

# *Research Update*

## *H. pylori* Infection in the Northwest Territories

**CANHelp** (Canadian North *Helicobacter pylori*) **Working Group**

Northern Health Services Network

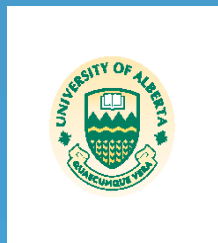
Northwest Territories Health and Social Services


University of Alberta



# Helicobacter in the Northwest Territories: the Aklavik project

Sander Veldhuyzen van Zanten  
Karen Goodman  
Justin Cheung, Amy Morse  
For the Aklavik Project Team





Thanks to John  
from Axcan Pharma  
for lunch

# Aklavik *H. pylori* Project

## Timeline

- Wave 1
  - Enrolment and clinical surveys Nov 2007 – Feb 2008
  - *H. pylori* breath tests Jan - Feb 2008
- Scope week Feb 4-8, 2008
- Histopathology assessment Feb – Apr 2008
- Microbiology, culture & susceptibility Feb – Sep 2008
- Pathology results reported to participants Apr 2008
- Epidemiology survey, initial phase Apr 2008
- Wave 2 Sep-Oct 2008
  - New enrolment campaign
  - Breath tests, surveys
- Treatment Oct-Nov 2008
- Long-term treatment follow-up through Dec 2009
- Inform community of research results Ongoing

# Aklavik *H. pylori* Project Participation ( Fall 08)

- Participants recruited: **314**
- Clinical surveys completed: 314
- Individuals with breath test results: **255**
- Aklavik residents appearing for endoscopy: 197
- Individuals from whom biopsies were obtained 193
- Epidemiology surveys completed to date
  - Household: 74
  - Individual: 119

# Aklavik *H. pylori* Project Prevalence (Fall 08)

- Proportion positive on breath test:
  - **57 %** (145/255)
- Preliminary positive result on biopsy culture:
  - 72% (140/195)\*

# Endoscopic findings

Esophagitis: n = 20

Barrett's esophagus: N = 5

Gastric Erosions: N = 12

Gastritis: N = 27

**Gastric Ulcer: N = 6**

Duodenal erosions: N = 1

Duodenitis: N = 13

Duodenal ulcer: N = 0 (surprising)

# Histology (n=184)

- Sydney classification was used

- Gastritis

Hp density

- SEVERE 43%

3+ 36%

- MODERATE 47%

2+ 37%

- MILD 10%

1+ 27%

- Atrophic changes 14%

- Intestinal metaplasia 16%





Gastritis much more severe than seen in Edmonton

# *Hp* Resistance Aklavik

- 33% Metronidazole resistance
- 13% Clarithromycin Resistance
- 4% both C and M

# Aklavik *H. pylori* Project

- Where are we going – what to do with the info from phase II...?
  - Phase III - Treatment

# Treatment Phase

Aklavik H. pylori Project

# Aklavik *H. pylori* Project

## Treatment Considerations

- *H. pylori* infection is difficult to eliminate with currently available antibiotics, and the most effective regimens at present combine 2-3 antibiotics with an acid-suppressing drug

- ???      How is *Hp* killed ?
- PPI decreases MIC some antibiotics
- Some antibiotics can cross gastric mucosa
- Direct anti-*Hp* effect in stomach or absorption first and then secretion into gastric lumen ?

# How do PPIs work in *Hp* Treatment ?

Direct anti-*Hp* effect

- increase killing capacity antibiotics (MIC)  
by raising pH
  - Clarithromycin and Amoxycillin MIC increase x10
  - Metronidazole no effect
- Change gastric milieu
  - Gastric juice volume

# Effect PPI

## MACH2 Study (N=514)

CM	69 %	
OCM	87 %	<u>GAIN 18%</u>
CA	26 %	
OCA	94 %	<u>GAIN 68%</u>

Gastroenterology 1999;116:248-253



# Twice daily PPI triple therapy

PPI- Clarithromycin and Amoxicillin (PPI-CA)

PPI- Clarithromycin and Metronidazole (PPI-CM)

are equally effective → > 70-80 %



# Aklavik *H. pylori* Project

## Treatment Considerations

- A few anti-*H. pylori* treatment regimens somewhat higher success rates in trial reports.

### 1) Quadruple therapy,

- proton pump inhibitor, bismuth, metronidazole and tetracycline

Estimated to be 87% in Canada.

### 2) 10-day sequential therapy

- proton pump inhibitor and amoxicillin for days 1-5,
- proton pump inhibitor in combination with tinidazole and clarithromycin days 6-10

# RCT Sequential vs PPI-CA

- N = 300

- Results

Sequential 89%

PPI-CA 77%

	<u>Sequential</u>	<u>PPI-CA</u>
• Clari-R	8/9 (89%)	6/21 (29%)
Clari-S	108/114 (95%)	86/91 (95%)

Ann Intern Med 2007;556-563

# Aklavik *H. pylori* Project

## Treatment Considerations

- Rationale for sequential therapy (De Francesco et al 2006).
  - amoxicillin, beta-lactam antibiotic,
  - compromises the cell wall
  - preventing efflux channel development for drugs like clarithromycin, making them more potent in phase two of the therapeutic regimen

# What is the impact of resistance?

- clarithromycin-resistant strains
  - decreased effectiveness in treating with clarithromycin based regimens
- metronidazole-resistant strains
  - high-prevalence populations,
  - Can use metronidazole - higher dose and/or if the regimen is taken for a longer duration.

# Objectives: Treatment Phase

1. Identify the most effective *H. pylori* therapy for infected individuals in the Aklavik *H. pylori* Project
2. Examine the effect of adherence to medication regimens and other clinical and demographic factors on treatment success

# Participants: Treatment Phase

Positive UBT and/or biopsy-based evidence of *H. pylori* infection  
(pathology or culture)

Subdivided based on their *H. pylori* resistance profiles and previous  
therapeutic intervention:

## 1) Treatment naïve:

Metronidazole resistant

Clarithromycin resistant

Susceptible to all drugs assessed

No resistance profile available

## 2) Treatment failures

# Inclusion Criteria

≥ 15 years old

evidence of *H. pylori* infection from initial study:

\*breath-test positive,

histopathology or culture consistent with *H. pylori* infection

\*Those without a breath test result at the outset of the trial will be required to complete one before enrolment. Those with inconsistent test results, will be offered the opportunity to repeat the breath test before deciding whether to undergo treatment, a decision that will be made in consultation with project physicians.



# Exclusion Criteria

Allergies to study medications

Treatment within the past 4 weeks with antibiotics

Severe cardio-respiratory, pulmonary, endocrine, hepatic or renal disease on anticoagulant therapy or other medication with serious drug interaction with study medications

Pregnant or lactating females

# Subject Requirements

- Pre-treatment C13-urea breath test (if there is no baseline breath test available from earlier phases of this study.)
- Measure adherence (bubble pack round-up)
- Post treatment questionnaire
- Follow-up breath-test at 6-8 weeks post-treatment – to determine the outcome of treatment
- Re-treatment option for participants who fail to eradicate

# Randomization

- Random number allocation
- If metro-R or without profile -> PPIAC vs ST
- If clari-R -> ST vs Q T
  
- Odd HP pack or QT (depending on their group allocation)
- Even to ST

RX for Aklavik H pylori Project: Phase III, Treatment

Patient: \_\_\_\_\_

DOB: \_\_\_\_\_

Healthcare number: \_\_\_\_\_

PLEASE BLISTER PACK MEDICATIONS.

MEDS TO BE DISTRIBUTED TO THE SUSIE HUSKY HEALTH CENTRE: Aklavik NT

Rx (circled regimen is regimen prescribed):

- a) **Conventional therapy – PPI- AC :**  
Rabeprazole 20mg po bid x 10/7  
Amoxicillin 1 gram po bid x 10/7  
Clarithromycin 500mg po bid x 10/7
  
- b) **Sequential therapy**  
Rabeprazole 20mg po bid x 10/7  
Amoxicillin 1 gram po bid x 5/7 (days 1-5)  
Clarithromycin 500mg po bid x 5/7 (days 5-10)  
Metronidazole 500mg po bid x 5/7 (days 5-10)
  
- c) **Quadruple therapy**  
Rabeprazole 20mg po bid x 10/7  
Bismuth 2 tablets qid x 10/7  
Tetracyclin 500mg po qid x 10/7  
Metronidazole 500mg po qid x 10/7

Repeats 0 (zero).

Dr Amy Morse R4 for Dr S van Zanten (Division of GI University of Alberta)

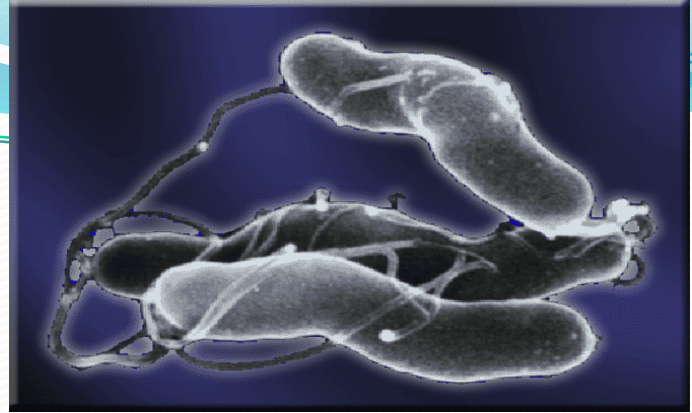
# Results

- **53 Rx for PPI AC**
- 3 Rx for Q uadruple therapy
- **55 Rx for ST**
  
- 74 (74/111 = 67%) packs returned thus far (as of Dec 28/08)
  
- 1 participant withdrawn for need for antibiotics for dental infection after treatment initiated

# What's next

- Follow-up U BT in Feb 09
- Q uestionnaire results pending
- Other communities...?

# 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 Team

