Investigating exposure to antibiotics in participants of community *H. pylori* projects in Arctic Canada

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Helicobacter pylori

- Spiral-shaped bacterium that colonizes the stomach
  - Infects around half of the world’s population, most often in childhood
  - Mode of transmission not fully known
  - Infection can come and go unnoticed, or persist long-term with or without symptoms

- Chronic infection can cause:
  - Gastritis (inflammation of stomach lining)
  - Peptic ulcer disease (~10% of cases)
  - Stomach cancer (~1% of cases)
H. pylori Prevalence in Canada

Study of multiple southern provinces:

- 68%
- 57%
- 58%
- 59%
- 30%
- 95%
- 35%
- 38%
Canadian North Helicobacter pylori Working Group

Research Approach
• Community-driven research approach used in northern communities to
  ➢ Characterize the burden of disease from H. pylori infection
  ➢ Exchange knowledge with community members and decision makers
to identify ways to reduce health risks from this infection

Goals
• Address community concerns about health risks from H. pylori infection
• Recommend H. pylori management strategies to health authorities
• Reduce health risks from H. pylori infection
Treatment & Antibiotic Resistance

Canadian Clinical Guidelines recommend:

- 3-drug therapy for initial treatment of *H. pylori* infection
  - PPI + two antibiotics (clarithromycin, amoxicillin and/or metronidazole) for 10 days

**Problem:**

Antibiotic resistant strains of *H. pylori*

Among CANHelp project participants, 43% (88/205) of *H. pylori* isolates are resistant to one or more antibiotics that can be used for the treatment of infection.
Risk factors for antibiotic resistance:

• *H. pylori* treatment failure due to
  - Poor adherence to treatment regimen due to complexity and duration
  - Treatment suspended due to side-effects

• Antibiotics taken frequently for other infections

• Incorrect/Empiric use of antibiotics
Aims of Analysis

To describe for Canadian Arctic communities with high *H. pylori* prevalence:

1) How the antibiotic dispensation rate varies by factors of interest

2) How this rate compares to that of the Edmonton outpatient population
Data Collection

Data from CANHelp Community Projects

• Chart review tool developed to standardize collection of information from health center medical charts

• Antibiotic prescription histories were collected for the 5-year period prior to enrolment for each participant; enrolment occurred during 2007-2012.

• Collected data included:
  o demographic factors;
  o frequency of antibiotic prescriptions;
  o type of antibiotic prescribed; and
  o reason for prescription.
Data Collection

Comparison Data from Edmonton, Alberta

*Interactive Health Data Application (IHDA)*

*(2010-2013)*

**Combined Data Sources:**

1) Pharmaceutical Information Network (PIN) Database;
2) Alberta Health Care Insurance Plan (AHCIP);
3) Adjusted Mid-Year Population Registry Files;
4) Alberta Health and Wellness Postal Code Translation File (PCTF).
## Study Population

**Table 1: Demographic characteristics participants.**

<table>
<thead>
<tr>
<th></th>
<th>Number of Participants</th>
<th>Average Age (Range) in years</th>
<th>Proportion of Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Communities</td>
<td>297</td>
<td>47.4 (8-86)</td>
<td>54.2%</td>
</tr>
<tr>
<td>Aklavik</td>
<td>164</td>
<td>44.5 (11-86)</td>
<td>51.8%</td>
</tr>
<tr>
<td>Old Crow</td>
<td>67</td>
<td>48.2 (8-81)</td>
<td>52.2%</td>
</tr>
<tr>
<td>Tuktoyaktuk</td>
<td>14</td>
<td>54.6 (10-81)</td>
<td>71.4%</td>
</tr>
<tr>
<td>Fort McPherson</td>
<td>52</td>
<td>53.3 (17-83)</td>
<td>59.6%</td>
</tr>
</tbody>
</table>
## Average Number of Antibiotic Prescriptions

Table 2: Average number of antibiotic prescriptions during 5-year review period by community and sex.*

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>95% CI</th>
<th>Female</th>
<th>95% CI</th>
<th>Male</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Communities</td>
<td>4.6</td>
<td>4.1, 5.1</td>
<td>5.6</td>
<td>4.8, 6.4</td>
<td>3.4</td>
<td>2.9, 3.9</td>
</tr>
<tr>
<td>Aklavik</td>
<td>4.2</td>
<td>3.5, 4.9</td>
<td>5.2</td>
<td>4.1, 6.3</td>
<td>3.1</td>
<td>2.4, 3.8</td>
</tr>
<tr>
<td>Old Crow</td>
<td>4.9</td>
<td>3.9, 5.8</td>
<td>5.3</td>
<td>3.9, 6.8</td>
<td>4.3</td>
<td>3.1, 5.6</td>
</tr>
<tr>
<td>Fort McPherson</td>
<td>4.5</td>
<td>3.3, 5.9</td>
<td>5.7</td>
<td>3.7, 7.7</td>
<td>3.0</td>
<td>2.0, 4.0</td>
</tr>
</tbody>
</table>

*Due to small sample size individual estimates are not presented for Tuktoyaktuk, NT.
## Top Reasons for Prescription

<table>
<thead>
<tr>
<th>Group</th>
<th>Reason</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All Participants</strong> (n=297)</td>
<td>Dental Abscess/Infection</td>
<td>12.5%</td>
</tr>
<tr>
<td></td>
<td>Urinary Tract Infection</td>
<td>11.9%</td>
</tr>
<tr>
<td></td>
<td>Otitis Media/Externa</td>
<td>8.2%</td>
</tr>
<tr>
<td><strong>Females</strong> (n=161)</td>
<td>Urinary Tract Infection</td>
<td>17.6%</td>
</tr>
<tr>
<td></td>
<td>Dental Abscess/Infection</td>
<td>8.3%</td>
</tr>
<tr>
<td></td>
<td>Otitis Media/Externa</td>
<td>7.9%</td>
</tr>
<tr>
<td><strong>Males</strong> (n=136)</td>
<td>Dental Abscess/Infection</td>
<td>20.4%</td>
</tr>
<tr>
<td></td>
<td>Laceration, Injury, Abrasions</td>
<td>12.0%</td>
</tr>
<tr>
<td></td>
<td>Otitis Media/Externa</td>
<td>8.6%</td>
</tr>
</tbody>
</table>
# Antibiotic Dispensation Rates in Arctic Communities

**Table 4:** Antibiotic dispensation rate by community.*

<table>
<thead>
<tr>
<th></th>
<th># of antibiotics dispensed/person-year</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Arctic Communities</td>
<td>0.94</td>
<td>0.89, 1.00</td>
</tr>
<tr>
<td>Aklavik</td>
<td>0.86</td>
<td>0.79, 0.92</td>
</tr>
<tr>
<td>Old Crow</td>
<td>1.01</td>
<td>0.91, 1.13</td>
</tr>
<tr>
<td>Fort McPherson</td>
<td>0.95</td>
<td>0.83, 1.07</td>
</tr>
<tr>
<td>Edmonton**</td>
<td>0.562</td>
<td>0.561, 0.563</td>
</tr>
</tbody>
</table>

**Rate Difference**  
(Arctic Communities – Edmonton)  
0.38  
0.33, 0.43

*Due to small sample size individual estimates are not presented for Tuktoyaktuk, NT.  
**Edmonton population ranged from 1,170,724-1,268,516 during 2010-2013, including both genders and all ages.
Discussion

The higher antibiotic dispensation rate observed in the Arctic communities relative to Edmonton may reflect some combination of:

1. A higher incidence of infectious diseases in Arctic communities;
2. Overuse of antibiotics due to limited availability of medical services and diagnostic technology, leading to dispensation of antibiotics prior to confirmed diagnosis;
3. Provision of health care in the Arctic communities primarily by nurses in phone consultation with physicians, while healthcare in Edmonton is primarily provided directly by physicians, which may alter prescribing patterns.
Next Steps

Estimate the effect of frequent exposure to antibiotics on:

1) Prevalence of resistant *H. pylori* infection;
2) Risk of treatment failure.
Acknowledgements
# Resistance Frequencies – Community Projects

## Table 5: Proportion of isolates with resistance to specific antibiotics by community.

<table>
<thead>
<tr>
<th></th>
<th>Amox</th>
<th>Cipro</th>
<th>Clari</th>
<th>Metro</th>
<th>Nitro</th>
<th>Rifam</th>
<th>Tetra</th>
<th>Any*</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Communities</td>
<td>0%</td>
<td>3.9%</td>
<td>15.6%</td>
<td>34.6%</td>
<td>0.97%</td>
<td>1.4%</td>
<td>0.48%</td>
<td>42.9%</td>
</tr>
<tr>
<td></td>
<td>0/205</td>
<td>8/205</td>
<td>32/205</td>
<td>71/205</td>
<td>2/205</td>
<td>3/205</td>
<td>1/205</td>
<td>88/205</td>
</tr>
<tr>
<td>Aklavik</td>
<td>0%</td>
<td>1.6%</td>
<td>8.3%</td>
<td>28.3%</td>
<td>1.6%</td>
<td>0%</td>
<td>0%</td>
<td>31.6%</td>
</tr>
<tr>
<td></td>
<td>0/120</td>
<td>2/120</td>
<td>10/120</td>
<td>34/120</td>
<td>2/120</td>
<td>0/120</td>
<td>0/120</td>
<td>38/120</td>
</tr>
<tr>
<td>Old Crow</td>
<td>0%</td>
<td>7.5%</td>
<td>24.5%</td>
<td>41.5%</td>
<td>0%</td>
<td>0%</td>
<td>1.8%</td>
<td>50.9%</td>
</tr>
<tr>
<td></td>
<td>0/53</td>
<td>4/53</td>
<td>13/53</td>
<td>22/53</td>
<td>0/53</td>
<td>0/53</td>
<td>1/53</td>
<td>27/53</td>
</tr>
<tr>
<td>Fort McPherson</td>
<td>0%</td>
<td>7.1%</td>
<td>28.5%</td>
<td>46.4%</td>
<td>0%</td>
<td>3.5%</td>
<td>0%</td>
<td>67.8%</td>
</tr>
<tr>
<td></td>
<td>0/28</td>
<td>2/28</td>
<td>8/28</td>
<td>13/28</td>
<td>0/28</td>
<td>1/28</td>
<td>0/28</td>
<td>19/28</td>
</tr>
</tbody>
</table>

**NOTE:** non-exclusive table (ie. isolates can be resistant to more than one antibiotic)

*Any = if participant is resistant to any antibiotic, or combination of antibiotics tested

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Amox – Amoxicillin (MIC>1ug/mL)
Cipro – Ciprofloxacin (MIC>1ug/mL)
Clari – Clarithromycin (MIC>1ug/mL)
Metro – Metronidazole (MIC>8ug/mL)
Nitro – Nitrofurantoin (MIC>2ug/mL)
Rifam – Rifampicin (MIC>4ug/mL)
Tetra – Tetracycline (MIC>4ug/mL) borderline resistance
## Resistance Frequencies – Community Projects

### Aklavik, NT
- 28% (34/120) to metronidazole
- 8% (10/120) to clarithromycin
- 7% (8/120) to more than one antibiotic
- 31.6% (38/120) to any antibiotic*

### Old Crow, YT
- 42% (22/53) to metronidazole
- 25% (13/53) to clarithromycin
- 21% (11/53) to more than one antibiotic
- 51% (27/53) to any antibiotic*

### Ft. McPherson, NT
- 46% (13/28) to metronidazole
- 29% (8/28) to clarithromycin
- 18% (5/28) to more than one antibiotic
- 68% (19/28) to any antibiotic*

*Any = if participant is resistant to any antibiotic, or a combination of antibiotics.
## Treatment Success – Community Projects

<table>
<thead>
<tr>
<th>Location</th>
<th>3-drug: Standard Triple Therapy</th>
<th>4-drug: Quadruple Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aklavik, NT</td>
<td>50% (24/49)</td>
<td>95% (21/22)</td>
</tr>
<tr>
<td>Seq: 70% (28/40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old Crow, YT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seq: 65% (13/20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-drug: 95% (21/22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ft. McPherson, NT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seq: 88% (21/24)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4-drug: 100% (15/15)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Reported to indicate project progress only; these estimates are highly uncertain due to small group sizes.

3-drug: Standard Triple Therapy
Seq: Sequential Therapy
4-drug: Quadruple Therapy