# Aids research in Africa –

# as if we were still in colonial times

## A study that has been stopped recently in Malawi sheds a scary-light on the reality of Aids research in Africa.

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A study organised by the John Hopkins University, School of Hygiene and Public Health, Department of Epidemiology in co-laboration with the Malawi College of Medicine was intended to save children by preventing mother to child transmission of HIV (MTCT). But it was stopped prematurely after details became public, which reveal the organisers had ignored the most basic principles of research in medicine.

Most striking was the fact that the women were approached for the first time 4 hours prior to delivery, while in labour. (8) Only few of them had ever been counselled or given any information on HIV and MTCT. During the 4 hours prior to delivery they were counselled and subsequently asked for consent to HIV testing. This counselling took place in an overcrowded delivery room with a complete lack of privacy. In case of a positive result, the women were than counselled for the result and got an introduction to the MTCT study, all this while in labour pain. A four-page patient information leaflet was handed out and consent for participation in the study was requested. No provision was made for longer counselling to explain this patient information to illiterate women. An important detail in a region where 55% of the women are illiterate. (6)

Not less important is the fact that an unknown number of women and new-borns were treated unnecessarily without being HIV infected. The following information is given in the product information of the HIV test used to diagnose whether the women were HIV-positive, that is infected with the virus or not: “Positive specimens should be retested using another method and the results should be evaluated in light of the overall clinical evaluation before a diagnosis is made.” (3) But this advice of the manufacturer was ignored and no retest was done in order to confirm the result. Also no doctor was involved whatsoever in making any diagnosis of possible symptoms. Giving a diagnosis of an HIV infection and administering drugs without respecting the necessary procedure is a clear violation of medical conduct and would lead to immediate legal consequences in developed countries.

Also the patient information was quite insufficient when it came to the side effects, although it was 4 pages long. It explained the obvious but did not contain the important list of potentially severe side effects. Only two side-effects were mentioned. At first women were told they and their children could experience some pain from the needles when the blood sample are taken. Than it is briefly mentioned that AZT, one of the drugs that is used can reduce the amount of blood in the child. One wonders why the women did not get the complete list of side-effects which even the companies hand out to all patients in the product information? Were the authors of the study too afraid to expose the following details: „Severe, life-threatening, and in some cases fatal hepatotoxicity ... Severe, life-threatening skin reactions, including fatal cases have occurred in patients treated with VIRAMUNE.... Some events occurred after short-term exposure to VIRAMUNE.“ Furthermore reference is made in the patient information to the results of a similar study performed in Uganda. Unfortunately the following findings on side-effects is not mentioned: The occurence of clinical or laboratory abnormalities in mothers was 80% and in babies, the rate of serious adverse events was 20%. (9)

No result of any diagnostic intervention done during the study, was given to the medical staff of the department, not even to the doctor responsible for the obstetrical treatment of the patients. This is an important aspect in a situation where resources are too scarce to perform even the most basic laboratory analysis on a routine basis. Even HIV positive results were withheld as well as the names of the patients who got anti-retroviral therapy. Consequently doctors could not take into account any of the information of the laboratory results nor whether or not the women or the child had been given anti-retroviral drugs. Therefore any symptoms from the mother or the newborn could not be interpreted as potential side-effects of the drugs. Even in the case of one maternal death no information from the study personal could be obtained as to whether the women had been given anti-retroviral drugs or not.

One of the drugs that was used in this study belongs to the most toxic drugs we have in medicine. They are used in so called Chemotherapy in cancer treatment. This is about the only condition where the strong and live threatening side-effects seem to be acceptable. On the other hand unborn and new-born children belong to the weakest group of humans. Consequently they are subject to a strong reluctance concerning any medical treatment because of fears of side-effects. It is incomprehensible that most of the media is following the bandwagon let by pharmaceutical companies to give the most

toxic drugs to the most vulnerable part of the population. And this is called a “treatment” which will “save lives”. Such a discrepancy between claimed and real intervention is unseen since bloodletting was finally abandoned more than 100 years ago.
The other drug used in this study has recently been refused registration for this indication by the Federal Drug Administration (FDA) in the US because the high incidence of side-effects but is nevertheless claimed to be safe in African mothers. (7)

The study has been stopped after the concerns about the details have been voiced. Or as the matron/chief nurse of the hospital put it: “studies which could not be conducted in the Western World should also not have a place in Malawi, misusing the poverty and the low educational status of a part of the patients.” The matron commented that she wondered how a credible ethical committee could approve such a study. She challenged that it was only because people in Malawi were poor that such a study could be done but she felt that Malawi should not be a dumping place for such problems. (2)

The saddest aspect in this story is the intention to save lives and to prevent harm has turned to the opposite. Women and new-borns have been declared as being HIV infected on the basis of one single unreliable test. Furthermore they have been exposed to the risk of side-effects of dangerous drugs.
The most positive aspect on the other hand is hidden in a letter and not transmitted to the public. After years of learning that Malawi has one of the highest HIV-infection rates in the world we are surprised to learn from the authors of this study that an additional centre had to be included because “the seroprevalence of HIV appears to be lower than what is estimate (30%) from pregnant women in Blantyre.” (1, 4, 5)

PS: In the meantime this study has been published in 2004 in the respected Journal of the American Medical Association. (10) Not surprisingly none of the ethical aspects described above were mentioned or discussed.

**Reference:**

1. Letter dated October 6, 2000 from the field director Dr. Newton I. Kumwenda, John Hopkins Project P.O. Box 1121, Blantyre, Malawi to The Cahirman, Colege of Medicine Research Committee, Chichiri, Malawi

2 The matron of Zomba Central Hospital, Mrs. Banda on a meeting held on February 4, 2002 in Zomba Central Hospital according to the minutes of the meeting.

3 product information of Determine™ HIV-1/2 Abbott Laboratories, Illinois, USA

4 Sentinel Surveillance Report 1997, HIV/Syphilis Seroprevalence in antenatal clinic attenders, National Aids Control Programm Malawi, Lilongwe, Malawi

5 Sentinel Surveillance Report 1999, HIV/Syphilis Seroprevalence in antenatal clinic attenders, National Aids Control Programm Malawi, Lilongwe, Malawi

6 Malawi Demographic and Health Survey 2000, National Statistical Office Zomba, Malawi, August 2001

7 Company Drops AIDS Drug Plan for US Fri Mar 22, comment by Reuters (please find the article at the end)

8 Study protocol (please find parts of it at the end)

9 Guay L et al. Intrapartum and neonatal single-dose nevirapine compared with zidovudine for prvention of mother-to-child transmission of HIV-1 in Kampala, Uganda: HIVNET 012 randomised trial, The Lancet, 1999, 4. September, Vol 354, No 9181

10 Taha E et al. Nevirapine and Zidovudine at Birth to Reduce Perinatal Transmission of HIV in an African Setting A Randomized Controlled Trial, JAMA. 2004;292:202-209.

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Company Drops AIDS Drug Plan for US Fri Mar 22, 5:22 PM ET
http://story.news.yahoo.com/news?tmpl=story&u=/nm/20020322/hl_nm/aids_plan_1&cid=594
WASHINGTON (Reuters) - A company that makes a key drug used to fight the AIDS (news - web sites) virus said on Friday it was dropping plans to try to get permission to widen marketing of the drug in the United States after irregularities were found in African trials of the drug.
Nevirapine has been found to reduce the risk that a mother infected with HIV (news - web sites) would pass on the virus to her baby during or soon after birth. Only small doses of the drug are needed to protect the baby.
German drugmaker Boehringer Ingelheim, a privately held company, had hoped to apply to market the drug in the United States for this use. Sold under the name Viramune, it is already widely prescribed for adults, and doctors are free to prescribe the drug any way they wish.
But Food and Drug Administration (news - web sites) (FDA) approval is needed for the company to actively promote the drug for use in preventing mother-to-child transmission in the United States.
When scientists started going through the data from the 1999 trial done in Uganda on nevirapine, some problems were found, Boehringer and the National Institute for Allergies and Infectious Diseases (NIAID) said in separate statements.
"Boehringer Ingelheim is aware that questions have been raised regarding reporting and documentation in a study conducted in Uganda for prevention of the transmission of HIV from mother-to-child during birth called HIVNET 012," the company said in a statement.
"Although no evidence has been found that the conclusions of HIVNET 012 (the Uganda trial) are invalid or that any trial participants were placed at an increased risk of harm,

certain aspects of the collection of the primary data may not conform to FDA regulatory requirements," the NIAID, which helped sponsor the trial, said in its own statement. "A comprehensive effort to access the primary data has begun to determine the applicability of the data collection processes to these regulatory requirements." Officials at NIAID and Boehringer were not immediately available for comment. "Since this NIAID and Boehringer Ingelheim review could not be completed within the remaining timeline for FDA action for the supplement, Boehringer Ingelheim has notified the FDA of its decision to withdraw the U.S. supplemental New Drug Application for prevention of mother-to-child transmission at this time," Boehringer said.

Part of the Study Protocoll:
3.0 STUDY DESIGN

3.1 Design summary
3.1.1 Objective
To determine if a short prophylactic regimen of oral single dose NVP alone or in combination with oral AZT (twice daily for a week) given to the newborn immediately after birth could reduce the rate of mother to child transmission (MTCT) of HIV.

3.1.2 Type of studv:
A randomized, open-label (nonmasked), controlled clinical trial (See Figure I).

*Group A Women:* These are women who attend the labour room relatively early. For this group, there is adequate time to conduct HIV counselling and testing (approximately more than 4 hours is anticipated between admission and delivery based on progress of labor). If a pregnant woman is found HIV positive she will be offered a single dose of NVP and her baby will be randomized to receive either NVP alone or NVP plus AZT.

*Group B women:* These are women who attend the labour room late. These are women in second stage of labour, with well established regular uterine contractions and advanced cervical dilatation. An approximate 4 hours duration from time of admission to the labour room to time of delivery should be used as a rough guide. Women who are expected to deliver in less than approximately 4 hours should be in this group. Among women who arrive late to the labour room, time to perform HIV counselling and testing is not adequate. These women are therefore counselled postnataly, and if they are HIV positive, their babies are randomized to receive the same regimen as babies born to men in Group A.

3.1.3 Intervention:
*HIV positive women* NVP 200mg tablets, single dose prior to delivery.

*Infants;* Randomized to receive either NVP 2 mg/kg birth weight, single oral dose alone, or NVP 2 mg/kg weight single oral dose plus AZT 4mg/kg birth weight every 12 hours for 7 days postnatally. Both NVP and AZT are offered as soon as possible after birth when the infant can swallow fluids (approximately within 12 hours following birth).

The study will be conducted at QECH (Queen Elisabeth Central Hosptial, Blantyre) and the health centers around the city of Blantyre. Eligible women are those who directly come to the labor ward from their homes, women attending the antenatal clinic but not eligible for enrollment in the Chorioamnionitis study, and women referred to the hospital for delivery.

3.1.5 Inclusion criteria for mothers:

- Willingness and ability to provide informed consent
- HIV positive at enrollment
- Willingness to take treatment as required by the protocol
- Willingness to return for follow up visits.

- Exclusion .criteria for mothers:
  - Inability to provide informed consent Refusal of HIV testing
  - HIV negative at enrollment

3.1.7. Exclusion criteria for infants.

- Preterm birth (<37 weeks gestation or birth weight <2.500 g)
- Low Apgar score (<5/10)
- Low hemoglobin levels (<l0g/d) on day 1-7.
- Conditions that require admission to the neonatal care unit

Children who are admitted to the neonatal care unit after they received the initial dose of study treatment, should continue to receive the assigned medication (this applies only to children receiving AZT since NVP is given only once - single dose) unless it is suspended by the attending clinician. In such situations a termination form should be completed.