



Pharmacy dean a pioneer in HIV/AIDS drug research

by CHUCK BROWN

Courtney Fletcher, Pharm. D., was there when an HIV/AIDS diagnosis was a death sentence.

When the disease first came to light in the 1980s, Dr. Fletcher, armed with his pharmacology expertise, joined other researchers on the figurative ground floor of HIV/AIDS research.

“When we started, the best you could do for a patient was extend life about six months on average,” said Dr. Fletcher, who is now dean of the UNMC College of Pharmacy. “Now we can think of HIV as a chronic disease – take your drugs and you can live a fairly normal life.”

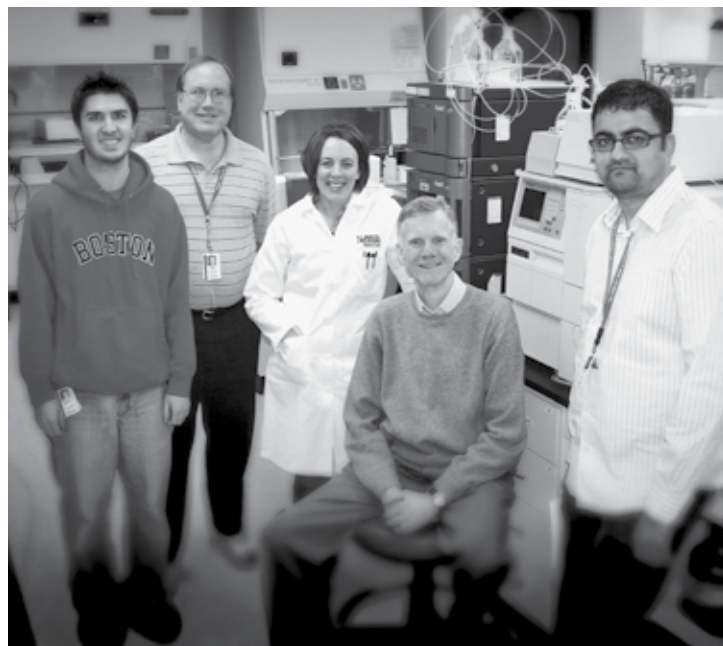
This is so thanks in large part to the work of Dr. Fletcher, who remains a preeminent force in HIV/AIDS drug research despite his full-time gig as UNMC pharmacy dean.

Dr. Fletcher’s path toward HIV/AIDS research was not intentional. As a researcher at the University of Minnesota in the early 1980s, he studied drugs to treat cytomegalovirus (CMV) infection – a type of herpes virus that is common and lethal in patients with weakened immune systems.

At the time, Dr. Fletcher and others interested in CMV focused more on transplant patients. But CMV became a major concern as HIV/AIDS came on the scene because the weakened immune system of those with HIV/AIDS made them vulnerable to the ravages of CMV.

As time went on, Dr. Fletcher and his colleagues began to help develop drugs to treat CMV disease in HIV/AIDS patients. And because they already worked with patients who had HIV/AIDS, Dr. Fletcher’s team also was asked to help with the development of pharmacological aspects of investigational drugs when they became available for the treatment of HIV infection.

“Our involvement with HIV/AIDS drug research really was born out of proximity,” Dr. Fletcher said. “We already were working on the drugs for treatment of one viral infection, CMV, so it was pretty natural for us to work on other drugs to this new viral infection, HIV.”



COLLEGE OF PHARMACY DEAN COURTNEY FLETCHER, PHARM.D., SECOND FROM RIGHT, WITH HIS RESEARCH TEAM. FROM LEFT, JOHN WEINHOLD, RESEARCH TECHNOLOGIST; BRIAN ROBBINS, PH.D., LAB DIRECTOR; SARAH NELSON, RESEARCH SPECIALIST; AND GAUTAM BAHETI, GRADUATE RESEARCH ASSISTANT.



**JOHN WEINHOLD,
RESEARCH
TECHNOLOGIST,
ANALYZES DRUG
CONCENTRATIONS
IN BLOOD SAMPLES
USING A MASS
SPECTROMETER IN
DR. FLETCHER'S LAB.**

As a pharmacology expert, Dr. Fletcher focuses on how drugs and patients interact. This work is particularly useful in setting proper dosages.

It's a delicate balance with many variables – too much of a drug and it becomes toxic – too little and it's ineffective.

To set proper dosages, Dr. Fletcher and his team monitor blood levels in HIV/AIDS patients to see if drug levels are high enough to effectively fight the virus and low enough to not harm the patient. Once they get enough data collected that shows a certain dose meets these requirements, they submit their information to the Food and Drug Administration (FDA) to approve the suggested dose.

As drugs were developed to treat HIV/AIDS, Dr. Fletcher and his team were there to help determine how much should be taken.

Mark Kline, M.D., is professor of pediatrics and chief of retrovirology at Baylor College of Medicine. He also runs a network of HIV/AIDS clinics for children that treat more than 30,000 patients in Africa and Romania. He has worked with Dr. Fletcher since the early 1990s and said the importance of Dr. Fletcher's work in the development of HIV/AIDS drugs cannot be overstated.

"Courtney and his team brought a level of sophistication to the table in terms of pharmacology that was absolutely critical in

the development of drugs to treat this disease," Kline said. "He brought a level of understanding of how these drugs interact with patients that physicians simply don't have."

Dr. Fletcher's work has been particularly important in the treatment of children with HIV/AIDS. In the early part of this decade, thanks to the pharmacology work of Dr. Fletcher and his team, the FDA approved the use of the drug efavirenz for children at nearly the same time it was approved for use in adults. Efavirenz – which inhibits the growth and replication of HIV/AIDS – is one of the most common and effective drugs used to treat the disease.

The speedy approval for use in children is nearly unheard of as drugs are typically approved for use in adults years before they are in children. This is so because proper dosages for children are hard to set because they are growing and their systems still developing.

Dr. Fletcher's team was at it again last year as their pharmacology work helped another effective drug – atazanavir – receive FDA approval for use in children. Like efavirenz, atazanavir inhibits the virus's growth and replication.

"Finding the right dose for a child is not as simple as just giving a child a smaller dose based on body weight," Dr.

Fletcher said. “There are differences in the way children and adults metabolize or excrete a drug ... and the way that a child metabolizes a drug when they are 3-years-old may not be the way they metabolize that drug when they are 4-years-old.

“So, in simple terms, finding the right dose for a child requires adjusting for a moving target.”

But Dr. Fletcher’s team was able to work through these issues and likely saved countless lives, Dr. Kline said.

“It’s fair to say there isn’t a child receiving HIV treatment today that hasn’t benefited from what Courtney has done,” Dr. Kline said.

“We don’t exactly know why the disease is able to replicate but one good lead we have developed suggests that we’re not getting the drugs to every spot we need to in the body,” Dr. Fletcher said.

Dr. Fletcher and his team will explore how the drugs get into reservoir sites and the characteristics associated with good and poor penetration so that they can develop strategies to improve drug availability into areas of the body they currently can’t access.

Susan Swindells, M.B.B.S., the Terry K. Watanabe Professor of Internal Medicine in the section of infectious diseases and

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Because of a proven track record in working with drug levels for children, Dr. Fletcher’s lab is one of just four in the United States that has National Institutes of Health (NIH) funding and approval to do pharmacology work for HIV/AIDS drugs in children. The other labs are at the University of California, San Francisco, the University of California, San Diego and the University of Alabama-Birmingham.

“The key to our success is that we have put together the expertise in one laboratory that allows us to design and conduct studies in children in a ‘real-time’ manner,” Dr. Fletcher said.

His lab at UNMC is directed by Brian Robbins, Ph.D., whom Dr. Fletcher recruited last year from St. Jude’s Children’s Hospital in Memphis, Tenn.

Recently, the lab received part of a five-year, \$12 million NIH program project grant that was awarded to a three-institution collaboration that includes the University of Minnesota and the University of Massachusetts.

The grant will be used to explore why – despite the presence of strong drugs such as efavirenz and atazanavir – HIV/AIDS still is able to replicate in patients. Researchers theorize that the virus hides and replicates in safe spots, or reservoirs, in the human body that drugs can’t reach.

medical director of the UNMC HIV Clinic, has worked with Dr. Fletcher for many years in the AIDS Clinical Trials Group.

“Dr. Fletcher is unassuming and very smart. I value his opinion highly and we are lucky to have him here in Nebraska,” she said.

Dr. Fletcher’s prowess as a top researcher was one of the key reasons he was hired as dean.

“Having a college leader who simultaneously is a well-funded researcher is a definite plus for UNMC’s entire research program,” said Tom Rosenquist, Ph.D., vice chancellor for research.

And increasing the college’s overall research potential is one of Dr. Fletcher’s main goals. He was particularly pleased when the American Association of Colleges of Pharmacy recently ranked UNMC sixth nationally among 110 pharmacy schools in terms of NIH research dollars per Ph.D. faculty member.

It confirmed Dr. Fletcher’s vision of the college as a research powerhouse.

“We have excellent talent and expertise here at the College of Pharmacy,” Dr. Fletcher said. “The way I see it, we should always be among the top pharmacy colleges in the country.” 