CRE – Carbapenem-Resistant *Enterobacteriaceae*

Epidemiology

Source: Human
Anatomical source: Stools, urine, skin, body fluids, secretions
Transmission
- Person-to-person (contact)
- Indirect: fomites

Incubation
- Undetermined, • follows colonization or asymptomatic infection
- Colonization may last 6 months

Complication: Sepsis
Death: up to 40-50%

Asymptomatic, Carriers

HEALTH CARE FACILITY ASSOCIATION
- 92% occur in patients with substantial exposures to HCF
- Reporting at least 1 case: 4% of acute care short stay, 18% of acute care long stay.
- 1% of *Enterobacteriaceae* cultured

HAI:
- **Surgical site infections (SSI),**
- **Blood stream infections (BSI) central line assoc. (CLABSI)**
- **HA pneumonias, Ventilator associated pneumonias (VAP)**
- **Urinary tract infections (UTI), catheter assoc. UTI (CAUTI),**
- **Wound infections**
- **Community infections**

Personal Risk Factors
- Severe underlying illness;
- High SOFA score
- ICU stay
- Diabetes
- Solid tumor

HCF related Risk Factors
- ICU stay
- Multiple HCF stays
- Wide spectrum antibioTx
- Tracheostomy
- Urinary cat insertion

Transmissible as long as microorganisms are present on secretions and excretions

Diagnosis

Microbiology
- ***Enterobacteriaceae*** *represent a large family of Gram-negative bacteria that includes genera s*uch as
  - Klebsiella, Escherichia, Enterobacter that may become carbapenem resistant,
  - Some *Enterobacteriaceae* have intrinsic resistance to imipenem: Morganella, Proteus, Providencia
  - Other *Enterobacteriaceae* include Salmonella, Shigella…
- **Carbepenem resistance (CR)** was uncommon before 2001,
  - Resistance due to production of **carbapenemase** (special β lactamase); a porin mutation that limits penetration ability of carbapenems; on transferable plasmids
  - First to spread was Klebsiella pneumonia carabapenemase (KPC),
  - Now *E.coli*, Enterobacter
  - Metallo-β-lactamases (MBLs), have become the more prevalent mechanisms for CRE. MBLs include New-Dehli (NDM), Verona Integron Encoded (VIM), imipenemase (IMP)
  - Associated with resistance to other antibiotics: Pan-resistant strains

Microbio Definition*: Enterobacteriaceae*
- Non-susceptible to doripenem, meropenem or imipenem AND
- Resistant to these 3rd generation cephalosporins: Ceftriaxone, cefotaxime, ceftazidime
- Ertapenem not yet included in definition

Table 1. Current CLSI Interpretive Criteria for Carbapenem Susceptibility for Enterobacteriaceae

	Current Breakpoints MIC (mcg/mL)		
Agent	Susceptible	Intermediate	Resistant
Doripenem	≤1	2	≥4
Ertapenem	≤0.5	1	≥2
Imipenem	≤1	2	≥4
Meropenem	≤1	2	≥4

CLSI: Clinical and Laboratory Standards Institute; MIC: minimum inhibitory concentration. Source: Reference 19.

Voluntary Report to LA health dept.

Lab Diagnosis
- **Culture to identify the genus and species**
- **Use MIC method to determine status of resistance**
- A **DNA microarray** enables detection of the most prevalent carbapenemases: NDM, VIM, KPC, OXA-48 and IMP and ESBLs SHV, TEM and CTX-M.

Treatment

Treatment 3 Options

1-Increase dose of carbapenem; risk of toxicity
2-Use a second-line antibiotic with Gram-negative activity for which resistance is not yet developed : colistin, tigecycline, gentamicin, fosfomycin but high toxicity
3- Combine first- and second-line antibiotics with the hope that synergistic interactions between antibiotics will lessen the need for extremely high antibiotic doses

Contact Precautions

Control

8 CORE MEASURES

1-Hand Hygiene
2-Contact Precautions
3-HCP Education
4-Minimize Use of Devices
5-Cohorting Infected Patients
6-Laboratory CRE Protocols
7-Antibiotics Stewardship
8-CRE Screening

CONTACT PRECAUTIONS (CP)

- Any patient colonized, infected, with history of col/inf
- Rectal carriage major risk for long term carriage
- Pre-emptive contact precautions for patients from facilities with CRE pending screening results
- Short term stay: Contact precautions for the duration of the stay

CONTACT PRECAUTIONS in LONG TERM FACILITIES

- Indications modified for LTCF
- Keep CP for high risk patients:
  - Patients totally dependent on HCP for activities of daily living
  - Ventilator dependent patients
  - Stool incontinent
  - Wound drainage difficult to control
- Others:
  - Relax CP,
  - Enforce Standard precautions

TRANSFERS (LA Rules)

- **The presence of CRE infection or colonization alone should not preclude the transfer of a patient from a facility to another (for example from an acute care to a long term care facility** .
- The source facility should ensure that the transporter and the receiving facility staff were notified.
- CP should be taken during the transfer
- The authority of the State Health Officer (or the Office of Public Health, his delegate) for communicable disease control is specified in Title 51:Public Health Sanitary Code; Part II. The Control of Diseases; §117. Disease Control Measures.

Specific measures are posted on DHH/OPH website under the title "Epidemiology Manual".

SURVEILLANCE

Review clinical cultures and antibiograms of K.peumo & *E.coli* to identify any presence of CRE; review archived results if not done previously

- If none: continue such surveillance,
- If CRE presence detected:
  - As community acquired: Collect culture on all suspected infections, request antibiograms
  - As Facility-Acquired: Carry out investigation to identify additional cases and units affected; survey and screening may be indicated
- Alert staff to report patients not responding to carbapenem treatment

SCREENING & POINT PREVALENCE SURVEY

- If review of clinical cultures is not sufficient to prevent CRE to be prevalent in a facility
- SCREENING is indicated to supplement clinical culture review
  - Start with epidemiologically linked patients,
    -patients with close contact
    -room mates
    -patients who have shared the same HCPs
  - Sites: rectum, peri-rectal area, wound, urine
- POINT PREVALENCE SURVEY:
  - May be a reasonable first step before deciding on systematic screening:
  - Screening in a one-time survey of all the patient in a ward /unit deemed at high risk,
  - If no important problem is identified, no follow-up is necessary
  - If the prevalence survey shows an important problem, follow up with ACTIVE SURVEILLANCE

ACTIVE SURVEILLANCE

- Culture all high risk patients regardless of their provenance
- Culture all epidemiologically-linked patients (see above description)
- Culture all patients coming from high risk facilities
- Culture all patients admitted to high risk units/wards (ICU, Long Term Acute Care)
- Do at admission, or if warranted regularly

ANTIBIOTIC STEWARDSHIP

- In addition to usual antibiotic stewardship measures
- Minimize use of class of antibiotics known to increase risk of CRE colonization: fluoroquinolones
- Restrict use of carbapenems

CHLORHEXIDINE BATHING

- Clorhexidine bathing (2%) or chlorhexidine wipes (2%) to bathe patients daily
- For high risk patients, for high risk units/wards