Updates on *H. pylori* research in Alaska

Bethel, Alaska, July 26th 2016

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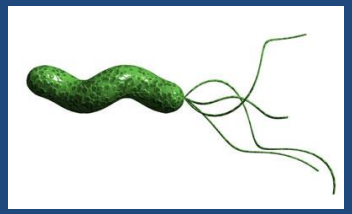
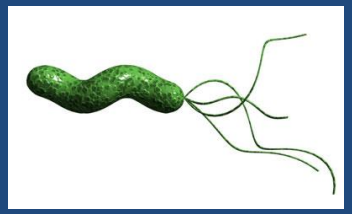


H. pylori Epi Background



- Organism: helical-shaped gram negative rod
- Reservoir: Humans
- Transmission: unknown
  - Probable fecal-oral
  - Possible oral-oral

What we have learned from previous studies in Alaska

- Seroprevalence among Alaska Native people is high: 75% overall*
- The proportion of isolates demonstrating antimicrobial resistance is high♦
- Treatment failure rate: 35%♦
- Reinfection rate at 2 years is high: 16%**
- *H. pylori* IgG antibody positivity is associated with gastric cancer in a case-control study╪

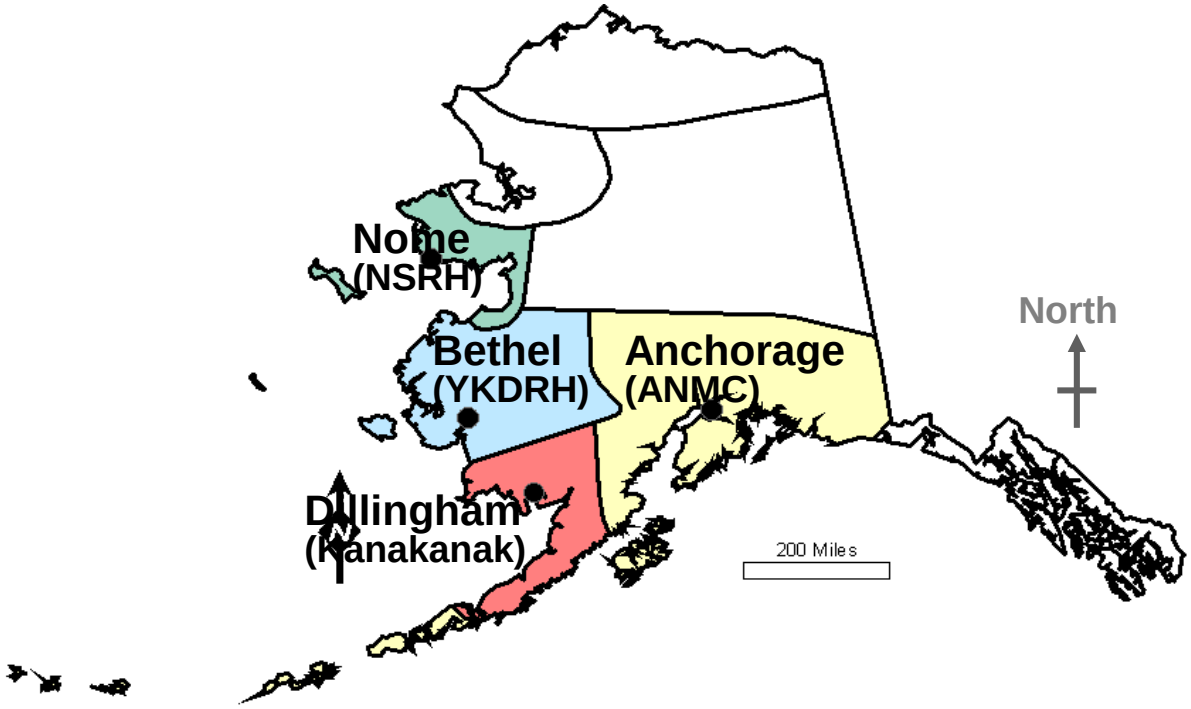
*Parkinson et al. *Clin Diagn Lab Immunol* 2000, ♦McMahon et al. *Ann Intern Med 2003*,
**Bruce et al. *Epi and Infection Journal* 2014, ╪Keck et al. *Can J Gastroenterol Hepatol* 2014

Ongoing Studies and Surveillance Alaska

- Antimicrobial resistance update from surveillance
- 12 year Reinfection study results
- Guidelines for diagnosis and treatment of *H. pylori* in Arctic Regions

Alaska Sentinel Surveillance for Antimicrobial Resistance

- **Norton Sound Regional Hospital (NSRH)**
- **Yukon Kuskokwim Delta Regional Hospital (YKDRH)**
- **Kanakanak Hospital**
- **Alaska Native Medical Center (ANMC)**



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Antimicrobial Resistance 2000-2014

Antibiotic	n/N	% Resistant
Metronidazole	308/676	**46%**
Clarithromycin	209/676	**31%**
Levofloxacin	97/630	**15%**
Amoxicillin	12/676	**2%**
Tetracycline	2/676	**0.3%**
Metronidazole & Clarithromycin	117/676	**17%**
Metronidazole & Clarithromycin & Levofloxacin	28/650	**4%**

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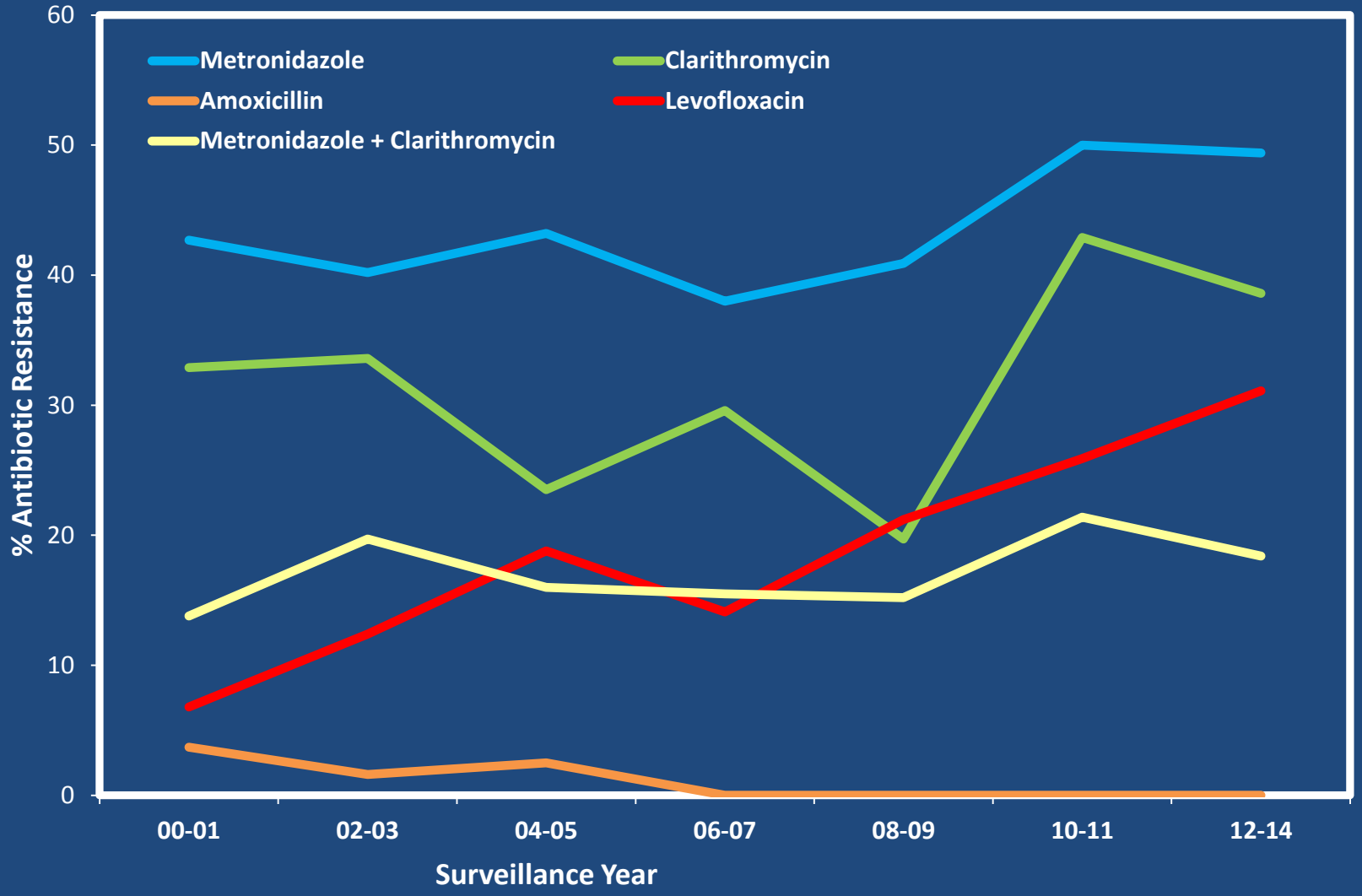
Trends in Antimicrobial Resistance 2000-2014



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Conclusions From Surveillance

- High proportion of *H. pylori* isolates are resistant to antibiotics in Alaska
- Rising levofloxacin resistance
  - >1 of 4 persons now demonstrate levofloxacin resistance
- Continued surveillance may help guide future antimicrobial therapy recommendations to medical providers for treatment of *H. pylori* infections in the AN/AI population

Participants
12 Year Reinfection Study

- Inclusion criteria
  - Urban Alaska Native & non-Native adults who participated in the 2 year reinfection study

Reinfection Rates with 12-year recruitment combined and separately

Time Period	Combined	Rural AN	Urban AN	Urban Non-AN
4-month	4.4%	10.1%	5.1%	3.2%
6-month	7.5%	13.0%	7.1%	8.2%
1-year	9.5%	16.0%	10.2%	8.2%
2-year	13.5%	22.1%	14.4%	12.0%
12-year	23.5%		26.9%	16.2%

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doi:10.1017/S0950268815001181

REVIEW ARTICLE
The diagnosis and treatment of *Helicobacter pylori* infection in Arctic regions with a high prevalence of infection: Expert Commentary

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SUMMARY

Helicobacter pylori infection is a major cause of peptic ulcer and is also associated with chronic gastritis, mucosa-associated lymphoid tissue (MALT) lymphoma, and adenocarcinoma of the stomach. Guidelines have been developed in the United States and Europe (areas with low prevalence) for the diagnosis and management of this infection, including the recommendation to 'test and treat' those with dyspepsia. A group of international experts performed a targeted literature review and formulated an expert opinion for evidenced-based benefits and harms for screening and treatment of *H. pylori* in high-prevalence countries. They concluded that in Arctic countries where *H. pylori* prevalence exceeds 60%, treatment of persons with *H. pylori* infection should be limited only to instances where there is strong evidence of direct benefit in reduction of morbidity and mortality, associated peptic ulcer disease and MALT lymphoma and that the test-and-treat strategy may not be beneficial for those with dyspepsia.

Key words: Antibiotic resistance, health policy, *Helicobacter pylori*, gastrointestinal infections.

H. pylori Treatment Guidelines

- Candidates for antimicrobial treatment:
  - Duodenal ulcers
  - Gastric ulcers
  - MALT* lymphoma
  - Severe gastritis *not* associated with use of NSAIDs or ETOH
- Treatment should consist of FDA approved regimens
  - Most often quadruple therapy

*mucosal-associated lymphoid tissue

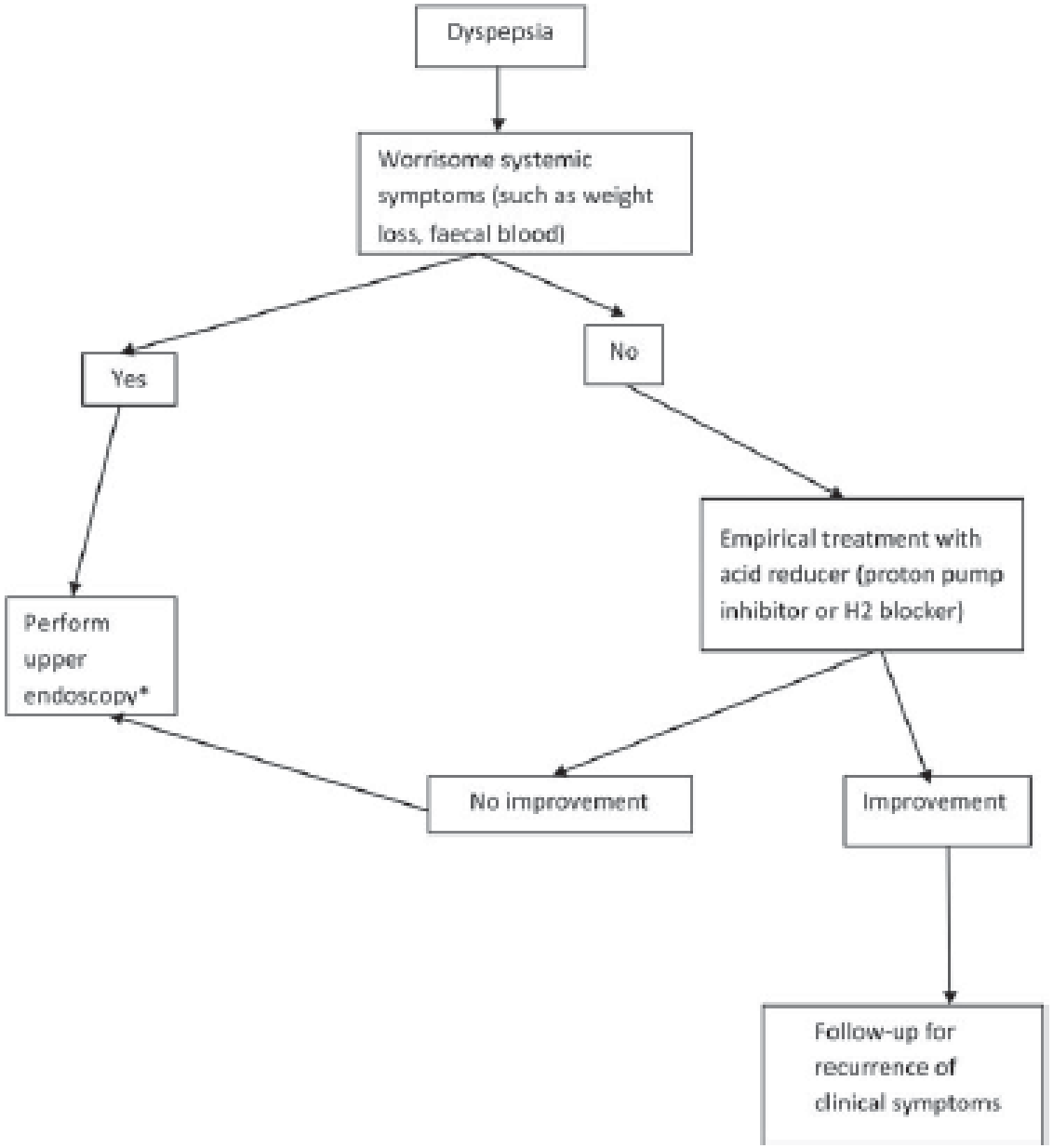

Fig. 1. Algorithm for management of dyspepsia in regions with high prevalence (>60% population infected) of *Helicobacter pylori* infection. * Further evaluation and treatment depending on findings of pathology found on endoscopy.

Main Focus in Alaska
H. pylori

- Surveillance for antimicrobial resistance
- Reinfection over time
- Diagnosis and treatment recommendations for Arctic populations with high *H. pylori* prevalence
- Risk factors for gastric cancer

Invasive Disease with *Haemophilus influenza* serotype a

Alaska 2000-2015

Bethel, Alaska, July 26th, 2016

Michael Bruce

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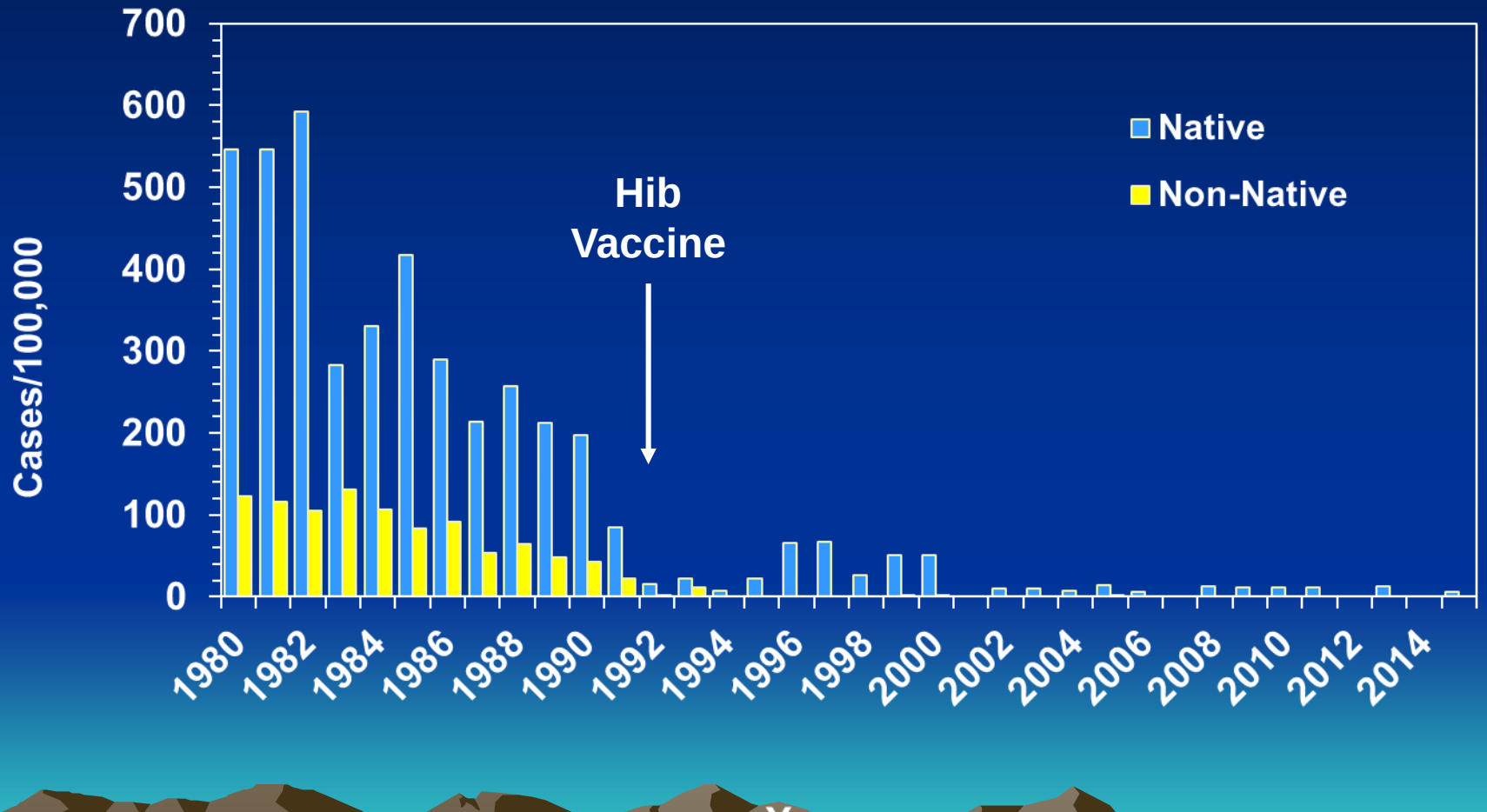
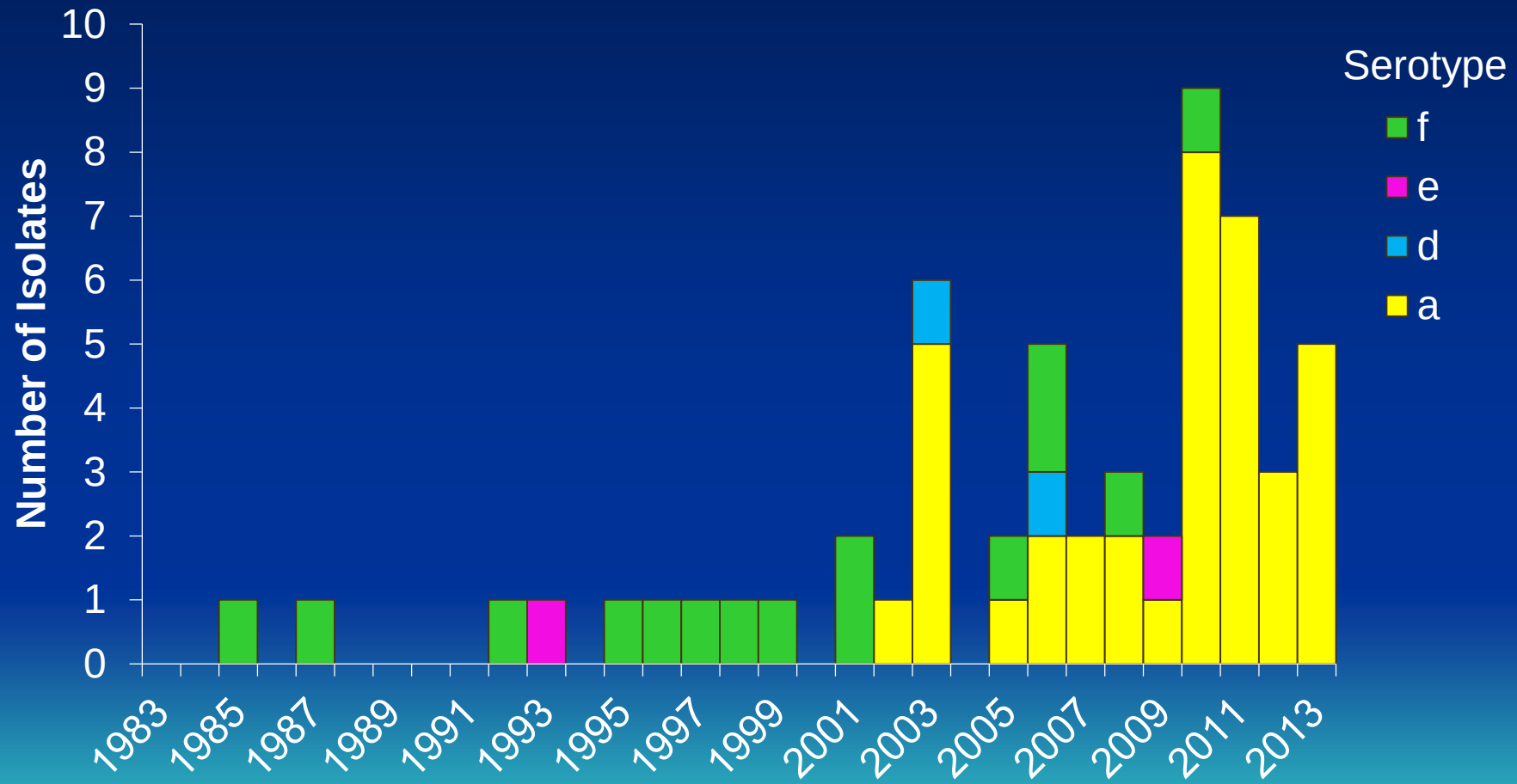
Haemophilus influenzae

- Gram-negative bacteria
- Colonizes the oral pharynx
- Clinical illness
  - Meningitis, epiglotitis, pneumonia, cellulitis, bacteremia, septic arthritis
- Polysaccharide capsule
  - 6 capsular types (a-f)

Invasive Hib Disease, Children Aged <5 Years, Alaska, 1980-November, 2015



Invasive non-b encapsulated *Haemophilus influenzae*, children <5, Alaska, 1983-2013



M Bruce, et al. EID 2013

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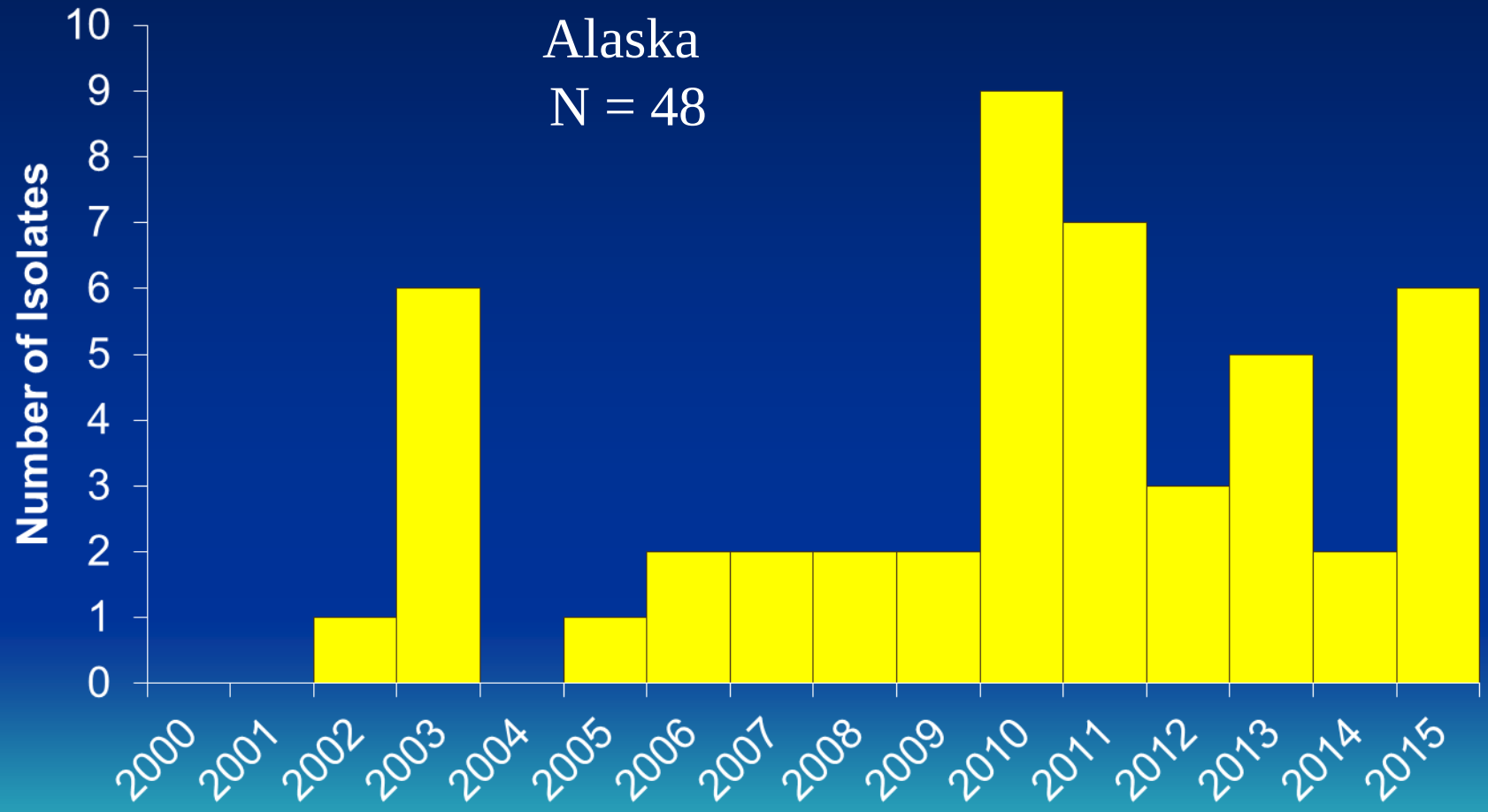
Objectives

- Characterize invasive Hia cases epidemiologically
- Describe initial clinical presentation
- Determine the incidence of invasive Hia disease in Alaska
- Assess relatedness by molecular typing
- Assess severity of infection and long term sequelae
- The Alaska Hib vaccine experience

Methods

- Case definition of invasive Hia:
  - Illness in a surveillance area resident with isolation of *Haemophilus influenzae* serotype a from a normally sterile site
- Data collected from Jan 2000 - Dec 2015 via Alaska population-based surveillance for invasive disease with Hia

Invasive Disease Caused by Hia
Alaska, 2000-2015



Characteristics of Persons with Invasive Hia 2000-2015

	Alaska N=48
Median Age (range)	8 months (0.3-60 years)
Gender (male)	32 (67%)
Indigenous	44 (92%)
Age appropriately vaccinated for Hib (< 10 years)	41 (91%)
Hospitalization	39 (81%)
Death	4 (8%)

Hia Clinical Illness in Children < 5 Years N=44

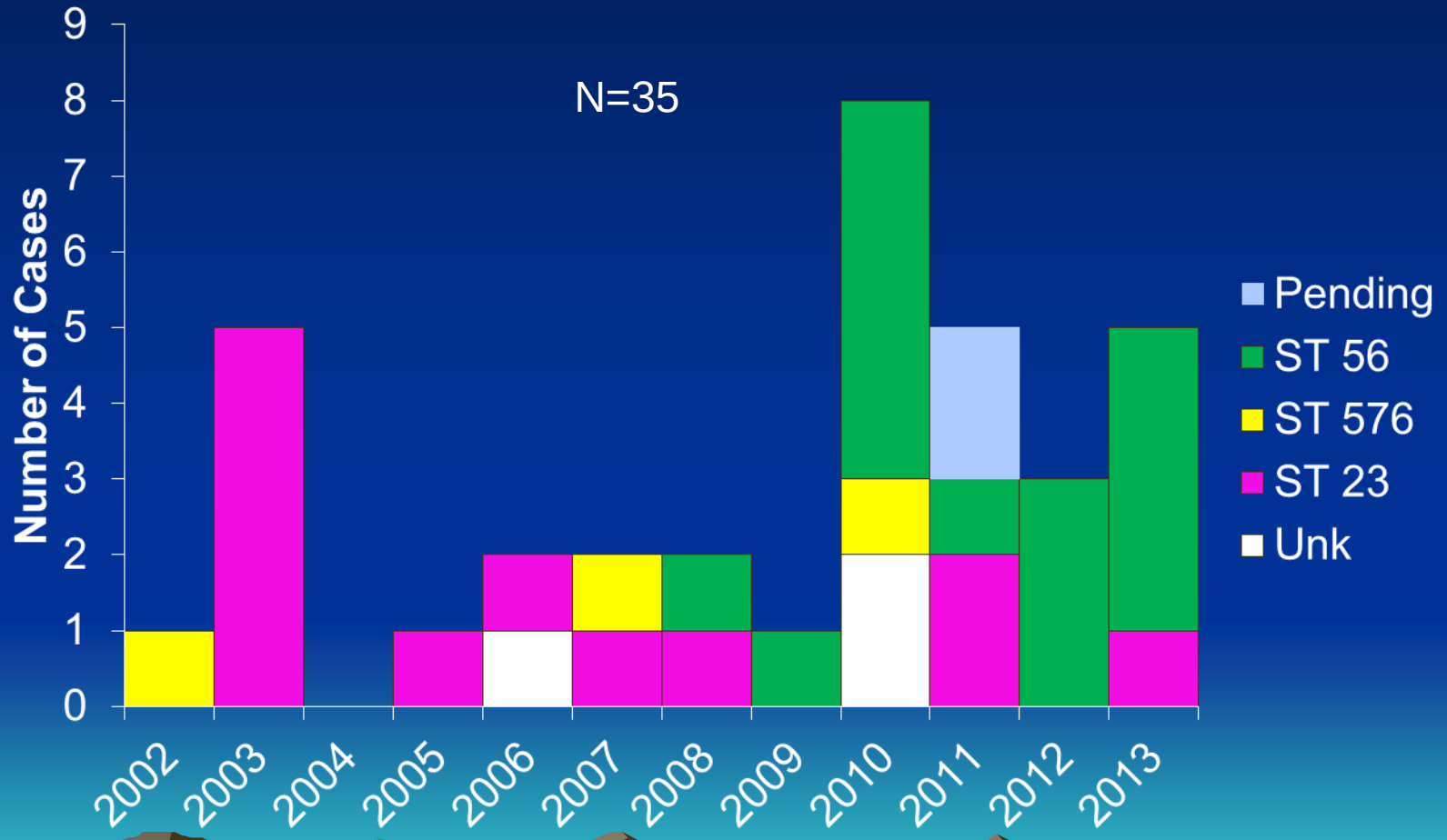
Meningitis	**17 (39%)**
Pneumonia	**9 (20%)**
Septic Arthritis	**8 (18%)**
Bacteremia	**4 (9%)**
Cellulitis	**3 (7%)**
Empyema	**1 (2%)**
Osteomyelitis	**1 (2%)**
Other	**1 (2%)**

Annualized Incidence* of Invasive Hia Disease, Alaska, 2000-2015

All Ages	# cases Rate (range)	48 0.5 (0-1.3)
< 2 years	# cases Rate (range)	40 13.2 (0-36.6)
< 2 years AK Native	# cases Rate (range)	38 44 (0-129.2)

* Rate is per 100,000 persons

Invasive Hia Disease Sequence Types Children Aged < 5 Years Alaska, 1980-2013



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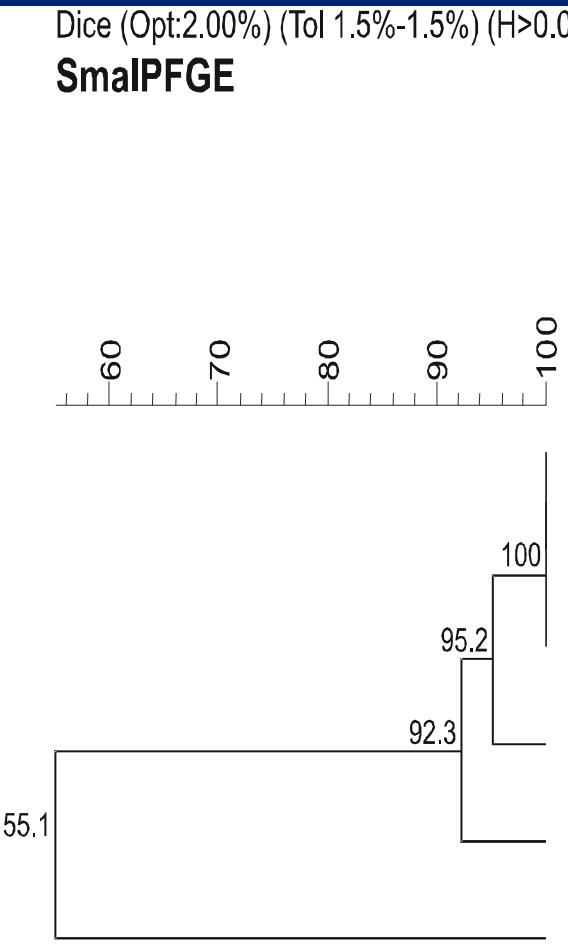
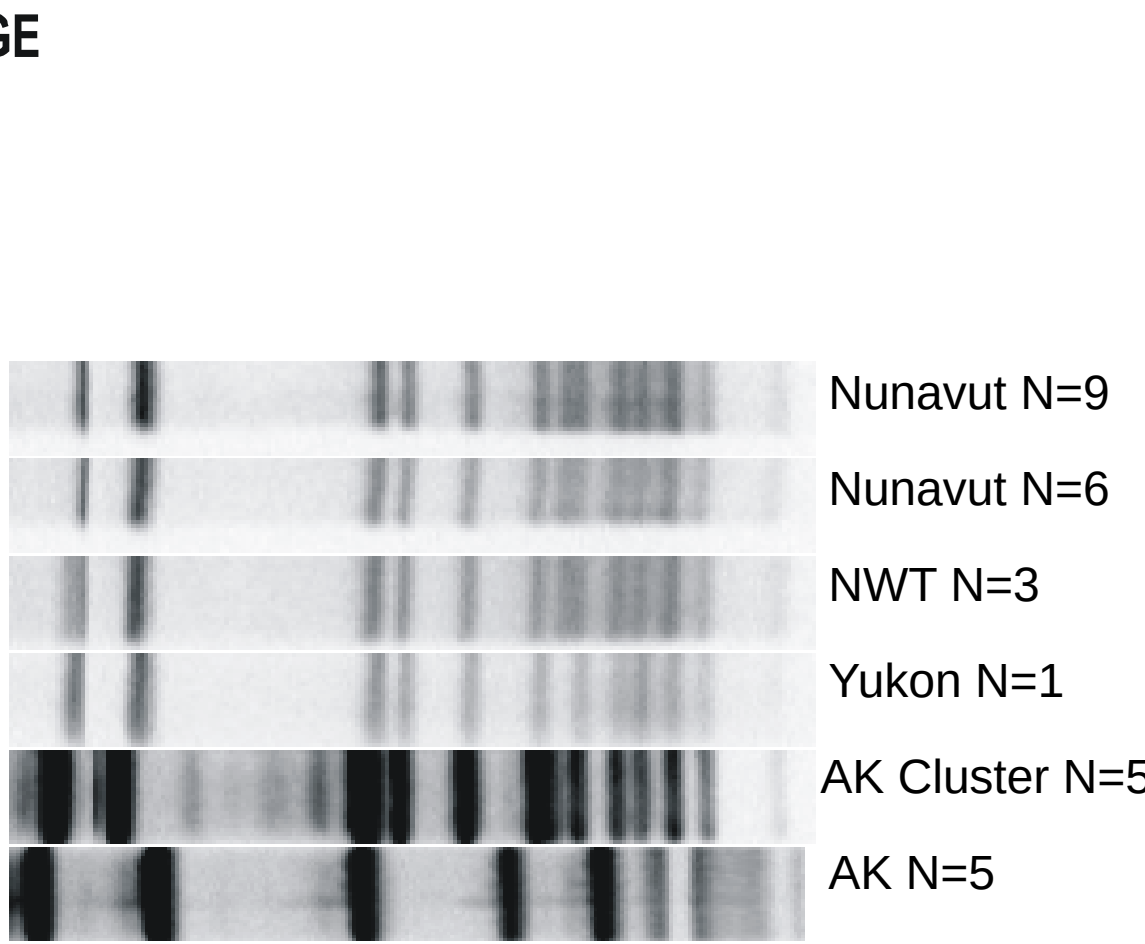
Hia Strain Typing by PFGE





Severity of Invasive *Haemophilus influenzae* Serotype A Infection in Children, Clinical Description of an Emerging Pathogen — Alaska, 2002–2014

Dr. Ian Plumb MBBS MSc

EIS Fellow, Arctic Investigations Program

Hia Severity Study

Invasive *Hia* disease in Alaska frequently leads to death or disability

- 25% died or had sequelae 1 year after illness
- 11% Case fatality if invasive *Hia* disease
- 21% Case fatality if meningitis or no localized source

Recurrent Disease with invasive Hia

- 3 recurrent invasive Hia cases since 2003
  - All in children < 1 year of age
  - Recurrence within 4-6 months after previous illness
  - 1 death
- Overall recurrence rate of 8%

Hia Vaccine

- Vaccine Working Group started 2014
  - Comprised of Canadian and Alaska representatives

1) Epi group

2) Vaccine Development and regulatory affairs

3) Business Plan Development

4) Government Support

5) Indigenous peoples' support

Thank you