1</sup>

Since the introduction of AZT as an AIDS drug in 1987, following a grossly corrupt clinical trial<sup>2</sup>, hundreds of research papers have reported AZT to be profoundly toxic to all cells of the human body<sup>3</sup> – predictably so, considering that AZT was specifically synthesized as a cell-poison to kill them. A brief overview is provided in the pamphlet *Why do President Mbeki and Dr Tshabalala-Msimang warn against the use of ARV drugs like AZT*<sup>4</sup>

It's virtually unknown by journalists, and therefore virtually unknown by the general public, that consistent with its basic pharmacological action as a cell-poison, dozens of studies have found that babies exposed to AZT in the womb and after birth by concerned, well-meaning doctors suffer a massively increased incidence of early death, serious disease, immunological disorders, brain damage, blindness, paralysis, spasticity, epilepsy, mental retardation, learning difficulties and other neurological injuries, as compared with unexposed babies born to untreated HIV-positive mothers.<sup>5</sup> Some of these findings are excerpted in the leaflet, *Why do Zackie Achmat, Nathan Geffen and Mark Heywood want pregnant African women and their babies to be given AZT? What AZT does to unborn and newly born children.*<sup>6</sup>

In *Corporate Crime in the Pharmaceutical Industry* (Routledge & Kegan Paul, 1984), John Braithwaite noted that 'Investigative journalists played a more important role than health regulatory authorities in many parts of the world in saving children from thalidomide.' Widukind Lenz, the German doctor who with his Australian colleague William McBride brought the thalidomide disaster to an end in the West, confirmed that 'the drug was withdrawn largely due to reports in the press'.

## *Appendix 2: Press Statement*

In the interests of a generation of South African children, mostly African, is there a single journalist in our country with the intelligence, the compassion, the diligence, the independence, the integrity, and the courage to follow the example of their European colleagues fifty years ago during the thalidomide disaster, and work towards averting another impending tragedy of thousands of children killed or maimed by AZT, some grossly, some slightly, by bringing the facts about the harm it causes to public attention? Even if the unborn and newly born children in jeopardy of being poisoned in South Africa are only African?

Adv Anthony Brink

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083 779 4174

CC: The Presidency, the Health Ministry, Cabinet, SANAC, ANC, MRC, and other interested parties

### **Footnotes:**

All articles and books mentioned below are accessible in the 'Quick links' column of the TIG website, [www.tig.org.za](http://www.tig.org.za).

1. *Inventing AZT* • 2. *Licensing AZT* • 3. *Debating AZT: Mbeki and the AIDS drug controversy* (2000); some reports published since 2000 are included in *Introducing AZT: 'A world of antiretroviral experience'* • 4. Online at [www.tig.org.za](http://www.tig.org.za) • 5. *Poisoning our Children: AZT in pregnancy* is a comprehensive survey of the medical and scientific literature on the foetal and neonatal toxicity of AZT, and a critical discussion of WHO and other institutional recommendations that pregnant women and their babies be given the drug • 6. Online at [www.tig.org.za](http://www.tig.org.za).



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18 December 2007

Dr M E Tshabalala-Msimang  
Minister of Health  
Private Bag X828  
Pretoria

And to cc list for information

Dear Dr Tshabalala-Msimang

## AZT IN PREGANCY

I refer to your Department's media statement on the 1<sup>st</sup>, announcing that 'Dual therapy for Prevention of Mother to Child Transmission of HIV should be implemented from the beginning of next year'. I haven't seen the 'draft treatment guidelines' currently being considered by the National Health Council, but 'Dual therapy' in this context conventionally means giving AZT or a similar nucleoside analogue drug to pregnant women and their babies in combination with nevirapine.

You'll recall President Mbeki's warning about AZT nine years ago in the National Council of Provinces on 28 October 1999:

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.

### *Appendix 3: A letter to Dr Tshabalala-Msimang*

As you correctly observed to journalists outside Parliament immediately afterwards (I quote a SAPA report), there was indeed:

a body of scientific research and information which indicated that AZT was a dangerous drug, and had not been designed for the treatment of HIV/AIDS. Because it was unable to target only the human immunodeficiency virus when it went to work in the body, it further weakened the immune system. There was also a danger that ... mothers taking the drug might produce children with disabilities. Tshabalala-Msimang said her ministry would not like to look back ten or fifteen years down the line and find it had exposed the vast majority of historically disadvantaged people in South Africa to a dangerous drug.

Two weeks later, on 16 November, you elaborated in Parliament:

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 ... AZT [*in the womb during gestation*], 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.

You need no reminding that the Medicines Control Council provided you with such disgracefully ignorant and inadequate 'assess[ments] ... [of] this data' that you turned to the Cochrane Centre, which then did no better. Some of your well-informed

### *Appendix 3: A letter to Dr Tshabalala-Msimang*

statements on AZT, supported by citations from the medical literature, are included in the enclosed introductory leaflet *Why do President Mbeki and Dr Tshabalala-Msimang warn against the use of ARV drugs like AZT?*

In the several years since 1999 when you and President Mbeki first expressed your concerns about AZT, particularly in regard to its harmful effects on unborn and newly born children, scores more research reports have been published confirming your worst apprehensions. This literature is canvassed in depth in a series of letters my group wrote to the Medicines Control Council, gathered in a compendium under the title *Poisoning our Children: AZT in pregnancy*. It can be downloaded free from our group's website mentioned in our letterhead. A few reports in this regard are included in the enclosed leaflet: *Why do Zackie Achmat, Nathan Geffen and Mark Heywood want pregnant African women and their babies to be given AZT? What AZT does to unborn and newly born children*.

According to the media statement, the new 'draft treatment guidelines' were developed on account of concerns about the 'limited effect and drug resistance associated with ... single drug nevirapine'. The problems with giving newborn babies, mostly African, even a single dose of nevirapine after birth are considerably graver than this. Official audits of HIVNET 012, the Ugandan study preceding nevirapine's conditional approval in this country by the MCC, found a very high incidence of unreported serious adverse events and many deaths among African babies exposed to this exceptionally toxic drug. This is detailed in my book *The trouble with nevirapine*, which can be downloaded free at my group's website.

In view of the focus of the 'process of consultation with experts and stakeholders', namely to 'try and address this challenge' of 'limited effect and drug resistance associated with ... single drug nevirapine', it seems unlikely that due attention was given during the 'process of consultation' to the proven serious harm that AZT has been shown in dozens of research reports to cause unborn

### *Appendix 3: A letter to Dr Tshabalala-Msimang*

and newly born children. This is because since the thalidomide disaster it's universally considered unconscionable to expose a pregnant woman to any drug known to harm the baby she's carrying. And it's equally unacceptable to treat a baby with a harmful drug that may seriously injure and possibly kill it. I enclose a copy of a press statement in this regard recently issued by my group on the 50th anniversary of the beginning of the thalidomide disaster, entitled *October 1957: Thalidomide and pregnancy; October 2007: AZT and pregnancy; Another tragedy of countless children killed and maimed foretold*.

In the interests of a generation of children, born to mostly poor African mothers, I implore you as a key member of the NHC to direct that an oral hearing be held at which I might present and be questioned on the medical research data that I've collected on how AZT and other nucleoside analogue drugs harm unborn and newly born children before the NHC accepts the new 'draft treatment guidelines' supporting their use.

You'll recall that although I'm a lawyer, a member of the MCC mentioned to you having been struck by the 'impressive detail' of my submissions concerning the foetal and neonatal toxicity of AZT, of which he said the MCC had been 'unaware'. The leading, most rigorous critics of AZT as an AIDS drug, Papadopoulos-Eleopoulos and her colleagues in Perth, Western Australia, have remarked to me: 'Clearly your knowledge-base in this subject extends far beyond ours.' In recognition of my expertise on the clinical and molecular pharmacology of AZT and nevirapine, which I've been studying for more than a decade, the scientists awarded me an honorary co-authorship credit of their 2001 monograph *Mother to child transmission of HIV and its prevention by AZT and nevirapine: A critical analysis of the evidence*. It can be downloaded from our website.

Section 6(1)(c) of the National Health Act 61 of 2003 requires that people should 'have full knowledge' of the 'risks' and 'consequences generally associated with each option' offered them by medical practitioners. Obviously, no pregnant African woman

*Appendix 3: A letter to Dr Tshabalala-Msimang*

would consent to exposing her baby to AZT (or similar) were she told of the proven 'risks' and 'consequences generally associated with' the drug, namely that

Numerous studies have found that children exposed to AZT in the womb suffer brain damage, neurological disorders, paralysis, spasticity, mental retardation, epilepsy, other serious diseases and early death

and

Hundreds of studies have found that AZT is profoundly toxic to all cells of the human body, and particularly to the blood cells of our immune system

as my group summarized the research in the *Mail&Guardian* on 22 November 2004 – a drug so toxic, especially to unborn children, that even its inventor Professor Richard Beltz disavowed it in an email to me 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.

I appreciate that you have been under enormous pressure by the pharmaceutical industry and its local agents to provide AZT and similar drugs to pregnant African women and their babies, and that South African National AIDS Council deputy chairperson Mark Heywood's AIDS Law Project acting on behalf of his and Zackie Achmat's Treatment Action Campaign menaced you with legal action in October, but it's unimaginable that apprised

*Appendix 3: A letter to Dr Tshabalala-Msimang*

of all the facts any judge would rule the government's reluctance to poison African babies with AZT unreasonable. And certainly no African judge.

Please act to avert this impending tragedy.

Yours sincerely

ADV ANTHONY BRINK

CHAIRMAN: TREATMENT INFORMATION GROUP

CC: President Thabo Mbeki; Department of Health Director-General Thamsanqa Mseleku; Department of Health Deputy Director-General Nthari Matsau; NHC members; all Provincial Health MECs; South African Local Government Association; South African Military Health Services; SANAC chairperson Deputy President Phumzile Mlambo-Ngcuka; SANAC deputy chairperson Mark Heywood; Parliamentary Health Portfolio Committee chairperson James Ngculu and all other members; Medical Research Council president Professor Anthony Mbewu; other interested parties, media, and online at [www.tig.org.za](http://www.tig.org.za)

## **FURTHER APPENDICES**

1. MCC reports on AZT in pregnancy
2. Cochrane report on same
3. Critical commentary on these reports