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Reducing Antimicrobial Resistance Through Infection Control and Antimicrobial Stewardship

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Objectives

- Describe antimicrobial stewardship in Human medicine
- Show some evidence of impact of a “stewardship” program
- Describe how stewardship improves patient quality and safety
- Summarize recent initiatives in promoting ASP
- Explain why ASP and IPAC need to work together

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Antimicrobial Stewardship: Why Now?

- ASP is **NOT** a new concept in healthcare
- 25% reduction of outpatient antibiotic prescriptions in Canada since 1998.
- Some parameters of resistance have stabilized.
- New antimicrobial resistant organisms (AROs) have emerged
- Carbapenemase Producing Enterobacteraceae (CPE)-NDM-1
- No effective antibiotics available and patients die
- Little new antimicrobials coming on the horizon
- Accreditation Canada made ASP an ROP

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Reaction to emerging ARO's

- WHO statement
- CDC policy
- Federal task force on ARO incl. a subcommittee on ASP
- AMMI Canada-Choose Wisely Canada
- Ontario: PHO, HQO, Artic program, CAHO and MOH all wanting to develop a comprehensive ASP for the Province

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But it gets worse:

- **Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study.**
- Lancet ID Feb 2016
- **It's here:** it's been found in a patient in N. America with resistant *E. coli* (May 2016)

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How Does Resistance Occur?

- Resistance is natural
- Some bacteria are inherently resistant to some classes of antibiotics
- Many mechanisms of resistance
- Some are inducible
- Some are constitutive
- Some are transferrable

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Effect on Resistance; Darwinian Selection

- Bacteria do NOT develop resistance
- Bacteria spontaneously mutate ($1/10^5$)
- Antibiotics act as the environmental stimulus, the selective pressure.
- Selection is of the “fittest”
- In the presence of an antibiotic, a resistance gene will confer a selective advantage

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MCR-1

- A plasmid that contains the resistance complex
- The plasmid can pass these resistance genes to other organisms
- The “mobile” plasmid, makes it scary as it can pass easily to “common” organisms. The complex resistance is no longer a rare hospital organism but can be seen widely.
- Found in animal excrement, then in food supply and finally in patients
- Large plasmids often inhibit growth under “normal” conditions

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How do we stop the spread of resistance?

- Prevent the passage of the organism from person to person
 1. Sanitation
 2. Hand hygiene
 3. Infection Control principles and practice
- Don't enable the organism to grow:
 1. Restrict the antibiotic environment which gives the organism its survival advantage
 2. Use effective antimicrobial which evades the resistance

Appropriate use of antibiotics....Antimicrobial Stewardship

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Antimicrobial Stewardship- Historical Approaches

- Control of usage was based on prescribing restriction, guidelines & pathways
- Hide susceptibility patterns to veer prescribers to certain antimicrobial classes or “cheaper” drugs.
- These approaches had limited beneficial impact

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Why Did Control Measures Not Work?

- Prescribers don't like to be told what to do
- Evidence for the restrictions was often lacking ... credibility gap.
- Guidelines were vague
- Guidelines often encourage broad spectrum coverage by being overly inclusive.
- Effective impact was not sustainable

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Myths about antibiotics

- More is better
“broad spectrum superior to narrow spectrum”
- Don't change what ain't broke
“stick with the meds which the patient has responded to”
- IV is superior to PO
- Narrow spectrum is inferior care- “simplification”
- Individual prescribing has no impact on resistance

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Goal of Antibiotic Therapy

- The right antimicrobial, dose and duration
- Goal: cure infection with minimal toxicity and minimal impact on selective (resistance) pressure.
- **Inappropriate Use** leads to:
 - Unnecessary exposure to antimicrobials
 - Increased cost
 - Antibiotic resistance and “super-infections”
 - Increased LOS

Does prescribing make a difference in preventing resistance?

- Is resistance inevitable?
- Is resistance futile?
- Is the problem a knowledge gap? An education gap?
- Is prescribing a behavior? Based on pattern recognition
- What are the influencers to effect change?
- Is it time to look at prescribing as a behavior rather than just a knowledge based activity?

Resistance is futile!

- Remove the selective pressure, you then remove the survival advantage of the organism.
- Over time, the resistance patterns will change.

Impact of Changing the Choice of Antibiotics

- Finland...’90...macrolides for Group A streptococcus
- Restrict the use of 3rd generation cephalosporins (ceftazidime) reduced ESBL's
- Rotate antibiotic classes...ICUs
 - cephalosporin, B-lactams (PiP/Tazo), carbapenem, quinolone

To prevent resistance to antibiotics in ICU

- Rotate the antibiotics

To prevent resistance to antibiotics in ICU

- Rotate the antibiotics

OR

- Rotate the attending physician

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Common Prescribing Errors

L. DeVreese, R. Zvonar; a TOH Audit

Chart review:

- Physicians don't define the diagnosis and rationale for choice of antibiotic in the chart (76%)
- Most antibiotic orders don't have stop dates (70%)
- Review of antimicrobial choice based on microbiologic data happens only 1/4 the time
- Taken as a bundle; only 21% compliance

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Evidence to discontinue antibiotics

- N. Singh et al....ICU patients... Suspected pneumonia
- If after 3 days, the cultures are negative, no adverse impact to discontinue antibiotics
- WHY?
- Many pneumonias are not actually pneumonia, the antibiotic was started empirically...so when to stop?
- "Easy to start antibiotics but very hard to stop" A Peloquin MD FRCPC

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When to discontinue antibiotics?

- After 3days/5days/1 week/more?
- UTI?
- CAP?
- HAP?

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Community Acquired Pneumonia

- Good evidence for 5 days with quinolones
- No such thing as a resp quinolone
- Why no such evidence for B-lactams? Study not done!
- This drove overuse of quinolone antibiotics in the community and in hospitals
- Resulted from aggressive multi-pharma marketing
- As a consequence, CDI associated with increased quinolone usage

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Health Care Associated Pneumonia

- including ventilator associated pneumonia (VAP)
- 8 days is sufficient except for pseudomonas aerogenosa
- For *P aerogenosa*...15 days
- Need 2 weeks if there is *S. aureus* bacteremia as well
- This info has been published in 2009 and has not been widely adopted. Why?
- Insecurity associated with otherwise very ill patients

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TOH ICU and General Medicine

- Randomized study of ASP:
- TOH 1100 bed , 2 campus model
- Each campus pilot was compared to its sister ward across town
- All sites had prescribing totals from the 3 months prior to the pilot and the same time period from the previous years

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Impact of ASP

- 30% reduction in antibiotic days
- 40% reduction in antibiotic cost on the wards tested
- Translated into \$160,000 annualized saving
- Hospital saved \$400,000 in antibiotic costs that fiscal year
- No negative impact seen (mortality, LOS, readmission)
- Spill-over effect on the non-intervention wards
- These wards are covered by the same Medical residents
- Is this a learning effect? Change in behavior?

ASP and AROs /ESBLs

- UK data: IPAC enhancements slowed down the *C. difficile* but the rapid fall in CDI only happened with aggressive reduction in antimicrobials
- Ontario data; 30% reduction in CDI outbreaks in past 2 years and significant decline in associated mortality.
- But no change in *C. difficile* infections
- How does this happen?
- Better patient recognition, better diagnosis, patient isolation reduce spread in the hospital! **Improved Infection Control**

C. difficile

- Many of our outbreaks are polyclonal isolates based on Molecular typing.
- Are these real outbreaks?
- Where is the CDI reservoir in our communities?
- IPAC goes only so far. Need aggressive reduction in discretionary antibiotic usage. **This is ASP**

CPES

- Rapid increase over the past 3 years
- More modest increase in 2013
- 70% colonization vs. 30% infection
- Risk factors are medical care or travel outside N. America
- Main infection site is UTI
- No antimicrobial utilization data is available to correlate cause and effect.
- Key reservoir in Ontario is in the Brampton Region

What are key barriers to reducing AROs in ONT.?

- Lack of data:
 - Limited resistance data for Ontario
 - Not comprehensive, limited to patient safety reporting
 - Very little community level data
 - Limited access to antimicrobial utilization/prescribing
- Identification of physician leadership
- LHIN leadership
- No provincial over-arching strategy
- Appropriate use of antibiotics is a key patient safety issue

PHO - Antimicrobial Stewardship Program

- To support community hospitals that do not have infectious Disease or Microbiology expertise
- Focus on support for the ICPs and pharmacists who become the front line advocates for ASP
- Focus on education and support
- Developed a suite of 32 evidence based ASP interventions and they are ranked based on priority and feasibility.
- These are available "on-line" at the PHO website

ASP at PHO

- Valery Leung... new ASP lead pharmacist
- Second pharmacist being hired to start July 2016
- ASP scorecard, will be sent out hopefully in late 2016 to help hospitals know how they compare with their peers
- Point prevalence survey of antibiotic usage
- Current pilot project of point prevalence
- Work with HQO, MOHLTC and colleagues to improve provincial data collection of antimicrobial utilization and HAI provincial surveillance database

PHO ASP Projects / Research

- Pilot of stewardship/management of UTIs in LTC.
- Using Implementation Science to evaluate the process and the outcomes of the intervention. First 2 pilot sites were in Oct-Dec 2015.
- Next step: 15 LTC homes across the province.
- Provincial role out next year?
- UTI Tools to be posted on the PHO website in the fall
- *C. difficile* reservoir studies.

Lessons learned

- Good data make believers out of skeptics
- Need strong senior leadership to implement the program and changes needed for potential success.
- Identifying local champions (early adopters) improves the chances of success and makes the project much more fun
- Work with people who at least are willing to consider change

Conclusions

- Individual prescribing patterns do impact resistance but it is hard to measure.
- If we adopt stewardship principles as a group we can effect profound impact on resistance and patient safety
- ASP and Infection Control programs should be coordinated. They are both needed to reduce resistance and *C. difficile*

Thank you!

Questions?
 Comments welcome