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## CARBAPENEM-RESISTANT ENTEROBACTERIACEAE INFECTIONS ASSOCIATED WITH ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY PROCEDURES LOS ANGELES COUNTY, 2015

### OVERVIEW

Carbapenem-resistant Enterobacteriaceae (CRE) infections associated with endoscopic retrograde cholangiopancreatography (ERCP) procedures have been reported in the literature, and several outbreaks have been investigated. Previous reports have identified breaches in cleaning protocols, including bacterial contamination of difficult to clean areas [1]. Other investigations report finding no breach in cleaning and reprocessing protocols or defects in the implicated scopes [2]. The scope's design has been implicated as a source of potential contamination due to the complexity of the elevator channel and the difficulty in ensuring adequate cleaning and disinfection [3].

In 2015, the Los Angeles County Department of Public Health (LAC DPH) Acute Communicable Disease Control (ACDC) program investigated three outbreaks of ERCP associated multidrug resistant organism (MDRO) infections at three separate hospitals. Each hospital performs a high volume of ERCP procedures, serves as referral centers for other hospitals, and often sees medically complex, high-risk patients.

### SUMMARY OF INVESTIGATIONS

#### Hospital A

In January 2015, the hospital infection preventionist (IP) notified ACDC of a cluster of patients who were carbapenem-resistant *Klebsiella pneumoniae* (CRKP) culture positive after undergoing an ERCP procedure. In mid-December 2014, an infectious disease physician alerted Infection Prevention and Control (IPC) to an unusual case of CRKP bacteremia in a patient shortly after undergoing ERCP. An investigation was initiated by the IPC, who requested a list of all 2014 CRE isolates identified by the laboratory. The laboratory identified 33 CRE positive patients in 2014, of which 23 were CRKP. Hospital A staff conducted a comprehensive investigation including extensive chart review of each case to identify potential risk factors, room locations, and IPC direct observation of duodenoscope reprocessing. The microbiology laboratory did further molecular testing on a subset of the CRKP isolates to determine relatedness. Molecular results were reviewed by IPC and further investigation was performed to determine the point source. Multiplex real-time PCR assay (rtPCR), which was used to detect carbapenemases, was negative for several CRKP.

A total of 15 patients met the case definition. A case was defined as a patient who was CRKP culture positive, infected or colonized at any site, who had an ERCP procedure between October 2014 and January 2015. Of these cases, three died during their hospitalization.

Initially, eight patients met the case definition, with clinical culture positive sites including blood (n=4), and abdominal sources including aspirate, drainage, or abscess (n=4). Seven isolates had identical sensitivity patterns and were resistant to carbapenems, aminoglycosides, penicillins, cephalosporins, and



fluoroquinolones and susceptible to colistin. One multiplex negative CRKP isolate underwent whole genome sequencing which identified the OXA-232 carbapenemase. Additional molecular testing by repetitive sequence-based polymerase chain reaction (repPCR) and high resolution melt analysis (HRM) was conducted by Hospital A's laboratory on CRE isolates from 17 patients in 2014 to determine relatedness. The unique carbapenemase OXA-232 strain was identified in CRKP isolates from ERCP-related patients (n=8). RepPCR and HRM results showed OXA-232 strains from all cases to be almost identical. When focusing on the strains that were highly related to each other, the only commonality between patients was ERCP during their hospitalization.

An index patient who was CRKP positive prior to their ERCP procedures in October 2014 was identified. This patient underwent multiple procedures with two duodenoscopes (duodenoscope 1 and duodenoscope 2). A total of 14 patients had subsequent ERCP exposure with duodenoscope 1; three additional patients had subsequent exposure to duodenoscope 2. There were no other common exposures identified among OXA-232 positive patients.

Once ERCP with duodenoscopes 1 and 2 was established as a risk factor for transmission of CRKP, patient notification was initiated by Hospital A. One hundred eighty-six (186) patients had ERCP with the implicated duodenoscopes between October 2014 and January 2015. Notification included phone calls and mailed letters informing of possible CRE exposure and offers to screen for CRE by rectal swab of all patients notified; 150 patients were screened, seven (5%) were positive for CRKP. Isolates from the surveillance cases were also identified as OXA-232.

Hospital A implemented many control measures including ceasing all ERCP procedures during the investigation, sequestering the two implicated duodenoscopes (1 and 2), assessing duodenoscope cleaning and disinfection process, culturing all seven adult duodenoscopes, reprocessing following manufacturer's guidelines, and sending duodenoscopes to a private company for additional ethylene oxide (EtO) gas sterilization. A Manufacturer and User Facility Device Experience report was submitted by Hospital A to the U.S. Food and Drug Administration (FDA). All seven duodenoscopes were cultured and all were negative for CRE.

A site visit was conducted by ACDC staff in February 2015, five days after the outbreak was reported. During this visit, duodenoscope cleaning and high level disinfection procedures were observed. Reprocessing was done by GI reprocessing technicians or GI registered nurses (RNs), both trained in reprocessing. Pre-cleaning was performed immediately after the procedure in the procedure room. The facility used an automated endoscope reprocessor. No breaches in technique to prevent infections were observed. Duodenoscopes were stored appropriately according to manufacturer instructions. Several consultations with the California Department of Public Health (CDPH), Centers for Disease Control and Prevention (CDC), and the FDA were conducted.



In late February 2015, ACDC sent an email to all acute care hospital IPs encouraging active surveillance for CRE infections following ERCP procedures, including a retrospective review. Additional clusters were identified and reported to LAC DPH.

### **Hospital B**

In February 2015, the director of IPC at Hospital B notified ACDC of four patients with CRKP infections since September 2014 following ERCP in their facility. In response to recent media attention surrounding the investigation at Hospital A, Hospital B initiated a review of CRE infections following ERCP in their facility and identified the four patients. A case was defined as a patient who was CRKP positive from any site after ERCP at Hospital B. IPC conducted a comprehensive review of patient medical records, ERCP procedures and microbiology review for other CRKP positive patients who may have undergone ERCP.

Five patients met the case definition. All cases underwent at least one ERCP procedure prior to their positive culture; three cases underwent two or more procedures prior to their positive culture. Four cases were CRKP culture positive in clinical specimens including blood (n=2) and bile (n=2); the fifth case was positive in a surveillance rectal swab tested after patient notification was initiated; two cases died.

IPC identified one duodenoscope as having been used by all cases prior to their positive culture. This duodenoscope was used frequently as it was preferred by the gastroenterologist who performed the larger volume of procedures at Hospital B. Reprocessing of the duodenoscopes was performed using an automated endoscope reprocessor.

Isolates for four cases were available for testing, including the case identified through surveillance. RepPCR performed by an outside laboratory identified two cases to be greater than 98% similar and 95% similarity among all four case isolates tested. Pulsed-field gel electrophoresis (PFGE) analysis performed at the LAC DPH Public Health Laboratory (PHL) on the initial three isolates available indicated that two cases were genetically indistinguishable. Isolates from all three cases were identified as genetically related.

Multiple control measures were implemented by the facility, including removing the implicated duodenoscope from use, postponing all elective ERCP procedures, and culturing of all duodenoscopes. Hospital B duodenoscopes were cultured twice using the CDC Interim Sampling Method for the Duodenoscope – Distal End and Biopsy Channel. The 10 scopes cultured were negative for CRE; all but two grew other organisms, including *Bacillus spp.* and coagulase negative Staph. In addition to culturing, Hospital B sequestered duodenoscopes for 48 hours after culture to ensure all samples were negative prior to further use, with the exception of urgent or emergent cases. Additional duodenoscopes were ordered to accommodate the 48 hour wait period after culture, and elective ERCPs resumed two weeks later. Apart from the use of the implicated duodenoscope in their ERCP procedures, no other common suspected source of infection was identified among the five cases.



IPC initiated patient notification for ERCP patients who were exposed to the implicated duodenoscope from August 2014 to February 2015. Notification letters were mailed to patients and included an FAQ on CRE and duodenoscopes as well as the number to a hotline that was established specifically for patients who were notified to call in with questions. Of the 67 patients notified, 34 (51%) requested rectal swab kits, and one patient tested CRKP positive.

ACDC conducted a site visit on February 2015, four days after notification by Hospital B, and observed the method used to reprocess duodenoscopes. No breaches in practices to prevent the spread of infections were noted. We reviewed infection control practices, scope reprocessing manuals, technician training and competency materials, and related policies and procedures. Several consultations with CDPH, CDC, and the FDA were conducted.

### **Hospital C**

In August 2015, ACDC was notified by IPC at Hospital C of three patients who became ill and were multi-drug resistant *Pseudomonas aeruginosa* (MDR-PA) culture positive in July 2015 following ERCP procedures in the facility. Hospital C initiated an ERCP surveillance program in May 2015 in response to two ERCP related MDRO outbreaks in other LAC facilities and identified three patients with blood cultures positive for MDR-PA after ERCP. ACDC notified the appropriate local health jurisdiction (LHJ) who led the investigation, with ACDC participating in a consultative role.

A case was defined as a patient who had received an ERCP procedure, inpatient or outpatient, at Hospital C between January 2013 and August 2015 who presented with a positive MDR-PA culture from any site within 90 days of ERCP. A comprehensive investigation was initiated by IPC staff, ACDC, and the LHJ, including review of ERCP procedure logs, medical records, administrative records, microbiology and culture results from patients, duodenoscopes, and environmental samples.

Sixteen patients met the case definition; eleven cases died. All cases had ERCP procedures performed between January 2013 and August 2015 with one or more of the three duodenoscopes linked to the outbreak. All cases were MDR-PA culture positive from at least one body site, including wound (n=4), blood (n=9), and other sites (4). Isolates were sent to the LAC DPH PHL for PFGE testing. Duodenoscopes were sent to CDC Environmental and Applied Microbiology Laboratory for testing.

A total of 41 MDR-PA isolates from 29 patients, three duodenoscopes, and one environmental site were sent for strain testing by PFGE at the LAC DPH PHL. Test results showed 16 case isolates and 8 duodenoscope isolates from three different scopes were identified as indistinguishable or closely related. One distinct MDR-PA strain was identified by molecular epidemiology. No commonalities other than ERCP procedure were identified among the 16 cases. Per the LHJ request, Hospital C sent the three epidemiologically linked duodenoscopes to the CDC Environmental and Applied Microbiology Laboratory for testing. Using the CDC Interim Duodenoscope Surveillance Protocol as well as more aggressive sampling techniques and sonication, many types of bacteria were identified, including *Pseudomonas*



*aeruginosa*, *Klebsiella pneumoniae*, *Citrobacter freundii*, and others. Sampled sites that demonstrated growth included the instrument channel, distal tip, and elevator.

Control measures recommended by ACDC and LHJ included removing the three epidemiologically linked duodenoscopes from service, double high-level disinfection, repairing and maintaining the scope storage room, monitoring and recording temperature and humidity, ceasing use of canned compressed air during drying, and discontinuing use of plastic scope covers during storage. Hospital C initiated periodic culturing of scopes in July 2015 in response to the outbreaks at Hospital A and B. During the outbreak, the recommendation was made to culture each scope after reprocessing. Once control measures were implemented, no further transmission was identified.

Patient notification was initiated at the recommendation of ACDC and LHJ. Eighty-eight patients who received an ERCP procedure with any duodenoscope from January 2015 to August 2015 were notified and offered testing. Fifteen patients requested testing, and none were positive for *Pseudomonas aeruginosa*. In addition, ACDC and the LHJ recommended Hospital C obtain consent for future ERCP procedures, inpatient and outpatient, including a verbal and written detailed review of the risks of infection and notification of the outbreak.

A site visit was conducted in August 2015, one day after notification by Hospital C, by ACDC, LHJ, and CDPH Licensing and Certification staff. Clinical, surveillance, and microbiology data was reviewed with Hospital C staff. Staff also observed duodenoscope reprocessing and storage. Immediate recommendations were made for control measures and patient notification. A second visit was made in mid-September 2015 to observe implementation of initial recommendations regarding storage and reprocessing procedures as well as to obtain environmental cultures. Several consultations with CDPH, CDC, and FDA were conducted.

## CONCLUSION

The epidemiology and lab analyses of these investigations suggest that the cause of these outbreaks is multifactorial, including that the complex design of the scope may impede effective cleaning, disinfection and reprocessing. In January 2016, the duodenoscope manufacturer initiated a recall of one scope model for replacement of the elevator mechanism [4]. In addition, several nationally recognized experts have recommended several options to enhanced reprocessing, including double high-level disinfection with periodic culturing of a sample of scopes and use of ethylene oxide sterilization after high-level disinfection [5]. The CDC, FDA, and CDPH provided guidance to hospitals and providers on duodenoscope reprocessing after ERCP. Professional associations that provide infection prevention and related information, e.g. the Association for Professionals in Infection Control (APIC) and the Society for Healthcare Epidemiology of America (SHEA) also provided reprocessing guidance.

Partnerships between hospitals performing ERCP procedures and LAC DPH are essential to ensuring optimal surveillance and coordination of prevention activities. The facilities experiencing these outbreaks were large, prestigious hospitals with robust infection prevention and control programs. Due to the design flaw of this instrument, hospitals could follow manufacturer guidelines and standard practices correctly



and still experience duodenoscope-related MDRO transmission. In addition, there may be other facilities with duodenoscope-related transmission of MDROs that may not have the expertise to conduct a complex investigation and implement effective prevention and control strategies. The involvement of LAC DPH in this issue is key to address these problems on a larger scale that will improve the safety of the patients these hospitals treat.

## REFERENCES

1. Wendorf KA, Kay M, Baliga C, et.al. Endoscopic Retrograde Cholangiopancreatography-Associated AmpC Escherichia coli Outbreak. *ICHE*. 2015;36(6):634-642
2. Epstein L, Hunter JC, Arwady MA, et.al. New Delhi Metallo- $\beta$ -Lactamase-Producing Carbapenem-Resistant Escherichia coli Associated with Exposure to Duodenoscopes. *JAMA*. 2014;312(14):1447-1455
3. Rutala WA, Weber DJ. ERCP Scopes:What Can We Do to Prevent Infections? *ICHE*. 2015;36(6):643-64
4. [http://medical.olympusamerica.com/sites/us/files/pdf/TJF-Q180V\\_reprocessing\\_compatible\\_materials\\_3.pdf](http://medical.olympusamerica.com/sites/us/files/pdf/TJF-Q180V_reprocessing_compatible_materials_3.pdf)
5. FDA Presentation "ERCP Scopes: What Can We Do To Prevent Infections?" William Rutala, Ph.D., MPH <http://www.fda.gov/downloads/AdvisoryCommittees/UCM447146.pdf> accessed October 5, 2016