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Emerging *Candida auris* Spreading in Healthcare Outbreaks

Fungus is epidemiologically similar to a 'superbug' bacteria

By Gary Evans, Medical Writer

A multidrug-resistant fungus, emerging globally, has now infected more than 60 patients in the United States, spreading more like a bacterial “superbug” than fungi, the CDC reports.

Candida auris causes high mortality, can transmit to patients on the hands of healthcare workers, persists in the environment, and can colonize people who then serve as a reservoir for outbreaks.

C. auris was an extremely rare infection in the U.S. when the CDC issued an alert¹ last year that it was causing healthcare-associated outbreaks with high mortality in several countries. It has now been reported in six states.

“We have 61 cases across the U.S., with 39 of those in New York,” says

Sharon Tsay, MD, an investigator in the CDC’s Epidemic Intelligence Service (EIS). “We also have identified 32 additional people who are [colonized] with *C. auris*.”

As has been demonstrated with multiple pathogens, the ability to persist in a colonized state means patients with no symptoms of infection could serve as a reservoir for spread to vulnerable patient populations, particularly those on IVs and other invasive devices that could

“WE HAVE 61 [CANDIDA AURIS] CASES ACROSS THE U.S., WITH 39 OF THOSE IN NEW YORK.”

seed bloodstream infections. *C. auris* has caused high mortality in outbreaks that involved bloodstream infections.

“They are not infected, but we are concerned that they also may be spreading it,” Tsay tells *Hospital Infection Control & Prevention*. “In hospitals

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or long-term acute care hospitals [LTACHs] they could be a source for ongoing [transmission].”

In acute care hospitals, patients with *C. auris* infection or colonization should be placed in single rooms under standard and contact precautions. The CDC originally recommended cleaning rooms and environmental surfaces with an antifungal agent, but has upgraded that to advise the use of a disinfectant that is EPA-approved to kill that most persistent of spore-formers — *Clostridium difficile*. (See CDC recommendations, in this issue.) That revision speaks volumes about both the ability of *C. auris* to persist in the environment and the CDC's concern that it could gain an endemic foothold in the U.S.

“We found that it exists in the environment in very high concentrations on beds and things closest to patients,” says **Paige Armstrong, MD**, a CDC EIS officer. “[It’s] even in the crevices and the corners of the room, meaning that we really need to focus on cleaning with the right [disinfectants] to kill this organism.”

Armstrong and Tsay were among several CDC investigators who reported on outbreaks of *C. auris* recently in Atlanta at the annual EIS conference.

“It has colonized people even after they were treated with antifungal medications — people still have it on their skin,” Armstrong says. “This is something that we don’t usually see with a fungus. These are things that we typically see with emerging or resistant bacteria.”

In addition, *C. auris* has the ability to develop resistance that is “very rare” in fungi, she says.

“There are only three main classes of antifungal medication,” Armstrong says. “So once you become resistant to all three of those,

there’s very little that can be done. It’s causing outbreaks in hospitals, which again, is something we typically attribute to bacteria. This is an emerging multidrug-resistant fungus that is acting like a bacterium — it’s acting like a super bug.”

Evidence of Transmission

In addition to New York, *C. auris* has also infected patients in five other states, including 15 in New Jersey, four cases in Illinois, and one each in Indiana, Maryland, and Massachusetts.

In a look-back study, the CDC identified the first eight fungal infections with the emerging pathogen that occurred at six health healthcare facilities in New York from May 2013 to Oct. 2016.² The patients had multiple indwelling devices, including urinary catheters, gastrostomy tubes, tracheostomy tubes, and central venous catheters. All had been in at least three healthcare facilities in the 90 days before the infection was diagnosed. Some had overlapping stays, raising the possibility of transmission. Three (38%) died within 28 days of diagnosis.

“A lot of these cases are in the sickest of the sick,” Tsay says.

Many of the *C. auris* isolates were highly related by whole genome sequencing and five were resistant to two antifungal drug classes, she reported. Three of four patients sampled had *C. auris* colonization in multiple body sites weeks after their first positive culture. The pathogen also was found in patient rooms and colonizing ward-mates. Inadequate contact precautions adherence was found at some long-term care facilities, Tsay concluded.

Strong evidence for transmission between patients was found in a *C.*

auris outbreak in Chicago reported at the EIS meeting. “Nearly indistinguishable” *C. auris* strains were isolated from patients in the same ward of an LTACH,³ investigators reported. In August 2016, the Chicago Department of Public Health was notified of two patients with *C. auris* infections who were treated at the same acute care hospital and LTACH. CDC investigators analyzed isolates using whole genome sequencing.

“*C. auris* was isolated from Patient 1’s bloodstream in May and Patient 2’s urine in July,” the CDC investigators found. “These patients had three overlapping [hospital] admissions during March–July, but wards differed. In April, three days separated their hospitalizations on the same LTACH ward. In August, we detected *C. auris* colonization of the index patients’ skin, nares, vagina, and rectum. *C. auris* was present on the mattress, bed rail, chair, table, and window ledge surfaces in Patient 1’s hospital room.”

In addition, three of 50 LTACH patients hospitalized on the same ward as both index patients were colonized with *C. auris*. All patient isolates were highly genetically related. Fortunately, both patients survived.

Deadly Outbreak

Evidence of the devastation possible by *C. auris* as a healthcare-associated infection (HAI) was demonstrated in an outbreak in several neonatal ICUs in hospitals in Colombia in 2016. Armstrong was the lead CDC investigator and reported the findings at the EIS conference.

“We’re talking about babies that have just been born, at times premature, so some of the most vulnerable patients,” Armstrong says. “When

CDC *Candida auris* Infection Control Measures

Infection preventionists that see a case of *Candida auris*, an emerging fungal infection that can be multidrug-resistant, should take the following measures, as recommended by the CDC.¹

Isolation: In acute care hospitals, patients with *C. auris* infection or colonization should be placed in single rooms under standard and contact precautions. The optimal duration for use of infection control precautions in health-care is unclear since the typical duration of *C. auris* colonization is unknown. Periodic reassessments for presence of *C. auris* colonization (e.g., every 1–3 months) might be needed to inform duration of infection control measures.

Assessments of colonization should involve testing of axilla and groin swabs for *C. auris*. Two or more assessments performed at least one week apart with negative results are needed before discontinuing infection control precautions is considered. The patient or resident should not be on anti-fungal medications active against *C. auris* at the time of these assessments.

Environmental cleaning: The fungal pathogen can persist on surfaces in healthcare environments. Healthcare facilities that have patients with *C. auris* infection or colonization should ensure thorough daily and terminal cleaning and disinfection of these patients’ rooms. CDC recommends the use of an Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against *Clostridium difficile* spores. This is a change from the original recommendation for use of an EPA disinfectant with an antifungal claim.

Nursing homes: Residents who are colonized or infected with *C. auris* should be housed in single rooms when available and placed on contact precautions. Residents do not need to be restricted to their rooms, but they should perform hand hygiene before exiting their rooms. If residents colonized or infected with *C. auris* use shared equipment (e.g., physical therapy equipment, recreational resources), items that residents handle extensively should be cleaned and disinfected after use.

Highly functional nursing home residents without wounds or indwelling medical devices (e.g., urinary and intravenous catheters and gastrostomy tubes) who can perform hand hygiene might be at lower risk of transmitting *C. auris*. Facilities may consider relaxing the requirement for contact precautions for these residents. However, in these instances, healthcare personnel should still use gowns and gloves when performing tasks that put them at higher risk of contaminating their hands or clothing. These tasks include changing wound dressings and linens, and assisting with bathing, toileting, and dressing in the morning and evening.

Transfer: When patients are transferred to other healthcare facilities, receiving facilities should receive notification of *C. auris* infection or colonization and the level of precautions recommended. In addition, state or local health authorities and CDC should be consulted about the need for additional interventions to prevent transmission. ■

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we got word of this and heard that it was very difficult to contain [and] curtail, we immediately responded and went down to Colombia.”

Working with investigators from the Instituto Nacional de Salud, Colombia’s CDC equivalent, Armstrong and colleagues visited four hospitals in three different cities. They identified 40 cases of *C. auris*, and more than half of them died. The in-hospital mortality rate was 56%. Forty-five percent of patients were infants. All patients had a central venous catheter, two-thirds had recent surgery, and half received parenteral nutrition during their stay, she reported.⁴ *C. auris* was isolated from 44 (14%) of 325 environmental samples, including some from rooms that had not had a case-patient present for up to six months. Of the six patients sampled, *C. auris* was cultured from either the groin or axilla of four.

Another troubling finding was that two nurses’ hands yielded *C. auris*, suggesting the route of transmission was transient colonization from other patients or equipment and environmental surfaces. Nine (23%) of 40 isolates were resistant to fluconazole and seven (18%) of 40 were resistant to amphotericin B. All isolates were highly related by whole genome sequencing.

“In Colombia, we were able to establish key fundamental pieces of information about this new emerging fungus,” Armstrong says. “Those tell us that we really need to be careful about basic things like hand hygiene, making sure people that are touching one person that might have this fungus on them aren’t going on and touching someone [else] to potentially spread it. I think there’s probably more than one reservoir within the healthcare setting.”

First reported in 2009 in Japan, *C. auris* has now been identified in

other parts of Asia, Africa, South America, and the United Kingdom.

“This fungus has now been reported in over a dozen countries worldwide,” Armstrong says. “One [concern] is that it’s affecting vulnerable populations. So, whether that be neonates, people in long-term care facilities, ICUs, or those that are already sick and may be receiving treatment for cancer — this infection can kill at very high rates.”

Unanswered Questions

At present, there are still more unknowns than knowns about *C. auris*, including whether it may spread in communities.

“We have a laundry list of questions we want to answer about this particular organism,” she says. “We’re working our way through them based on what we think are of the utmost priority and those that can impact the most, and save the most lives. As far as how it came into the healthcare system, that’s really a question of, ‘Is this something that exists in the community?’ That’s a question that we’re still trying to answer. Is this something, like other multidrug-resistant organisms, that does exist in the community and we’re just seeing it when people get sick from it in the healthcare setting? We don’t have a good answer to that quite yet.”

In addition to being multidrug-resistant, the emerging pathogen also is difficult to identify with standard laboratory methods, which can result in inappropriate treatment. With healthcare outbreaks a clear threat, rapid identification of *C. auris* in a hospitalized patient is critical to prevent subsequent transmission, the CDC emphasizes.⁵ The range of infections includes bloodstream,

wound, and ear. Concerning the latter, the “auris” name comes from the Latin word for “ear.”

According to the CDC, risk factors include recent surgery, diabetes, broad-spectrum antibiotic and antifungal use, and central venous catheter placement. While the sporadic outbreaks thus far certainly underscore the emergence of *C. auris*, a recent commentary on the new pathogen did not mince words on the ultimate threat.

“The fear is that biologic and epidemiologic factors are aligned for more extensive, worldwide emergence and/or dissemination of *C. auris* infections,” the authors warned.⁶ “...If events come together, we could witness the fungal counterpart to the worldwide expansion of carbapenem-resistant Enterobacteriaceae (CRE).”

Two scenarios — which are not necessarily mutually exclusive — could result in a major global public health problem, they explained. On the one hand, various *C. auris* strains, particularly those resistant to antifungal drugs, could continue to emerge independently and spread clonally, they noted. On the other, in perhaps a more concerning scenario, a single predominant strain of multidrug-resistant *C. auris* could emerge, which is somewhat analogous to the virulent NAP1 strain that has made *C. diff* so difficult to control.

“Growing cohorts of colonized and infected patients in countries with large populations and far-reaching international diasporas attest to [this] feasibility,” the authors noted. “In troubling publications from India, *C. auris* already accounted for [more than] 5% of candidemia in a national survey of ICUs, and as much as 30% of candidemia at individual hospitals. Other properties of *C. auris* may contribute to this perfect storm, including difficulties

in timely and definitive identification by commonly used commercial methods, intrinsic virulence ... [and] the ability to cause lengthy outbreaks and possibly persist within hospital environments.”

While the use and overuse of antifungal agents may have selected out drug-resistant *C. auris* strains — the classic paradigm for antibiotic resistance — something else seems to be going on, the authors concluded.

“Antifungal selection is unlikely to be the sole determinant,” the note. “It is conceivable that changes to *C. auris*’ ecological niches have brought the fungus into greater contact with susceptible humans.” ■

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Mysterious Paralysis Cases Continue in Children

Recent cases more severe, striking younger patients

A cryptic polio-like illness of unknown etiology is increasing, causing more severe symptoms in younger patients than when it first emerged in 2014, a CDC investigator reports.

After a decline in cases in 2015, there was more than a four-fold increase last year, including patients that presented with altered mental status and needed mechanical ventilation.

“Acute flaccid myelitis (AFM) is characterized by a sudden onset of a limb weakness, meaning an arm or a leg may lose strength or may be difficult to move,” says **Tracy Ayers**, PhD, an epidemiologist in the CDC Epidemic Intelligence Service. “Sometimes there’s facial drooping, sometimes there’s difficulty swallowing.”

The AFM syndrome emerged in 2014 in the U.S. in conjunction with an outbreak of Enterovirus D68 (EV-D68), which was

initially strongly suspected as the infectious etiology. However, EV-D68 has been identified in some cases of AFM, but is not present in others with identical symptoms, says Ayers, who presented the investigation recently in Atlanta at the annual EIS Conference.

“EV-D68 specifically is one of the many enteroviruses that we tested for,” Ayers says. “A portion of the specimens do test positive for EV-D68, but we also have a portion that test positive for other enteroviruses, and a large portion that don’t testify positive for any of those. I think at this time it’s inconclusive what is the definitive cause. But we will continue to look at EV-D68, as well as many other enteroviruses. We’re thinking about things that are maybe non-infectious as well.”

The investigation has taken on a sense of urgency because more recent cases are striking

younger children with more severe clinical presentation. Ayers and co-investigators examined a cluster of cases in children last year in Arizona.

“I was able to speak to some of the parents of some of the cases and interview them,” she says. “The idea was to explore with open-ended questions so we could learn as much as possible. They also recounted the onset of illness because this is such a new disease for us. So [we are] just learning how it progresses.”

‘The Bed Hurt’

One parent said her daughter felt fine during the day, gradually began feeling weak and ill, and by bedtime that evening had become hypersensitive and could not touch anything without experiencing pain, Ayers says.

“By the time it came time to go to bed, the bed hurt,” she says. “Everything hurt to touch. She couldn’t touch anything. So the mother put her in the bathtub because that felt better to have the water on her skin. At that point, she lost even more muscle tone and her head went a little floppy as well. So the mother was holding her in the bathtub, very scared, as you can imagine as a parent and not knowing what to do. That’s when she immediately took her to the emergency room. That’s often how these cases happen. They’re detected at the point of paralysis and taken to the emergency room.”

When Ayers examined the child two weeks later, she was regaining a little bit of strength in her upper arms and was engaged in physical therapy.

“Unfortunately, she was only one case out of 134 for 2016,” she says. “We’ve tested for over 250 different organisms that potentially could be the cause of this. We haven’t found a consistent organism causing this at this point. So we’ve expanded a lot of our laboratory testing now.”

Since the condition emerged, some cases have fully recovered and others remain at least partially symptomatic. No deaths have been attributed to AFM.

“We don’t know what the long-term outcomes are,” Ayers says. “There are very few cases and it’s brand new. We’re also working very closely with our state and public health partners because what we really want to do is make sure we [raise] awareness in the forefront of all clinicians’ minds. [We need to make sure] they’re reporting and suspecting AFM [and] collecting specimens as early as possible. It is a rare disease, but it’s such a severe one that we need as much

information as possible so we can learn more about what may be causing this and can prevent [future cases in] other families.”

Not Related to Zika

In a CDC review, confirmed cases were defined as acute flaccid limb weakness and spinal cord gray matter lesions on MRI. A total of 311 confirmed AFM cases were reported between August 2014 and October 2016. Compared to the first cases in 2014, those confirmed in 2016 had a lower median age (5 vs. 7 years), were more likely to present with altered mental status, (26% vs. 11%), have more than two limbs affected (48% vs. 32%), and require mechanical ventilation (33% vs. 20%), Ayers and colleagues reported.¹

The first cluster of AFM cases occurred in Denver in August 2014.² Earlier in 2014, California clinicians had noted an excessive number of acute flaccid paralysis cases in children.³ The CDC issued a health advisory and began active surveillance for AFM cases on Sept. 21, 2014.

Just to clarify, the current AFM syndrome is not caused by the polio virus and it emerged before Zika, which has complicated things because it produces a similar paralytic condition called Guillain-Barré Syndrome.

“There are different parts your spinal cord [connected] to the nerve junction in your muscles that can cause paralysis,” Ayers says. “And Guillain-Barré is one where at the nerves, the demyelination happens on its way to your muscle, and you can get paralysis that way. What we’re looking at for acute flaccid myelitis, very

specifically, is the infection is happening in the spinal cord.”

Another investigation at the meeting established a strong link between GBS and Zika infection in an investigation in Puerto Rico. During local Zika virus transmission in 2016, the Puerto Rico Department of Health reported 66 GBS cases with laboratory evidence of Zika infection. That essentially doubled the typical GBS annual rate of about 60 cases to 120 with the addition of the Zika-related cases.⁴

“It’s important to remember that Guillain-Barré is a post-infectious autoimmune disorder,” says **Emilio Dirlikov**, MD, the GBS team lead for the CDC’s Zika response in Puerto Rico. “It can be caused by Zika — attributed to Zika virus, but there are many other triggers, including bacteria and viruses. So, for our surveillance system, under the Zika virus response, we asked providers to report any case that had a suspicion of GBS.” ■

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Wild, Wild West: Clinic Outbreak Breaks Rules

Seventeen oncology patients infected, three die

How egregious were the infection control violations in an outbreak in a New York City outpatient oncology clinic? Three patients died and investigators agreed it could have been much worse. The staggering array of breaks in basic practice prompted investigator **Joel Ackelsberg**, MD, MPH, to dub the outbreak “the wild, wild west.”

“It’s quite possible that this is a fairly common situation in all outpatient settings, let alone in oncology practices,” says Ackelsberg, an epidemiologist in the bureau of communicable disease at the New York City Department of Health and Mental Hygiene. “We heard about this outbreak because it was noticed in an ICU where two patients from the same provider were hospitalized at the same time. It was fortunate we heard about it. It was also fortunate that a more pathogenic and virulent [infection] wasn’t involved in this outbreak.”

Several investigators involved in the outbreak recently participated in a webinar held by the CDC. Among them was **Amber Vasquez**, MD, MPH, an EIS officer in the CDC division of healthcare quality promotion.

“The investigation began on May 24, 2016, when an infectious disease physician at hospital A notified the New York City Department of Health and Mental Hygiene of two cases of *Exophiala dermatitidis* bloodstream infections that occurred on May 14-15,” she says. “This prompted review of hospital A’s network laboratory to search for more cases. Two more were found. All four of these case patients had underlying cancer and

were receiving care from the same physician at an outpatient oncology clinic.”

The clinic physician reached out to patients to be tested, even if they had no symptoms, and on May 27 a fifth case was found of *E. dermatitidis*, a common environmental fungus, she says.

“It has been seen in prior healthcare-associated outbreaks, including an outbreak of neurologic infections resulting from steroid injections from a compounding pharmacy in 2002,” Vasquez says. “But infections with this fungus are quite rare, and generally affect the nervous or respiratory systems. Bloodstream infections are extremely rare.”

The CDC acted quickly, knowing that oncology patients are at high risk because they are immunosuppressed.

“They are on therapy as well as [having] their underlying cancer,” she says. “They can also be at increased risk of bloodstream infections due to the long-term presence of central venous catheters [CVCs], such as implanted port catheters and peripherally inserted central catheters.”

The outbreak occurred at a small, independently managed clinic, unaffiliated with any hospital. In addition to the physician, the clinic had a nurse, a phlebotomist, and a few staff running the front desk.

“They do medical evaluations and follow-up visits, phlebotomies, and infuse chemotherapy,” she says. “Patients often use Hospital A, a nearby but separate facility for select services such as inpatient admission, or procedures like port placement.”

After the first cases were discovered

in the hospital, the CDC conducted a thorough look-back investigation that included current, former, and deceased patients at the clinic.

“Since the fifth patient had no symptoms and was only found because of a surveillance blood culture, we asked all patients with a CVC or who had received IV medication at the clinic to have surveillance blood cultures drawn,” she says. “Review of the clinic records revealed an additional case from March who had been seen at a hospital out of state. This patient was infected with another type of fungus called *Rhodotorula mucilaginosa*, which is also a common environmental yeast.”

Ultimately, a total of 17 cases were identified, primarily infected with *E. dermatitidis*. None of the deceased patients had evidence of infections. All 17 case patients had an underlying cancer malignancy, including 15 with solid organ disease.

“All of the case patients had a CVC present, and nearly all of those were port catheters,” Vasquez says. “All 17 case patients were hospitalized for CVC removal and to initiate antifungal therapy. This included 12 asymptomatic patients.”

The 90-day mortality rate was 18%, with three of the 17 patients dying, respectively, at 10 days, 74 days, and 78 days after the diagnosis.

“All of the cases were exposed to a compounded IV flush solution that was used to flush CVCs,” she says.

Median flushes for cases were 12, compared to four for non-cases, suggesting a dose-response relationship. A further review of the records found all patients had been exposed to the same bag of flush solution, which was drawn in advance

and used over a prolonged period. The bag was no longer available for culturing, but the epidemiological evidence was compelling.

“This was a solution compounded at the clinic by taking a 1-liter bag of normal saline and adding small amounts of two antibiotics and a blood thinner to it,” Vasquez says. “It was stored in a refrigerator and accessed multiple times a day with individual 10 ml syringes drawn from the bag over a four- to eight-week period until it was depleted. This was a highly unusual practice.”

The compounding was performed by a clinic nurse who had no pharmaceutical training nor performance assessment, she says. In addition, no pharmacist or pharmacist-trained staff were providing supervision. “For compounding the flush, the nurse had handwritten notes she used for reference,” she says.

The compounding was performed under a biological safety cabinet, which is intended to protect healthcare workers and the product being created.

“There were potentially contaminated materials in the critical sterile area such the outside plastic coverings of saline bags and the use of non-sterile gloves,” she says. Adding considerable insult to this series of injuries, the safety cabinet had not been inspected since 2014, when it was rejected for failing to meet adequate air flow requirements. The rejection notice was still on the hood, she says.

Procedures in Question

What else happened? The better question might be what didn't, as Vasquez went through a damning comparison and contrast between

CDC recommended practices and those being performed at the clinic.

For example, the CDC recommends that outpatient clinics develop written infection control and prevention policies and procedures based on guidelines, regulations, and standards. In addition, healthcare personnel should be trained in infection control on hire and annually thereafter.

“No formal or written policies or procedures were found at the clinic. Nor could we find an individual designated to enforce infection control standards,” she says. “Only one staff member had reportedly received infection control training four years prior, but no documentation could be provided.”

The CDC recommends that medications should be drawn in a designated “clean” medication area, and prefilling and storing batch-prepared syringes should be avoided.

“No designated clean medication area existed and IV medications were in multiple areas of the clinic, including in the lab area and patient rooms,” she says. “In the clinic, batches of IV flush syringes were being prepared every morning based on the number of patients scheduled that day. And this was recurring for weeks at a time with repeated entry allowing for more opportunities for potentially contaminating solutions.”

In addition, the CDC recommends that medications that require refrigeration be stored in a dedicated, labeled refrigerator. Medications should always be discarded according to the manufacturer's expiration date, even if not opened.

“The IV flush solution bag and

syringes were stored in a refrigerator that was also used for the occasional storage of staff food items,” she says. The expiration date “is the final day that the manufacture guarantees full potency and safety of a medication. But we found 39 vials of expired medications at clinic A. Some had been expired for years, but it is unclear how many may have been in use.”

Failed Awareness

Thus, in addition to the substandard compounding of the IV flush solution and prolonged storage which allowed repeated re-entry into the bag, there was a profound absence of an infection control culture.

“Most important was a lack of awareness in basic infection control and prevention practices,” Vasquez says. “There was a failure to be aware of and meet minimum standards for infection control and patient safety.”

Public health officials shut down the clinic for several months, allowing it to be reopened only after thorough evidence of infection control training and establishment of proper policies and protocols. Compounding is no longer conducted on site.

Similar challenges “exist across many outpatient settings, such as pain management and orthopedic clinics, where injections often occur,” she says. “There are likely many more outpatient facilities performing similar medication and injection services. Few outpatient healthcare facilities are licensed or accredited. As a result, many facilities are opened and operated without being held to minimum safety standards for infection control

or other aspects of patient care.”

To use Ackelsberg’s analogy, patients seeking care at such clinics may run a risk akin to walking into a bar in the old west.

“It’s unclear to what extent the comprehensive guidelines developed by the CDC have actually penetrated into the ongoing practice of ambulatory

care medicine in general, and in oncology specifically,” he says. “I think it is a cautionary tale. There is probably more of this going on.” ■

Drugs, Death, and Infectious Diseases

A surveillance artifact is uncovered in Minnesota

The intersection of the national opioid epidemic and infection control has reached some strange and critical crossroads, from drug-diverting healthcare workers infecting patients to addicted admissions infecting themselves by injecting through their IV lines. Now, we have another twist: the distinct possibility that infectious diseases could be masking some of the national death toll of opioids.

Victoria Hall, MD, a CDC epidemic intelligence officer at the Minnesota Department of Health, described her findings recently in Atlanta at the annual EIS conference.

“In early spring, we were notified of an unexplained death — a middle-aged man who died suddenly at home,” she says. “Two days prior, he had seemed ill to his family, but he didn’t want to go to the hospital. He was also slurring his words some. He was on long-term opioid therapy for some back pain and his family was a little bit concerned that he was abusing his medication.”

On autopsy, however, the medical examiner listed the cause of death as pneumonia, and it was subsequently referred to the health department’s unexplained deaths group.

“Further testing diagnosed an influenza pneumonia, but also detected a toxic level of opioids in his system,” Hall says. “[Again], on the death certificate, it only listed pneumonia

and listed no mention of opioids. So this death wasn’t counted in the state opioid surveillance death system.”

The case was detected because of the Minnesota Department of Health’s Unexplained Deaths and Critical Illness of Possible Infectious Etiology (UNEX), which has conducted surveillance since 1995.

“This was started by CDC in many states,” she says. “Today, Minnesota is the only state that has maintained the program. It was developed to constantly be on the lookout for these new and emerging health threats, particularly infectious diseases. It takes cases that have no clear explanation for deaths and looks further into it. It helps facilitate more testing to try to find answers, and try to find any new diseases that might be emerging.”

What also is emerging is a national opioid epidemic that the CDC estimates causes some 90 overdoses every day. It turns out, that may be an underestimate.

The Nexus

“[UNEX] has also allowed us to look into the opioid epidemic from an infectious disease standpoint,” Hall says. “We know that deaths involving infectious diseases like pneumonia or endocarditis can be complicated if there are opioids in the system. Opioids at therapeutic

or higher than therapeutic levels could impact the immune system. It actually makes your immune cells less effective at fighting off illness. They are also sedatives, so they have side effects such as a decrease in your breathing. [That] makes you less prone to cough, makes your breathing more shallow, and makes it easier for something like a pneumonia to really set in.”

Hall and co-investigators reviewed deaths detected through UNEX as well as opioid use during 2006–2015.¹ Fifty-nine (3.5%) of 1,676 UNEX deaths had evidence of opioid use. Twenty-two deaths involved toxic opioid levels, but lacked correct ICD-10 codes to be reported by statewide opioid death surveillance. Thirty-two of 59 UNEX deaths with opioid use had pneumonia. A pathogen was identified in 20 (63%) pneumonia cases, including *Streptococcus pneumoniae* and *Haemophilus influenza A*. “There’s no national standardization for how to fill out a death certificate,” she says. “We found that if you have a really profound infectious disease, like really bad pneumonia, that may be the only thing written on the death certificate. It’s not going to be picked up in opioid surveillance, which is quite concerning because it means that the epidemic, which is already quite severe, could potentially be even

worse.” Beyond the numbers, there may be other aspects of both opioids and infectious diseases that can be revealed by studying their nexus.

“We found a lot of suggestions of interactions between the two. Opioids may make you more prone to get infectious diseases, but if you have a really severe infectious disease, you are [also] more prone to opioid-related illness or deaths,”

Hall says. “This is especially true in pneumonia cases where even at normally prescribed and at overdosed levels, opioids seem to be playing a big role in illness. Understanding how opioid use and the infectious diseases like pneumonia interact with each other might better inform our future guidance for clinicians. So we can handle these cases while people are still alive and not catch them

through a system like ours.” ■

REFERENCE

1. Hall V, Lynfield R, Wright N, et al. Deaths Associated with Opioid Use and Possible Infectious Disease Etiologies Among Persons in the Unexplained Death (UNEX) Surveillance System — Minnesota, 2006–2015. CDC EIS Conference. Atlanta, April 24–27, 2017.

First Hep A Transmission by Transplant

Three nurses exposed while treating patient

Though hepatitis A virus (HAV) has spread via blood transfusion, the virus had never transmitted from a transplant patient. Now, through a circuitous chain of events, it has. Indeed, HAV spread from an organ donor to the transplant recipient, and then to three nurses providing post-transplant care, the CDC reports.¹

The investigation began in August 2015 when two home healthcare workers in Texas were diagnosed with hepatitis A, which causes a range of symptoms from diarrhea, nausea, abdominal and joint pain, and fever. The nurses were not vaccinated for HAV.

“Hepatitis A is a reportable disease, so two separate local health departments in Texas received notifications of these two separate nurses’ infections and that were kind of clustered in time,” says **Monique A. Foster**, MD, MPH, the lead author of the investigation and a medical epidemiologist at the CDC. “It was then noticed that they worked for the same home health company.”

They cared for one patient in common, a seven-year-old who underwent liver, small bowel, and pancreas transplantation. The transplant

patient had been previously immunized for HAV, but was in an immune-compromised state that must have undermined vaccine efficacy.

“The only thing they had in common was the same patient,” Foster says. “So initially, when the investigation started, we thought maybe one of the parents [of the transplant patient were infected]. We initially didn’t think that the HAV came from the patient because she had been previously vaccinated. But when we did the laboratory testing we found out that she was, indeed, the source of the nurses’ infections. The index case spread it to all three nurses — the home health nurses, and a nurse who took care of the patient in the hospital.”

The hospital nurse developed jaundice, diarrhea, and joint pain, and was hospitalized. HAV infection was diagnosed by serologic testing, and this nurse also had not received hepatitis A vaccination.

“[That nurse] was hospitalized briefly and that is not uncommon with hepatitis A,” Foster says. “About 20% of people will be hospitalized when they are infected. It’s a very acute illness. It’s short, but older people tend to

have a worse course [of infection]. Anyone who has any underlying liver disease or other diseases can end of being hospitalized. Thankfully, no one died. Sometimes in large hepatitis A outbreaks, there will be one or two deaths.”

CDC: No Changes to Guidance

Though none of the nurses were vaccinated for HAV and one was ill enough to be hospitalized, the outbreak does not warrant changing current employee health recommendations, the CDC concluded.

“We don’t recommend universal vaccination for healthcare workers because nosocomial spread of hepatitis A is incredibly rare,” says Foster. “If someone is symptomatic enough to be hospitalized [with HAV] it’s usually known, and healthcare workers are pretty adherent to wearing gloves and other precautions that would prevent spread of a fecal-oral pathogen.”

Also, the home health nurses were spending 12 hours per shift inside the patient’s home, where they ate meals and shared space with the

patient's family, the CDC reported.

"Studies conducted before childhood vaccine was universal show that the longer you spent time with someone with hepatitis A, the more likely you are to get infected," Foster says. "The nurses from the home health company definitely would be considered, from our standpoint, as household contacts. That is why we recommend post-exposure prophylaxis [PEP] with hepatitis A vaccine for any household contact of someone who has been diagnosed with HAV."

While contacts of the nurses received PEP vaccination, the health-care workers had to ride out the infection until all fully recovered.

"We only recommend PEP for people who are exposed to hepatitis A, not for those who already have it," she says. "You basically have to wait it out. There is really no medication or intervention we can do."

Care for the organ recipient provided by all three nurses included exposures to watery feces while changing diapers and ostomy bags.

"So even if the nurses were adhering to perfect hand hygiene, it is really hard not to become infected," Foster says. "I'm sure the nurses were involved in changing her stoma bag and things like that, where they would come into contact with fecal materials."

It was later discovered that the organ donor — an eight-year-old who died in a car accident — had not been immunized and had acute HAV infection at the time of death.

"We were able to get a specimen from her donor," Foster says. "And for the donor to end up positive was also surprising. In an acute illness, the donor would have only been infectious for a few weeks. To have died in a car accident at the same time that they were infec-

tious with HAV — which led to the recipient getting it — is all kind of a one-in-a-million type of thing."

Vaccine Uptake Low

Specimens from the nurses, the recipient, and the donor contained genetically identical HAV, showing that the virus was transmitted to the recipient through the transplanted organs. Vaccination of the organ donor might have prevented the subsequent chain of infections.

"Unfortunately, the data that we have show that HAV vaccine — even though it has been recommended universally as part of childhood vaccination for the last 20 years — still has pretty low uptake compared to the other childhood vaccines," Foster says. "So only around 53% of children age 15 to 35 months — who should have received both doses of HAV vaccine at that age — have actually received two doses."

However, no screening tests for HAV infection are required for blood, organ, or tissue donation in the United States. Because of the low U.S. incidence of HAV infection and typically brief self-limiting course of disease, an HAV-unvaccinated organ donor is unlikely to be acutely infected at death and transmit HAV to

a patient, the CDC reports.

Once the infection was detected, contact precautions were instituted during subsequent hospitalizations, the local health department recommended the patient's home health nurses be fully vaccinated against HAV, and no further transmissions to healthcare workers were detected during the subsequent eight months of continued viral shedding in the patient's feces.

"For someone to be infected that long is very surprising, as typical infection only lasts two to four weeks — and that is symptomatic infection," she says.

Additional recipients of the donor's heart and kidneys had evidence of immunity and probably were protected through previous HAV vaccination.

"The acute nature of HAV infection, low population HAV infection rate, and low rate of HAV infection-associated hospitalization make universal vaccination of healthcare workers and testing for patients impractical," the CDC concluded. ■

REFERENCE

1. Foster MA, Weil LM, Jin S, et al. Transmission of Hepatitis A Virus through Combined Liver–Small Intestine–Pancreas Transplantation. *Emerg Infect Dis* 2017 23;(4):590-596.

COMING IN FUTURE MONTHS

- Search for source of gram-negative BSIs in hemodialysis patients
- Cutting edge: What IPs need to know about new CDC surgical infection guidelines
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CME/CE QUESTIONS

1. Regarding removal of *Candida auris* from the environment, the CDC originally recommended cleaning rooms and environmental surfaces with an antifungal agent, but has upgraded that to advise use of a disinfectant that is EPA-approved to kill:

- A. *Clostridium difficile*
- B. Norovirus
- C. Carbapenem-resistant Enterobacteriaceae
- D. *Acinetobacter baumannii*

2. What was the in-hospital mortality rate for patients infected with *C. auris* in hospital outbreaks in Colombia?

- A. 22%
- B. 37%
- C. 46%
- D. 56%

3. Cases of acute flaccid myelitis in children have now been traced to non-infectious exposures to allergens that specifically affect the spine.

- A. True
- B. False

4. Which of the following infection control violations were found in an outbreak at an outpatient oncology clinic in New York City?

- A. 39 vials of expired medications
- B. Substandard compounding of an IV flush solution
- C. Drawing syringes in advance from same flush bag
- D. All of the above

CME/CE OBJECTIVES

Upon completion of this educational activity, participants should be able to:

1. Identify the clinical, legal, or educational issues encountered by infection preventionists and epidemiologists;
2. Describe the effect of infection control and prevention issues on nurses, hospitals, or the healthcare industry in general;
3. Cite solutions to the problems encountered by infection preventionists based on guidelines from the relevant regulatory authorities, and/or independent recommendations from clinicians at individual institutions.