Carbapenemase-Producing Enterobacteriaceae (CPE)
Where are we now?

Kasey Gambeta
February 21, 2019
IPAC PANA
Overview

• Provide an overview of the current epidemiology in Ontario
• Identify some essential IPAC considerations
• Discuss thoughts for the future
A Bit of Background
Sorting out the Acronyms

- Carbapenem-resistant organism (CRO)
- Carbapenemase-producing organism (CPO)
- Carbapenem-resistant Enterobacteriaceae (CRE)
- Carbapenemase-producing Enterobacteriaceae (CPE)
What are Carbapenemase Producing Enterobacteriaceae (CPE)?

- *Enterobacteriaceae* are a family of bacteria commonly found in the gastrointestinal tract
- CPEs are resistant to carbapenem antibiotics through the production of carbapenemase enzymes
- 16.5% risk of infection following colonization
- High rates of mortality

CPE Versus CPOs

<table>
<thead>
<tr>
<th>Classification</th>
<th>Enzyme</th>
<th>Most Common Bacteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Class A</td>
<td>KPC, SME, IMI, NMC, GES</td>
<td>Enterobacteriaceae and rarely pseudomonas</td>
</tr>
<tr>
<td>Class B (metallo-b-</td>
<td>NDM, IMP, VIM, GIM, SPM</td>
<td>P. aeruginosa</td>
</tr>
<tr>
<td>lactamases)</td>
<td></td>
<td>Enterobacteriaceae</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Acinetobacter spp.</td>
</tr>
<tr>
<td>Class D</td>
<td>OXA</td>
<td>Acinetobacter spp.</td>
</tr>
<tr>
<td></td>
<td>OXA-48</td>
<td>Enterobacteriaceae</td>
</tr>
</tbody>
</table>

As CPOs are increasing in numbers, they may require more focus

Compliments of Dr. Samir Patel
Testing for CPE

Step 1
• Susceptibility testing using meropenem or ertapenem to screen for presence of carbapenem resistance (e.g. broth microdilution, disk diffusion)
  • * PHO accepts specimens if there is a high MIC (minimum inhibitory concentration) – remains true during outbreaks and for point prevalences

Step 2
• If MIC is high, then perform phenotypic testing (identifies if the bacteria hydrolizes carbapenems) e.g. Rosco, CarbaNP testing
  • If positive, report out as “presence of carbapenemase activity”

Steps 3
• Refer the isolate for PCR testing for confirmation
  • Identifies the type of carbapenemase (e.g. KPC, NDM, OXA-48)
  • Final report: Positive for carbapenemase gene

PHO turn-around time: 4-5 days

Compliments of Dr. Samir Patel
The Short Life Span of Antibiotic Drugs

The Antibiotic Pipeline

- 9-15 that may provide a treatment for CPE
- However, at different phases of testing, only 1/5 make it through trials and may not be approved in Canada

Why are we Concerned?

• CPE can share the genes that cause antibiotic resistance with other bacteria
• Treatment options are limited
  • Last-line antibiotics may be required
• There is a high mortality rate associated with infections
• Patients/residents can remain colonized for prolonged periods of time
Reporting
It’s now Mandatory

• Revision to Health Protection and Promotion Act, 1990 (HPPA) includes CPE colonization or infection as a disease of public health significance (DOPHS)

• Previously voluntary reporting in Ontario (Dec. 2011-April 2018)
Resources: Surveillance and Reporting

- **Appendix A: Disease-specific chapter** – outlines epidemiology, prevention and control measures
- **Appendix B (Case definition)** – outlines case and outbreak definitions
Table Talk: Identification of a CPE Case

A 68 year old male, Mister C., is admitted to a hospital orthopedic unit on August 30, 2018 following a hip replacement surgery. During the admission assessment, the following was identified:

- Patient visited the surgical outpatient clinic in January 2018 and again two weeks ago
- Patient travelled to India in December 2017 to visit family
- Patient has Type 1 diabetes
- Patient has not previously been admitted to hospital

1. Does this patient have risk factors for CPE?
2. Should a specimen be collected to test for CPE? If so, what specimen would you collect?
Table Talk

You get a call from your lab that Mister C.’s rectal specimen is positive for a *Klebsiella pneumoniae* NDM-1 type CPE.

When checking the lab report, you notice that Mister C. actually had a rectal specimen collected in March 2018 during an outpatient visit, which grew *Klebsiella pneumoniae* NDM-1.

Do you need to report this infection to your public health unit (for PHUs: is iPHIS entry required)?
Two weeks later, Mister C. develops a surgical site infection and a specimen is sent to the lab. Your lab reports the specimen is positive for an *Escherichia coli* NDM-1.

Do you need to report this infection to your public health unit (for PHUs: is iPHIS entry required)?
Surveillance and Reporting: Sporadic Case Definition

• Laboratory confirmation of CPE by an Ontario microbiology laboratory.
• Both colonization detected from active screening and clinical infections are considered confirmed cases of CPE.

Note: The first positive isolate from any individual identified as colonized or infected with CPE is reportable. Subsequent positive isolates from the same patient are reportable only if the patient tests positive for a different CPE (i.e., different carbapenemase).

• Suspect Outbreak Definition
• Confirmed Outbreak Definition
Resources: Surveillance and Reporting

- CPE investigation tool
- iPHIS data entry user guide

https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/IDLandingPages/carbapenamase-producing-enterobacteriaceae.aspx
The Ontario Epidemiology
Summary of reported CPE cases by sex and age
May 1, 2018 to Jan 31, 2019

- 220 cases reported in 209 patients
- 18 cases associated with 6 outbreaks
- 202 sporadic cases

Source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2019/02/07].
Carbapenemase Producing *Enterobacteriaceae* (CPE) rates by public health unit, May 2018 to Nov 2018

Rate Range (per 100,000 population)
- 0.0
- 0.1 - 1.0
- 1.1 - 2.0
- 2.1 - 3.0
- 3.1 - 4.0

Health Unit Code
(Case Count, Rate)

Cases: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2018/12/03].
Ontario Population: Population Projection, 2016-2041, Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted: [2017/10/24].

PublicHealthOntario.ca
Total Unique CPE Cases Reported in Ontario

Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2019/02/19]
Infection versus Colonization
Percentage of CPE Cases

Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2019/02/19]
CPE by Type
Percentage of Cases

Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2019/02/19]
The Numbers Explained

• NDM - promiscuous

• OXA-48 – lower resistance levels
  • Rapid increase in numbers may be explained by two factors:
    • PHO has a low threshold level for testing OXA-48s (0.25 mg/L versus >2 recommended by CLSI), and is therefore more likely to identify them
    • Due to lower resistance levels, OXAs are more likely to be missed and transmit from person to person without recognition, until it reaches someone carrying bacteria with other resistance that creates a higher level carbapenemase

• VIM – sporadic cases without risk factors – very difficult to develop from antibiotic use so hard to identify where the cases are coming from
## CPE Risk Factors May to November 2018

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic illness/underlying medical condition</td>
<td>115</td>
<td>16</td>
<td>131</td>
<td>(88)</td>
</tr>
<tr>
<td>Hospitalization in Canada in the last 12 months</td>
<td>84</td>
<td>38</td>
<td>122</td>
<td>(69)</td>
</tr>
<tr>
<td>Med/surg procedure in Canada in the last 12 months – excluding endoscopic procedures</td>
<td>47</td>
<td>43</td>
<td>90</td>
<td>(52)</td>
</tr>
<tr>
<td>Travel outside Canada in the last 12 months</td>
<td>55</td>
<td>53</td>
<td>108</td>
<td>(51)</td>
</tr>
<tr>
<td>Other medical risk factors</td>
<td>41</td>
<td>40</td>
<td>81</td>
<td>(51)</td>
</tr>
<tr>
<td>Hospitalization outside of Canada in the last 12 months</td>
<td>31</td>
<td>67</td>
<td>98</td>
<td>(32)</td>
</tr>
<tr>
<td>ICU admission in Canada in the last 12 months</td>
<td>28</td>
<td>65</td>
<td>93</td>
<td>(30)</td>
</tr>
<tr>
<td>Previous colonization with CPE</td>
<td>19</td>
<td>48</td>
<td>67</td>
<td>(28)</td>
</tr>
<tr>
<td>Med/surg procedure outside of Canada in the last 12 months</td>
<td>19</td>
<td>62</td>
<td>81</td>
<td>(23)</td>
</tr>
<tr>
<td>Endoscopic procedure in Canada in the last 12 months</td>
<td>15</td>
<td>60</td>
<td>75</td>
<td>(20)</td>
</tr>
<tr>
<td>Other behavioural risk factors</td>
<td>9</td>
<td>48</td>
<td>57</td>
<td>(16)</td>
</tr>
<tr>
<td>Contact with confirmed case in the last 12 months</td>
<td>6</td>
<td>46</td>
<td>52</td>
<td>(12)</td>
</tr>
</tbody>
</table>

Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2018/12/03]
Risk Factors are not all Foreign!

- 160 total cases
- 55 reporting travel/hospitalization outside of Canada
- 53 reporting no travel outside of Canada
- Unknown for 52 cases
- At least 1/3 of cases have no foreign travel/hospitalization history
Infection Prevention and Control
CPE Transmission

• Colonized or infected patients/residents are the main reservoir for CPE (mainly found in the lower gastrointestinal tract)

• Transmission is likely via direct and indirect contact
CPE Screening

• Admission screening
  • Received health care outside of Canada
  • Known contact of a case
* Risk factors may change as CPE evolves
  • E.g. Travel to CPE endemic countries, those hospitalized in Canada

• Ensure your lab has the capacity to test for CPE and develop communication plan

• Specimens:
  • Rectal or stool
  • Urine, wound or exit sites may be indicated

Stakeholder Query

Should LTCHs be following PIDAC screening protocols for AROs?

• Although PIDAC Annex A appears to focus on acute care, it is actually guidance for all health care settings, risk factor screening is important for all health care settings
CPE Management and Prevention

• Routine Practices plus Contact Precautions for those that are CPE positive or have a risk factor
  • Acute Care
    • Gloves must be worn on entry to a patient’s room or bed space
    • Long-sleeved gown if skin or clothing will come in contact with the patient or their environment
  • Non-acute settings
    • Gloves and gown are required for activities that involve direct care
  • Visitors – PPE for direct care
  • Single room and toileting facilities
  • Minimize clutter

Interesting Study

• A model-based strategy to control the spread of Carbapenem-resistant *Enterobacteriaceae*: Simulate and Implement, 2016

• Estimate of health-care worker being colonized after having unprotected contact with a CPE case
  • 45% of opportunities were colonized
  • 10% when using glove and gown

• Estimate probability of a patient becoming colonized after contact with a HCW who did not conduct HH
  • 22% of volunteers hands became colonized

• Estimate of continued colonization after hand hygiene
  • No colonization detected

CPE Contact Investigation and Management

• Conduct full unit point prevalence if feasible
  OR
• Minimum - screen roommates and those patients exposed to the case

• Place contacts on precautions until CPE ruled out
• Discontinue precautions for those with risk factors:
  • Minimum 3 sets of specimens, different days
  • At least one taken 21 days after last exposure
  • Re-screen if ongoing transmission of CPE
• Screening of household contacts is not required, unless admitted to a health care facility
• Flag cases and contacts
Stakeholder FAQ

• Our lab is denying CPE point prevalence specimens that we send in.
  • Follow-up with private labs revealed that their policy requires facilities to notify the lab ahead of time if they are sending >5 specimens for CPE testing at one time – the testing must be approved by the microbiologist
Drains need Attention!

- Sinks have the potential to become contaminated with CPE
- Routine cleaning with particular attention to drains (sinks, showers)
  - Consider enhanced sink and drain cleaning
e.g. letting chemicals rest in pipes, flushing, steaming, brushing, etc.
- Sample procedure in PIDAC’s Environmental Cleaning for Infection Prevention and Control
- Consider sink testing upon discharge
- Avoid body fluid disposal in the sinks

Antimicrobial Stewardship in Long-Term Care

Antimicrobial Stewardship in Primary Care

• Series on shared decision making: Building the capacity of your patients to help make informed decisions regarding their need for antibiotics

• Four tools – ear, sore throat, sinus infection, bronchitis

Discontinuing Precautions

• For a positive case, contact precautions should remain in place for the duration of acute care hospitalization

When should we re-screen patients to identify ongoing colonization with CPE?

• There is currently no recommendation for when follow-up screening should occur or how often it should be repeated
• Decision must be made through discussion with members of the care team
Patient Discharge FAQ

What if a long term care home (LTCH) is not willing to accept a returning CPE patient back to their own LTCH? Any recommendations on how we can go about planning the discharge?
Table Talk

An Infection Control Professional from a long-term care home (LTCH) has called to ask you about a resident currently at your facility who will be returning to the LTCH. While at your facility, the patient developed CPE colonization.

They have never managed a CPE case before and she is looking for assurance on what she should do.

What would you consider?
Table Talk: Risk Factors for Transmission?

- Consider patient risk factors for transmission
  - Cognitive impairment or confusion
  - Ambulatory
  - Accommodation
  - Indwelling devices, wounds, incontinence
  - Dedicated personal hygiene products
  - Risk assessment prior to engagement in group activities, dining and communal spaces
- Risk factors other residents
- Education
- Refer to resources
  - PHO, PIDAC, PHU
CPE Outbreak Management

- Each facility should have an outbreak management policy
- Form an outbreak team
- Attempt to identify a source for the outbreak
- Conduct prevalence screens
- Consider closing a floor/unit
- Ensure that the laboratory is saving isolates
- Consider requesting assistance from the local Public Health Unit, PHO regional IPAC offices, or an academic Health Sciences Centre if there is a lack of resources to manage the outbreak
CPE Outbreak Management

• Sinks and drains
  • Testing
    • Speak to lab about specimen collection
  • Removal and replacement of the horizontal drainage system may be necessary to prevent ongoing transmission

• Chlorhexidine bathing

• Decolonization?


https://www.cdc.gov/infectioncontrol/guidelines/environmental/background/sampling.html#box15
CPE Outbreak Management

Should hospital staff be screened in any situation?

Routine staff screening is not recommended. Staff screening is recommended as a potential strategy where there is ongoing transmission, no other known source, and a staff member may be epidemiologically linked to new acquisitions

- Focus on particular staff members that may have an epidemiological link to new acquisitions
- If a staff member is positive, follow OHA communicable disease protocols
  - If there is a strong potential link to transmission, a case-by-case review of their work and the risks associated must be done
  - If the decision is made to keep the staff member working, there should be a focus on strict hand hygiene.

Resources

• Provincial Infectious Diseases Advisory Committee

Public Health Ontario Resources

- Information sheets for patients and staff
- CPE FAQs
- Sample screening form

https://www.publichealthontario.ca/en/BrowseByTopic/InfectiousDiseases/Pages/IDLandingPages/carbapenamase-producing-enterobacteriaceae.aspx

The Bottom Line

- Screening is essential to identify and manage those with risk factors.
- The epidemiology and risk factors of CPEs are evolving.
- Implementing and strictly adhering to IPAC strategies is essential.
- Consistent reporting is essential to track and understand the organism.
Future Thoughts

CRISPR

• Technology that is used to target foreign DNA and RNA
  • Examples of use: genetic engineering and gene regulation, record exposure to light, antibiotics, and viral infection or document internal molecular events in bacteria, treat cancer, etc.

• IPAC uses: phages (natural bacterial enemy) deliver CRISPR system into the genome of antibiotic resistant organisms

• The system destroys antibiotic resistant-conferring plasmids (re-sensitizes bacteria) and programs lytic phages to kill only antibiotic-resistant bacteria

• Potential for hospital surface sprays and hand sanitizers to facilitate the replacement of antibiotic-resistant organisms with sensitive ones

CPE and One Health

Aims to achieve optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment (WHO, 2019: https://www.cdc.gov/onehealth/index.html)

- 2018 systematic review of studies identifying CPE in wildlife, food-producing, and companion animals (68 studies)
- Livestock and seafood (49 studies)
  - VIM, KPC, NDM, OXA, IMP reported
  - Low prevalence in European countries
  - High prevalence in China (15% milks samples), Algeria (6% in milk, 26% in chickens), India (1-3% in piglets), Lebanon (2.5% in fowl)


CDC: https://www.cdc.gov/onehealth/domestic-activities/index.html
CPE and One Health

- Companion animals and wildlife (21 studies)
  - CPE isolated in USA, Algeria, Germany, France, Spain, China, Australia
  - Isolated in gulls, wild boar, cats, dogs, horses
- Transmission from animals to humans (2 studies)
  1. Identified 3/6 chicken farm workers in China were CRE positive
     - 2/3 were closely matched to tested animal samples
  2. Identified 4/30 poultry farm workers, and 1/19 veterinarians in Egyptian poultry farms carried a CRE - matched samples collected from poultry
- Retail seafood in Canada, 2016 Study
  - 8 (0.6%) of 1328 seafood samples positive for CPE – all from SE Asia


CDC: https://www.cdc.gov/onehealth/global-activities/index.html
PHO Regional IPAC Offices

• Central – ipaccentral@oahpp.ca
• East – ipaceast@oahpp.ca
• West – ipacwest@oahpp.ca
• Central West - ipaccentralwest@oahpp.ca
• North - ipacnorth@oahpp.ca
• General inquiries - ipac@oahpp.ca
Resources


Resources


Resources
