

# Medical Journal of Therapeutics *Africa*

Volume 1 Number 3  
September 2007  
*Liver Diseases*



*Children in school in Kenya. Photos courtesy of Cornelius D Pitts PharmD.*

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## *From the Editor-in-Chief*

Our first 2 issues of *Medical Journal of Therapeutics Africa* focused on 2 of the 3 reputed main killers of Africans, malaria and HIV/AIDS. Our fourth issue, publication date Jan 2008 will focus on the third of the 3 main killers, tuberculosis. We chose liver diseases for the focus of issue 3 because focusing on an organ attacked by parasites gave us an opportunity to discuss water-borne diseases and revisit malaria.

And with each issue we will continue to revisit malaria. Malaria is completely preventable and completely curable; its existence and continued potency pours shame on industrialized nations. We will also continue to update on the work of humans whose major efforts are focused on preventing malaria through physical and chemical barriers to mosquitoes and through vaccines.

In this issue we include interviews with 2 extraordinary health-care professionals. John A Rich MD is an American physician based in Philadelphia whose work with urban adolescent males at risk for violent death led to his award of the MacArthur "Genius" award. Cornelius D Pitts IV PharmD is an American pharmacist and USP alumnus who has worked for GlaxoSmithKline for 25 years and who takes time every other year to work in Kenya to work taking care of the needs of a school in Majengo, Kenya.

During production of this issue I visited Africa and was able to discuss diseases and therapies first-hand with healthcare professionals, professionals far outside healthcare and non-professionals who toil long hours for little pay. I spent 2 weeks in Lagos, the biggest city in Nigeria (and perhaps the world), and 1 week in Ekpoma, a small town in Edo State not far from Benin. From the minute I arrived in Lagos I was cared for by MJoTA's Osagie Lawrence Egoro-Ighalo and his family. Pastor Egoro arranged visits to the School of Pharmacy at the University of Lagos, which included filming footage for the MJoTA movie on malaria, and also a week-long visit to Ambrose Alli University in Ekpoma where I was the guest of the Dean of Natural Sciences, Afe Ekundayo PhD, Professor of Microbiology. At Ambrose Alli University I gave a huge public lecture on diabetes, plus workshops on writing manuscripts, grant proposals and presentations. A major reason for my visit was to encourage submissions of articles from African universities to our journal: MJoTA can only be a dialog between pharmaceutical industry professionals in the US and Africa if we hear from more Africa.

We are delighted to publish articles from Africa. An article describing the road to regulation of a drug in Nigeria came by courier mail from the University of Lagos while Ndu David Ifudu PhD, its Dean of Pharmacy, visited us in Philadelphia. The author, Herbert Coker PhD is a pharmacist and Professor Ifudu's predecessor at University of Lagos. The final paper in this issue is the first collaborative paper between our institution and an African institution: Ms Joan Schertz connected with Robert Kalyesubula MD in the Spring when she wrote a story about the African Children's Choir™. Dr Kalyesubula was an orphan educated by the choir all the way through medical school. He is now an infectious disease specialist working in his home country of Uganda with patients who have HIV/AIDS. These articles truly represent our dreams, our goals, and what is so magnificently right about African professionals who work in Africa.



*Dr Dodgson and the Dean of Natural Sciences at Ambrose Alli University and with faculty at Pax Herbs*

## INSTRUCTIONS TO AUTHORS

For consideration by the Editors and the Editorial board, all manuscripts must be written according to the uniform requirements for manuscripts submitted to biomedical journals, which are posted on [www.icmje.org](http://www.icmje.org). We also adhere to the Editorial Policy Statements prepared by the Council of Science Editors (CSE) at [http://www.councilscienceeditors.org/services/draft\\_approved.cfm](http://www.councilscienceeditors.org/services/draft_approved.cfm).

Our style and editing guidelines can be obtained from the Editor-in-Chief. In brief, add only 1 space between sentences, number the references sequentially in the text and list the references in the same style as PubMed.

The preferred manner of submission is as an attachment on an e-mail, with pictures of figures and tables sent camera-ready as high resolution jpg files. Under special circumstances, manuscripts will be accepted by posted mail or fax.

We accept letters, literature review articles and data articles giving original research, and magazine articles telling stories. Articles should generally have under 3,000 words.

Original data articles need to be in the form Abstract (200 words maximum), Introduction, Methods, Results, Discussion.

Magazine articles are narratives and have no prescribed structure; accompanying photographs are encouraged. They may be as short as 200 words or as long as 10,000 words, however, they must be focused and tightly written.

We do not pay for medical journal articles or for magazine articles. You will retain the copyright for your journal or magazine article when you assign to us rights to publish your article in an issue of *Medical Journal of Therapeutics Africa*.

Each journal and magazine article is reviewed by at least 2 members of the editorial board and the editor-in-chief, and outside reviewers as the need arises. We adhere to the requirement of the National Library of Medicine for inclusion of journals in their database is that "neither the advertising content nor

commercial sponsorship should raise questions about the objectivity of the published material."

All articles published are required to meet the standards of the National Library of Medicine. Our major criteria for selecting each article are scientific merit, relevance to our target audience quality of writing, and relevance to the focus of the issue.

We invite submission of articles reporting any data or information that will nurture the dialog between pharmaceutical industry professionals in Africa and the United States. These articles will include clinical and preclinical studies, reviews of current clinical and preclinical studies, discussion of devices and medications, case reports.

Submissions of review articles and case reports must be preceded by communication with the Editor-in-Chief. We also invite submission of letters to the Editor, which should address observations in clinical practice, early results of studies, discussion of applications of basic research to clinical practice or discussion of clinical guidelines.

We will only accept for submission for consideration by the Editorial Board articles sent as attachments to e-mail letters. Please first send an e-mail with a cover letter, then send a second e-mail with the article attached. We will only lay out articles for publication if the manuscript has been prepared in Microsoft Word or equivalent word-processing program.

When we accept the article for review, we will e-mail you a form which you need to sign, stating that you are the senior author of the article under review and that all tables and figures are either original or you have proof that you are permitted to reproduce them. We also need you to give us permission to publish the article in *Medical Journal of Therapeutics Africa* and permission for your article to be downloaded in context with other articles.

Send articles to:

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River in Lagos. Photo courtesy of Pastor OL Egoro-Ighalo.

## MALARIA IN THE NEWS

### QUICK TEST FOR MALARIA APPROVED BY FDA

*Press release from United States Food and Drug Administration <http://www.fda.gov>, 26 Jun 2007.*

**The US Food and Drug Administration has cleared for marketing the Binax NOW Malaria Test, the first US-authorized rapid test for malaria for use in laboratories.**

Standard laboratory tests for malaria require identifying parasites in a blood sample under a microscope. With the Binax NOW test, results are available in 15 minutes after a few drops of whole blood are placed on a dipstick. The test differentiates the most dangerous malaria parasite, *Plasmodium falciparum*, from less virulent malaria parasites. Results still need to be confirmed using standard microscopic evaluation.

Humans infected with malarial parasites may develop a high fever, chills, and flu-like illness. Untreated, they may develop severe complications and die.

Malaria was eliminated from the United States in the 1950s. According to the Centers for Disease Control and Prevention, 1,528 newly-reported cases of malaria were reported in the United States in 2005, including 7 deaths. **Nearly all deaths from malaria can be prevented if the infection is diagnosed and treated early.**

The Binax NOW test was 95% accurate compared with standard microscopic diagnosis in a multi-center study outside the United States in areas where malaria is prevalent.

The Binax NOW test is manufactured by Binax Inc, a subsidiary of Inverness Medical Innovations Inc, Scarborough, Maine.

**Filho FSF, Arcanjo ARL, Chehuan YFM, Costa MR, Martinez-Espinosa FE, Vieira JLF, et al. Chloroquine-resistant *Plasmodium vivax*, Brazilian Amazon. Emerg Infect Dis. 2007 Jul. At <http://www.cdc.gov/EID/content/13/7/1125.htm>**

From September 2004 to February 2005 the Foundation for Tropical Medicine of Amazonas in Manaus, Brazil tested the effectiveness of standard supervised chloroquine therapy on 166 volunteers with uncomplicated *P vivax* malaria. Each volunteer was administered uncoated, scored, 150-mg chloroquine tablets (10 + 7.5 + 7.5 mg/kg at 24-hour intervals). Primaquine was withheld until day 28 (dose regimen of 30 mg/day for 7 days). Of the 109 volunteers completing the in vivo test, 19 had

positive blood smears within the 28-day follow-up (1 on day 14, 3 on day 21, and 15 on day 28). All were required to be treated with mefloquine, which was the alternative therapy.

Chloroquine absorption was confirmed adequate in these humans on day 2 with a mean±SD chloroquine plasma concentration of 785.4±800.1ng/mL (n=10). Suspected therapeutic failure (*P vivax* chloroquine resistance) was confirmed in 11 of 109 patients with a mean isolated chloroquine plasma concentration >10ng/mL (356.6±296.1ng/mL). Plasma desethylchloroquine concentrations were not measured.

The proportion of failures was 10.1%; even though 89.9% of the *P vivax* infections were successfully evaluated and adequate clinical and parasitologic responses were obtained. The amount of therapeutic failures indirectly indicates the possible regional spread of *P vivax* chloroquine-resistant strains.

We believe our findings are important and merit the attention of local public health authorities. Considering the possibility of emerging underestimated *P vivax* chloroquine resistance in Manaus, we feel it is essential to clarify whether such documented resistance can copromote *P vivax* malaria outbreaks in malaria-endemic areas within the Amazon.

This study was supported by the Brazilian Ministry of Health and the US Agency for International Development as part of the scientific program of the Amazonian Surveillance Network for Antimalarial Drugs Resistance (RAVREDA).

**Compiled and edited by SJ Dodgson PhD**



**Cashew tree in Lagos. Cashew bark is used to treat malaria. Photo courtesy of Pastor OL Egoro-Ighalo.**

## DIETHYLENE GLYCOL (DEG) KILLS



Display case at Univ Sciences Philadelphia. SJ Dodgson.

### DRUGS CONTAMINATED WITH DIETHYLENE GLYCOL IMPORTED FROM CHINA

*Reported 04 Jul 2007 by Kathia Martinez of The Associated Press*

Ms Martinez reported that the Panama prosecutor claimed to have evidence that at least 94 humans died from drugs contaminated with diethylene glycol since Jul 2006, that 293 more deaths are under investigation, and that deaths continued after the medicine was pulled from shelves in Oct 2006.

DEG was in cough syrup, antihistamine tablets, calamine lotion and rash ointment made in a Panama government laboratory.

The prosecutor's office found that DEG was made by a Chinese company which lied that it sold 99.5% pure glycerin to a Spanish company. That company sold what this to Panama's Medicom SA, which sold in turn it to a government laboratory.

Officials in Panama exhumed and tested humans who had swallowed medicines containing DEG and who died last year, and reported finding the medicines killed them.

The 293 suspected cases were brought to the police by family members, but the causes of death had not yet been confirmed forensically.

Three Medicom executives were imprisoned, charged with crimes against public health.

### POISONED MEDICINE FROM CHINA?

*Reported by Debo Abdulai's in "Poisoned medicine from China?" in Nigerian newspaper Tribune*

Mr Abdulai reported that Nigeria has been open to China since the economic depression started. Drugs

from China are cheaper, easily found on drug shelves and come in approved by the National Agency for Foods Drugs Administration and Control (NAFDAC). He claims that almost every Nigerian has used Chinese products to fight diseases.

In July 2007, the former head of China's top food and drug safety agency was executed a few days after being sentenced to death after pleading guilty to corruption and accepting USD850,000 in bribes (see page 188). Zheng Xiaoyu was commissioner of the Food and Drug Administration from its founding in 1998 until mid-2005, and was arrested Feb 2007 as part of a government investigation into corruption at the agency. The government is now reviewing more than 170,000 production licenses issued by the food and drug agency over the past decade.

In 2007, 2 Chinese companies were accused of shipping contaminated food ingredients to the United States, leading to a nationwide pet food recall.

The Chinese government is investigating how DEG ended up in cough syrup and toothpaste in Latin America. This deadly adulteration led to more than 365 deaths in Panama last year after officials unwittingly mixed DEG into 260,000 bottles of cold medicine. Toxic toothpaste was removed from drug shelves in Dominican Republic and Nicaragua.

In China, tainted injections were reported to have killed 11 persons, and 6 were reported to have died and 80 sickened after taking an antibiotic that was produced with what was later discovered to be a substandard disinfectant.

According to Mr Abdulai: "Effects of China's unsafe drugs are not recent. In 1998, 155 Americans were sickened by impure gentamycin sulfate made by a Chinese firm. Around the same time, 89 children died in Haiti after taking cough medicine made with antifreeze from China.

"The danger to Nigerians is therefore grave. We are open to Chinese drugs which incidentally are relatively cheaper; we are no longer sure if the drugs we use are not made in Onitsha, Lagos or Kano markets while those from Europe are out of the reach of the common man because they are very expensive. God save us all."

### FDA ADVISES MANUFACTURERS TO TEST GLYCERIN FOR POSSIBLE CONTAMINATION. GLYCERIN CONTAMINATED WITH DIETHYLENE GLYCOL REMAINS A POTENTIAL HEALTH HAZARD TO CONSUMERS

*From FDA press release*

The United States Food and Drug Administration (FDA) is warning pharmaceutical manufacturers,

## DIETHYLENE GLYCOL (DEG)

suppliers, drug repackers, and health professionals who compound medications to be especially vigilant in assuring that glycerin, a sweetener commonly used worldwide in liquid over-the-counter and prescription drug products, is not contaminated with diethylene glycol. This is a known poison used in antifreeze and as a solvent. Today, the agency is issuing guidance to industry recommending methods of testing glycerin and other controls to identify any contamination with DEG before use in the manufacture or preparation of pharmaceutical products.

FDA has no reason to believe that US glycerin is contaminated, though the agency knows of recent reports from other countries of deaths from DEG-contaminated glycerin. FDA emphasizes the importance of testing glycerin for DEG because of the severity of the problem.

DEG poisoning is an important public safety issue and FDA is exploring how supplies of glycerin become contaminated. In addition, FDA is working with manufacturing and pharmacist organizations to raise awareness of this risk and to put into place controls to ensure that this problem does not happen in the U.S. or elsewhere.

The most recent incident was in Panama in Sep 2006 and involved DEG-contaminated glycerin used in cough syrup, which resulted in dozens of hospitalizations for serious injury and more than 40 deaths. In late 1995 and early 1996, at least 80 children died in Haiti from DEG-contaminated glycerin in acetaminophen syrup. Between 1990 and 1998, similar incidents of DEG poisoning were reported from Argentina, Bangladesh, India, and Nigeria and resulted in hundreds of deaths. In 1937, more than 100 people died in the United States after ingesting DEG-contaminated Elixir Sulfanilamide, a drug used to treat infections. These deaths led to the enactment of the Federal Food, Drug, and Cosmetic Act, which is the nation's primary statute on the regulation of drugs.

### **Guidance for industry Testing of Glycerin for Diethylene Glycol**

posted on

<http://www.fda.gov/OHRMS/DOCKETS/98fr/07D-0135-gdl0001.pdf>

All pharmaceutical manufacturing operations, including the re-packaging and re-labeling of ingredients like glycerin, must conform to current good manufacturing practice (CGMP). The guidance provides recommendations for complying with CGMP and is intended to help manufacturers, compounders, repackers, and suppliers avoid the use of glycerin that is contaminated with DEG and prevent incidents

of DEG poisoning.

### **DEG POISONING IN NIGERIAN CHILDREN**

*Summary of article abstract by Okuonghae HO, Ighogboja IS, Lawson JO, Nwana EJ in Ann Trop Paediatr. 1992;12:235-8; Dept Paediatrics, Jos Univ Teaching Hosp, Nigeria.*

From Jun to Sep 1990, 47 children died at Jos University Teaching Hospital, Nigeria after ingesting paracetamol syrup adulterated with DEG. Children's symptoms included anuria, fever, vomiting, diarrhoea, convulsions, tachycardia, acidotic breathing, pallor, oedema, and hepatomegaly. Laboratory findings included hyperkalaemia, acidosis, elevated creatinine, and hypoglycaemia. Treatment was to correct dehydration and acidosis plus administration of antibiotics; none were given kidney dialysis. All died within 2 weeks of admission.

### **DEG KILLED PATIENTS IN THE US IN 1937**

*Summary of article by Carol Ballentine in FDA Consumer Magazine, June 1981*

Sulfanilamide was a wonder drug in the 1930s, the precursor to more powerful antibiotics, and it was delivered in tablet form. The manufacturers SE Massengill Co, in Bristol, Tennessee, were asked by patients to manufacture it in liquid form. The company chemist dissolved sulfanilamide in DEG, compounded the solution and sent 633 shipments around the country.

The first shipments were sent out in early Sep 1937. On 11 Oct 1937, the American Medical Association (AMA) received reports from physicians in Oklahoma, that an unfamiliar sulfanilamide compound had killed patients. The AMA asked for samples of the drug and wired the Massengill Co, requesting the composition of the compound. The AMA laboratory isolated DEG as the toxic ingredient and immediately issued a warning, through newspapers and radio, that Elixir Sulfanilamide was toxic and deadly.

The Food and Drug Administration was told about the deaths on the 14 Oct 1937 by a New York physician. An inspector from the agency's Kansas City Station confirmed that 8 children and 1 adult died after taking a product labeled "Elixir Sulfanilamide, the SE Massengill Co, Manufacturing Pharmacists, Bristol, Tenn.-Va."

Inspectors were dispatched to the firm's headquarters in Bristol and to branch offices in Kansas City, New York, and San Francisco. They found that the firm had already learned of the poisonous effects of the liquid sulfanilamide and had sent telegrams to

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more than 1,000 salesmen, pharmacists, and doctors. The telegrams requested the return of the product without saying that the drug was lethal. At FDA's insistence, the firm sent out a second wave of messages: "Imperative you take up immediately all elixir sulfanilamide dispensed. Product may be dangerous to life. Return all stocks, our expense."

FDA then tried to retrieve all the drug. Most of the 239 FDA inspectors and chemists was assigned to retrieve all drug. State and local health officials joined the search. Newspapers and radio stations continued to issue warnings.

The staff checked the company's shipping records and the distribution lists in the 4 distributing houses and in a number of wholesale and retail drugstores. Thousands of order slips were examined. In one establishment, 20,000 sales slips were checked.

FDA employees tracked down the firm's 200 salesmen and questioned them about the dispersion of shipments and physician samples. Finding the salesmen was the first problem. Once found, salesmen were not all forthcoming about their distribution information. One man in Texas gave the necessary information after being jailed by state authorities.

In some drugstores, the solution had been sold without prescriptions to unknown purchasers. Additionally, physicians had incomplete records of the names and addresses of patients for whom they had prescribed.

Even when the purchaser was located, the inspectors frequently had trouble finding what happened to the drug. Many doctors and pharmacists did everything in their power to recover the drug. One physician postponed his wedding to help an FDA chemist search for a 3-year-old boy.

Other physicians lied that they had prescribed the drug, or lied about their patients' subsequent health. One inspector was told that a shipment of 1 gallon had been returned to the manufacturer after only 1 dose had been dispensed. The manufacturer reported that 3 doses had been dispensed and subsequent questions determined that 2 patients had died. Similarly, a physician told an inspector that none of the 5 patients dispensed the medicine had died, however, after asking questions, the inspector found that 4 of them died.

Victims of poisoning were ill 7 to 21 days. All victims, which included children, had kidney failure: urine flow stopped, severe abdominal pain, nausea, vomiting, stupor, and convulsions. They were in intense, unrelenting pain before death.

Tests on experimental animals would have demonstrated the lethal properties of the liquid sulfanilamide. A review of the current existing scientific lit-

erature would have shown that other studies had reported that DEG was toxic and could cause kidney damage or failure. But in 1937 the law did not prohibit the sale of dangerous, untested, or poisonous drugs.

Through the persistence of federal, state, and local health agencies and the effects of the AMA and the news media, most liquid sulfanilamide was recovered. Of 240 gallons manufactured and distributed, 234 gallons and 1 pint was retrieved; the remainder was consumed.

Twenty-five seizures were made under federal law. The charge was misbranding. "Elixir," FDA said, implied the product was an alcoholic solution. If the product had been called a "solution" instead of an "elixir," no charge of violating the law could have been made. FDA would have had no legal authority to ensure the recovery of the drug and many more people probably would have died.

FDA Commissioner Walter Campbell: "It is unfortunate that under the terms of our present inadequate Federal law, the Food and Drug Administration is obliged to proceed against this product on a technical and trivial charge of misbranding. ...[The Elixir Sulfanilamide incident] emphasizes how essential it is to public welfare that the distribution of highly potent drugs should be controlled by an adequate Federal Food and Drug law. ... We should not lose sight of the fact that we had many deaths and cases of blindness resulting from the use of another new drug, dinitrophenol, which was recklessly placed upon the market some years ago. Deaths and blindness from this [drug] are continuing today. We also should remember the deaths resulting from damage to the liver that have occurred from cinchophen poisoning, a drug often recommended in such painful conditions as rheumatism. We also have unfortunate poisoning, acute and chronic, resulting from thyroid and radium preparations improperly administered to the public.

"These unfortunate occurrences may be expected to continue because new and relatively untried drug preparations are being manufactured almost daily at the whim of the individual manufacturer, and the damage to public health cannot accurately be estimated. The only remedy for such a situation is the enactment by Congress of an adequate and comprehensive national Food and Drugs Act which will require that all medicines placed upon the market shall be safe to use under the directions for use. ..."

The liquid sulfanilamide experience resulted in the 1938 Federal Food, Drug, and Cosmetic Act.

*Compiled and edited by SJ Dodgson PhD*