A Question Of Medical Ethics

Experimental Ebola Drugs Are Raising Vigorous Moral Debate

BY MATTHEW HAY BROWN

BALTIMORE — As the Ebola virus ravages West Africa, two American health workers who contracted the disease in Liberia were airlifted back to the United States to be treated with an experimental drug. They have since recovered.

But colleagues of a doctor in Sierra Leone, stricken as he led his country's fight against the virus, decided against giving him the same medicine. He has since died.

The worst Ebola outbreak in history, combined with the existence, in small amounts, of untested drugs that might prove effective in combating it, is raising questions about the ethics of fighting an epidemic.

Chief among them: Can a drug be used to treat the sick when it has yet to be tested for efficacy, or even safety? When supplies of such drugs are scarce, who should get them first? And who should decide?

"Everybody has the same goals here," said Dr. Nancy Kass, a professor of bioethics at the Bloomberg School of Public Health at the Johns Hopkins University. "To treat people if it works, and to not treat people if it doesn't work — and certainly not treat people if it's harmful.

"The problem is, we're looking at this black box, and not knowing what the answers are."

The lethality of Ebola has helped make the answer to the first question easier. The World Health Organization estimates the case mortality rate of the virus at up to 90 percent. With at least 1,350 dead, this outbreak is on pace to surpass the death toll from all previous outbreaks combined.

In the face of such statistics, the Food and Drug Administration eased a restriction this month on the use of the experimental drug TKM-Ebola, developed by a Canadian firm on a U.S. Defense Department contract. A panel of ethicists convened by the World Health Organization has voted unanimously to support the use of experimental treatments such as ZMapp, the medicine given to Dr. Kent Brantley and Nancy Writebol, the Americans who were airlifted from Liberia to Emory University in Atlanta. And the National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health in Bethesda, said last week that it would move up clinical trials for a promising Ebola vaccine.

Under the circumstances, Dr. Henry Silverman said, the decision to try drugs that might work seems "noncontroversial."

"In a time of epidemic, when we have limited time to go through the normal regulatory procedures, you have to weigh risk and benefit," said Silverman, a physician and bioethicist who chairs the ethics committee at the University of Maryland Medical Center. "In this case, this is an illness with a high fatality rate, and we don't have any other good medicines."

Still, there remain questions about who should get such drugs, given the limited quantities in which they tend to be produced.

The supply of ZMapp, used to treat the two Americans, three Liberian doctors and a Spanish priest, is now "exhausted," according to San Diego-based Mapp Biopharmaceutical Inc. Tekmira Pharmaceuticals, the British Columbia firm behind TKM-Ebola, has yet to allow the drug to be used to treat the sick.

"For the first time, we have a range of potential treatments and vaccines that could be important assets supporting our efforts to control Ebola virus disease," Marie-Paule Kieny, assistant director general of the World Health Organization, told reporters in Geneva.

She added: "I don't think that there could be any fair distribution of something which is available in such a small quantity."

Silverman calls the question of who gets the experimental drugs the "justice issue." It makes sense to prioritize health workers, he says, for at least a couple of reasons.

"You want to keep a functioning health care structure in place," Silverman said. And doctors, nurses and other professionals are likely to be the most able to give informed consent.

Kass adds a third reason to prioritize health workers. She points to the case of Brantley and Writebol.

"These were not any two Americans, but they were two Americans who had volunteered to go into the heart of this really terrible epidemic," she said. "I think when someone is willing do that, we have to have certain kinds of commitments to them, both to give them as much protective equipment and training as possible on the front end, and to also make a promise that if you get sick, we're going to airlift you home, we're going to do everything we can."

After health workers, Silverman said, authorities may weigh a variety of criteria for determining whom to prioritize: Those who are most vulnerable, those who are most sick, those who stand to benefit most.

"This is traditional triage," he said.

History offers some examples. During the H1N1 pandemic in 2009, the Centers for Disease Control recommended giving the limited vaccinations to pregnant women, caregivers for children under 6 months and health and emergency services workers.

But each emergency will demand its own reasoning, Silverman said. He said transparency is vital.

"When you're drawing up criteria, you want to make sure you have representation from all of the stakeholders," he said. "So especially people in West Africa, you want to make sure you have those voices at the table, because they may have a different value system from Westerners."

One guiding principle, Kass and Silverman both say, is to manage expectations around an experimental treatment. If an untested drug proves ineffective — or harmful — the results can be catastrophic.

"There is already a fair amount of distrust and rumor (in West Africa) surrounding both why people are getting the disease and what the response should be and whether the health care providers are helping or not," Kass said. "If you put into that context a treatment that turns out not to work, there is a potential that you inadvertently create even more distrust.

"And what is needed right now, much more than a treatment that might be available to 25 or 30 people in the short run, is having as many people as possible cooperating with regard to when they're supposed to assemble and when they're not, whether or not they're supposed to cross borders, how they're supposed to care for people who are sick, how they're supposed to handle the bodies of people who have died," Kass said.

That the ZMapp might have failed was reportedly a concern of the colleagues of Sheik Umar Khan, who decided last month not to give him the drug. According to The New York Times, a treatment team from Doctors Without Borders and the World Health Organization feared stoking the already considerable suspicion of Western medical institutions.

"What they really didn't want to do was kill Dr. Khan with their attempt at therapy," Dr. Armand Sprecher, a public health specialist at Doctors Without Borders, told The Times. "If word got out that (Doctors Without Borders) killed Dr. Khan, that would have implications for outbreak control."

Khan died — as did the Rev. Miguel Pajares, the Spanish priest who was given ZMapp.

"Before there's going to be any kind of program, there has to be a really intelligently designed communication program that happens alongside it," Kass said.

Kass said exploring the use of experimental drugs is important. But in the current outbreak, she said, the focus should be on existing tools.

"Ultimately, the best hope for containing things is going to be in the public health systems of Africa — which are, in general, woefully inadequate," she said. "Given that a lot of people are not optimistic that the drug will be a magic bullet — it might be helpful, but it's not going to be black and white, just everybody pop a pill and make Ebola go away — maybe there's not enough discussion still about what kinds of work can the United States or other wealthier countries be contributing to, not only in drug development or drug access, but in bolstering the health systems."

JOHN SPINK/ATLANTA JOURNAL-CONSTITUTION/MCT

Dr. Kent Brantly hugs members of the medical team at Emory University Hospital in Atlanta following his discharge from the facility on Thursday, Aug. 21, after being successfully treated for Ebola. American missionary Nancy Writebol was also treated and was discharged.