Addressing Concerns about Health Risks from \textit{H. pylori} infection in Northern Canada

\textit{Integrating Research and Health Care}

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Rachel Munday, RN, RM (UK), MSc
Aklavik Health Center, NWT

Medicine Grand Rounds
October 22, 2010
Background

Canadians at High Risk from H. pylori Infection

- In 2006, the Canadian Helicobacter Study Group identified 3 groups of Canadians at high risk from *H. pylori*-associated disease:
  - Elderly people
  - Immigrants from high-prevalence regions
  - Aboriginal peoples
Background

H. pylori and Associated Diseases in Aboriginal Peoples of Canada
Aboriginal Peoples of Canada: 
% of Population by Province

<table>
<thead>
<tr>
<th>Province</th>
<th>% Aboriginal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nunavut</td>
<td>85</td>
</tr>
<tr>
<td>NWT</td>
<td>51</td>
</tr>
<tr>
<td>Yukon</td>
<td>23</td>
</tr>
<tr>
<td>Manitoba</td>
<td>14</td>
</tr>
<tr>
<td>Saskatchewan</td>
<td>14</td>
</tr>
<tr>
<td>Alberta</td>
<td>5</td>
</tr>
<tr>
<td>BC</td>
<td>4</td>
</tr>
<tr>
<td>Ontario</td>
<td>2</td>
</tr>
<tr>
<td>Quebec</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

http://images.google.com/ Map_Canada_political-geo.png
Northern Canada

Political Definition

- **Northern Territories**
  - Nunavut
  - NWT
  - Yukon

Physiographic Definition

- **North of Tree Line**
  - Most of Nunavut
  - Northern parts of
    - NWT
    - Yukon
    - Manitoba
    - Ontario
    - Quebec
    - Labrador
Aboriginal Peoples of Northern Canada

- Aboriginal Groups (2001 Census Data)
  - North American Indian (First Nations)
    - ~29% of Northwest Territories population
    - ~20% of Yukon population
  - Metis (mixed European and First Nations ancestry)
    - ~10% of Northwest Territories population
  - Inuit
    - ~85% of Nunavut population
    - ~12% of Northwest Territories population
# People of Northern Canada

- **2006 Population**

<table>
<thead>
<tr>
<th>Region</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nunavut</td>
<td>29,474</td>
</tr>
<tr>
<td>Northwest Territories (NWT)</td>
<td>41,464</td>
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<tr>
<td>Yukon</td>
<td>30,372</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>101,310</strong></td>
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</tbody>
</table>
## H. pylori Prevalence in Canada

### Multi-ethnic Populations

<table>
<thead>
<tr>
<th>Place</th>
<th>Population</th>
<th>Age (yrs)</th>
<th>n</th>
<th>HP+%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nova Scotia</td>
<td>Health insurance registry</td>
<td>18-72</td>
<td>316</td>
<td>38</td>
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<tr>
<td>Van Zanten 1994</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manitoba</td>
<td>Healthy persons</td>
<td>&gt;20</td>
<td>469</td>
<td>35</td>
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<tr>
<td>Perez-Perez 1997</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 provinces</td>
<td>Dyspeptic patients,</td>
<td>18-86</td>
<td>1013</td>
<td>30</td>
</tr>
<tr>
<td>Thomson 2003</td>
<td>49 family doctor practices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Southern Quebec</td>
<td>Births (cord blood)</td>
<td>Maternal</td>
<td>99</td>
<td>10</td>
</tr>
<tr>
<td>Northern Quebec</td>
<td>Nunavik Inuit births</td>
<td></td>
<td>100</td>
<td>27</td>
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<tr>
<td>Hodgins 1998</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern Manitoba</td>
<td>Wasagamack Cree (First Nations) village</td>
<td>Adult</td>
<td>306</td>
<td>95</td>
</tr>
<tr>
<td>Bernstein 1999; Sinha 2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nunavut</td>
<td>Inuit communities</td>
<td>All ages</td>
<td>256</td>
<td>51</td>
</tr>
<tr>
<td>McKeown 1999</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northwest Territories</td>
<td>Inuvialuit (Inuit) &amp; Gwich’in (First Nation) hamlet</td>
<td>All ages</td>
<td>333</td>
<td>58</td>
</tr>
<tr>
<td>Goodman, unpublished</td>
<td></td>
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<td></td>
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</table>
**H. pylori Prevalence in Northern Canada & Other Circumpolar Populations**

<table>
<thead>
<tr>
<th>Place</th>
<th>Population</th>
<th>Age (yrs)</th>
<th>n</th>
<th>HP+%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Northern Manitoba</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bernstein 1999; Sinha 2002</td>
<td>Cree (First Nations) village</td>
<td>Adult</td>
<td>306</td>
<td>95</td>
</tr>
<tr>
<td><strong>Nunavut</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McKeown 1999</td>
<td>Inuit communities</td>
<td>All ages</td>
<td>256</td>
<td>51</td>
</tr>
<tr>
<td><strong>Northwest Territories</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goodman, unpublished</td>
<td>Inuvialuit (Inuit) &amp; Gwich’in (First Nation) hamlet</td>
<td>All ages</td>
<td>333</td>
<td>58</td>
</tr>
<tr>
<td><strong>Chutkotka, Russia</strong></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Reshetnikov 1998</td>
<td>Chutkotka Native coastal Arctic village, males</td>
<td>Mean=32</td>
<td>34</td>
<td>77</td>
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<tr>
<td><strong>Nuuk, Greenland</strong></td>
<td></td>
<td></td>
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<tr>
<td>Milman 2003</td>
<td>Population survey</td>
<td>22-76</td>
<td>71</td>
<td>47</td>
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<tr>
<td><strong>Sismiut, Greenland</strong></td>
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<td></td>
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<tr>
<td>Koch 2005</td>
<td>Population-based sample</td>
<td>15-87</td>
<td>685</td>
<td>58</td>
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<tr>
<td><strong>Norton Sound, Alaska</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Zhu 2006</td>
<td>Rural Alaska Native villages</td>
<td>All ages</td>
<td>610</td>
<td>80</td>
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</tbody>
</table>
# H. pylori Prevalence in Children

## Multi-ethnic Population

<table>
<thead>
<tr>
<th>Place</th>
<th>Population</th>
<th>Age (yrs)</th>
<th>n</th>
<th>HP+%</th>
</tr>
</thead>
</table>
| 4 provinces
  *Jacobson 2005*   | Endoscopy patients, 4 academic centres               | 5-18      | 246| 5    |
| **Northern Manitoba** | Cree (First Nations) village                         | 0-12      | 163| 56   |
  *Bernstein 1999; Sinha 2002*
| **Nunavut**           | Inuit communities                                    | 0-15      | 28 | 32   |
  *McKeown 1999*
| **Northwest Territories** | Inuvialuit (Inuit) & Gwich’in (First Nation) hamlet | 0-14      | 59 | 52   |
  *Goodman, unpublished*
| **Norton Sound, Alaska** | Rural Alaska Native villages                         | 0-24      | 610| 72   |
  *Zhu 2006*

## Aboriginal Populations


Little Data on *H. pylori*-associated Disease in Aboriginal Canadians

- **Peptic Ulcer Disease**
  - Increased ratio of gastric to duodenal ulcer
    - Inuit of northern Labrador, *and also*
      - Alaska Natives
      - Native Greenlanders
      - Residents of Arctic Norway
  - Increased hospitalizations associated with peptic ulcer disease diagnoses
    - In Manitoba, Registered Indians had nearly 2x rate of other persons (*Bernstein 1999*)
Little Data on \textit{H. pylori}-associated Disease in Northern Canada

- **Gastric cancer**
  - Compared to Canadian average, increased rates in
    - NWT men
    - First Nations and Inuit men in NWT, \textit{and also}
      - \textit{Alaska Native men relative to US average}
      - \textit{Native Greenlanders relative to Danes}
    - But not in Manitoba Registered Indians \textit{(Bernstein 1999)}
Addressing Concerns about Health Risks from *H. pylori* infection in Northern Canada

*Integrating Research and Health Care*

Population Health and Clinical Investigators Conducting Community-driven Research on *H. pylori* Infection in Northern Aboriginal Communities
Case Study
Convergence of Research and Patient Care Goals

- Aboriginal communities in Northwest Territories and Yukon express concern about health risks from *H. pylori* infection and seek research to find solutions
- Health authorities in Northern Canada seek information
  - To improve clinical management of *H. pylori* infection given perception of frequent treatment failure
  - To inform public health policy related to *H. pylori* infection
- Northern communities are remote with respect to advanced medical services and research infrastructure
A CRY FOR HELP
Case Study

Patient Care Issues Prompting Research

- Anxiety about cancer risk from *H. pylori* infection

- For patients presenting with dyspepsia, test and treat approach leads to:
  - High risk of prescribing the wrong treatment
  - High risk of treatment failure regardless of regimen
  - High risk of successful treatment not improving symptoms

- For patients presenting with dyspepsia and family history of gastric cancer, eradication may or may not prevent gastric cancer

- Patients requiring treatment may have already failed multiple attempts
Case Study
Community Health Issues Prompting Research

- Widespread anxiety about cancer risk from highly prevalent *H. pylori* infection leads to high demand for infection control solutions

- Test and treat approach leads to:
  - Frequent treatment failure
  - Increased prevalence of resistant bacterial strains

- People with *H. pylori* infection are often asymptomatic, even when they have severe gastric inflammation
CANHelp (Canadian North Helicobacter pylori) Working Group

Community Organizations
- Aklavik Health Committee
- Vuntut Gwitchin First Nation General Assembly, Old Crow
- Crystal Lennie, Inuvialuit Regional Corporation

NWT Agencies
- Rachel Munday, Nurse in Charge, Aklavik Health Center
- Leah Seaman, Public Health Physician, Beaufort-Delta Regional Health Authority
- Kami Kandola, Chief Public Health Officer, NWT Health and Social Services
- John Morse, Former Medical Director, Stanton Territorial Health Authority
- Susan Chatwood, Director, Institute for Circumpolar Health Research

Yukon Agencies
- Brendan Hanley, Yukon Medical Officer of Health
- Jodi Butler Walker, Arctic Health Research Network Yukon
- Norma Kassi, Arctic Health Research Network Yukon
- Nurse in Charge, Old Crow Health Centre
- Darius Elias, MLA, Yukon Legislature

Alberta Health Services
- Robert Bailey, Director, Northern Health Services Network
CANHelp (Canadian North Helicobacter pylori) Working Group

Investigators

University of Alberta
- Epidemiology: Karen Goodman
- Global Health: Janis Huntington
- Anthropology: Christopher Fletcher
- Gastroenterology: Sander van Zanten, Richard Fedorak
- Microbiology: Monika Keelan
- Pathology: Safwat Girgis

External
- Health Policy: Carl Phillips
- Arctic Investigations: Michael Bruce

Trainees

Public Health Sciences:
- Ashley Wynne
- Laura Aplin
- Megan Johnston
- Katharine Fagan-Garcia
- Amy Colquhoun

Gastroenterology:
- Justin Cheung
- Amy Morse

Microbiology:
- Maysoon Mahmood
- Megan Burlet
We use a collaborative and participatory approach in pursuit of the following aims:

» To obtain representative data from diverse Arctic communities for developing public health strategies for control of \textit{H. pylori} infection in the circumpolar north.

» To conduct policy analysis to identify cost-effective \textit{H. pylori} management strategies that account for ethics, economics, and local cultural concerns for northern communities.

» To develop knowledge exchange strategies that help northern communities understand \textit{H. pylori} health risks, available solutions and unsolved challenges for reducing these risks.
CANHelp Working Group
Pilot Project
The Aklavik *H. pylori* Project
Hamlet of Aklavik, Northwest Territories

- 2006 population: 590*
  - 90% Inuvialuit (Inuit) or Gwich’in Dene (First Nation)

- Access
  - Reached only by water, air, or winter ice-road (or spring partially-thawed road)
Aklavik Health Centre
Initial Study Community
Aklavik, NWT

Why Aklavik?

- Suggested by NWT health authorities
  - Community leaders
  - High level of community concern
  - Enthusiasm from local health authorities
    - Rachel Munday, Nurse-In-Charge
      - Outstanding research facilitator and collaborator
Initial Research Project
Aklavik H. pylori Project Goals

1) Investigate *H. pylori* infection in Aklavik
2) Include community members in research planning and conduct
3) Develop effective activities to inform community members of the research results
Aklavik H. pylori Project
Integrating Scientific and Patient Care Goals

5 Components:
» Community Survey
» Endoscopy
» Treatment
» Knowledge Exchange
» Policy Development
Questionnaire items: knowledge of *H. pylori* and reasons for community concern

2. Have you heard of *Helicobacter pylori* or *H. pylori* infection?
   - Yes
   - No
   - Unsure / don’t remember
   - Refused to answer

If yes:

2a. Can you tell me what kind of illness it causes as far as you know or from what you have heard?
   - Yes; specify all the illnesses: __________________________________________
   - No
   - Unsure
   - Refused to answer

2b. Do you know or have an idea about how people get it?
   - Yes; specify: _______________________________________________________
   - No
   - Unsure
   - Refused to answer

2c. How did you find out about *H. pylori* infection? (mark all that apply)
   - TV/Radio
   - Health Centre
   - Family members who had it
   - Other; specify: _____________________________________________________
   - Unsure/don’t remember
   - Refused to answer

3. Do you believe *H. pylori* infection is a community concern?
   - Yes: please specify the main reason for concern: ______________________
   - No
   - Unsure
   - Refused to answer

- 345 of Aklavik’s 590 residents participated in survey
- 299 were age 12+ (responded on their own)
Have you heard of *Helicobacter pylori* or *H. pylori* infection?

- Of the 299 respondents aged 12+ years, 167 (56% [50-62]) indicated they had heard of *H. pylori* infection.
Have you heard of *Helicobacter pylori* or *H. pylori* infection?

- Of the 299 respondents aged 12+ years, 167 (56% [50-62]) indicated they had heard of *H. pylori* infection
  - 72% could describe illnesses
  - 48% how people got *H. pylori*
Do you believe *H. pylori* infection is a community concern?

- 229 (77% [71-81]) believed that *H. pylori* is a community concern
Do you believe *H. pylori* infection is a community concern?

- 229 (77% [71-81]) believed that *H. pylori* is a community concern
- 19% stated they were unsure why they believed it was a concern

![Bar chart showing reasons for concern](chart.png)
Breath Test Results

- 333 people were tested for *H. pylori* by UBT
  - 58% were positive

Impact on recruitment
## Aklavik *H. pylori* Project
### Selected Findings

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>152</td>
<td>62</td>
</tr>
<tr>
<td>Women</td>
<td>181</td>
<td>55</td>
</tr>
<tr>
<td><strong>Ethnicity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inuvialuit (Inuit)</td>
<td>183</td>
<td>66</td>
</tr>
<tr>
<td>Gwich’in Dene (First Nation)</td>
<td>89</td>
<td>55</td>
</tr>
<tr>
<td>Non-aboriginal</td>
<td>41</td>
<td>25</td>
</tr>
</tbody>
</table>
Aklavik H. pylori Project
Endoscopic Abnormalities
### Aklavik H. pylori Project

**Endoscopic Abnormalities**

<table>
<thead>
<tr>
<th>Apparent inflammation</th>
<th>Gastritis</th>
<th>13.8%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Duodenitis</td>
<td>6.7%</td>
</tr>
<tr>
<td><strong>Erosions</strong></td>
<td>Gastric</td>
<td>6.2%</td>
</tr>
<tr>
<td></td>
<td>Duodenal</td>
<td>0.5%</td>
</tr>
<tr>
<td><strong>Ulcers</strong></td>
<td>Gastric</td>
<td>3.1%</td>
</tr>
<tr>
<td></td>
<td>Duodenal</td>
<td>0</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Esophagitis</strong></td>
<td></td>
<td>10.4%</td>
</tr>
<tr>
<td><strong>Barrett’s Esophagus</strong></td>
<td></td>
<td>2.6%</td>
</tr>
</tbody>
</table>
Prevalence of selected histopathology classifications

<table>
<thead>
<tr>
<th></th>
<th>All $H. pylori+$</th>
<th>All participants</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$n$</td>
<td></td>
</tr>
<tr>
<td></td>
<td>129</td>
<td>194</td>
</tr>
<tr>
<td>Inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (%)</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td>Moderate (%)</td>
<td>47</td>
<td>31</td>
</tr>
<tr>
<td>Severe (%)</td>
<td>43</td>
<td>29</td>
</tr>
<tr>
<td>Atrophy (%)</td>
<td>21</td>
<td>14</td>
</tr>
<tr>
<td>Intestinal Metaplasia (%)</td>
<td>11</td>
<td>8</td>
</tr>
</tbody>
</table>
Aklavik *H. pylori* Project
Endoscopy

<table>
<thead>
<tr>
<th>Condition</th>
<th>n</th>
<th>% Asymptomatic</th>
<th>% No visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastritis</td>
<td>27</td>
<td>42</td>
<td>52</td>
</tr>
<tr>
<td>Duodenitis</td>
<td>13</td>
<td>23</td>
<td>54</td>
</tr>
<tr>
<td>Gastric Erosion</td>
<td>12</td>
<td>33</td>
<td>42</td>
</tr>
<tr>
<td>Gastric Ulcers</td>
<td>6</td>
<td>50</td>
<td>33</td>
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</table>
Aklavik *H. pylori* Project

Histopathology

<table>
<thead>
<tr>
<th>Condition</th>
<th>n</th>
<th>% Asymptomatic</th>
<th>% No visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrophy</td>
<td>27</td>
<td>33</td>
<td>73</td>
</tr>
<tr>
<td>Intestinal metaplasia</td>
<td>16</td>
<td>25</td>
<td>56</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No inflammation</td>
<td>61</td>
<td>46</td>
<td>43</td>
</tr>
<tr>
<td>Mild inflammation</td>
<td>13</td>
<td>23</td>
<td>62</td>
</tr>
<tr>
<td>Mod/severe inflammation</td>
<td>116</td>
<td>35</td>
<td>71</td>
</tr>
</tbody>
</table>
Aklavik *H. pylori* Project

UBT

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>% Asymptomatic</th>
<th>% No visits</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. pylori</em> positive</td>
<td>176</td>
<td>36</td>
<td>73</td>
</tr>
<tr>
<td><em>H. pylori</em> negative</td>
<td>125</td>
<td>49</td>
<td>62</td>
</tr>
</tbody>
</table>
Aboriginal residents of Aklavik, NWT have a high prevalence of *H. pylori* infection with elevated frequencies of:

- Erosions and ulcers of the gastric corpus relative to the duodenum
- Gastric cancer precursors

Severe disease, not presenting for care
Aklavik *H. pylori* Project

Conclusions

- Elevated risk of gastric cancer
- Community worries over cancer risks from *H. pylori* infection are well-placed
- Plans to expand
Next Steps – Expand Research to Include…

- 6 Yukon First Nations Communities
- 5 Inuvialuit Settlement Region Communities
- International Collaboration
  - Alaska
  - Greenland
Next Steps – Expand Research to…

- 5 NWT Inuvialuit communities
Next Steps – Expand Research to…

- 6 Yukon First Nations
Supporters

- Alberta Heritage Foundation for Medical Research
- Canadian Institutes of Health Research (CIHR)
  - Institute of Aboriginal People’s Health
  - Network Environments for Aboriginal Health Research (NEAHR)
    - Anisnabe Kekendazone, Ottawa
    - Nasivvik, Universite Laval
  - w/ Canadian Association for Gastroenterology & Industry Partners
- ArcticNet National Centre of Excellence
- Social Sciences and Humanities Research Council of Canada
- Indian and Northern Affairs Canada
- Canadian Circumpolar Institute
- Public Health Agency of Canada
And now we will hear from…

Rachel Munday,
Nurse-In-Charge
Aklavik Health Center
Case Study

Evidence-based Clinical Pearls for Patient Care
Case 1

- 50 year old male
- Mother died of Gastric Cancer age 55
- Asymptomatic

- Anything we can do?
Case 2

- 58 year old male
- Smoker
- Bleeding GU, benign, *Hp* positive
- Treated with therapeutic endoscopy
- How do we manage?
After Martin Blaser
Gastric Cancer risk factors

- Smoking
- Diet
- Age
- Helicobacter
- Pernicious anemia
- Genetic factors → E-cadherin
Outcomes of *H. pylori* colonization

- 5-15% Duodenal or Gastric ulcer
- < 1% gastric cancer
- 85% gastritis (dyspepsia ?)
## Hp-Gastric Cancer
### Relative Risk

<table>
<thead>
<tr>
<th>ATROPHY</th>
<th>Relative Risk</th>
<th>Gastritis Distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>none/mild</td>
<td>1.0</td>
<td>antral predominant 1.0</td>
</tr>
<tr>
<td>moderate</td>
<td>1.7</td>
<td>pangastritis 15.6</td>
</tr>
<tr>
<td>severe</td>
<td>4.9</td>
<td>corpus predominant 34.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Intestinal metaplasia</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>absent</td>
<td>1.0</td>
</tr>
<tr>
<td>present</td>
<td>6.5</td>
</tr>
</tbody>
</table>

Body Gastritis with Atrophy
Normal gastric epithelial cells.

Intestinal (goblet cell) metaplasia
High Grade Dysplasia
(Early Gastric Cancer)
Gastric Cancer

- Progressive gastritis body
- Acid Output decreases

- Intestinal metaplasia
- atrophy

- Gastric cancer
Annual Gastric Cancer Incidence within 5 years

- Atrophic Gastritis 0.1% (N= 22365)
- Intestinal metaplasia 0.25% (N= 61707)
- Mild to moderate dysplasia 0.6% (N= 7616)
- Severe dysplasia 6% (N= 562)

de Vries et al, GE 2008;134:945-952
Case Family History Gastric Cancer

- Test for Hp (by UBT)
- Treat, if positive

- Then do endoscopy and look for histology
  - Always biopsy antrum and body

- Come back for gastroscopy in 5 years?
TREATMENT
Anti-Hp Antibiotic Activity
How do PPIs work in Hp Treatment?

- Direct anti-Hp effect
- Increase killing capacity antibiotics (MIC) by raising pH
  - Clarithromycin and Amoxicillin  MIC increase x10
  - Metronidazole: no effect
- Change gastric milieu
  - Gastric juice volume
Effect PPI

**MACH2 Study (N=514)**

- CM: 69%
- OCM: 87% **GAIN 18%**
- CA: 26%
- OCA: 94% **GAIN 68%**

*Gastroenterology 1999;116:248-253*
## PPI-CA

<table>
<thead>
<tr>
<th>Paper</th>
<th>Regime</th>
<th>Days</th>
<th>n/N</th>
<th>% (95% CI)</th>
<th>% wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>van Zanten et al</td>
<td>OAC 20b:1000b:500b</td>
<td>7</td>
<td>119/152</td>
<td>78% (71%-84%)</td>
<td>14.3</td>
</tr>
<tr>
<td>Lind et al</td>
<td>OAC 20b:1000b:500b</td>
<td>7</td>
<td>29/30</td>
<td>97% (83%-99%)</td>
<td>17.8</td>
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<tr>
<td>Lind et al</td>
<td>OAC 20b:1000b:250b</td>
<td>7</td>
<td>28/34</td>
<td>82% (65%-93%)</td>
<td>9</td>
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<tr>
<td>Laine et al</td>
<td>OAC 20b:1000b:500b</td>
<td>10</td>
<td>114/137</td>
<td>83% (77%-90%)</td>
<td>15.5</td>
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<tr>
<td>van Zanten et al</td>
<td>OAC 20b:1000b:500b</td>
<td>7</td>
<td>39/50</td>
<td>78% (64%-88%)</td>
<td>9.5</td>
</tr>
<tr>
<td>van Zanten et al</td>
<td>OAC 20b:1000b:500b</td>
<td>7</td>
<td>27/33</td>
<td>82% (65%-93%)</td>
<td>8.7</td>
</tr>
<tr>
<td>van Zanten et al</td>
<td>EAC 20b:1000b:500b</td>
<td>7</td>
<td>35/39</td>
<td>90% (76%-97%)</td>
<td>12.9</td>
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<tr>
<td>van Zanten et al</td>
<td>LAC 30b:1000b:500b</td>
<td>7</td>
<td>58/71</td>
<td>82% (71%-90%)</td>
<td>12.3</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>7</td>
<td>449/546</td>
<td>84% (79%-90%)</td>
<td>100</td>
</tr>
</tbody>
</table>

## PPI-CM

<table>
<thead>
<tr>
<th>Paper</th>
<th>Regime</th>
<th>Days</th>
<th>n/N</th>
<th>% (95% CI)</th>
<th>% wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chiba N</td>
<td>OMC 20b:500b:250b</td>
<td>14</td>
<td>28/34</td>
<td>82% (65%-93%)</td>
<td>8.9</td>
</tr>
<tr>
<td>Lind et al</td>
<td>OMC 20b:400b:250b</td>
<td>7</td>
<td>33/35</td>
<td>94% (81%-93%)</td>
<td>13.5</td>
</tr>
<tr>
<td>Lind et al</td>
<td>OMC 20b:400b:500b</td>
<td>7</td>
<td>37/39</td>
<td>95% (83%-99%)</td>
<td>14.1</td>
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<tr>
<td>van Zanten et al</td>
<td>OMC 20b:400b:250b</td>
<td>7</td>
<td>41/48</td>
<td>85% (72%-91%)</td>
<td>10.8</td>
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<tr>
<td>van Zanten et al</td>
<td>EMC 20b:500b:250b</td>
<td>7</td>
<td>144/190</td>
<td>76% (69%-82%)</td>
<td>11.6</td>
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<tr>
<td>van Zanten et al</td>
<td>OMC 20b:500b:250b</td>
<td>7</td>
<td>137/189</td>
<td>72% (66%-79%)</td>
<td>11.0</td>
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<tr>
<td>Chiba et al</td>
<td>OMC 20b:500b:250b</td>
<td>7</td>
<td>109/145</td>
<td>75% (67%-82%)</td>
<td>11.1</td>
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<tr>
<td>Chiba, Marshall</td>
<td>OMC 20b:500b:250b</td>
<td>7</td>
<td>41/51</td>
<td>80% (67%-90%)</td>
<td>9.7</td>
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<tr>
<td>Chiba, Marshall</td>
<td>OMC 20b:500b:250b</td>
<td>7</td>
<td>39/49</td>
<td>80% (66%-90%)</td>
<td>9.4</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>7</td>
<td>609/780</td>
<td>82% (76%-88%)</td>
<td>100</td>
</tr>
</tbody>
</table>

% eradication range from 60% to 100%.
Twice daily PPI triple therapy

PPI- Clarithromycin and Amoxycillin (PPI-CA)
PPI- Clarithromycin and Metronidazole (PPI-CM)

are equally effective $\geq 70\%-80\%$
Pre Primary treatment Resistance Over Time

<table>
<thead>
<tr>
<th>Year</th>
<th>CLA</th>
<th>MET</th>
</tr>
</thead>
<tbody>
<tr>
<td>NS 1995-96</td>
<td>2</td>
<td>NA</td>
</tr>
<tr>
<td>NS 1997-98</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>NS 1999-01</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>NS 2002-04</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Can 1999</td>
<td>20</td>
<td>23</td>
</tr>
</tbody>
</table>
Quadruple therapy Second Line
7-14 days

Most data: PPI-BMT → 75-80 %

PPI bid
Bismuth qid
Metronidazole 250-500mg qid
Tetracycline 500mg qid

APT 2002;16:1047-1057
Sequential Therapy

- PPI bid
  Amoxycillin 1 g bid } x 5 days

- PPI bid
  Clarithromycin 500 mg bid } x 5 days
  Metronidazole 500 mg bid
RCT Sequential vs PPI-CA

- N = 300

- Results

<table>
<thead>
<tr>
<th>Sequential</th>
<th>PPI-CA</th>
</tr>
</thead>
<tbody>
<tr>
<td>89%</td>
<td>77%</td>
</tr>
</tbody>
</table>

- Clari-R
  - 8/9 (89%) 6/21 (29%)

- Clari-S
  - 108/114 (95%) 86/91 (95%)

Ann Intern Med 2007;556-563
Concomitant Therapy

- All drugs given for 10 days
- PPI bid
- Amoxicillin 1b bid
- Metronidazole 500mg bid
- Clarithromycin 500mg bid
Concomitant vs. Standard Triple Therapy

<table>
<thead>
<tr>
<th>Study</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treiber (1998)</td>
<td>1.67 (0.26-10.61)</td>
</tr>
<tr>
<td>Neville (1999)</td>
<td>6.50 (2.24-18.86)</td>
</tr>
<tr>
<td>Nagahara (2000)</td>
<td>7.92 (0.92-67.84)</td>
</tr>
<tr>
<td>Catalano (2000)</td>
<td>1.95 (0.53-7.11)</td>
</tr>
<tr>
<td>Nagahara (2001)</td>
<td>2.99 (1.02-8.79)</td>
</tr>
<tr>
<td><strong>Pooled OR (95% CI)</strong></td>
<td><strong>3.52 (1.95-6.38)</strong></td>
</tr>
</tbody>
</table>

Odds Ratio

- Favors standard triple therapy
- Favors concomitant therapy

Graham and Fischbach 2010
<table>
<thead>
<tr>
<th>Grade</th>
<th>Cure Rate (ITT)</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>≥95%</td>
<td>Excellent</td>
</tr>
<tr>
<td>B</td>
<td>90-94%</td>
<td>Good</td>
</tr>
<tr>
<td>C</td>
<td>85-89%</td>
<td>Acceptable</td>
</tr>
<tr>
<td>D</td>
<td>81-84%</td>
<td>Poor</td>
</tr>
<tr>
<td>F</td>
<td>≤80%</td>
<td>Failure</td>
</tr>
</tbody>
</table>
Treatment Success Triple therapy (PPI-CA)

Graham et al, Gut 2010;59:1143-53
Treatment Success Concomitant Quadruple Rx
Listed in order of publication

Graham et al, Gut 2010;59:1143-53
Aklavik *H. pylori* Project
Percentage of H. pylori Isolates Resistant to Antibiotics

- Metronidazole: 25%
- Clarithromycin: 10%
- Ciprofloxacin: 1%
- Nitrofurantoin: 1%
- Amoxicillin: 0%
- Rifampicin: 0%
- Tetracycline: 0%

Antibiotic
Aklavik RCT

Treatment Allocation (among participants with post-test)

Treatment naïve

- **LCA Triple** 60% (29/48) 95% CI 45-74
- **Sequential therapy** 74% (29/39) 95% CI 58-97

(Quadruple therapy - one person with multiple resistance successfully treated)

Previous treatment failure

- **Quadruple therapy**
  - 9 trial failures, 1 pre-trial failure 90% (9/10)
- **Sequential therapy**
  - 4 pre-trial failures 50% (2/4)
Bleeding GU Case

• Treat Hp with ????

• PPI bid x 8 weeks, then od

• **Do not stop PPI** unless documentation patient is Hp negative

• UBT on PPI 20% false negative

• Need to stop PPI 7-14 days prior to UBT
Conclusions

- Working with the Aklavik community has been rewarding and is feasible
- There is a very high prevalence of *Hp*
- The histologic gastritis in Aklavik is more severe than in Edmonton
- Epidemiological research and RCTs will help establish how we can manage the *Hp* related burden of illness in Aklavik
The Aklavik Project Endoscopy Team