

# Drug-Resistant *Pseudomonas aeruginosa* and Medical Tourism from the United States to Mexico

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

[Sarah Gregory] Hello, I'm Sarah Gregory, and today I'm talking with Dr. Cal Ham, a medical officer at CDC in Atlanta. We'll be discussing extensively drug-resistant infections linked to medical tourism from the United States to Mexico.

Welcome, Dr. Ham.

[Cal Ham] Thank you so much, Sarah. I'm very excited to be here.

[Sarah Gregory] Well, we're excited to have this conversation.

So let's start with some definitions. What is carbapenem and how is it used and why is it used?

[Cal Ham] Carbapenems are a type of broad-spectrum antibiotics that are used to treat severe infections caused by certain types of bacteria that are resistant to other types of antibiotics. And these really are some of our last line antibiotics that can be used effectively against highly resistant organisms. They've been a mainstay of treatment for infections caused by highly resistant bacteria since they were first approved by the FDA back in 1985, and some of the types of infections that they are used to treat include bloodstream infections, complicated urinary tract infections, pneumonia, and complicated skin and soft tissue infections. Now, they are typically given intravenously in healthcare facilities and currently there are four that are approved for use in the United States, and those include imipenem, meropenem, doripenem, and ertapenem.

[Sarah Gregory] Okay. So what are carbapenemase?

[Cal Ham] So carbapenemases are actually enzymes that are produced by bacteria and inactivate carbapenem antibiotics. But not just carbapenem antibiotics, they also inactivate nearly all beta-lactam antibiotics, which is one of the major classes for antibiotics that we have available (penicillin was the first in that class of antibiotics). Genes for these carbapenemase enzymes are often carried on these mobile genetic elements such as plasmids that can be transferred from one species to another, and thereby allowing resistance of spread between different bacterial species.

Now one of the reasons we are concerned about these is that they are associated with rapid spread, particularly in healthcare settings, and can lead to very rapid increases in the percent of bacteria that are resistant to carbapenems and other antibiotics. I will say there are several different types of carbapenemases that are of public health concern, but their prevalence and incidence varies globally.

[Sarah Gregory] So could you explain a little further on how they evolved?

[Cal Ham] Absolutely. So keep in mind that antimicrobials (including antibiotics) are often natural products. So for example, penicillin was first identified in a mold. So it's thought that enzymes like carbapenemases that inactivate antibiotics evolved as part of natural bacterial defense systems against these products, such as antibiotics, that other organisms evolved.

So when we use antibiotics, especially when they are overused or misused, that actually creates a selective pressure for bacteria that have these types of defense systems. Because, of course, bacteria with the defense systems will survive and those without will die in the presence of an

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antibiotic. Bacteria can also acquire the code or the DNA for that defense system from other bacteria, and this ability to share DNA again means that the number of bacteria with the code or the genes for these carbapenemase enzymes can rapidly increase.

[Sarah Gregory] And when did we first start diagnosing them?

[Cal Ham] The first carbapenemase identified in the United States—we refer to it as KPC, which stands for *Klebsiella pneumoniae* carbapenemase—it was actually first reported in 2001 and it was identified from an isolate that was actually collected back in 1996 in North Carolina. Since then, we've seen very rapid expansion of KPC across the United States. So it started off in just a couple of states, and since then (and currently) it's been identified in all 50 states. Now, KPC is the most common carbapenemase in the United States. However, worldwide the most common carbapenemase is called NDM, which stands for New Delhi Metallo-beta-lactamase.

[Sarah Gregory] Okay. So what is *Pseudomonas aeruginosa*?

[Cal Ham] *Pseudomonas* is a type of bacteria that's found commonly in the environment, and the type of *Pseudomonas* that most commonly infects humans is called *Pseudomonas aeruginosa* and it can cause bloodstream infections, pneumonia, and surgical site infections. And often times these can be very serious infections and can lead to severe illness and even death.

Now, *Pseudomonas* is intrinsically resistant to many antibiotics, which makes preserving the antibiotics that are effective against *Pseudomonas* critically important (and including carbapenems). So the good news, though, is that in the US, cases of multidrug-resistant *Pseudomonas* actually declined about 30% among hospitalized patients from 2012-2017. Currently, at least carbapenemases are pretty rare to be found in *Pseudomonas* isolates in the United States. But one of our concerns is if they become more common, this could reverse trends of decreasing highly resistant *Pseudomonas* that we've seen over the last few years.

[Sarah Gregory] Your study was about extensively drug-resistant carbapenemase-producing *Pseudomonas aeruginosa* and medical tourism from the United States to Mexico. Tell us what extensively drug-resistant carbapenemase-producing *Pseudomonas aeruginosa* is.

[Cal Ham] Extensively drug-resistant carbapenemase-producing *Pseudomonas aeruginosa*, which is quite the mouthful—

[Sarah Gregory] Yes.

[Cal Ham] —is a type of *Pseudomonas* that produces a carbapenemase enzyme, which we were just talking about, and is resistant to nearly all antibiotics (including carbapenems). And these cause infections that are incredibly difficult to treat with limited therapeutic options. And again, due to the presence of carbapenemase gene, these have the potential to rapidly spread and increase carbapenem resistance in healthcare facilities. Now for this paper, the specific type of carbapenemase that we found in these *Pseudomonas* isolates that we refer to as VIM, which stands for Verona integron-encoded Metallo-beta-lactamase.

[Sarah Gregory] I think you said these pathogens aren't really commonly found in the United States right now. Is that what you were saying?

[Cal Ham] That's correct. So carbapenemase-producing *Pseudomonas*, in general, are rare in the United States. Now, *Pseudomonas* itself is certainly more common. So in 2017, it was estimated that drug-resistant *Pseudomonas aeruginosa* caused a little over 32,000 infections among hospitalizations and 2,700 deaths in the United States. But again, those include *Pseudomonas* that weren't necessarily carbapenemase-producers. So in terms of carbapenemase-producing *Pseudomonas*, you're correct. Those are relatively rare in the United States. And for those that carry this specific carbapenemase gene VIM, through December 31st of 2021, there has been (reported to us at CDC) just over 500 cases.

[Sarah Gregory] Okay. So how do these pathogens spread?

[Cal Ham] In healthcare settings, which is where most of the serious infections occur, *Pseudomonas* can be spread on the hands of healthcare workers or even by medical devices that are used on multiple patients that get contaminated during patient care. And subsequently, either the device isn't properly cleaned or if the healthcare worker doesn't perform hand hygiene, they can then be passed from one patient to another. Importantly, I want to note that patients can become colonized with this organism, meaning that they carry the bacteria but they don't actually show signs or symptoms of clinical infection. And these colonized patients may not be recognized because, again, they're not showing signs or symptoms of clinical infection but, importantly, they can transmit to other patients via one of the mechanisms I just discussed.

[Sarah Gregory] Tell us about medical tourism. What is it and why do people do it?

[Cal Ham] Yeah. So medical tourism is a term that's commonly used to describe international travel, expressly for the purpose of receiving medical care. And so that's different from someone who is traveling to another country, say for vacation or work, and then gets sick while in that other country and requires medical attention at that point. So these are individuals who are traveling expressly for the purpose of receiving medical care.

Now, medical tourists, we know they can pursue medical care abroad for a variety of reasons. Some of these reasons include lower cost of the procedure they're pursuing, a recommendation from friends or family, the opportunity to combine medical care with a vacation destination, or to receive a procedure or therapy that may not be available in their country of residence.

[Sarah Gregory] About how many people in the United States engage in medical tourism yearly? Do we know?

[Cal Ham] So our best estimate is that annually, up to 750,000 US residents participate in medical tourism. Though it's thought that the actual number may be much higher than that. It's a large number of US residents who participate in medical tourism annually.

[Sarah Gregory] Are there certain countries where it's more popular to go to do this?

[Cal Ham] Medical tourists from the US most commonly travel, as you can imagine, to Mexico and Canada, as well as some other countries in Central America, South America, and the Caribbean.

[Sarah Gregory] Are there certain procedures that are more popular than others?

[Cal Ham] From a 2016 survey that was done among US medical tourists in 11 different states, the number one procedure that people pursued were actually dental procedures or dental care

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(just over 50%). And some other common ones include cosmetic surgery, orthopedic surgery, and even organ transplants. And then bariatric surgery, in general, is also a popular choice among US medical tourists. Now, bariatric surgery is actually...it's a type of weight loss surgery that works by making changes to the digestive system that restrict the amount of food the stomach can hold, or by reducing the body's ability to absorb nutrients. Some examples that you may have heard of these types of surgeries include gastric bypass, gastrectomy, and adjustable gastric band surgeries.

[Sarah Gregory] Your study was about this problem occurring in medical tourism in Mexico in particular. How were you alerted that these infections were occurring?

[Cal Ham] A little bit of background, so in the US it's recommended that each case of these unusually resistant bacteria, such as VIM *Pseudomonas*, be investigated. And these initial investigations, they are often carried out by state and local healthcare-associated infection programs at public health departments, and we work very closely with these health departments with these responses.

So these state and local health departments really play a critical role in containing the spread of these highly resistant bugs in healthcare settings through a variety of different activities, and these include activities such as conducting onsite infection control assessments to make sure appropriate measures are implemented to prevent their spread; performing colonization screening and other case finding activities; and importantly, gathering epidemiologic information and exposure histories when these bugs are identified, which they can be shared with CDC to assess for emerging trends. In addition, testing of resistant bacteria in the US for carbapenemase genes occurs through CDC's Antibiotic Resistance Laboratory Network (or we like to refer to it as AR Lab Network) which is a national network of 55 public health laboratories, which really allows us to identify these highly resistant organisms early and take steps to prevent their spread.

So we were first alerted to this on September 28th, 2018, when we received a report from the Arizona Department of Health Services of a highly antibiotic-resistant *Pseudomonas aeruginosa* carrying that VIM carbapenemase gene. The isolate came from a stomach wound on an adult patient under the age of 40, which is a little atypical because we typically identify these in older individuals. But this patient had recently undergone bariatric surgery in Tijuana, Baja California, Mexico. From late September through late November of 2018, we received six reports of VIM *Pseudomonas* isolates from patients who had undergone bariatric surgery in Tijuana, and four of these patients had actually undergone surgery at the same facility (which I'll refer to as facility A) and by the same surgeon (who I'll refer to as surgeon 1). All four of these patients also used the same US-based travel agency (which I'll refer to as travel agency A) who helped, essentially, arrange their travel to Mexico as well as the procedure at this facility.

Using these reports from multiple health departments across multiple jurisdictions and laboratories and laboratory results from the AR Lab Network, we were able to identify this unusual epidemiologic signal of multiple VIM *Pseudomonas* cases occurring in US residents, all of whom who had recently undergone bariatric surgery in Tijuana and most at the same facility and by the same surgeon. Based on this, CDC in collaboration with the Secretariat of Health in Baja California in Mexico launched an outbreak investigation.

[Sarah Gregory] So overall, what time period did you investigate?

[Cal Ham] We cast a pretty wide net to find as many affected individuals as possible. And so the exact time period we investigated were for US residents who underwent invasive medical procedures in Mexico between January 1st, 2018-December 31st, 2019.

[Sarah Gregory] So a two-year period. Okay.

And how many people were affected that you found?

[Cal Ham] So in total, we identified 38 US residents from 18 different states who were affected following an invasive medical procedure in Mexico during the investigation period. There were also an additional six suspected cases, however they did not have a culture collected so we were unable to identify *Pseudomonas* as being a cause of infection. But however, all six of those did have signs and symptoms of infection.

[Sarah Gregory] So tell us a little bit more about how you went about this study.

[Cal Ham] It was really an international collaboration between CDC and public health authorities in Mexico, and of course our state and local public health partners as well. It was also really a multipronged approach, so I'll talk about a couple of different aspects of the investigation. The first is really case findings. So you know after we received those six initial reports, we took some additional measures to find other cases of VIM *Pseudomonas*.

And so we did both passive and active case findings, including telephone notifications, patient interviews, and sending out notification letters. And on November 19th, 2018, CDC issued a call for cases on the Epidemic Information Exchange for *Pseudomonas aeruginosa* isolated from patients who reported bariatric surgery in Tijuana, and we posted an Emerging Infections Network notification on November 23rd, 2018. And then a few months later in March of 2019, that travel agency that I mentioned earlier (travel agency A) actually provided us with the contact information for patients who had undergone bariatric surgery at facility A in Tijuana between August 1st, 2018, and February 15th, 2019.

So for those who were at high risk for having an active infection or a current hospitalization based on their surgery dates, CDC and state and local health departments conducted telephone notifications and structured interviews to obtain demographic information, clinical and exposure detail, and information about factors that influence their decision to have surgery at facility A. For lower risk individuals, we also recommended that state and local health departments send out notification letters as well, and some health jurisdictions actively contacted those individuals. We also, in addition to case findings, we posted patient and provider (healthcare provider) notifications online.

So in January 2019, we posted an online notification for patients and their US healthcare providers and an Alert Level 2 Travel Health Notice, which were covered by several major media outlets at the time. These notifications included warnings describing the risk of bacterial infections after surgery. And some individual states also issued their own health alerts as well to increase awareness of the potential outbreak.

In addition to patient and provider notifications, the Federal Commission for Protection against Sanitary Risk in Mexico was able to conduct an infection control assessment at facility A. And this took place in December 2018. They actually identified multiple infection control lapses, including poor hand hygiene practices, incomplete medical records, and lack of chemical or biological indicators that are really in place to ensure that medical equipment and devices are

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appropriately sterilized and reprocessed after their use. Unfortunately, no CDC staff were able to go on site for that IPC assessment and investigation and we subsequently received minimal epidemiologic information on hospital stays in Mexico.

And then the last part of the investigation I'll talk about is related to laboratory characterization. So we received 22 VIM *Pseudomonas* isolates from affected patients, and we actually performed whole genome sequencing on those 22 isolates to assess for their relatedness to each other.

[Sarah Gregory] Is there anything else that you found that you care to tell us about?

[Cal Ham] Yeah. I think a lot of important results came from this investigation. So most of the cases, actually 36 out of the 38, occurred among US residents who underwent elective bariatric surgery in Tijuana, Baja California, Mexico; 31 underwent surgery by the same surgeon (surgeon 1), and 27 at the same facility (facility A); 34 out of 38 (so about 90%) of the patients were female; and the median age was 39 years of age. The surgery dates ranged from August 2018 to August 2019. Cases in patients who underwent surgery at facility A really peaked in January 2019.

The most common procedure that these patients reported was a sleeve gastrectomy. Actually, 34 of the 38 patients reported sleeve gastrectomy. And following bariatric surgery in Tijuana, 16 of these patients were hospitalized in the United States and at least four were actually admitted to an intensive care unit. Additionally, six of the patients had to undergo an additional surgery because of their infection from VIM *Pseudomonas* and one patient died. Now whether or not the VIM *Pseudomonas* infection or the surgery actually contributed to their death is a little unclear from the medical records that we had available. Importantly, based on our investigation, there was no evidence of onward transmission in US healthcare facilities where these patients were hospitalized.

In terms of what we learned from the patient interviews—so we actually wound up interviewing 160 individuals who underwent and had surgery at facility A. So not all of them actually had a VIM *Pseudomonas* infection. But we learned that the most common reason they reported for having surgery at facility A was lower cost (so 83% reported that), and this was followed by recommendations from friends or family at 52%, 23% reported that they did not meet weight qualifications for surgery in the US, and 23% responded saying that convenience or shorter wait time was one of the reasons that they decided to have surgery at facility A.

In terms of the whole genome sequencing results, of the 22 isolates that were sequenced, 17 were determined to be highly related and formed a distinct cluster. All 17 of these were associated with surgeon 1, except for one where the surgeon was actually unknown. And primarily these were taken from individuals who underwent surgery at facility A. So these closely related strains from case patients after surgery performed by surgeon 1 across multiple facilities and the infection control lapses identified at facility A led us to hypothesize that a persistently contaminated mobile medical device such as a laparoscope (which is a device that's used to perform these bariatric surgeries) was a plausible source of the outbreak. Some alternative explanations include persistently contaminated environmental or water source, or a healthcare worker carrying the bacteria but not actually having symptoms of illness.

And finally, facility A was closed in March of 2019, and then ongoing monitoring through December of 2019 did not identify any additional cases linked to facility A after January of 2019, or to surgeon 1 after July of 2019.

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[Sarah Gregory] That's some good news.

Have there been other infectious outbreaks related to medical tourism?

[Cal Ham] Yeah, there has. Some of the more recent ones include nontuberculous mycobacteria surgical site infections among medical tourists from the US and Switzerland who underwent cosmetic surgery in Latin America. Another one is Q fever among US medical tourists who receive live cell therapy in Germany. However, I do want to point out that all healthcare abroad—not just medical tourism—is a risk for acquiring multidrug resistant organisms. And that's why providers should really take travel history when seeing patients and patients should of course share travel information, and it really helps ensure appropriate treatment and protect other patients from potential transmission.

[Sarah Gregory] This is all public health. Just tell us a little bit more about how this impacts public health in the United States, carrying these pathogens back here.

[Cal Ham] First, this investigation really underscores the potential for medical tourism to introduce rare and highly concerning pathogens into the US healthcare system. Several lines of epidemiologic and laboratory findings from this investigation support a point source outbreak linked to surgeon 1, who primarily operated at facility A, although the exact source of the pathogen was not identified. Providers who care for patients with a history of recent invasive procedures in Mexico should be aware of the potential for infections caused by resistant pathogens, such as VIM *Pseudomonas*. And for those with signs of infection, healthcare providers should really obtain cultures, provide antimicrobial susceptibility testing to guide treatment, and have any carbapenem-resistant strains of *Pseudomonas* and *Enterobacterales* tested for VIM and other plasmid-mediated carbapenemase genes.

Since July 2020, we have identified additional cases of VIM *Pseudomonas* among US residents undergoing procedures in Tijuana, however these recent infections appear to be sporadic and unrelated to each other. However, they do underscore the potential for US residents to acquire these highly resistant bacteria even in the absence of a recognized outbreak.

[Sarah Gregory] Are there any ways that other countries can reduce these problems?

[Cal Ham] Yeah, absolutely. One thing is establishing and ensuring adherence to these core infection prevention and control practices in healthcare facilities, really to prevent infections and to prevent transmission between the patients. Another thing that can be done is to build laboratory capacity and surveillance systems for detection of these highly resistant bugs so that when they do occur, they can be rapidly identified and appropriate interventions can be put in place to prevent further spread. And then finally, I think antibiotic stewardships or using antibiotics responsibly, not overusing or misusing them, which we discussed earlier can create that really selective pressure for some of these highly resistant bugs.

[Sarah Gregory] Does CDC have any recommendations for people considering having procedures done in other countries?

[Cal Ham] We do. So first and foremost, I think it's important for you to do research when choosing a healthcare facility abroad. Anyone who is considering medical tourism and US healthcare providers caring for prospective or returned medical tourists should be aware that standards for infection control, as well as regulations and enforcement practices, vary from

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country to country and as well as from facility to facility within a country. So you really want to do your research for any healthcare facility that you're considering.

Another thing for those thinking about medical tourism is to consider visiting facilities that have been accredited for infection prevention and control by national and even international bodies. A healthcare facility that's accredited by an external body may have better developed infection control practices than a nonaccredited facility. Some accrediting groups include the Joint Commission International, DNV GL International Accreditation for Hospitals, and the International Society for Quality in Healthcare. And they all have lists of standards that facilities must need to be accredited.

However, it is important to note that all surgeries carry some risk, and accreditation does not necessarily guarantee a successful outcome or eliminate the risk of pathogen transmission in healthcare. And finally, I'll say that people planning for medical tourism should also really consider getting a pre-travel consultation with a healthcare provider at least four to six weeks before traveling to discuss their health status, the procedure itself, and other healthy travel options. And for those of you who are interested, for more information on CDC recommendations, you can please check out our website. It's [cdc.gov/travel/page/medical-tourism](https://www.cdc.gov/travel/page/medical-tourism).

[Sarah Gregory] Okay. Good to have that.

Dr. Ham, tell us about yourself and what you do at CDC.

[Cal Ham] Yeah. My background, I'm a physician and an epidemiologist by training. I am the deputy lead of the antimicrobial resistance team in the division of healthcare quality promotion at CDC, and most of my work focuses on the prevention and response to these highly drug-resistant organisms that are found in healthcare settings. Some examples include MRSA or methicillin-resistant *Staph aureus*, CRE or carbapenem-resistant *Enterobacterales*.

[Sarah Gregory] I imagine you like to travel, as most of us at CDC do. Do you have any favorite countries, medical tourism aside?

[Cal Ham] I really do enjoy traveling, and it's certainly hard to pick just one country. I guess if I had to pick just one, I'm a big history buff so I really enjoyed a trip I took a few years ago to Italy. I think seeing all the historic sites around Rome was truly amazing and a dream come true.

[Sarah Gregory] What period of history? My passion is medieval history. What period of history are you most engaged with?

[Cal Ham] I'm certainly no expert by any means, but I would say ancient Roman and Greek history are the two time periods that I'm most interested in.

[Sarah Gregory] Well, thank you so much for taking the time to talk with me today, Dr. Ham.

[Cal Ham] Absolutely. Thank you so much for having me, it was a pleasure.

[Sarah Gregory] And thanks for joining me out there. You can read the January 2022 article, Extensively Drug-Resistant Carbapenemase-Producing *Pseudomonas aeruginosa* and Medical Tourism from the United States to Mexico, 2018–2019, online at [cdc.gov/eid](https://www.cdc.gov/eid).

I'm Sarah Gregory for *Emerging Infectious Diseases*.

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