IS THIS YOUR STOP?
Antimicrobial Stewardship

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Chair Antimicrobial Stewardship Team

16th CHICA-HANDIC ANNUAL EDUCATION DAY
Objectives

1) Consequences of antibiotic (over)use
2) Goals of Antimicrobial Stewardship
3) Urinary tract infections: Stewardship needed?
Consequences of Antimicrobial (over) use
Goal

To improve patient outcomes
Common Goal

1) New Antimicrobials

2) Containment

3) Optimize use of existing antimicrobials

Antimicrobial Resistance and *C. difficile*

Patient Outcomes
Collateral damage

Antimicrobial Use

???

Patient Outcomes
Juravinski Hospital ramps up C. diff measures outbreak
Six patients affected, but no new cases in unit

BY NICOLE O’REILLY

Juravinski Hospital has implemented C. difficile control measures in one of its units, after an outbreak affecting six patients was declared June 17.

None of those patients remains in the affected unit — four are in other areas of the hospital, one has been transferred to Brantford and one has died, though not from C. diff.

All are believed to have contracted the infection while in the F3 medicine unit.

The hospital didn’t have its face-to-face meeting with public health until Monday, said Dr. Dominik Mertz, medical director of the infection prevention and control program at Hamilton Health Sciences. For that reason and since there have been no new cases on the unit since June 10, the hospital didn’t notify the public about the outbreak until Tuesday, he said.

Legislation does not require hospitals to notify the public about outbreaks of the infection, rather they report to public health and some numbers are disclosed at designated intervals through the Ministry of Health and Long-Term Care website.

The patients in the unit became ill between June 6 and 10. Some patients who were transferred out didn’t develop symptoms until June 14 and 15, Mertz said.

Four of the patients didn’t develop symptoms until being transferred, including the one who went to Brantford.

However, Mertz said there’s no sign of any ongoing outbreaks anywhere else in the hospital — we don’t have any new cases potentially linked to those cases.

The Juravinski is taking special precautions to contain the outbreak, including hand-cleaning audits, and ramping up its cleaning to include an anti-sporicide.

C. difficile is a spore-forming bacteria that causes diarrhea and fever. The elderly, those with underlying medical conditions and those taking antibiotics are the most vulnerable because antibiotics kill “good bacteria,” allowing the infection to grow.

The bacteria are spread through inadequate hand and environmental cleaning.

Recent provincial statistics found that Juravinski workers only wash their hands about half the time before caring for a patient. This is the lowest rate among area hospitals and well below the provincial average.

The hospital posted a 36 per cent hand-washing rate in 2006-07. That improved to 49 per cent the next year and went up to 55 per cent this year.

“In general, hand washing is needed to prevent C. difficile from spreading, but I can’t say specifically in this case,” said Dr. Chris Mackie, an associate medical officer of health in Hamilton.

Mertz agreed, adding he believes the outbreak may help raise awareness about hand washing and improve overall practices across the hospital.

Public health is testing to see if the patients were made ill by one strain — passed among them — or by separate strains.

Mackie said he doesn’t know why the hospital announced the outbreak.

Married couple dies from C. Diff 10 weeks apart

July 2, 2011

At 85, Thomas Dawson accepted he would die from lung cancer.

He’d lived a good life and believed he had enough time left to see his granddaughter’s wedding in August and his 65th wedding anniversary in December.

He died April 8, only a couple of weeks after his diagnosis. But it wasn’t cancer that killed him — it was C. difficile.

And he had no idea the same gruesome disease would also claim his wife — 84-year-old Maude Dawson.
Antibiotics and Resistance

Antibiotic utilization = major driver for resistance:

- Δ in resistance is paralleled by Δ in antimicrobial use
- Resistance is more prevalent in the health care setting
- Hospital areas with highest antimicrobial use have the highest rates of resistance

Ecological studies
- Association over time
  - Cross-sectional

Table 2. Causal associations between antimicrobial use and the emergence of antimicrobial resistance.

| Changes in antimicrobial use are paralleled by changes in the prevalence of resistance. |
| Antimicrobial resistance is more prevalent in health care-associated bacterial infections, compared with those from community-acquired infections. |
| Patients with health care–associated infections caused by resistant strains are more likely than control patients to have received prior antimicrobials. |
| Areas within hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use. |
| Increasing duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms. |

Antibiotic utilization = major driver for resistance:

- Prior exposure to antimicrobials associated with risk for resistance in health-care associated infections
- Duration of exposure associated with higher likelihood of colonization by resistant pathogens

Individual level studies
  - Exposure
  - Duration of exposure

Table 2. Causal associations between antimicrobial use and the emergence of antimicrobial resistance.

Changes in antimicrobial use are paralleled by changes in the prevalence of resistance.
Antimicrobial resistance is more prevalent in health care-associated bacterial infections, compared with those from community-acquired infections.
Patients with health care-associated infections caused by resistant strains are more likely than control patients to have received prior antimicrobials.
Areas within hospitals that have the highest rates of antimicrobial resistance also have the highest rates of antimicrobial use.
Increasing duration of patient exposure to antimicrobials increases the likelihood of colonization with resistant organisms.
Collateral damage

Antibiotics and Resistance

% MRSA in *S. aureus*

Portugal, Spain, Italy, Greece, and Turkey:
- Highest MRSA rates
- Highest utilization of Antimicrobials
- Antimicrobials over the counter

From the European Antimicrobial Resistance Surveillance System
Collateral damage

Canadian Nosocomial Infection Surveillance Program (CNISP)
Collateral damage

Overall VRE incidence rates per 1,000 patient admissions, 1999-2010

Canadian Nosocomial Infection Surveillance Program (CNISP)
Collateral damage

Overall VRE incidence rates per 1,000 patient admissions, 1999-2010

Canadian Nosocomial Infection Surveillance Program (CNISP)
Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-NET)
Antimicrobial Resistance is one of three greatest threats to human health
Goal

Antimicrobial Resistance and *C. difficile*

Antimicrobial Use

Patient Outcomes
Collateral damage

Clinical implications of resistant bacteria:

- Worse outcomes
- Higher mortality rates
- Longer length of stay
- Greater costs

as compared to their susceptible counterparts

Collateral damage

Clinical implications of *Clostridium difficile*:

- Worse outcomes
- Higher mortality rates
- Longer length of stay
- Greater costs

Song et al. Infect Con Hosp Epidemiol 2008; 29: 823-828
Forster et al. CMAJ; DOI:10.1503/cmaj.110543
1) New Antimicrobials

Antimicrobial Resistance and *C. difficile*

Antimicrobial Use

Patient Outcomes
1) New Antimicrobials

Figure 1. New antibacterial agents approved in the United States, 1983–2007, per 5-year period [2, 3].
The solution

1) New Antimicrobials

October 2011: 9 drugs reported to be in phase I-III clinical trials

Figure 1. New antibacterial agents approved in the United States, 1983–2007, per 5-year period [2, 3].
1) New Antimicrobials

Antimicrobial Resistance and *C. difficile*

Antimicrobial Use

Patient Outcomes
Solutions

1) New Antimicrobials

2) Containment

Antimicrobial Resistance and *C. difficile*

Antimicrobial Use

Patient Outcomes
2) Containment

Infection Prevention & Control

Challenges:
- Screening
- Compliance
- Private rooms
- Costs
- Community...
2) Containment

% MRSA in *S. aureus*

From the European Antimicrobial Resistance Surveillance System
2) Containment

% MRSA in *S. aureus*

MRSA Search & Destroy strategy successful:
- Netherlands
- Scandinavian Countries

From the European Antimicrobial Resistance Surveillance System
Antimicrobial Resistance and *C. difficile*

Common Goal

1) New Antimicrobials

2) Containment

Antimicrobial Use

Patient Outcomes
Common Goal

1) New Antimicrobials

2) Containment

3) Optimize use of existing antimicrobials

Antimicrobial Resistance and C. difficile

Antimicrobial Use

Patient Outcomes
Goals of Antimicrobial Stewardship Programs (ASP)
• 2\textsuperscript{nd} most commonly prescribed class of drugs in US (likely similar here in Canada)

• Account for \textbf{at least} 20\% of hospital pharmacy budgets

• > 40\% of all hospitalized patients receive antibiotics

• \textbf{Repeatedly demonstrated that up to 50\% of antimicrobial use is inappropriate}
What is ASP?

- Optimization of antimicrobial therapy via appropriate:
  - Choice
  - Dose
  - Route
  - Duration
What is ASP?

- Optimization of antimicrobial therapy via appropriate:
  - Choice
  - Dose
  - Route
  - Duration

“I am not sure whether we have a problem with inappropriate use of antibiotics here”
Goals of ASP

Quality improvement and patient safety initiative

- Optimize clinical outcomes
- Minimize unintended consequences of anti-infective use
  - Toxicity
  - Selection of pathogenic organisms (such as *C. difficile*)
  - Emergence of resistance
Goals of ASP

Quality improvement and patient safety initiative

- Optimize clinical outcomes
- Minimize unintended consequences of anti-infective use
  - Toxicity
  - Selection of pathogenic organisms (such as *C. difficile*)
  - Emergence of resistance
- Also shown to reduce costs...
Quality improvement and patient safety initiative

- Optimize clinical outcomes
- Minimize unintended consequences of anti-infective use
- Toxicity
- Selection of pathogenic organisms (such as C. difficile)
- Emergence of resistance
- Also shown to reduce costs...

Win – Win – Win
(patient – resistance – costs)
Elements of ASP

The single best element of ASP? ‘Multi’: multiple elements and multidisciplinary

- Prospective audit & feedback (AII)
- Restrictions (AII)
- Guidelines & clinical pathways (AII)
- Dose optimization (AII)
- Streamlining (AII)
- IV to PO switch (AII)
- Antibiotic order forms (BII)
- Education (AIII)
- Microbiology consultations
- Rapid diagnostics
- MDR surveillance
- Adverse effects surveillance
- Process measure
- Outcome measure
- Decision support systems
Urinary tract infections: Stewardship needed?
Definitions

- Urinary tract infection (UTI)
  = ???

- Asymptomatic bacteriuria
  = ???
Definitions

- **Urinary tract infection (UTI)**
  
  = positive culture + signs/symptoms

- **Asymptomatic bacteriuria**
  
  = positive culture in the absence of signs/symptoms
Definitions

- Urinary tract infection (UTI) = positive culture + signs/symptoms

- Asymptomatic bacteriuria = positive culture in the absence of signs/symptoms

‘Positive urine culture’

- Women: >10^5 cfu/ml bacteria clean catch voided urine (x2)
- Men: >10^5 cfu/ml bacteria clean catch voided urine or 1x >10^2 cfu/ml in a catheterized specimen
Definitions

- **Urinary tract infection (UTI)**
  
  = positive culture + signs/symptoms

- **Asymptomatic bacteriuria**

  = positive culture in the absence of signs/symptoms

**Symptoms:**

- Dysuria, frequency, urgency, suprapubic pain, hematuria

- Pyelonephritis: and/or Fever, chills, flank pain, costovertebral angle tenderness, nausea/vomiting

- Signs/symptoms
Clinical implications

- Urinary tract infection (UTI)
  = positive culture + signs/symptoms

- Asymptomatic bacteriuria
  = positive culture + no signs/symptoms (with few exceptions)
Clinical implications

- Urinary tract infection (UTI) = positive culture + signs/symptoms

- Asymptomatic bacteriuria = positive culture in the absence of signs/symptoms

Implications of urine analysis?

- No clinical implications due to lack of predictive value:
  - Nitrite: sensitivity ~20-30%, specificity ~ 94-100%
  - Leukocyturia: specificity ~60-70% (for UTI), positive culture in patient with no Lc in urine most likely contamination
Asympt. bacteriuria: Epidemiology

Women:
- 1% in schoolgirls to >20% >80 years
- Diabetics: 8-14%
- Pregnant women: 7%

Men:
- Rare in the young, 6-15% >75 years

Microbiology

Uncomplicated UTI:

*E. coli* 75-95%

Other enterobacteriaceae (*P. mirabilis, K. pneumoniae*, *S. saprophyticus*)

Complicated UTI:

Plus *Pseudomonas, Serratia, and Providencia* species, enterococci, staphylococci, and fungi

# Microbiology

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<th>Organism</th>
<th>Number of Isolates</th>
<th>Ampicillin</th>
<th>Cefazolin</th>
<th>Ceftriaxone</th>
<th>Ceftazidime</th>
<th>Piperacillin</th>
<th>Piperacillin-Tazobactam</th>
<th>Imipenem</th>
<th>Ertapenem</th>
<th>Meropenem</th>
<th>Gentamicin</th>
<th>Tobramycin</th>
<th>Amikacin</th>
<th>Nitrofurantoin (urine only)</th>
<th>TMP/SMX</th>
<th>Ciprofloxacin</th>
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<td>91</td>
<td>83</td>
<td>95</td>
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</table>

*Note: The table above represents the percentage of isolates resistant to various antibiotics. The values indicate the percentage of resistance.
Antimicrobial Treatment

Uncomplicated UTI:

- Cystitis (female):
  - Nitrofurantoin (100mg BID x 5 days)
  - TMP/SMX (1 DS tablet BID x 3 (-7) days)
    - Ciprofloxacin (500mg BID x 3 days)
    - Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin
    - Fosfomycin (n/a)

Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin

Fosfomycin (n/a)
Uncomplicated UTI:

- Cystitis (male):
  - Nitrofurantoin (100mg BID x 5 days)
  - TMP/SMX (1 DS tablet BID x 3 (-7) days)
  - Ciprofloxacin (500mg BID x 3 days)
  - Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin
  - Fosfomycin (n/a)

Insufficient tissue levels (prostatitis) / lack of data
Antimicrobial Treatment

Complicated UTI:

- **Cystitis:**
  - Nitrofurantoin (100mg BID x 5 days)
  - TMP/SMX (1 DS tablet BID x 3 (-7) days)

1st choice: Ciprofloxacin (500mg BID x 3 days)

- Betalactams: amoxi/clav, cefpodoxime, cefaclor, cephalexin
- Fosfomycin (n/a)

Resistance rates in complicated UTI
Symptomatic catheter related bacteriuria:
- fever, suprapubic tenderness, costovertrabral angle tenderness, or otherwise unexplained systemic symptoms (altered mental status, hypotension, SIRS)

AND
- $>10^{(5)}$ cfu/ml irrespective of urine specimen
- $>10^{(3)}$ cfu/ml with evidence of pyuria

While indwelling catheter or 48h after removal
Catheter-related: Epidemiology

- Most common hospital-acquired infection
- Bacteriuria in 3-10% per catheter day
- 10-25% of these will become symptomatic
- Risk factors for symptoms: female sex, diabetes, prolonged catheterization, errors in catheter care

Pathogenesis: mostly extraluminal (2/3 of cases)

Catheter-related: Treatment

- Who to treat?
- All patients with significant pyuria and bacteriuria?
- Empiric treatment indicated?
- Spectrum of antibiotics?
- Duration?
- Management of indwelling catheter?
Catheter-related: Treatment

- **ONLY SYMPTOMATIC PATIENTS**
- Pyuria and bacteriuria per se does not need to be treated
- Symptomatic patients:
  - Treatment according to susceptibility results
  - If needed, empirically ceftriaxone, ciprofloxacin, ceftazidime
  - Duration 14 days
- Remove or replace catheter whenever possible
In-house data

Hamilton Health Sciences
Problem: treatment of asymptomatic bacteriuria
Methods: review all patients with positive urine cultures
Assessment of symptoms: charts and discussion with teams
Outcome: appropriate management of positive urine culture
Stewardship initiative UTI

Problem: treatment of asymptomatic bacteriuria

Methods: review all patients with positive urine cultures

Assessment of symptoms: charts and discussion with teams

Outcome: appropriate management of positive urine cultures

Results:

- >100 patients with positive urine cultures
- about 50% obtained from asymptomatic patients
- >50% of asymptomatic patients were treated
Take Home Messages

- Order urine cultures only if there is an indication for treatment:
  - Signs or symptoms of UTI
  - Pregnancy or urological intervention
  - >20% of *E. coli* isolates resistant to FQ or TMP/SMX
  - Consider nitrofurantoin in non-complicated UTI
Take Home Messages

- Order urine cultures only if there is an indication for treatment:
  - Signs or symptoms of UTI
  - Pregnancy or urological intervention
- >20% of E. coli isolates resistant to FQ or TMP/SMX
- Consider nitrofurantoin in non-complicated UTI

- Abx can harm
- Abx indicated if potential benefit > potential harm
- Need to treat patients, not lab results