Aklavik *H pylori* Project Treatment Phase: seeking an effective therapy for a Canadian Arctic hamlet.

Morse AL, Goodman KJ, Munday R, Morse J, Van Zanten SV, CANHelp Working Group
CANHelp (Canadian North Helicobacter pylori) Working Group

Aklavik Community Organizations
- Rachel Munday, Nurse in Charge, Aklavik Health Centre
- Aklavik Health Committee
- Billie Archie, Arctic Health Research Network, Aklavik Chapter

NWT Agencies
- Andre Corriveau, Former Chief Medical Officer, Health and Social Services, NWT
- John Morse, Former Medical Director, Stanton Territorial Health Authority
- Leah Seaman, Beaufort-Delta Regional Health and Social Services Authority
- Susan Chatwood, Director, Arctic Health Research Network

Capital Health
- Robert Bailey, Director, Northern Health Services Network

University of Alberta
- Principle Investigator: Karen Goodman, Epidemiology
- Gastroenterology: Sander van Zanten, Justin Cheung, Amy Morse, Richard Fedorak
- Microbiology: Monika Keelan, Joanne-Simala Grant
- Pathology: Safwat Girgis
- Anthropology: Christopher Fletcher
- Health Policy: Carl Phillips
BACKGROUND: WHAT IS THE AKLAVIK HP PROJECT?
Project Goals

• To address community concerns about health risks from *H. pylori* infection

• To recommend *H. pylori* management strategies to health authorities

• To reduce health risks from *H. pylori* infection
Initial Research Project

Aklavik *H. pylori* Project Aims

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 so that the resulting knowledge becomes part of the community knowledge base
Study Community: Aklavik, NWT

Location:

• On Peel Channel of Mackenzie River Delta
• North of Arctic Circle
• 113 km south of Arctic coast
Study Community: Aklavik, NWT

• 2004 population: 631
  – 90% Inuvialuit (Inuit) or Gwich’in Dene (First Nation)

• Access
  – Reached only by air or by winter ice-road from Inuvik
Selected Study Community
Aklavik, NWT

Why Aklavik?

• Selected by NWT health authorities as a starting place for this research
  – High level of community concern due to stomach cancer deaths in some families
  – Enthusiasm for the research from local health authorities

• Other communities to be included later for comparison
BACKGROUND: HP AND TREATMENT
Why the concern regarding Hp?

- Chronic bacterial infection
- Association with gastritis, peptic ulcer disease and gastric cancer (Van Zanten 1994)
- Chronic *H. pylori* infection is thought to be acquired in childhood and has been associated with overcrowding and having family members with the infection.
- The Canadian Helicobacter Study Group has identified three groups at high risk of *H. pylori* infection and subsequent disease – 1) the elderly, 2) immigrants and 3) First Nations and Inuit populations.
Why the concern regarding Hp?

• Earlier phases of the Aklavik *H. pylori* Project found the prevalence of Hp infection to be 58% (UBT), and 67% with endoscopy and histopathology.
Treatment of Hp

- Current recommendations for first time therapy for *H. pylori* infection in Canada, including the NWT, endorse triple therapy
  - PPI plus clarithromycin and amoxicillin/metronidazole (PPI-CA or PPI-CM).
- Canadian eradication rates: 84% and 82% (Rodgers & van Zanten 2007).
- There are no reports of the effectiveness of these treatments in Canada’s Arctic populations, but anecdotal impressions among clinicians in the Canadian North *Helicobacter pylori* (CANHelp) Working Group are that treatment failure is a common problem.
Treatment of Hp con’t

- A few anti-\textit{H. pylori} treatment regimens somewhat higher success rates in trial reports.

1) Quadruple therapy,
   - including a PPI, bismuth, metronidazole and tetracycline (PPI-BMT),
   - Estimated to be 87% in Canada.
Treatment of Hp con’t

2) 10-day sequential therapy
   – PPI and amoxicillin for days 1-5,
   – PPI with tinidazole and clarithromycin days 6-10
   • Superior to standard triple therapy (89% vs 77% in one trial) (Vaira et al 2007).
   • Further supported by a recent meta-analysis (Nadim, Horung and Howden, 2008) that estimated eradication in 93% with sequential therapy.
   • There is no data to date on the success of sequential therapy in a Canadian population
Treatment of Hp con’t

• Rationale for sequential therapy
  – Amoxicillin (beta-lactam antibiotic) compromises the cell wall during the initial phase of therapy thus preventing efflux channel development for drugs like clarithromycin, making them more potent in phase two of the therapeutic regimen (De Francesco et al 2006).
Inclusion/Exclusion Criteria

- ≥15 years old
- Evidence of *H. pylori* infection from initial study: *breath-test positive*, histopathology or culture consistent with *H. pylori* infection
- *All participants required to have a breath test as that is the parameter to be followed for eradication, repeat endoscopy and biopsy not feasible

- Allergies to study medications
- Treatment within the past 4 weeks with antibiotics. Unless breath-test done in interim is positive reflecting on-going infection.
- 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
What about the Hp positive persons who were not eligible or not interested in the treatment trial?

• Offered treatment outside the trial.
Randomization for Treatment Naive

- Random number allocation
- Odd PPI-AC
- Even to ST

- Please note that if sensitivities were available for an individual they were not randomized to a regimen that was felt to be ineffective
RESULTS
Participants

• 157 adults with Hp
• 111 patients randomized
• *103 treatment naive patients randomized (*12 persons with documented treatment failures)
• 71 treatment naive participants with repeat UBT results
  – 35 ST vs 36 PPIAC
Eradication Rates

- PPIAC: 66
- ST: 77
• Exact 95% confidence intervals
  – PPIAC: 0.67 (0.490-0.814)
  – ST: 0.77 (0.599 - 0.896)
  – P = 0.165
DISCUSSION
Is there really a difference between the regimens?

- Trend seems there
- BUT, not powered enough to see if the difference is real
- Plan: continue to evaluate the two regimens in Circumpolar (Old Crow) and Canadian populations (Edmonton)
Why are the eradication rates lower than anticipated?

• treatment failure is more common in high-prevalence populations.
  – Typically achieve success in 80-90% of patients (Graham & Shiotani, 2008) treatment failure is more common in high-prevalence populations.
  – ? Re-infection

• Both regimens have clarithromycin
  – Some participants had no biopsy therefore no C&S results
  – 33% of the Aklavik *H pylori* was metronidazole resistant, **13% was clarithromycin resistant** and 4% was resistant to both
  – Evaluation of resistance patterns within the specific groups pending

• What proportion of persons completed all doses?
  – Post-treatment patients were asked to turn in blister packs with untaken medications left in, analysis pending
Special Thanks

• Karen Goodman and Sander Van Zanten
• Julianne and the team at Rexall Drug Inuvik
• Rachel Munday and the team at the Susie Husky Health Centre
• Mike Arget and Janis Huntington
• Community coordination team in Aklavik (Evelyn Wilson, Sally Kasook and Joanna Hartley)
• Aklavik Health Committee (Robert Buckle, Chair)
• The Hamlet of Aklavik for their hospitality and drive to take control of their health.
Aklavik Project Funding Agencies

• Alberta Heritage Foundation for Medical Research
• Canadian Association for Gastroenterology with Canadian Institutes for Health Research / AstraZeneca
• Social Sciences and Humanities Research Council
• Public Health Agency of Canada
• Indian and Northern Affairs Canada
• Canadian Circumpolar Institute
Aklavik Project Supporters

[Logos of the supporters]
The Aklavik Project Team

Questions???
PPI bid
Amoxicillin 1g bid
Levofloxacin 500 mg bid

In Italy > 80%
In Canada ?, USA