Neisseria gonorrhoeae: The Ontario perspective

Michael Whelan and Dr. Vanessa Allen

PHO Grand Rounds, May 5, 2015
Objectives

• Participants will be able to:
  • Describe preferred specimen collection for testing and list the antibiotics that are considered first line treatments for gonorrhea in Ontario
  • Explain the current epidemiology of gonorrhea in Ontario
  • Identify and discuss two approaches to be used to further investigate gonorrhea epidemiology and effectiveness of public health guidelines in Ontario
BACKGROUND FOR THE DEVELOPMENT OF GONORRHEA GUIDELINES IN ONTARIO
Gonorrhea Infections

- Etiologic agent: *Neisseria gonorrhoeae*
  - Gram-negative intracellular diplococcus
- Infects mucous membranes
- Incubation period ~ 1 – 14 days
- Modes of transmission
  - Sexual transmission
    - oral, vaginal, anal
  - Vertical transmission
### Sequelae

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<td>Increased risk of HIV transmission and acquisition</td>
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Rates of sequelae from the pre-antibiotic era range from 10-24%
Primary Challenges for the Surveillance and Treatment of *N. gonorrhoeae*

1) Antibiotic resistance
   - Loss of sulfa based compounds, penicillin, tetracyclines and ciprofloxacin as empiric therapy due to high rates of resistance
   - Imminent risk of losing cephalosporins (cefixime and ceftriaxone) the last reliable class of antibiotics

2) Change in number of positive culture specimens vs. positive NAAT specimens
   - No susceptibility data available for non-culture specimens
History of Antimicrobial Resistance in *Neisseria gonorrhoeae*

- **1936:** Sulfonamides introduced for the treatment of gonorrhea
- **1943:** Penicillin developed for the treatment of gonorrhea
- **1945:** A third of *N. gonorrhoeae* resistant to sulfonamides
- **1950:** > 90% resistant to sulfonamides
- **1952:** Tetracycline introduced
- **1955:** Penicillin first used to treat gonococcal urethritis
- **1960:** Spectinomycin developed for the treatment of *NG*
- **1967:** Spectinomycin resistance (pen S & later in 1981 in pen R)
- **1970:** Increasing penicillin resistance (altered PBPs), dose recommended now 4.8 million units and probenecid
- **1972:** Increasing penicillin resistance described in Hawaii (QRNG)
- **1976:** Plasmid mediated penicillin resistance described
- **1981:** Spectinomycin resistance acquired
- **1984:** Large outbreak of penicillin resistance *NG* in North Carolina, penicillin no longer recommended
- **1985:** Plasmid mediated tetracycline resistance acquired
- **1986:** Tetracycline resistance acquired
- **1989:** First high level ceftiraxone resistant strain of *NG* in Japan
- **1990:** Quinolone resistance described in *NG*
- **1991:** Quinolone resistance described in Hawaii (QRNG)
- **1995:** Seattle outbreak of QRNG
- **2000-2007:** Series of US recommendations regarding when ciprofloxacin cannot be used empirically
- **2001:** Rx failure with oral cephalosporin in Japan
- **2009:** First high level ceftriaxone resistant strain of *NG* in Japan
- **2010:** Sequential loss of each class of antimicrobials as effective therapy for *Neisseria gonorrhoeae*
Cephalosporin Susceptibility of *N. gonorrhoeae* in Ontario

Increasing cefixime resistance among *Neisseria gonorrhoeae* isolates in Ontario
Case Reports of Treatment Failure Associated with the Cephalosporins

Two cases of verified clinical failures using internationally recommended first-line cefixime for gonorrhoea treatment, Norway, 2010


GONORRHOEA TREATMENT FAILURES TO CEFIXIME AND AZITHROMYCIN IN ENGLAND, 2010
CA Ison (catherine.ison@hpa.org.uk), J Hussey, K N Sankar, J Evans, S Alexander

1. Sexually Transmitted Bacteria Reference Laboratory, Health Protection Agency, London, United Kingdom
2. Carlton Street Clinic, Blyth, Northumberland, United Kingdom
3. New Croft Centre, Newcastle upon Tyne, United Kingdom
4. Health Protection Agency North East, Newcastle General Hospital, Newcastle upon Tyne, United Kingdom

Successful treatment of gonorrhoea is the mainstay of public health control. Cefixime and ceftriaxone, highly active third generation cephalosporins, are today the recommended first-line agents in most countries and azithromycin is a second-line agent. However, there is increasing evidence of decreasing susceptibility and emergence of therapeutic failures. In this report two cases of clinical failure to cefixime are described, one of which additionally shows failure to azithromycin and selection of a less susceptible strain during treatment.
Nine clinical failures with cefixime (9/133, 6.77%)

Urethral, pharyngeal and rectal sites of infection
  • MSM, MSW, women

Two cases initially treated with cefixime 800 mg
Diagnosis of of *N. gonorrhoeae*: Shift to Molecular Testing

Currently, Susceptibility Testing for *N. gonorrhoeae* is only Possible on Cultured Isolates

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<th>Total Labs (%)</th>
<th>Total Tests</th>
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Access to GC Culture for Medical Purposes

| Yes                      | 33 (36.7) |
| No/NA                    | 57 (63.3) |
NAAT Testing is Primary Method for Diagnosing Gonorrhea in Ontario
Use of Culture for Diagnosing Gonorrhea in Ontario
Implications

• Clinical failures of gonorrhea associated with the use of cefixime in North America

• First quantification of the risk of failure with cefixime

• Suggests a lower threshold for cefixime resistance
  • If true, the problem of cephalosporin resistance is much larger than estimated by PHAC, the CDC and the WHO

• Offers some approaches for tracking ongoing clinical failures
  • Increased use of culture
  • Test of cure
GUIDELINES FOR TESTING AND TREATMENT OF GONORRHEA IN ONTARIO, 2013
Guidelines for Testing and Treatment of Gonorrhea in Ontario, April 2013

• Recommendations are based on:
  • Ontario surveillance data of gonorrhea
  • Pharmacokinetic/pharmacodynamics modeling studies
  • Clinical efficacy data

• The recommended treatment approach is similar to the CDC, aimed to effectively treat gonorrhea given current trends of antimicrobial resistance and aim to mitigate further resistance in Ontario
Testing Recommendations (for Symptomatic Patients)

Gonorrhea Testing Recommendations
(for individuals presenting with symptoms and risk factors consistent with gonorrhea)

Symptomatic patients
Choose specimen site based on patient gender and history
(Include test for chlamydia)

- **Males**
  1. Urethral culture (preferred)
  2. Urine NAAT (if culture not locally available or acute urethral discharge)

- **Females**
  1. Cervical culture (preferred)
  2. Cervical NAAT

- **Additional rectal / pharyngeal specimens**

- **Culture**
Screening Recommendations (for Asymptomatic Patients)

Gonorrhea Screening Recommendations
(for individuals presenting with risk factors for gonorrhea, but without associated symptoms)

Asymptomatic patients
Choose specimen site based on patient gender and history
(Include test for chlamydia)

- **Males**
  - Urine

- **Females**
  - Urine or cervical swab

- Additional rectal / pharyngeal specimens
  - (indicated for all MSM with unprotected sexual exposure at these sites)

- NAAT
- Culture
Treatment Recommendations and Follow-up for Gonorrhea
Additional Resources


Gonorrhea is the second most commonly reported sexually transmitted infection in Ontario and North America. Left untreated, gonorrhea can lead to a host of complications including pelvic inflammatory disease, infertility, and blood stream infections. Cephalosporin, the last available class of antibiotics recommended for the treatment of gonorrhea, have been failing worldwide. In response to Ontario and global clinical failures, Public Health Ontario's new guidelines recommend an injectable drug (ceftixime), in combination with a pill (azithromycin).

Public Health Ontario's Guidelines for Testing and Treatment of Gonorrhea in Ontario provide the evidence, rationale, and recommendations to effectively diagnose and treat persons infected with N. gonorrhoea. The recommendations are based on current scientific evidence, Ontario epidemiology and antimicrobial susceptibility profiles of N. gonorrhoea, and available laboratory testing methods in Ontario. The guidelines cover:

- Laboratory testing recommendations, including when to perform a Gram stain, bacterial culture or nucleic acid amplification testing (NAAT);
- Treatment recommendations for uncomplicated urogenital, rectal and pharyngeal N. gonorrhoea infections; and
- Recommendations for follow-up of N. gonorrhoea infections, including public health reporting, testing and treatment of sexual contacts, indications for test of cure, and follow up testing.

- Frequently Asked Questions
- Quick Reference Guide: a two page document that highlights the testing, screening and testing recommendations in addition to symptoms and risk factors and reporting obligations.
- Online Training Module: an interactive tool to help health care professionals become more familiar with the guidelines.
- Press Release

Ontario Ministry of Health and Long-Term Care Resources:

- Patient Information Sheet
- Sexual Health and Sexually Transmitted Infections Prevention and Control Protocol, 2013

Topics
- A-Z Index
- Chronic Diseases and Injuries

Quick Links
- Events
- Laboratory Testing Information
Potential Impact on Guidelines on Public Health Practice

• Provision of optimal and effective therapy to each individual

• Preliminary evidence shows this may slow down the development of resistance in community strains of *N. gonorrhoeae*

• Expedited partner therapy is no longer an option

• Public Health Nurses only be able to complete cultures under medical directive

• Test of cure could cause capacity issues for health care practitioners
EPIDEMIOLOGY OF GONORRHEA IN ONTARIO
Overview of Gonorrhea Epidemiology

• STI data reporting and collection in Ontario

• Descriptive epidemiology of gonorrhea for Ontario
  • E.g. by year, gender, age, public health unit, risk factors

• Treatment data

• Gonorrhea-HIV co-infection
Gonorrhea reporting in Ontario

• Gonorrhea is reportable under the *Health Protection and Promotion Act*

• Public health units report cases of gonorrhea using the integrated Public Health Information System (iPHIS)
  • All analyses for this presentation are based on data extracted from iPHIS
  • Data are subject to change based on health unit reporting updates through iPHIS
  • Cases were identified as ‘MSM’ if:
    • Client Gender = ‘MALE’, and
    • Answer for risk factor ‘SEX WITH SAME SEX’ = ‘Y’
Incidence of gonorrhea by year: Ontario, 2005-2014

Data Sources: Case data: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19]. Population data: Population Estimates [2005-2013], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted by Public Health Ontario [2014/07/03].

Notes: * Counts for 2014 are more likely to change as data in iPHIS are updated. The rates for 2014 were calculated using the population for 2013. ** Provincial rates include cases that did not specify male or female.
Incidence of gonorrhea in males: Ontario, 2014

Data Sources:  
- **Case data**: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19].  
- **Population data**: Population Estimates [2005-2013], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted by Public Health Ontario [2014/07/03].
Incidence of gonorrhea in females: Ontario, 2014

Data Sources:
- **Case data**: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19].
- **Population data**: Population Estimates [2005-2013], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted by Public Health Ontario [2014/07/03].

PublicHealthOntario.ca
Incidence of gonorrhea by age: Ontario, 2005-2014

Data Sources: Case data: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19]. Population data: Population Estimates [2005-2013], Ontario Ministry of Health and Long-Term Care, IntelliHEALTH ONTARIO, extracted by Public Health Ontario [2014/07/03].
Incidence of gonorrhea by public health unit: Ontario, 2014

Data Sources:
Case data: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19].
## Incidence of gonorrhea by public health unit: Ontario 2005-2014

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<td>6.6</td>
<td>4.6</td>
<td>6.6</td>
<td>8.5</td>
</tr>
<tr>
<td>Porcupine</td>
<td>7.7</td>
<td>16.7</td>
<td>27.9</td>
<td>51.8</td>
<td>116.5</td>
<td>102.2</td>
<td>79.7</td>
<td>34.3</td>
<td>17.3</td>
<td>6.9</td>
</tr>
<tr>
<td>Chatham-Kent</td>
<td>17.8</td>
<td>30.3</td>
<td>23.4</td>
<td>19.1</td>
<td>12.9</td>
<td>14.9</td>
<td>15.0</td>
<td>8.5</td>
<td>10.4</td>
<td>5.7</td>
</tr>
<tr>
<td>Leeds, Grenville And Lanark District</td>
<td>2.4</td>
<td>5.9</td>
<td>3.6</td>
<td>5.9</td>
<td>8.3</td>
<td>9.5</td>
<td>5.9</td>
<td>5.3</td>
<td>8.9</td>
<td>5.3</td>
</tr>
<tr>
<td><strong>Ontario</strong></td>
<td>26.5</td>
<td>30.4</td>
<td>31.0</td>
<td>30.0</td>
<td>27.3</td>
<td>30.2</td>
<td>31.7</td>
<td>30.5</td>
<td>33.6</td>
<td>43.0</td>
</tr>
</tbody>
</table>
## Risk Factors reported by gonorrhea cases by gender: Ontario 2012-2014

<table>
<thead>
<tr>
<th>Gender</th>
<th>Risk factor</th>
<th>2012</th>
<th></th>
<th>2013</th>
<th></th>
<th>2014</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>MALE</td>
<td><strong>Cases reporting at least one risk factor</strong></td>
<td>1,964</td>
<td>82.3%</td>
<td>2,427</td>
<td>85.2%</td>
<td>3,168</td>
<td>83.5%</td>
</tr>
<tr>
<td></td>
<td>No condom use</td>
<td>1,444</td>
<td>73.5%</td>
<td>1,869</td>
<td>77.0%</td>
<td>2,344</td>
<td>74.0%</td>
</tr>
<tr>
<td></td>
<td>MSM*</td>
<td>800</td>
<td>40.7%</td>
<td>1,091</td>
<td>45.0%</td>
<td>1,294</td>
<td>40.8%</td>
</tr>
<tr>
<td></td>
<td>More than one sexual contact in past six months</td>
<td>597</td>
<td>30.4%</td>
<td>672</td>
<td>27.7%</td>
<td>837</td>
<td>26.4%</td>
</tr>
<tr>
<td></td>
<td>New sexual contact in past two months</td>
<td>556</td>
<td>28.3%</td>
<td>619</td>
<td>25.5%</td>
<td>750</td>
<td>23.7%</td>
</tr>
<tr>
<td></td>
<td>Anonymous sex</td>
<td>186</td>
<td>9.5%</td>
<td>228</td>
<td>9.4%</td>
<td>359</td>
<td>11.3%</td>
</tr>
<tr>
<td></td>
<td>Met contact through internet</td>
<td>32</td>
<td>1.6%</td>
<td>50</td>
<td>2.1%</td>
<td>92</td>
<td>2.9%</td>
</tr>
<tr>
<td>FEMALE</td>
<td><strong>Cases reporting at least one risk factor</strong></td>
<td>1,335</td>
<td>78.2%</td>
<td>1,328</td>
<td>78.8%</td>
<td>1,574</td>
<td>78.0%</td>
</tr>
<tr>
<td></td>
<td>No condom use</td>
<td>967</td>
<td>72.4%</td>
<td>1,019</td>
<td>76.7%</td>
<td>1,171</td>
<td>74.4%</td>
</tr>
<tr>
<td></td>
<td>New sexual contact in past two months</td>
<td>221</td>
<td>16.6%</td>
<td>232</td>
<td>17.5%</td>
<td>285</td>
<td>18.1%</td>
</tr>
<tr>
<td></td>
<td>More than one sexual contact in past six months</td>
<td>184</td>
<td>13.8%</td>
<td>223</td>
<td>16.8%</td>
<td>279</td>
<td>17.7%</td>
</tr>
<tr>
<td></td>
<td>Anonymous sex</td>
<td>28</td>
<td>2.1%</td>
<td>37</td>
<td>2.8%</td>
<td>69</td>
<td>4.4%</td>
</tr>
<tr>
<td></td>
<td>Met contact through internet</td>
<td>3</td>
<td>0.2%</td>
<td>9</td>
<td>0.7%</td>
<td>20</td>
<td>1.3%</td>
</tr>
</tbody>
</table>

**Source:** Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public health Ontario [2015/01/19].

*Cases with a client gender of male and the risk factor ‘sex with same sex’ selected*
Treatment of gonorrhea cases: Ontario, 2014

- Treatment data reported for **91.9%** (5,354/5,825) of cases

- **55.9%** (2,992/5,354) treated according to Ontario’s provincial treatment guidelines.
  - Additional 4.8% (255/5,354) received the alternate first-line treatment outlined in the Canadian guidelines.

- **39.4%** (2,107/5,354), received treatment regimens that did not meet provincial or federal guidelines
  - 20.9% of these (441/2,107) received monotherapy (e.g. cefixime, azithromycin etc)
Co-infection with HIV

• STIs can enhance the risk of HIV infection and transmission*
  • Lesions resulting from an STI may facilitate HIV transmission more easily
  • Increased HIV viral load as a result of STI
  • HIV infection may also accelerate progression of inflammatory processes associated with an STI (e.g. multiple lesions or treatment failure with syphilis infection)

• Co-infections defined
  • For gonorrhea cases: HIV reported to public health prior to or concurrently (within 30 days) with gonorrhea diagnosis

Gonorrhea and HIV co-infection: Ontario, 2006-2013

Source: (Gonorrhea case data) Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario [2014/10/28]; (HIV case data) Date extracted [2014/09/09].
Summary of gonorrhea epidemiology in Ontario

• A marked increase in gonorrhea incidence has been noted in 2014 compared to 2013 and previous years

• Higher proportion of cases reported by males

• Highest age specific rates:
  • In males observed among the 20-24 and 25-29 year-olds
  • In females observed among 15-19 and 20-24 year-olds

• The highest rates of gonorrhea were reported in Toronto in 2014
  • Incidence in southern Ontario increased, but declined in Northern Ontario compared to 2013
Summary of gonorrhea epidemiology in Ontario

• From 2012-2014:
  • Most commonly report risk factor is ‘no condom use’
  • Over 40% of male cases identified as MSM, highest in 2013 at 45%

• In 2013, over 20% of cases in MSM had a known HIV co-infection compared to non-MSM at just over 1%

• Cause of the increase in gonorrhea incidence not identified at this time further investigation is warranted
GONORRHEA IN ONTARIO 2015:
UPDATE ON RESISTANCE AND NEXT STEPS
Where are we now?

- In 2013 there was an improvement seen in the resistance patterns of *N. gonorrhoeae* in Ontario after the release of the guidelines but this was short-lived
  - In 2014, 10.1% of cases tested at Public Health Ontario had reduced susceptibility compared to 8.1% in 2013
Total Number of *Neisseria gonorrhoeae* Isolates Received for Antimicrobial Susceptibility Testing In Ontario by Gender, January 2010- March 2015

Source: Public Health Ontario Laboratory Information System, extracted March 20th, 2015
Proportion of Isolates of *Neisseria gonorrhoeae* with Decreased Susceptibility to Cefixime by Gender in Ontario (MIC Values >= 0.12 mg/L), January 2010- March 2015

Source: Public Health Ontario Laboratory Information System, extracted March 20th, 2015
Cefixime Resistance Patterns in *Neisseria gonorrhoeae* Isolates from Women In Ontario by Month, March 2013-February 2015

Gonorrhea clinical failures associated with cefixime MIC => than 0.12 mg/L
Cefixime Resistance in Neisseria gonorrhoeae among Men in Ottawa and Toronto, 2011-2015

Data from PHO Online STI Laboratory Data Tool, extracted March 20 2015
Cefixime Resistance in *Neisseria gonorrhoeae* among women in Ontario, 2011-2015

**Antibiotic Susceptibilities by Minimum Inhibitory Concentration**
(Combined - Annually)

**Distribution of Minimum Inhibitory Concentrations**

**Age Group**
- < 1
- 1 - 4
- 5 - 9
- 10 - 14
- 15 - 19
- 20 - 24
- 25 - 39
- 40 - 64
- 65 +
- Unknown

**Year**
- 2010
- 2011
- 2012
- 2013
- 2014
- 2015

**MIC Group**
- <= 0.03 mg/L
- 0.06 mg/L
- 0.12 mg/L
- 0.25 mg/L

Data from PHO Online STI Laboratory Data Tool, extracted March 20, 2015
Proportion of *Neisseria gonorrhoeae* Isolates Resistant to Azithromycin by Gender in Ontario, January 2010- March 2015

```
Proportion of Samples

Year

F
M
U
Total

Source: Public Health Ontario Laboratory Information System, extracted March 20th, 2015
```
Azithromycin Resistance Patterns in *Neisseria gonorrhoeae* Isolates from Women In Ontario by Month, March 2013-February 2015
Proportion of *Neisseria gonorrhoeae* Isolates Resistant to Ciprofloxacin by Gender in Ontario, 2010-2015

Source: Public Health Ontario Laboratory Information System, extracted March 20th, 2015
EVALUATION OF GONORRHEA GUIDELINES IN OTHER JURISDICTIONS
Effectiveness of Change to Ceftriaxone + Azithromycin: the UK experience

- 2010, the UK changed their guidelines to recommend ceftriaxone 500 mg intramuscularly + azithromycin 1 gm orally due to increases in cefixime resistance

<table>
<thead>
<tr>
<th></th>
<th>2007 (N=1024)</th>
<th>2008 (N=1097)</th>
<th>2009 (N=1298)</th>
<th>2010 (N=1145)</th>
<th>2011 (N=1194)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefixime only</td>
<td>112 (11)</td>
<td>133 (12)</td>
<td>95 (7)</td>
<td>88 (8)</td>
<td>8 (1)</td>
</tr>
<tr>
<td>Cefixime and azithromycin</td>
<td>454 (44)</td>
<td>566 (52)</td>
<td>635 (49)</td>
<td>439 (38)</td>
<td>42 (4)</td>
</tr>
<tr>
<td>Cefixime and doxycycline</td>
<td>117 (11)</td>
<td>59 (5)</td>
<td>52 (4)</td>
<td>44 (4)</td>
<td>4 (&lt;1)</td>
</tr>
<tr>
<td>Cefixime as part of treatment</td>
<td>702 (69)</td>
<td>764 (70)</td>
<td>789 (61)</td>
<td>568 (50)</td>
<td>55 (5)</td>
</tr>
<tr>
<td>Cefixime only</td>
<td>73 (7)</td>
<td>54 (5)</td>
<td>81 (6)</td>
<td>123 (11)</td>
<td>24 (2)</td>
</tr>
<tr>
<td>Cefixime and azithromycin</td>
<td>95 (9)</td>
<td>156 (14)</td>
<td>289 (22)</td>
<td>287 (25)</td>
<td>947 (79)</td>
</tr>
<tr>
<td>Cefixime and doxycycline</td>
<td>45 (4)</td>
<td>21 (2)</td>
<td>49 (4)</td>
<td>46 (4)</td>
<td>135 (11)</td>
</tr>
<tr>
<td>Cefixime as part of treatment</td>
<td>232 (23)</td>
<td>253 (23)</td>
<td>439 (34)</td>
<td>470 (41)</td>
<td>1114 (93)</td>
</tr>
<tr>
<td>Azithromycin only</td>
<td>13 (1)</td>
<td>10 (1)</td>
<td>8 (1)</td>
<td>11 (1)</td>
<td>11 (1)</td>
</tr>
<tr>
<td>Azithromycin as part of treatment</td>
<td>583 (57)</td>
<td>762 (69)</td>
<td>965 (74)</td>
<td>783 (68)</td>
<td>989 (83)</td>
</tr>
</tbody>
</table>

Data are the number of patients (%). \( N = \) total number of isolates for which antibiotic prescribing data are available.

*Table 3: Prescribing practice for patients with gonorrhoea attending GRASP clinics between 2007 and 2011*

Ison et al. Lancet Infectious Diseases. September 2013
Effectiveness of Change to Ceftriaxone as the Backbone of Therapy for Gonorrhea: the UK experience

Evidence of Early Reduction in Prevalence of Resistant Isolates of *N. gonorrhoeae*

<table>
<thead>
<tr>
<th></th>
<th>Ceftriaxone</th>
<th></th>
<th>Ceftriaxone</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;0.125 mg/L</td>
<td>≥0.125 mg/L</td>
<td>Total</td>
<td>&lt;0.125 mg/L</td>
</tr>
<tr>
<td>2007</td>
<td>1043 (98.5%)</td>
<td>16 (1.5%)</td>
<td>1059</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Cefixime</th>
<th>Ceftriaxone</th>
<th></th>
<th>Cefixime</th>
<th>Ceftriaxone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;0.125 mg/L</td>
<td>≥0.125 mg/L</td>
<td>Total</td>
<td>&lt;0.125 mg/L</td>
<td>≥0.125 mg/L</td>
</tr>
<tr>
<td>2011</td>
<td>1159 (89.2%)</td>
<td>140 (10.8%)</td>
<td>1299</td>
<td>0 (0.0%)</td>
<td>1299</td>
</tr>
<tr>
<td>Total</td>
<td>5629 (91.1%)</td>
<td>547 (8.9%)</td>
<td>6176</td>
<td>9 (0.1%)</td>
<td>6176</td>
</tr>
</tbody>
</table>

Data are number of isolates (%). Decreased susceptibility deemed to be MIC ≥0.125 mg/L. MIC = minimum inhibitory concentration.

*Table 1*: Genitourinary isolates showing decreased susceptibility to ceftriaxone and cefixime between 2007 and 2011

Ison et al. Lancet Infectious Diseases. September 2013
Effect of Geographically Different Approaches to the Treatment of Gonorrhea: Ciprofloxacin discontinuation in California 2002

Ciprofloxacin no longer recommended in California

California guideline change was not associated with a reduction in the prevalence of resistant *N. gonorrhoeae*

Reduction only occurred after national guideline change

*Figure 1. Prevalence of CipR GC isolates with corresponding 95%*
Effect of Geographically Different Approaches to the Treatment of Gonorrhea: Ciprofloxacin discontinuation in California 2002

Replacement of Ciprofloxacin Resistant Clones of *N. gonorrhoeae*

Persistence of ciprofloxacin resistant clones in California hypothesized to be due to ongoing importation from other US states

Figure 3. Percentage of G437, G1407, and G3112 within the tested isolate population (n = 460) from 2005 to 2009.
GONORRHEA IN ONTARIO 2015: NEXT STEPS
Prescription Practices Since the Roll out of the Gonorrhea Guidelines in 2013

• Poor adherence to guideline recommendations (< 60%)
• Suggestion to remove “second line” options
• Working with Public Health Units and Public Health Ontario Communications and Knowledge Exchange to strategize new ways of promoting and integrating the gonorrhea guidelines into routine practice
The gonorrhea guidelines are a first for Ontario

- Previously practitioners followed the Canadian Guidelines for Sexually Transmitted infections for testing, treatment and follow-up

The treatment recommendations in the Ontario guidelines differ from the current PHAC gonorrhea treatment recommendations

- The Ontario Guidelines recommend intramuscular ceftriaxone and oral azithromycin as the only front line therapy (similar to the US CDC and the UK BASHH)
- Initial feedback from Health unit colleagues has been to remove second line options (currently under review)
Guideline Evaluation Objectives

• The objectives of the evaluation will be to determine:
  • The implementation of the guidelines
  • The impact of the guidelines
  • Describe the changes in gonorrhea testing patterns
  • Describe the changes in gonorrhea treatment patterns
  • Determine the impact the changes in gonorrhea testing and treatment practices have had in reducing the incidence of gonorrhea cases with reduced susceptibility to cephalosporins and azithromycin resistance in Ontario
STI Ontario Surveillance (SOS)

- Establishing a prospective sentinel surveillance system for sexually transmitted infections initially focused on gonorrhea
- In collaboration with public health units, STI clinics, and Public Health Ontario
- Obtain and synthesize relevant data from diverse regions throughout Ontario based on location, population distribution and access to priority populations
  - 7 health units participating
  - First report out in 2015
SOS - *N. gonorrhoeae* project objectives

- Monitor trends and prevalence of *N. gonorrhoeae* with reduced susceptibility throughout Ontario in various diverse locations and populations
- Analyze and compare risk factors associated with *N. gonorrhoeae* and drug resistant *N. gonorrhoeae*
- Monitor the minimum inhibitory concentration of *N. gonorrhoeae* specimens
- To use data from this to inform gonorrhea management recommendations in Ontario
Summary

- Data from several sources suggest initial decrease in *N. gonorrhoeae* resistance rates with change of treatment guidelines
  - More recent reemergence of resistance throughout Ontario more broadly
- Uniform approach across populations may assist in eradication of resistant clones
- Multiple efforts to develop evidence and establish next steps
  - Efforts to understand guideline uptake
  - Evaluation of Ontario treatment recommendations
  - Establishment of sentinel surveillance system
- Your help is very important to addressing the issue of resistance
Acknowledgements

- Public Health Units
- PHO Laboratories and Communicable Diseases
- PHO Communications
- Ministry of Health and Long-Term Care
QUESTIONS?
THANK YOU!
Select Public Health Ontario resources

• Guidelines for Testing and Treatment of Gonorrhea in Ontario (April 2013)

• Infectious Disease in Focus sections of PHO’s Monthly Infectious Disease Surveillance Reports
  • Gonorrhea:
    • November 2012 edition
    • February 2015 edition

• Reportable Disease Trends in Ontario:
  • 2011 Report
  • 2012 Report