Pre-exposure treatment

CU Researchers Join New Front in Battle against HIV

University of Colorado is part of an expanding worldwide effort to fight the deadly human immunodeficiency virus on a new front: preventing its transmission in people not yet infected by the virus.

The Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), Bill and Melinda Gates Foundation, and Family Health International are sponsoring multiple trials in places such as Thailand and Botswana to test the safety and efficacy of two antiretroviral medications – tenofovir and emtricitabine – that could greatly slow the spread of AIDS and other diseases that prosper when human immune systems become compromised.

Separately, researchers at CU’s schools of Medicine and Pharmacy are gathering data for an NIH study of the pharmacologic properties of the drugs. It could provide key data for researchers in the Thailand and Botswana trials, among many others.

Antiretroviral medications prevent viruses with ribonucleic acid in their genetic material – HIV is one – from replicating in the host’s cells.

New use? The two medications are already used to treat people infected with HIV, typically in combination with other antiretroviral medications. Combination antiretroviral therapy has also been used to prevent HIV transmission after high-risk exposures such as accidental needle sticks, sexual exposures to infected partners, and from infected mother to fetus during pregnancy.

Meditz (left) and Anderson are investigating drug concentrations of antiretroviral drugs in hopes of helping other researchers find the right doses to keep HIV-negative patients healthy.
The new work explores the possibility of using a daily, oral combination of tenofovir/emtricitabine as “pre-exposure prophylaxis” (or “PrEP”). In other words, it would protect people before they are exposed to the virus, said Amie Meditz, MD, an assistant professor in the Infectious Disease Division at the School of Medicine.

Meditz is co-investigator with primary investigator Pete Anderson, PharmD, associate professor in the Department of Pharmaceutical Sciences of CU’s School of Pharmacy, in the NIH-sponsored study. The aim: collect data to characterize how the drug concentrates in the cells of non-HIV patients, and compare the results to those of HIV-positive patients.

**Collaborative work.** Researchers in studies such as the CDC-sponsored trials in Thailand and Botswana will, in turn, correlate that pharmacologic data to outcomes in studies that test the efficacy of the oral tenofovir/emtricitabine medication in preventing HIV transmission.

Clinicians have plenty of past experience and data to use when they administer anti-retroviral medications to HIV-infected patients or those who have been exposed to the virus, Meditz noted. The oral tenofovir/emtricitabine combination, however, has not been used to prevent sexual transmission prior to exposure.

“We’re trying to study the pharmacology in people who don’t have HIV,” she says. Understanding how the drugs concentrate in the cells of the body before exposure could help researchers determine safe and effective dosing regimens, Meditz explained. It would be a key to obtaining a potential new indication for the drugs from the Food and Drug Administration.

“Other researchers are going to put our concentration data in the context of their own studies,” added Anderson. “We will define the build-up of the drug, then collaborate with others in measuring outcomes.”

The study uses a testing methodology Anderson developed with a team of lab partners that allows researchers to test extremely minute amounts of the drug inside cells (see accompanying story).

Anderson, who has been working for years on the pharmacology of HIV treatments, said his work with Meditz on the present study builds on thousands of previous hours of lab time.

“We already know how the drugs build up in HIV-positive patients,” he said. “This is now a new way to use the medication.”

Defining intracellular concentrations in HIV-negative patients, he added, allows researchers “to ask the next question: is there a best way to dose it?”

**Social ramifications.** Studies such as those in Thailand and Botswana are part of a new wave of HIV-related research that could also have profound social repercussions, Meditz believes.

For example, a recently completed trial in South Africa of a tenofovir-based gel,
applied topically by women before and after sex, demonstrated success (compared to a placebo) in reducing HIV transmission.

Women apply the gel into the vagina with a cartridge-shaped applicator during the 12 hours before sex and within 12 hours after, Meditz explained. Provided it is carefully introduced, she said, the preventive approach could give women a new measure of control over their lives and health, especially in HIV-plagued continents like Africa.

“The problem in Africa and some other [areas],” she said, “is that women often don’t have control over condom use by their partners. This treatment is a female-controlled option for reducing the transmission of HIV.” Being able to apply the gel hours before and after intercourse, she adds, also gives women a way to protect themselves in a discreet and convenient way.

The new treatments could help stem the tide of new HIV infections – about 2.7 million a year, according to the CDC – but Meditz cautioned that simply proving their clinical effectiveness won’t ensure their success without a program that addresses cultural issues like the South African trial did.

“The medications require extensive education and training,” she noted. “Their acceptability to the community has to be established.”