TEACHING the History & Social Aspects of Pharmacy

New Series No. 3 (Fall 2002)

An online newsletter of the American Institute of the History of Pharmacy. Copies are available as well at the Institute website of www.aihp.org.

Welcome to the third issue of *Teaching the History and Social Aspects of Pharmacy*. This newsletter is issued twice a year (Autumn and Spring) in an electronic format and distributed via email from a list managed by Greg Higby, Director of the American Institute of the History of Pharmacy (please contact Greg at: ghigby@mhub.facstaff.wisc.edu to be placed on the mailing list). The Newsletter also is posted on AIHP's website (www.aihp.org).

As the editor, I have been receiving positive feedback on the first two issues, but very few contributions. The quality and value of this newsletter represents only what the readers have contributed to it: short articles on courses and course materials; book, film, museum, software, and other reviews; updates from the social sciences; announcements for conferences, grants, and publishing opportunities; news stories; interesting websites; viewpoints and commentaries; and most importantly, feedback on its content and format.

This issue contains course materials, one on ethical issues in testing new treatments for AIDS and the other on constructing patient package inserts. Along with one of the articles on course materials, the review and announcement were written by the editor. In other words, I received only one contribution for this issue, and it was from a colleague at work. This newsletter is in dire need of more involvement from its readers, if it is going to survive, let alone thrive.

I eagerly await your comments and suggestions for improving the newsletter, and most importantly, your contributions. The success of this newsletter depends on dedicated and involved readers, especially those of you who have something to say about history and the social sciences in pharmacy. To that end, I am releasing this issue a bit late, and I have set an earlier deadline for submissions for the next issue. I hope that by reading this issue over the holidays and winter school break, some readers will be motivated and have the time to write and submit a contribution of their own. Please contribute your ideas and experiences for the benefit of others and Enjoy!

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The next issue of ***Teaching the History and Social Aspects of Pharmacy*** will be published during Spring of 2003. The **deadline** for submitting items, announcements, and materials for that issue is **15 February 2003**. Please submit materials electronically in **MS Word** to: Mike Montagne at mmontagne@mcp.edu (Mass. College of Pharmacy & HS, 179 Longwood Ave., Boston MA 02115; phone: 617-732-2995; fax: 617-732-2236).

Courses & Course Materials

HIV-Positive Pregnant Women and Newborns in South Africa: Medical Hope, Moral Risk

A decision by the Constitutional Court of South Africa this year offers a mix of medical hope and moral risk. *Treatment Action Campaign vs. Minister of Health* trumpets hope that HIV positive pregnant women and their newborns will receive treatment, decreasing the likelihood that certain children will inherit the disease. At the same time, the case effectively carries the risk that we may fail to study questions raised by the very medical milestone we celebrate, losing an opportunity to learn from some of pharmacotherapy's richest "teachable moments." As pharmacy educators we enjoy the privilege of joining our students in squarely facing the hope, the risk, and their companion questions.

Medical Hope in South Africa

The medical hope finds root in the AIDS pandemic.

People living in Sub-Saharan Africa account for 10% of the world's population, 71% of the world's 40 million people living with HIV or AIDS, 81% of the world's women of childbearing age living with HIV or AIDS, and 87% of the world's children infected with the disease. The rate of perinatal HIV transmission reaches 43% in some areas of Sub-Saharan Africa. The region's annual per capita health care expenditures range from $2 to $40.

This year, South African law bypassed certain ethical questions, noted others, turned its back on politics, and then bowed to medicine, allowing HIV-infected pregnant women to anticipate a more promising future for their unborn offspring.

Researchers had learned that a single dose of nevirapine or zidovudine given to mothers at delivery and to newborns within 72 hours of birth can reduce vertical transmission by 33 to 50%. Slightly better results attach when newborns are then formula-fed rather than breastfed. In light of these findings, the World Health Organization (WHO) and UNAIDS recommended that developing countries provide this short-course perinatal antiretroviral therapy and that they advise HIV-infected women not to breastfeed infants if safe.

But like leaders of developed countries, those running developing nations do not always appreciate unsolicited advice. Thabo Mbeki, president of South Africa, is no exception. Moreover, he has consistently opposed medical intervention for HIV and AIDS. This year his stance was challenged in court. Mbeki lost the case. The Constitutional Court of South Africa ordered the government to develop a program to prevent perinatal HIV transmission, including counseling pregnant women, testing pregnant women, and making appropriate treatment available. Students can read this landmark case on line as noted below. For the foreseeable future, enforcement of the decision may consume time and attention of many South African residents and their advocates.

So there's the hope: the Court's decision may be followed, the short-course treatment may continue to prevent vertical transmission of HIV infection among certain patients, and more people may live.

Moral Risk in America

The moral risk? We may allow enforcement of the South African Court's decision to eclipse a potentially discomforting chapter in American and African history. We may forget how we learned about short-course protocols. The route that brought us short-course regimens left central ethical issues unresolved. In short, the danger remains that as a society we may refrain from asking, learning, and taking a stand.

In 1994, the United States and France conducted the first randomized controlled trial in which an intervention reduced the incidence of HIV infection. The AIDS Clinical Trial Group Study 076, known as the ACTG Study 076, reduced the risk of HIV infection from mother to offspring by about 70%. Less than two months after the initial results were analyzed, the study was terminated. The 076 protocol became the standard of care for HIV positive pregnant women in the U.S., in France, and soon enough, in the rest of the developed world.

By now many are familiar with the ACTG 076 protocol as introduced in the United States and France. As initially formulated, AZT is administered orally to HIV-positive women while they are pregnant, IV during labor, and orally to newborns for 6 weeks. Initially the price tag ran about $800 per person. Today, with discounts, it runs at about $200 per person.

In 1994 when the ACTG 076 protocol became the standard of care, WHO convened a group to assess the time, money, and scientific validity associated with alternatives. Specifically, they wanted to prevent vertical transmission of AIDS with less time involved in treatment and monitoring, at a price underdeveloped countries could afford, and through a scientifically valid assessment of drug regimens.

Ethical rules governing research in the United States and most developed countries require that when conducting a randomized clinical trial comparing two treatments for a disease, there must be no evidence for thinking one treatment is better than the other. But when working outside our own and other developed countries, we appear relatively unrestrained by such research methodology.

And so in 1997, for example, the New England Journal of Medicine reported on results of 18 randomized controlled trials involving 17,000 women. Two were conducted in this country, sixteen elsewhere. The two in the United States gave subjects access to AZT and other drugs. The sixteen outside our borders – with one exception – gave treatment groups shorter regimen AZT, and gave control groups placebos and no access to AZT. Accounts conflict as to whether informed consent was obtained. Again, our information about ACTG 076 protocol would have pro-

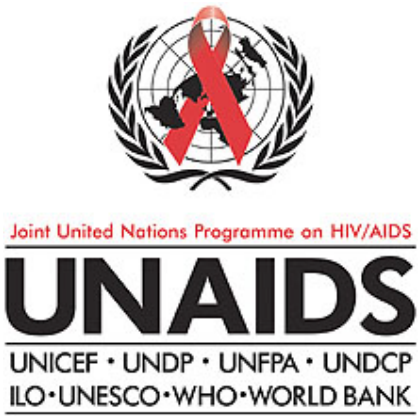
hibited use of sugar pills in our own country, and in any event, our laws would have required strict adherence to rules associated with procuring and documenting informed consent.

After a series of such short-course clinical trials in developing countries, we unveiled the regimen that was recently endorsed by the Constitutional Court of South Africa.

Some Questions

In the aftermath of these clinical trials, some commentators and panels began raising questions. No consensus has emerged. As a large group or working in small groups, students can address questions formulated by others and can add their own.

Was WHO the appropriate party to identify and assess options? If not that organization, then what other individual or entity? What collaboration procedures should be followed between the researcher-sponsors and the host country? In deciding what those procedures should be, what qualifications should we require of the procedure-designers? Should we have particular concerns when a government effectively blocks medical treatment for HIV/AIDS? Should we have particular concerns when a government does not consider placebo trials exploitative even with life-threatening epidemics when there is a known treatment with significant benefits? What role should our values play here? Do we have a right to pass moral judgment on another country when we are willing to discard primary ethical principles as soon as we are working with people in impoverished nations? Should we worry about exploitation when performing placebo trials in developing countries under circumstances that we would label exploitative and unethical in our own country? Should American researchers in developing countries use the same standards as we use here? If so, why? If not, why not? Should we follow a single international standard of ethical research? Are alternative modes of experimentation impractical? Should pharmaceutical researchers assure that every person – including those in a control group, if any – receive the best proven therapy? What if the people involved have limited health coverage, such that they would not be receiving the medicine if they were not participating in the study? Are we using impoverishment as justification for exploitation? What duty is owed to research subjects in other countries (a) during a clinical trial and/or (b) after completion of the research? Do extreme circumstances justify extreme measures? Can we justify the use of placebos based on the need for speed? How should we factor in the scant available financial and medical resources of the developing countries? What about our failure to use the results of our experiments to offer subsidized treatment? Is it relevant that the subjects of these experiments could not possibly benefit from their participation? Do the ends justify the means? Does the Golden Rule have a place in these discussions? Do all these questions miss the mark? Is all this relevant to students of pharmacy? Why or why not?



Suggested Resources:

UNAIDS. "Report on the Global HIV/AIDS Epidemic 2002". July 2002. Accessed November 3, 2002 at < http://www.unaids.org > .

Treatment Action Campaign vs. Minister of Health (2002) (4) BCLR 356. Accessed November 3, 2002 at < http://www.concourt.gov.za/date2002.html > .

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Deconstructing/Constructing a Patient Package Insert (PPI)

As part of my elective course, Drug Education, I have developed a four session exercise in which students deconstruct a manufacturer's package insert for a specific drug product, and then they construct a patient package insert (PPI) from the manufacturer's package information.

This exercise, while initially boring, long, and seemingly simplistic to most students, typically results in the students learning and appreciating PPIs to a much greater extent than before this exercise. Most students comment that they "had never before looked closely and carefully at a PPI and what it was all about." Later in their college careers, during the 6th year of clinical rotations, students are tasked to create patient information materials. Students who have taken the Drug Education course, and who experienced this exercise, have commented that the PPI exercise taught them all of the basic principles and approaches to developing patient information materials, and that similar work they performed during their clinical year seemed much easier.

This exercise takes place over four consecutive 75-minute class sessions. A secretary sometimes is available to assist with typing up each segment of the PPI that is produced by each student group.

Format and Process for PPI Exercise

The United States Pharmacopeia's model (for generating individual drug monographs for USP-DI) is based on a consensus-building process. Following the USP model, advisory panels are formed consisting of 3-4 students per panel (current panels cover heart medications, psychiatric medications, and antibiotics). The manufacturer's package insert for a specific medication is distributed to each group. The best approach appears to be one in which three to four specific medications are used in this exercise each semester, and at minimum (for benefit of comparison), two different panels (student groups) are tasked to develop a PPI for the same medication. The panels meet over three class sessions and develop their PPI based on the format below. The primary approach is to: 1) determine what information from the manufacturer's package insert should be transferred to the patient's package insert; and 2) rewrite the manufacturer's technical information to make it more readable and understandable for the patient (focusing on a variety of medication literacy issues). Each panel's PPI is typed up and presented to the other panels (i.e., all other students in the course). In the fourth class session, the students' PPIs are compared to each other, to USP-DI PPI monographs, and to other PPI versions that are available on the same medication, and there always is a lively discussion about content, format, and related issues regarding these student-generated PPIs.

FORMAT FOR PATIENT PACKAGE INSERTS (USP MODEL)

<u>Session 1:</u>

Introduction to PPIs and the Development Process

PPI Part 1: About Your Medicine/Description of Medicine
- What is it (names and pronunciations)?
- What does it look like?
  - Dosage forms (strength, type, size, color)
- How does it work and for what is it used?
  - Pharmacology (mechanism of action)
  - Indications for use (accepted, off-label, not accepted)
- Other descriptive information

<u>Session 2:</u>

PPI Part 2: Before Using & Proper Use
- Contraindications
- Precautions/Warnings (allergies, other medical problems)
- Proper use (dosing, timing, administration, storage)
- Use by different subgroups (children, older adults, pregnancy,
  - breast-feeding)
- Interactions (food, tests, drugs)

<u>Session 3:</u>

PPI Part 3: Side Effects/Problems/ Additional Information
- Side effects/adverse reactions (% occurrence in

most package inserts)
(common vs. rare; bothersome vs. serious)
Overdose
Addiction potential
Other problems
Other patient consultation issues

Session 4:

Review, Comparison, and Discussion of Student-generated PPIs.

Key Issues

What information should the patient know/read for self?
What information should be reserved for the pharmacist to discuss?
Do you list all indications for use?
Do you list all types (categories) of precautions/warnings?
Do you list all potential interactions?
Do you list all side effects or some? Which ones?
How do you categorize side effects?

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Review

Quack, Quack, Quack: The sellers of nostrums in prints, posters, ephemera & books. By William H. Helfand, New York: The Grolier Club, 2002 ($40 hardcover).

A very interesting exhibition and catalogue has been curated and written by William Helfand and presented at the Grolier Club in New York. The exhibition, unfortunately, closed on November 23, 2002, but the wonderfully written and illustrated exhibition catalogue provides a memorable record of that event. This was "an exhibition on the frequently Excessive & flamboyant Seller of Nostrums as shown in prints, posters, caricatures, books, pamphlets, advertisements & other Graphic arts over the last five centuries."

The exhibition was divided into 10 sections: The Itinerant Quack, The Ways of the Quack, Systems, Morison's Pills, Vin Mariani, Anatomical Museums & Medicine Shows, Selling Sex Cures, Addiction and Electricity Cures, Quacks in the Arts, and The Evils of Quackery. The catalogue includes the full exhibition, along with an introductory section of 9 chapters on quacks, quackery, and advertising. The catalogue is profusely illustrated with many of my favorites in color.

Works by William Hogarth, Honore Daumier, Jules Cheret (Vin Mariani), Maxfield Parish (No-To-Bac), H.G. Wells (Tono-Bungay), and Weir Mitchell (The Autobiography of a Quack and The Case of George Dedlow) are included in the exhibition, as well as a variety of materials by many known and unknown artists and writers.

Helfand has one of the largest collections of printed material on pharmacy, drug products, and related subjects. He has curated numerous exhibitions and written five books (e.g., The Picture of Health; Medicine and Pharmacy in American political prints, 1765-1870; Potions, pills, & purges: The art of pharmacy; and Pharmacy: An Illustrated History with, David Cowen) based on his collection and materials from other collections, including the Ars Medica Collection at the Philadelphia Museum of Art. For those of you who missed the exhibition, the catalogue is highly recommended.

THE TRAVELLING QUACK.

Announcement

ICIUM 2004: The Second International Conference on Improving the Use of Medicines.
March 30 to April 2, 2004, Chiang Mai, Thailand

Mark your calendars now for the Second International Conference on Improving the Use of Medicines. In April 1997, researchers and policymakers from around the world gathered in Chiang Mai, Thailand for the first international conference on this topic. This conference, sponsored by a variety of international health groups, was an important and educational event. The second conference will focus on cost-effective interventions to improve the use of medicines. Registration is limited to 500 participants. Details about this conference will be available on the ICIUM 2004 website, which should be up by December 1, 2002. [This listing was obtained from the E-drug site, where it was described by Dr. John Chalker, INRUD Coordinator for Management Sciences for Health (www.msh.org)].