My Spidey Sense is Tingling

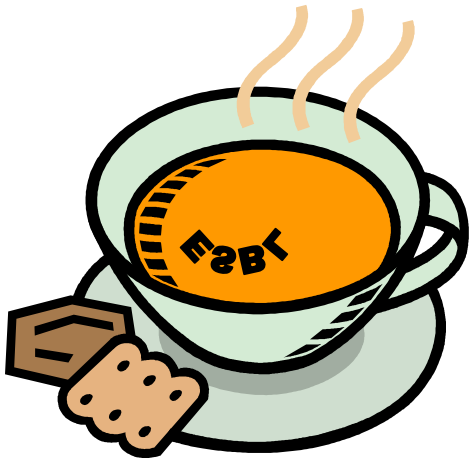
CHICA Manitoba Conference

June 1, 2012

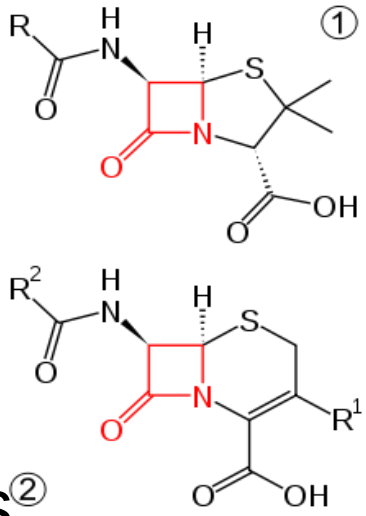
Infection Control Issues and Trends

- VRE outbreak
- C.difficile outbreaks
- New environmental treatments
  -hydrogen peroxide vapours
  - Copper covered furniture and equipment
- Antimicrobial stewardship programs

ESBL and CRGNB's
Alphabet soup or actual threat?



What are they?



- ESBL
  - Extended Spectrum Beta Lactamases
  - Possess enzymes that hydrolyze the beta-lactam ring
  - Confers resistance to all beta lactams: penicillins, cephalosporins and aztreonam
  - Inhibited by beta-lactamase inhibitors (eg. clavulanic acid)
  - Most are plasmid mediated (eg. TEM-1, SHV)

- Often also resistant to other classes, eg. aminoglycosides, fluoroquinolones, sulfonamides making them multi-drug resistant
- Predominantly in enterobacteriaceae, in particular *E. coli* and *Klebsiella pneumoniae*

- AmpC beta-lactamases
  - Chromosomes
  - Inducible in presence of beta-lactam antibiotics
  - Similar antibiotic profiles as ESBL
  - Found in *Enterobacter sp, Citrobacter fruendii, Morganella morganii, Serratia and Pseudomonas*

- Carbapenamase Resistant Gram Negative Bacteria (CRGNB)
  - Gram negative bacteria such as *E. Coli* and *Klebsielle Pneumoniae* which are resistant to Carbapenems (eg. meropenem, imipenem and ertapenem)
  - Most common is *Klebsiella pneumoniae* Carbapenemases (KPC) which contain the bla_{KPC} gene

- Metallo-beta-lactamases have been found since the 1960's but generally in non-pathogenic or infrequent pathogens such as stenotrophomonas and bacillus sp.
- VIM type seen mostly in *Pseudomonas* and *Acinetobacter sp*. ,
- New Delhi strain (NDM-1) which was mostly seen in *E.coli* and *K.pneumoniae*

Where did they come from?

- Bacteria are smarter then us
  - June 1964, ampicillin released
  - December 1964, first case of *E.coli* resistant to E.coli detected
  - September 1981- cefotaxime released
  - March 1982- first case of *Klebsiella* resistant to cefotaxime.

Risk Factors

- ESBL
  - ICU
  - Foreign bodies
  - Long hospitalization
  - Nursing home
- CRE
  - ICU
  - Foreign bodies
  - Long hospitalization
  - Organ/stem cell transplant
  - Nursing home

- Community acquired ESBL first reported in Canada, Spain and UK
- Often in UTI’s and resistant to all first line options
- Usually CTX-M, worldwide/cdn strain is ST 131

CRGNB

- First KPC reported in North Carolina in 2001
- Spread though eastern US and now in South America, Europe and China
- First 3 cases reported in Ottawa (2 were person to person transmission) 2008
- Also outbreak in Montreal 2009-2010, outbreak in ICU of 8 isolates initially

- NDM-1 first described in 2009 from Sweden (previously hospitalized in New Dehli), found in *Klebsiella* in the urine and *E.coli* in the stool
- Subsequent review in UK found 29 patients with NDM-1 gene in *K.pneumoniae* and *E.coli* strains of which 17 had travelled to Indian subcontinent

Where do they come from?

- ESBL
  - Food
  - Veterinary use
  - Overuse/misuse of antibiotics as outpatients
- NDM
  - Drinking water and sewage in New Dehli

How big of a problem are they?

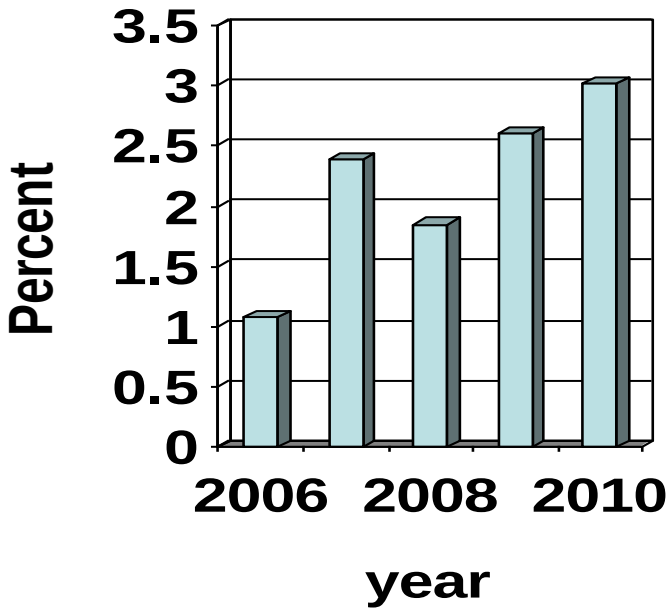
Canada

Study Year	Total ESBL-E.coli	Total ST-131	Rate
2007	53	26	49.1
2008	55	27	49.1
2009	47	25	53.2
2010	30	18	60
2011	46	33	71.7

Canada ESBL types

- CTX-M-15 for 33/46 (72%)
- CTX-M-27 for 7/46 (15%)
- CTX-M-14 for 3/46 (7%)
- rare SHV-12 and CTX-M-3.

SBH E.coli ESBL producers



CRGNB

- US
  - *Klebsiella pneumoniae* isolates, meropenem resistance was 0.6% in 2004, rose to 5.6% by 2008
  - 2007 data
    - *E. coli*, carbapenem resistance 4%
    - *K. pneumoniae* 10.8%

CRE- KPC

- 2002-2003 surveillance NYC
  - 9/602 *K. pneumoniae* with KPC gene
  - 2004, 20 more isolates
- 2010 reported in 36 states, Washington DC and Puerto Rico
- 2006- outbreak in Israel involving 8 hospitals and 5 chronic care centers

NDM-1

- Global
- Many with links to Indian subcontinent but also evidence of links to eastern European countries (Bosnia, Kosovo, Serbia)
  - Also spread to other GNB (*acinetobacter, vibrio, pseudomonas*)
  - Pakistan military- 27.1 % inpatients and 13.8% outpatients are carriers
  - Most NDM strains isolated in India were from community onset infections

- US
  - 2009-2011
    - 13 isolates of MBL containing enterobacteriaceae
    - 7/13 were NDM

CRGNB

- WRHA 2011
  - Only 1 carbapenamase (KPC) in *S.marcescens* imported from Montreal
  - 9 other carbapenem resistant isolates (*E.coli, Klebsiella and E.cloacae*)- not carbapenamases

Why are they important?

- ESBL
- Increased morbidity and mortality
  - Some studies showed higher mortality, mostly related to delayed effective treatment
  - Others show same mortality but increased hospitalization length and cost
  - Metanalysis 2007
    - Crude mortality 34% in ESBL producers vs 20% in non-ESBL

- Treatment options
  - Current guidelines suggest usage of carbapenems for treatment of serious ESBL infections
- Increased carbapenem use increases promotion of CRGNB which have very little treatment options

CRE

- Carbapenamses are difficult to treat because they are usually also resistant to multiple other classes of antibiotics and occasionally have no known options.
- May be still sensitive to colistin and tigecycline
- KPC –independently associated with increased mortality
  - Montreal outbreak, crude mortality of 57.1%

- NDM-1 is plasmid mediated, concerning because of the rapidity of spread and the organisms involved

Are they an infection control problem?

- Come from development of resistance in the patient's own previously sensitive strain or by transmission from another individual
- Worldwide reports of ESBL and CRE outbreaks
- Not much reported on AmpC producers

Transmission

- **Transmit like VRE**
  - fecal and skin carriage
  - Fecal oral spread
  - Spread on hands of HCW and shared patient equipment

Managing Outbreaks

- Many reports of success in controlling outbreaks using traditional IC practices
  - Screening of contacts
  - Contact Precautions
  - Increased Hand hygiene

What should we doing?

Current Lab Protocols

- ESBL
  - Automated system flags if MIC >1 mg/L for ceftriaxone or cefotaxime
  - Disk test for ESBL is done
  - If positive then all cephalosporins are reported as Resistant regardless of their MIC and fax to IPC
  - If negative then sensitivities are reported as found according to old CLSI breakpoints

- CRE
  - Automated system flags isolates with meropenem >0.5 mg/L
  - Ertapenem disk set up to confirm
  - Modified Hodge test done
  - If MH is positive then cephalosporins and carbapenems are reported as Resistant and fax to IPC
  - If MH is negative, cephalosporins are carbapenems are reported as found (unless ESBL +)

Breakpoints

Current

Antibiotic	Sensitive	Resistant
Ceftriaxone	≤8	≥64
Ceftazidime	≤ 8	≥ 32
Meropenem	≤ 4	≥ 16
Ertapenem	≤ 2	≥ 8

Proposed

Antibiotic	Sensitive	Resistant
Ceftriaxone	≤1	≥ 4
Ceftazidime	≤ 4	≥ 16
Meropenem	≤ 1	≥ 4
Ertapenem	≤ 0.5	≥ 1

Proposed Changes

- ESBL
  - Report as found for all cephalosporins based on new lower breakpoints
  - ? Fax all reports of ceftriaxone resistant to IPC
- CRE
  - If elevated MIC to meropenem or ertapenem, stop for review
  - Report according to new CLSI breakpoints
  - Add comment regarding reduced susceptibility to carbapenems
  - Report to IPC

ESBL recommendations

- Manitoba Health
  - ESBL should be reported to IPC by lab
  - Contact precautions for acute care facilities
  - Routine practices for LTC
    - contact precautions IF draining wounds that cannot be contained, extensive skin disorder OR acute diarrhea
  - Routine admission screening not required
  - Contact follow up not routinely required

Future changes?

- CTX-M now predominant ESBL type in Canada
  - Most are community-acquired
- ? Isolation in hospital useful in non-outbreak situation
  - Very little data
  - Systemic review by Goddard and Muller, AJIC 2010
    - Only 4 uncontrolled retrospective studies to review
    - No scientifically based suggestions for management of ESBL in non outbreak situation

CDC recommendations for CRGNB

- Review microbiology records for preceding 6-12 months to determine if any CRE cases were present
- If previously unrecognized cases are identified, to do point prevalence cultures in high risk areas (eg. ICU, wards with previous cases) to identify cases
- Contact precautions for all identified cases

PHAC recommendations for CRGNB

- If patient found to have CRGNB> 48 hours after admission
  - Consider
    - Clinical screening (ie wounds, urine, etc) of roommates
    - Retrospective review of lab reports (6-12 mo)
    - If 2 or more patients with same strain (species) strongly consider active surveillance testing on patients with contact with index cases
- Contact precautions
- Single room or cohort with other CRGNB with same strain