



Aklavik *H. pylori* Project

## **Aklavik *H. pylori* Project Progress Report**

**1 Apr 2015**



*The Aklavik H. pylori Project is the initial project of a collaborative effort of the Canadian North Helicobacter pylori (CANHelp) Working Group to investigate H. pylori infection in northern Canada with goals of addressing community concerns, improving clinical management and reducing health risks.*

**Report Date:** 1 Apr 2015

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## Overview of Project Timeline and Findings

What has been done so far?

- Around 65% of Aklavik residents have participated in this project.
- Completed components of the project include *H. pylori* screening by breath test, collection of questionnaire data, endoscopy, and treatment.

What remains to be done?

- Long-term follow-up is ongoing, as is analysis of questionnaire data and reporting research results back to the community.

What have we learned?

- Of participants screened by breath test, 58% were positive for *H. pylori* infection.
- Of those who had a scope test and whose stomach biopsies revealed *H. pylori* when examined by a pathologist, 91% had moderate to severe chronic inflammation of the stomach; this frequency of moderate to severe chronic inflammation is consistent with an increased risk of stomach cancer in this community.
- Of treatments investigated in Aklavik, Old Crow, and Fort McPherson, early results show that a 4-drug regimen is much better than the 3-drug regimen most commonly used in Canada to treat *H. pylori* infection (HP-Pac), but we need more data to be sure about this.
- Available treatments for eliminating *H. pylori* infection are burdensome and more research is needed to find out how to make them more effective.
- Follow-up *H. pylori* testing in Aklavik suggests that most people who were successfully treated remained *H. pylori*-free for 2 years or longer.
- CANHelp Working Group research so far has not pinpointed an environmental source of *H. pylori* in Aklavik or other communities where *H. pylori* projects are being carried out; this is consistent with findings of research around the world: the evidence suggests that most people with *H. pylori* infection get it from direct contact with a person who has the infection.

### **Aklavik *H. pylori* Project Timeline**

- Wave 1 data collection
  - Recruitment and health questionnaires Nov 2007 to Feb 2008
  - *H. pylori* screening by breath test Jan to Feb 2008
- Endoscopy Feb 4 to 8 2008
- Pathology Feb to Apr 2008
- Microbiology Feb to Nov 2008
- Pathology results reported to participants Apr 2008
- Wave 2 data collection
  - Breath testing, participant questionnaires Apr 2008
- Wave 3 data collection
  - Breath testing, participant questionnaires Sep to Nov 2008
  - Knowledge transfer strategy development Apr to Oct 2008
- Treatment Nov to Dec 2008
- Short-term treatment follow-up & participant questionnaires Jan to Mar 2009
- Long-term treatment follow-up Nov 2011 to Mar 2012
- Inform community of research results Ongoing

### **Participation and Data Counts**

- Participants recruited: 376
- Interviewer-administered health questionnaires completed: 345
- Breath tests completed: 333 (332 have a positive, negative, or borderline result)
- Aklavik residents consenting to endoscopy: 200
- Aklavik residents completing endoscopy: 195 (194 completed with biopsies)
- Biopsies available for *H. pylori* testing: 194
- Interviewer-administered participant questionnaires completed:
  - 285 individual respondents
  - 145 household respondents (reporting household data for 295 individuals)
- Participants consenting to treatment: 181
- Participants assigned treatment: 126
- Treatment trial participants: 113
- Post-treatment breath tests completed: 112 (111 have a positive, negative, or borderline result; 1 had an unclassifiable result)
- Interviewer-administered post-treatment questionnaires completed: 94

## Findings to Date

- Proportion positive on breath test: 58% (193/332)
- Endoscopic findings from 195 Aklavik residents:
  - Gastritis: 14% (27/195)
  - Gastric erosions: 6% (12/195)
  - Gastric ulcer: 3% (6/195)
  - Duodenitis: 7% (13/195)
  - Duodenal erosion: 1% (1/195)
  - Duodenal ulcer: 0
  - Esophagitis: 10% (20/195)
  - Barrett's esophagus: 3% (5/195)
- Pathology findings (Sydney classification) from 194 Aklavik residents:
  - Chronic gastritis: 68% (132/194)
    - Severe: 29% (56/194)
    - Moderate: 31% (61/194)
    - Mild: 8% (15/194)
  - Atrophic changes: 14% (27/194)
  - Intestinal metaplasia: 8% (16/194)
  - *H. pylori* positive: 67% (129/194)
    - Among 129 *H. pylori*-positive participants :
      - Chronic gastritis: 100% (129/129)
        - Severe gastritis: 43% (56/129)
        - Moderate gastritis: 47% (61/129)
        - Mild gastritis: 9% (12/129)
      - Atrophic changes: 21% (27/129)
      - Intestinal metaplasia: 11% (14/129)
- Microbiology findings from 194 Aklavik residents:
  - Culture positive: 73% (142/194)
  - Antibiotic susceptibility tests were performed on 120 isolates obtained from culture:
    - Resistance to any antibiotics tested: 32% (38/120)
      - Metronidazole: 28% (34/120)
      - Clarithromycin: 8% (10/120)
      - Ciprofloxacin: 2% (2/120)
      - Nitrofurantoin: 2% (2/120)
      - Amoxicillin, tetracycline, rifampicin: 0
    - Resistance to multiple (2 or 3) antibiotics: 7% (8/120)
      - Clarithromycin + Metronidazole: 5% (6/120)
      - Clarithromycin + Metronidazole + Ciprofloxacin: 1% (1/120)

- Clarithromycin + Metronidazole + Nitrofurantoin: 1% (1/120)
- Treatment success among 89 treatment-naïve trial participants with post-treatment breath test:
  - Standard triple therapy: 59% (29/49)
  - Sequential therapy: 70% (28/40)

The breath test prevalence (proportion positive) of 58% is a better reflection of the prevalence of *H. pylori* infection in Aklavik than the 67% positive by pathological assessment of biopsies (or the 73% positive by culture) among those with biopsies from endoscopy. Since residents who were informed of positive breath test results were motivated to undergo endoscopy, there are proportionally more positives in the latter group. The *H. pylori* prevalence of 58% is similar to what has been observed in other Inuit communities in Canada and Greenland. (See: Goodman KJ, Jacobson K, Veldhuyzen van Zanten SJ. *Helicobacter pylori* Infection in Canadian and Related Arctic Aboriginal Populations. *Can J Gastroenterol*, 22:289-95, 2008)

## Summary of On-going and Previous Project Activities

### 1. On-going Project Activities

#### 1.1 Recent Activities

Ethnographic Fieldwork Lead, Dr. Sally Carraher, traveled to Aklavik May to June 2014 to continue her ethnographic research on the local kinship system, and to supervise and assist other CANHelp team members with data collection. During her time in Aklavik, Sally also updated the Aklavik *H. pylori* Project Planning Committee on several ongoing projects, including the continuation of the water study, investigating antimicrobial effects of traditional medicines on stomach health, and the expansion of the knowledge exchange program.

MSc student Kate Williams traveled to Aklavik in July 2013 and again in June 2014 to collect antibiotic exposure histories from medical charts of participants who had *H. pylori* cultured from stomach biopsies and tested for antibiotic susceptibility and/or were treated and completed a post-treatment breath test. For each of these participants, information was collected for the five-year period before project enrolment on: demographic factors; frequency of antibiotic prescriptions; type of antibiotics prescribed; and reason for prescription. Kate will use this information for her MSc thesis, to estimate associations of antibiotic exposures on two health outcomes: 1) the prevalence of antibiotic-resistant *H. pylori* infection and 2) success of treatment to eliminate *H. pylori* infection.

Emily Hastings, PhD student and Data Dissemination Lead, travelled to Aklavik in May 2014 to conduct semi-structured qualitative interviews with key informants from the community to identify specific research questions that address predominantly-expressed community concerns

about the health effects of regular exposure to environmental contaminants. Emily will use this information, along with information from similar interviews conducted in other communities, to focus her PhD dissertation work. She completed 2 interviews in Aklavik, which were recorded, transcribed and analyzed to identify major themes. Some aspects of this analysis are ongoing.

## **1.2 Upcoming Activities**

Sally Carraher will return to Aklavik during June to August 2015 to follow up with residents about their knowledge of *H. pylori* and try to gauge how much people in the community have learned through years of involvement in a long-term project like the Aklavik *H. pylori* Project, particularly whether or not perspectives of *H. pylori* and *H. pylori*-related science are changing.

## **2. Previous Project Activities**

### **2.1 First Wave of Data Collection (Nov 2007 to Feb 2008)**

Community coordinators Evelyn Wilson and Trevor McNutt initiated informed consent and clinical questionnaire contacts in November 2007, actively recruiting participants at strategic community locations. The research assistant team joined the community coordination team to boost the field work efforts from December 29 through to January 12. During January 2008, our recruitment and screening efforts prioritized obtaining endoscopy consents from those who were prepared to agree regardless of breath test results, and breath testing for those whose willingness to be scoped depended on breath test results. At the same time, we told participants about the advantages of having both the breath test and endoscopy, regardless of test results. To increase recruitment, project staff set up recruitment posts at the supermarket and post office. The project staff created a map of the hamlet to track door-to-door coverage of households. During January 11 to 13, Aklavik staff members were trained on the breath test protocol. The new infrared breath test analyzer (IRIS-2, Wagner, Germany) was installed and functional by January 24. On January 28, we began reporting breath test results to participants.

Aklavik resident Heather Stewart was hired in January to assist the community coordination team. Radio announcements to encourage participation were ongoing throughout the same month. Once breath test results were available, we announced the prevalence of positive results in Aklavik residents who had been tested so far (consistently around 55%). Following endoscopy week, the project office remained open during reduced hours to conduct breath tests.

### **2.2 Community Response to Initial Recruitment Efforts**

Initial recruitment efforts were met with a positive response from the community. Most residents contacted indicated a desire to participate. The biggest challenge was getting potential participants to follow through on scheduled appointments to complete the informed

consents, questionnaires, and breath test. The field team used active recruitment with multiple invitations and reminders. A challenge for the endoscopy phase of the project was the fraction of participants who indicated they were willing to be scoped only if they had a positive breath test. Of the initial 100 questionnaires completed, 40 respondents indicated a willingness to consent to endoscopy, another 30 or so said they would do so if they had a positive breath test, and the remainder were too young for endoscopy. This response shows that a very high proportion of participants were willing to consider endoscopy, particularly if they had a positive breath test result, but highlighted the need to have breath test results available before endoscopy, as well as the need to inform community members that endoscopy would provide a more thorough evaluation than the breath test, so those who were breath-test negative were also encouraged to have an endoscopy.

### **2.3 Community Response during Endoscopy Week (Feb 4 to 9, 2008)**

The endoscopy team arrived in Aklavik on Sunday, February 4, 2008. That evening, a community meet-and-greet was held and was well attended. Each evening during the week, residents were called to schedule appointments for the next day. In addition, team members went on the radio to encourage residents to come to the health centre to be scoped. Many team members engaged in outreach at various social events and during casual interactions with community residents. Community activities that were arranged for team members included: lunch at the preschool, a youth dance presentation at the community arena, lunch at the Indian Band offices, health careers presentations by team members to high school students, tours of the school, curling, visits to the market and crafts shop, and evening patrols.

Upper gastrointestinal endoscopies were performed at the Aklavik Health Centre in temporary endoscopy units equipped with rented endoscopy towers and gastroscopes, with technical support from Olympus Canada. Experienced endoscopy nurses and service workers assisted the gastroenterologists. Study participants 15+ years of age who wished to undergo endoscopy were eligible, as were children whose parents request that they be included, at the gastroenterologist's discretion.

The number of individuals who appeared at the health centre to be scoped each day were as follows: 39 on Monday, February 4; 37 on Tuesday, February 5; 54 on Wednesday, February 6; 43 on Thursday, February 7; and 24 on Friday, February 8. Of 200 residents who appeared at the health centre to be scoped, 191 completed the ultra-thin scope procedure without sedation (mostly with transnasal insertion), 5 were sedated, 5 were not able to complete the procedure, and another 1 participant could not have biopsies taken. No adverse effects occurred during the endoscopies, with the exception of a few minor nosebleeds and mild to moderate discomfort. A post-endoscopy patient satisfaction questionnaire indicated that most of those scoped tolerated the procedure well and would be willing to have it in the future if needed.



## **2.4 Biopsy Data**

Dr. Safwat Girgis, the team Pathologist, completed pathologic assessment of biopsies in April 2008. During April 23 to 30, 2008, Dr. Justin Cheung returned to Aklavik to report pathology findings to each participant individually.

The team microbiologist Dr. Monika Keelan's lab processed biopsies for culture, encountering a number of samples that grew very slowly. Preliminary identification of *H. pylori* was performed with biochemical testing and morphology (wet mount); confirmation was performed by 16S rRNA gene sequence analysis. Twelve isolates were damaged in the lab by an anaerobic jar seal failure. Antibiotic susceptibility testing was initiated during summer 2008 and took much longer than anticipated. Genotyping was initiated during winter 2009 and has led to new projects expected to continue for a few years.

## **2.5 Waves 2 & 3 of Data Collection**

Data collection continues whenever there is an opportunity for project staff to collect more questionnaires or conduct more breath tests. The epidemiology questionnaire was launched during Justin Cheung's April 2008 visit to take advantage of the large number of project participants who come into the health centre. Aklavik residents were informed that the end of September 2008 would be their last chance to be tested for *H. pylori* in time to participate in the treatment phase, which was initiated in late November 2008.

## **2.6 Treatment Trial**

Dr. Amy Morse, University of Alberta Gastroenterology Fellow, coordinated the treatment phase of the project. Working with Dr. Goodman (Scientific Director) and Dr. van Zanten (Lead Gastroenterologist), Amy Morse developed a treatment protocol and study information sheet for informed consent, which were reviewed by the Aklavik Study Planning Committee and approved by the University of Alberta ethics board. In late November 2008, Amy Morse went with Dr. John Morse, and Sander van Zanten to Aklavik to evaluate candidates for treatment and to oversee the administration of therapy with the support of Rachel Munday, the Aklavik Health Centre Nurse in Charge. Aklavik project staff Sally Kasook and Joanna Hartley coordinated the activities at the Aklavik Health Centre. This included phone reminders to participants in the treatment trial during the course of treatment as well as collection of bubble packs to count unused medication and administration of a post-therapy questionnaire. The treatment trial randomized 113 participants; 95 had a post-treatment breath test, 65% of which were negative. Used bubble packs were collected from 43 participants. Treatment was also given to 12 adults and 16 children who were not in the trial. Several trips were made in 2009 to conduct the post-treatment breath tests.

## **2.7 Knowledge Exchange**

Janis Geary (previously Huntington) traveled to Aklavik April 4 to 15 and June 25 to July 24 of 2008 to work on her funded project: "Knowledge Transfer of Health Research Findings to Community Members of Aklavik, NWT," for which she obtained community input to use in the development of effective knowledge exchange strategies under the guidance of

anthropologist Dr. Chris Fletcher. This research identified several preferred strategies including some already being used (radio announcements, newsletters, flyers, meetings with local organizations) and some to be developed (discussion groups involving youth and elders, presentations at community events, and a video documentary). Christopher White, a filmmaker from Yellowknife, was hired to make the documentary. It was filmed in Aklavik from May to June of 2009, and in Edmonton from July of October of 2009. In 2010, the health committee screened “Never say die: The Aklavik *H. pylori* Project”, a documentary produced by the CANHelp Working Group which aims to help community members understand the research process and results. Initial reactions to the documentary were very positive. A formal evaluation of this type of media as a knowledge exchange tool is currently pending.

### **2.8 Chart Review Follow-up**

Ashley Wynne traveled to Aklavik from May to June 2011 to complete her funded project on improving our instrument for conducting chart reviews at the Aklavik Health Center. The chart review included collecting information regarding previous stomach and esophageal complaints (during the past 5 years) as well as previous testing and treatment for *H. pylori* infection. A comprehensive assessment of the previous chart review tool was conducted, and the tool was improved based on these findings. The new chart review tool was then used to thoroughly re-review all charts with any history of gastrointestinal complaints (n=120). The first and second rounds of chart review have been merged and are now ready for analysis.

### **2.9 Treatment Follow-up**

PhD student Sally Carraher (now Ethnographic Fieldwork Lead) traveled to live in Aklavik from mid-September 2011 to mid-June, 2012, to conduct an ethnographic study of the Aklavik *H. pylori* Project. Ethnography in the project serves as a way to augment and enrich the descriptive epidemiology of *H. pylori* infection risk factors, by exploring local kinship organization and socio-economic structure. Ethnography also serves a knowledge translation role, as important issues regarding different worldviews and understandings of current *H. pylori* research practices and findings are investigated through the use of participant observation. By strengthening communication between various parties involved in community-based research, this project aims to help promote the direct application of research knowledge into effective *H. pylori* screening and treatment practices, both in Aklavik and other remote northern communities throughout Canada.

During this time, Sally also followed up with treatment participants to determine the proportion of individuals re-infected with *H. pylori* since the trial was carried out in November 2008 and with participants who did not have *H. pylori* when first tested to see if any of them have become infected.

In November 2011, PhD student Megan Lefebvre traveled to Aklavik to follow-up with treatment participants who had not yet completed a post-treatment questionnaire. She carried out an analysis of the post-treatment questionnaire data looking at adherence and

barriers to completing treatment. Findings from this analysis may lead to developing community-specific strategies to improve adherence.

### **2.10 Knowledge Exchange Program**

In 2011, the CANHelp Working Group received a CIHR “Meetings, Planning, and Dissemination” grant to develop an innovative strategy for making microbiology research results meaningful to community members. In consultation with the Aklavik Health Committee, Monika Keelan, Amy Colquhoun and Sally Carraher have launched an exchange program that facilitates sustained contact between two community members and three Aklavik *H. pylori* Project researchers, in an effort to develop an iterative, participatory data dissemination project. Sally and Monika traveled to Aklavik in September 2012 to meet with community members and organizations and recruit two youth for the exchange project. In October 2012, two community members traveled to the CANHelp microbiology lab in Edmonton to learn how the *H. pylori* bacteria and DNA were isolated, characterized, and analyzed, and how to interpret the microbiology results. They also met with the public health researchers and gastroenterologists in the CANHelp and University of Alberta Hospital offices respectively.

During November-December 2012, the two community members worked with Aklavik’s grade 10 general science students to develop materials for educating community members about *H. pylori* microbiology research. The resulting dissemination materials will be used to help present Aklavik *H. pylori* Project results to other interested Arctic communities. Evaluation of this exchange program will be used to improve CANHelp Working Group collaborative research methodologies and knowledge dissemination initiatives.

The two community members also traveled to Vancouver in December 2012 to assist Sally Carraher with presenting on our microbiology data dissemination project at the ArcticNet annual scientific conference, where they won an award for best poster presentation!

### **2.11 Dissemination Activities**

Dr. Sander van Zanten, Lead Gastroenterologist, and Emily Hastings, Data Dissemination Lead, travelled to Aklavik from March 25 to 31, 2013 to meet with project participants and present results from Emily’s MSc thesis research on environmental exposures and transmission of *H. pylori*. Sander and Emily went on the radio to present results from the project so far and to answer questions that community members called in. They were also available to meet with community members interested in hearing more about the project and discussing results at the health center. The following is a summary of results presented to community members:

Emily’s thesis results indicate that *H. pylori* infection did not occur more frequently in individuals exposed to investigated environmental sources that could potentially be contaminated with the bacteria, relative to participants who were not exposed to these sources. This includes environmental exposures such as untreated water, sewage, cats and dogs. Since contamination of local water sources with the bacteria is a commonly expressed concern in communities across

the north, continued analysis of the role of environmental exposures in transmission of *H. pylori* will include testing water samples from northern communities to determine whether living *H. pylori* organisms are in local water sources.

Preliminary analysis of the effect of exposure to mice indicates that *H. pylori* infection was more frequent in individuals who reported having evidence of mice in their home, relative to those who did not report having evidence of mice in their home. Further research is needed to address whether there is a potential role for mice in transmission of *H. pylori* or if evidence of mice in the home is a marker for another source of transmission. It should be noted that a very small proportion of participants reported exposure to mice. Therefore, even if it is possible for mice to transmit the bacteria, it is not likely that this the usual route by which *H. pylori* spreads.

During this trip, Emily also completed follow-up breath tests with participants who had received treatment through the project to ensure that the infection was cleared. Individuals were then notified of their infection status and further care was arranged for participants who were still positive.

In May and June 2013, Dr. Sally Carraher returned to Aklavik to meet with the Aklavik Health Committee and other community stakeholders. During that time, she provided copies of her dissertation results to community organizations and the health centre, presented the findings of her ethnographic research at different community events, and sought feedback to use in our continuing data dissemination and knowledge translation efforts.

### **2.12 Pilot Water Study**

In 2013, with guidance from the Aklavik *H. pylori* Project Planning Committee, Dr. Keelan supervised a summer student, Yashna Beesoon, in a pilot study to test local water sources for living *H. pylori* organisms. Water samples were collected from treated water and untreated surface water sources in July and filtered for DNA and RNA extraction; the filters were cultured in an attempt to grow any *H. pylori* organisms present. The cultures did not yield *H. pylori* isolates and no *H. pylori* DNA was detected in the water samples. Failure to detect organisms, however, cannot be interpreted as ruling out water as a mode of transmission, because the methods used in this investigation might not be sufficiently sensitive. In particular, larger water sample volumes may be required to collect a sufficient number of organisms for detection. Planning committee members have requested that additional approaches to water testing be attempted to overcome the limitations of the pilot project.