

Reemergence of Intravenous Drug Use as Risk Factor for Candidemia, Massachusetts, USA

[Announcer] This program is presented by the Centers for Disease Control and Prevention.

[Sarah Gregory] Today, I'm talking with Dr. Stuart Levitz, a professor of medicine and microbiology at the University of Massachusetts Medical School. We'll be discussing the reemergence of IV drug use and candidemia. Welcome, Dr. Levitz.

[Stuart Levitz] Thank you, Sarah, it's a pleasure to be talking to you.

[Sarah Gregory] I understand that illegal intravenous drug use has become endemic and this has created a surge in deaths and infections. What's happening?

[Stuart Levitz] Yes, I would say endemic and epidemic. Illicit use of intravenous drugs has long been a problem in the United States. However, in recent years, the problem has really worsened significantly. For instance, it's now estimated that over 60,000 people a year die from drug overdoses in the United States, that's from using illicit drugs. And this is greater than a six-fold increase compared to what was seen several decades ago, for instance in the early 1990s. In addition to the staggering number of overdose deaths, acute and chronic infections can be transmitted by intravenous, or IV, drug use. To give you an example, the World Health Organization estimates that globally, or worldwide, the prevalence of hepatitis C in injection drug users is 67 percent. In other words, two out of three illicit injection drug users are infected with hepatitis C. Other infections can be seen. For example, HIV is also commonly transmitted by the sharing of needles.

[Sarah Gregory] We hear a lot about opioids now, but many of us may not really know what they are. Would you explain to us what opioids actually are?

[Stuart Levitz] Yes. Opioids are a class of drugs, and simply defined, they're a class of drugs that act on opioid receptors. These receptors are primarily found in the brain, spinal cord, peripheral nerves, and also in the gastrointestinal tract. Medically, opioids are most commonly prescribed for pain relief, of course, but they also have other accepted uses, including the treatment of diarrhea. Many opioids are available legally by prescription, for example, morphine, codeine, oxycodone. Others, such as heroin, of course, are illegal in the United States. The potent synthetic opioid drug, fentanyl, which is available by prescription, is relatively inexpensive to manufacture. And what's happened is that much of the heroin sold in the United States, illicitly, is cut with fentanyl or is actually entirely fentanyl. Because of its relatively potency and low cost, this has led to a lot of overdoses.

[Sarah Gregory] Your article specifically discusses candidemia infections associated with intravenous drug use. Tell us about these infections—what they are and how do they usually spread?

[Stuart Levitz] Well, as a physician specializing in infectious diseases, I see a lot of infections associated with illicit intravenous drug use. I already mentioned to you hepatitis and HIV, but I also see acute bacterial infections, particularly staphylococcal infections, or staph infections, as

they're commonly known, including MRSA. However, at the beginning of this decade, we began to see cases of candidemia. So, candidemia are bloodstream infections that are due to the fungus candida. This was very unexpected, and as the number of these infections grew, we decided to study them. Now, as far as your question in terms of what they are and how they usually spread, the "spread" part is that we don't know the source of the candida in these patients, and I can only speculate. Candida normally lives on the skin. It also can be found in the gastrointestinal tract, including the mouth. Thus, we speculate that the candida got into the blood because the skin wasn't cleaned properly prior to the injection of drugs. Alternately, it should be noted that many drug users actually lick their needles prior to injection of the drugs. So, in those cases, the source could have been saliva, but we really don't know, and this remains a mystery to us.

[Sarah Gregory] Where did you conduct the study and how did you go about it?

[Stuart Levitz] Well, the study was conducted at UMass Memorial Hospital. This is an approximately 800 bed teaching hospital that serves Central Massachusetts. A talented infectious disease fellow in our program, Nongnooch Poowanawittayakom, reviewed the hospital records of all patients 14 years of age and older who had a positive blood culture for candida, over a seven year period beginning in 2010. What she found was that there were a 198 such cases of candidemia in the hospital. And then, after reviewing the records, what she found was that 24 of those 198 cases had a history of illicit intravenous drug use. What we then did was we compared the cases associated with intravenous drug use with those that did not have such an association.

[Sarah Gregory] So, what did you discover?

[Stuart Levitz] Well, we had several discoveries. First, as expected, the patients with a history of drug use were younger and were much more likely to be infected with hepatitis C. Interestingly, of the 24 cases associated with drug use, we found four different species of candida. So this strongly argued against a common source of infection in all the patients. In addition, whereas the species called *Candida albicans* was responsible for over half the cases not associated with drug use, it was responsible for less than 30 percent of the drug use-associated cases. We also found some other differences. Infections of the bone and the heart were more common in the drug users. Although the numbers were low, they were still statistically significant in terms of the differences. Five of the 24 patients that had, had drug use, died of the candida infection, emphasizing that this can really be a lethal infection. In addition to the morbidity, there was fairly large mortality. And, finally, it's worth pointing out that the number of candidemia cases associated with drug use went up in the last year of the study. So, nine of the 24 cases were found in 2016, the year that our study ended. And this to us ominously suggested that this problem might be getting worse.

[Sarah Gregory] What are the common treatments for candida and do you have suggestions for treatments different from them?

[Stuart Levitz] Yes, the most recent guidelines from the Infectious Disease Society of America for the treatment of candidemia, these guidelines recommend starting with a class of drugs called echinocandins. There are three licensed members of this class in the United States, called caspofungin, micafungin, and anidulafungin. So this is the drug that we usually use when we see a patient that has candidemia. Now, there's some problems with the echinocandins, and

particularly in this population. The echinocandins must be given intravenously and drug users, when you, when you have intravenous lines in them, they sometimes use these lines to illicitly inject drugs, so the patients need to be observed closely while they're on the drugs, and they can't, they can't go home with intravenous lines. So, some patients we do switch to fluconazole, but it's only those patients that the candida isolate is susceptible to that medication and that they're medically stable.

[Sarah Gregory] This is a side question, but your article mentions that lemon juice was used to dissolve heroin. It seems that lemon juice can be contaminated and cause candida infections. Since lemon juice is an acid and is also touted to be somewhat antimicrobial, how is it able to be contaminated?

[Stuart Levitz] Yeah, Sarah, thanks for asking about this, as I think this is a fascinating story. So, back in the 1970s to 1990s, much of the heroin that was sold in the United States and in Europe was impure. It was called "brown heroin." Normal heroin would be white, so the brown reflected the impurities of the heroin. And the heroin did not dissolve in water, so what drug users did to dissolve the heroin is they used lemon juice, which, as you mentioned, is acidic. Well, it turns out that, whereas most bacteria do not like acid and do not grow under acidic conditions, fungi, including candida, grow very well at low pH, at acidic pHs. Well, the lemon juice got contaminated with candida and then the injection drug users ended up shooting the candida into their veins. Interestingly, candidemia was rare in those patients back then. Those patients mostly got skin lesions and some got eye infections. When the street heroin got purer in the late 1990s, the problem largely went away, although now, as our article suggests, it seems to be reappearing in a new form.

[Sarah Gregory] What are your conclusions about illegal opioid use and candida after doing this study?

[Stuart Levitz] Well, although many of the press reports surrounding illicit opioid use have centered on deaths from overdose, I want to emphasize that infections remain a serious cause of illness and death in persons with intravenous drug use. The morbidity and mortality associated with candidemia is quite high, so clinicians should be on the lookout for cases, and aggressively treat them when they occur. Some major unanswered questions that I have is how widespread the problem of candidemia associated with injection drug use is. Is this mostly limited to the geographical area where I practice or are other medical centers also seeing cases? I'm very curious to find out. And also, as I already mentioned, I'm very curious to know where the candida is coming from.

[Sarah Gregory] Would you like to tell us about your position at UMass Memorial Hospital and how you are involved in studying drug use and candida?

[Stuart Levitz] Yes, I'm an attending physician that specialize in infectious diseases at UMass Memorial Hospital. I'm also a professor of medicine at the University of Massachusetts Medical School, which is affiliated with the hospital. I run a research lab that studies fungal immunology; in particular, we're trying to develop vaccines to protect persons against fungal infections. When I make what I think is an interesting clinical observation, I try to get one of our trainees interested in researching the cases. I was very fortunate that Nongnooch took a strong interest in

the project. She really did an outstanding job collecting and analyzing the data. I also want to give some kudos to two other physicians that helped a lot with the study—Sankaru Touray and Dick Ellison, who's the head of infection control at our hospital, as well as two statisticians—Anamika Dutta and Shannon Stock.

[Sarah Gregory] Thank you Dr. Levitz, for talking with us today. Listeners can read his April 2018 article, Reemergence of Intravenous Drug Use as Risk Factor for Candidemia, Massachusetts, USA, online at cdc.gov/eid.

I'm Sarah Gregory for Emerging Infectious Diseases.

[Announcer] For the most accurate health information, visit cdc.gov or call 1-800-CDC-INFO.