Helicobacter pylori and Antibiotic Resistance - what the Guidelines say and beyond …

My Child's H. pylori Will Not Go Away (The Resistant Bug)

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  - **Johnson&Johnson - Consultant, Advisory Board; honorarium**
  - **Pfizer, Inc. - Consultant, Advisory Board; honorarium**
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Educational objectives

- Briefly discuss the epidemiology and transmission of *H. pylori* infection, and,
  - how this might affect treatment success and antimicrobial resistance;
- Review the established gastroduodenal and extra-gastric diseases caused by *H. pylori* infection
- Describe, in brief, the evidence-based methods for diagnosis and testing for cure of *H. pylori* infection in children
- Present the therapeutic approaches to *H. pylori* infection and the reasons for treatment failure; in particular;
  - Epidemiology of *H. pylori* antibiotic resistance
  - Mechanisms for antimicrobial resistance of *H. pylori*
  - Guidelines for salvage therapy; or how treat when the first regimen you tried fails

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Case Study

- 8 yr old boy originally referred by pediatrician with a 14 month history of abdominal pain, nausea and hemoccult negative stools
  - HPI
    - *H. pylori* serology negative (performed by PCP)
    - Abdominal pain; epigastric, awakens from sleep 5 nights/wk
    - Daily medications; PPI qd, H2RA qhs
  - FHx
    - Parents, US born, 2nd generation from the Dominican Republic
    - Reflux, peptic ulcer disease, recurrent anemia
  - Work-up after referral to Peds GI
    - Labs: Hgb 9.1, Hct 30.5, MCV 61; guaiac (+) stools
    - UGI: normal anatomy

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Case Study cont'd

- Work-up cont'd
  - EGD (initial)
    - Esophagus: esophagitis (histology)
    - Gastric: nodular gastropathy, gastric erosions; chronic active gastritis; H pylori (+) on both CLO and histology
    - Duodenum: duodenitis (histology)
  - Treated with triple therapy x 14 days
    - Amoxicillin (75 mg/kg/day); clarithromycin (20 mg/kg/day)
    - PPI bid – which was continued after antibiotics finished
    - Supplemental iron
  - Outcome: stay tuned…

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Medical Pioneers, Scientific Discovery and the Nobel Prize

2 Australians Win Nobel Prize in Medicine
Australians Barry J. Marshall and Robin Warren Win 2005 Nobel Prize in Physiology or Medicine by Matt Moore, Associate Press Writer

Marshall and Warren share the check of $1.3 million for their 2005 Nobel prize

STOCKHOLM, Sweden Oct 3, 2005 — *Australians Barry J. Marshall and Robin Warren won the 2005 Nobel Prize in physiology or medicine for showing that bacterial infection, not stress, was to blame for painful ulcers in the stomach and intestine.*
The 1982 discovery transformed peptic ulcer disease from a chronic, frequently disabling condition to one that can be cured by a short regimen of antibiotics and other medicines, the Nobel Prize committee.
Thanks to their work, it has now been established that the bacterium Helicobacter pylori is one of the most common cause of peptic ulcers.

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Previously Published Guidelines

- **CANADA (Canadian *HELICOBACTER PYLORI* Study Group)**
  - Sherman P, Hassall E, Hunt RH, Fallone CA, Veldhuyzen van Zanten S, Thomson ABR. **Canadian Helicobacter Study Group Consensus Conference on the Approach to *Helicobacter pylori* infection in Children and Adolescents.** *Can J Gastroenterol* 1999;13:553-559.
  - Update/Revised Guidelines: Jones NL, Sherman P, Fallone CA et al. **Update on the approach to *Helicobacter pylori* infection in children and adolescents - An evidence-based evaluation.** Can J Gastroenterol 2005; 19:399-408.
- **EUROPE (ESPGHAN)**
  - Drumm B, Koletzko S, Oderda G et al. ***Helicobacter pylori* infection in children : A consensus statement.** J Pediatr Gastroenterol Nutr 2000; 30:207-213.
- **UNITED STATES (NASPGHAN)**
  - Gold BD, Colletti RB et al. ***Helicobacter pylori* Infection in Children: Recommendations for Diagnosis and Treatment**. J Pediatr Gastroenterol Nutr 2000;31:490-497.

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Epidemiology and *Transmission* of *H. pylori* Infection

If infection can be prevented, then bad outcomes (i.e., bacterial resistance, cancer) won't occur…

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Potential Determinants of *H. pylori* Infection Acquisition

- Necessary: exposure to the organism
  - Living in or originating from high-prevalence areas
  - Infected family members and large family size
  - Infected contacts in the community
  - Environmental reservoirs
  - Behavior and other factors increasing exposure
    - Intimate contact, gastroenteritis, poor sanitary facilities

Kivi M et al. Scan J Infect Dis 2006;38:407-417
Torres J et al. Arch Med Res 2000;31:431-469
Kivi M et al. Epidemiol Infect 2005;133:645-652

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Potential Determinants of *H. pylori* Infection Acquisition

Additional factors contributing to transmission

- Host factors
  - Expression of gastric receptors
  - Host defenses: gastric acid secretion, immune responses
  - Other factors affecting the gastric environment
    - Young age
- Bacterial factors
  - Protected localization
    - Motility, adhesion
    - Withstanding host defense
      - Urease activity, immune evasion
    - Adaptive evolution

Kivi M et al. Scan J Infect Dis 2006;38:407-417
Aspholm-Hurtig M et al. Science 2004;305:519-522
Bjorkholm B et al. Helicobacter 2005;5:149-154

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Intra-familial Transmission
Is it Mom, Dad, brother or sister?

- Multi-generation Vietnamese Study
  - Community-based, cross-sectional study
    - 533 participants, 135 households
  - *H. pylori* infection detected by validated, research-based IgG ELISA
  - *H. pylori* infection significantly associated with
    - Infection in mothers and grandmothers (OR 2.5; CI 1.19-5.26), not fathers or grandfathers
    - Infection in both parents (OR 4.14; CI 1.29-13.23)
- Cross sectional Israel/Arab Study
  - 4 separate, rural geographic regions; north, central, south and east Israel; children ages 3-5 years (N=197)
  - *H. pylori* testing by polyclonal stool antigen test
  - Village of residence (OR 3.3; CI 1.03-11) and *H. pylori* (+) sibling (OR 4.4; CI 1.3-14.6) were significantly associated

Van Bang N et al Eur J Epidemiol 2006;21:459-463
Muhsen KH et al Epidemiol Infect 2006;134(5):990-996

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Transmission of *H. pylori* Infection: Are Children the "Effectors"?

- **Familial Clustering**
  - U.S.-Mexico Study: binational cohort from El Paso, Texas (US) and Juarez, Mexico
    - 4 *H. pylori*-infected family members had *H. pylori* isolation from fecal specimens
    - all 4 were infected with the same *H. pylori* strain - genotype of *vac*A s1a/m2
    - *H. pylori isolated from sewage and water sources, particularly in Juarez cohort (suggests water reservoir)*
- **Parent to child transmission**
  - Aboriginal Canadian study
    - homologous DNA in soother (i.e., pacifier) soaking water and maternal saliva suggest oral-oral route of transmission via mother - child

Liang S et al Helicobacter 2003;8(5):561-7
Owen RJ et al J Med Microbiol 2003;52 (supp 1):514-524
Chang PS et al Acta Pediatr Taiwan 2003;44(6):336-338
Sinha SK Helicobacter 2004;9(1):59-68

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Transmission of *H. pylori* Infection

Maternal and sibling transmission, as well as birth origin: major determinants of infection acquisition

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Epidemiology of *H. pylori* Infection

- **Reservoir**
  - Humans (fecal-oral; oral-oral; gastro-oral)
  - Environmental: water; food sources
  - Other: zoonotic (flies, cats, dogs, sheep)?
- **Primary acquisition**
  - Childhood
- **Risk factors**
  - Developing countries/populations, poor hygienic conditions
  - Lower socioeconomic circumstances
  - Intra-familial clustering
  - Immigrants in industrialized nations
  - Crowded conditions
    - day care, orphanages, foster homes

Robinson LG et al J Infect Dis 2002;186(8):113-1137
Glynn MK et al. Clin Infect Dis 2002;35(9):1059-1065
Crone J and Gold BD. Helicobacter 2004;9(supp 1):49-56
Malaty H et al. Clin Infect Dis 2003;37(8):1067-1072

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Diseases Associated with *H. pylori* Infection

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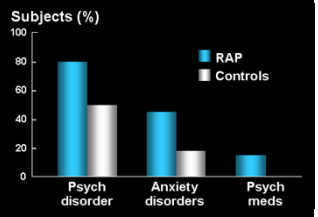
Adult Diseases Often Begin in Childhood

- Inflammatory bowel disease
  - early onset (ie, <2 yrs) and poor treatment response results in increased complications
- *H. pylori*-associated gastroduodenal disease (ulcers, gastritis, and adenocarcinoma)
  - early childhood acquisition results in *more severe* adult disease outcomes
- Obesity
  - 12-fold increase of adult morbid obesity if BMI >85% at 10 years of age
- Functional bowel disease
  - adult outcomes of childhood onset recurrent abdominal pain
- Lung cancer (smoking); skin cancer (sun exposure); liver cancer (hepatitis B)



Marx G, et al. J Pediatr. 2002; 140:470.
Silverstein, et al. Gastroenterology. 1999; 17:49
Malaty, et al. Lancet. 2002; 359:931.
Campo, et al. Pediatrics. 2001; 108:1.

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Are there Good, O.K. and…BAAAD *H. pylori*?

"The only good *Helicobacter* is a dead *Helicobacter*" Graham 1997

↓

"In a world of black and white, *H. pylori* is gray" Blaser 1999

↓

"Save the *H. pylori*" Fennerty 2000

↓

"*Helicobacter pylori* is not and never was protective against anything, including GERD " Graham 2003

↓

"*Helicobacter pylori* may be good in some, bad in others, and not so bad in most" Blaser 2008

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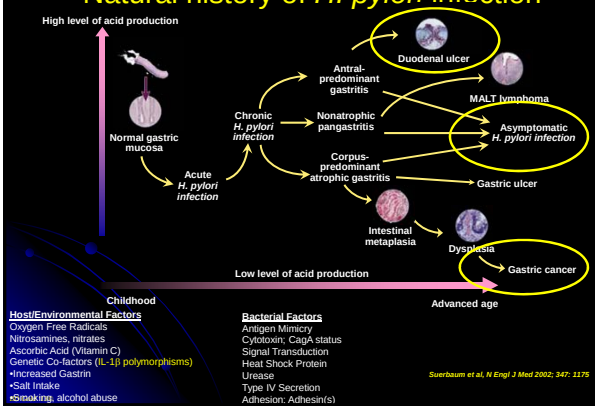
Natural history of *H. pylori* infection



Infection and Malignancies
The *H. pylori* Paradigm

- Infection-attributed malignancy
  - 1.9 million cases per year
  - 17.8% of global cancer burden
  - Viruses, schistosomes and specific bacteria
- *H. pylori* is leading factor responsible for 5.5% of all cancers
- Other bacterial infections and cancer
  - Chronic inflammation +/- toxins that change cell cycle resulting in altered cell growth
  - "Carcinogenic bacteria" are highly site-specific
    - *Salmonella typhi* and gallbladder cancer
    - *Streptococcus bovis* and colon cancer
    - *Chlamydia pneumonia* and lung cancer

Starzynska T et al Helicobacter 2006;11(Supp 1):32-35
Parkin DM Int J Cancer 2006;118:3030-3044
Mager DL J Translational Med 2006;4(14):1-18

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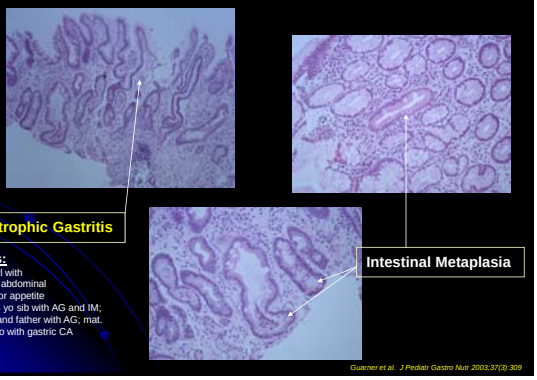
H. pylori and Disease Outcomes in Children – Gastric Cancer in Childhood?



Cases:
11 yo girl with anemia, abdominal pain, poor appetite
FHx: 13 yo sib with AG and IM; mother and father with AG; mat. Grandmo with gastric CA

Guarner et al. J Pediatr Gastro Nutr 2003;37(3):309

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H. pylori-associated Gastroduodenal Disease in Children and Adults

- Gastritis
  - ~100% of infected persons
  - Majority asymptomatic; inflammation does not always = symptoms
- Ulcers
  - 5-15% of infected persons; unknown population-based prevalence in children
  - Duodenal > gastric
  - Role of non-steroidal anti-inflammatory agents?
- Atrophy with/without Intestinal Metaplasia
  - <2%; true prevalence not known
  - at-risk populations?
- Gastric adenocarcinoma
  - Case reports
  - At-risk population; biomarkers identifiable in childhood
- MALT-lymphoma
  - < 1%; true prevalence is not known
  - Eradication = disease resolution

Kato S et al J Gastroenterol 2004;39(8):734-738
Guarner J et al. J Pediatr Gastroenterol Nutr 2003;37(3):309-314
Plummer M et al. IARC Sci Pub 2004;157:311-326
Kalapachi B et al. J Clin Gastroenterol 2004;38(3):248-251
Zheng PY and Jones N. Can J Gastroenterol 2003;17(7):448-454

GI Symptoms or GERD (Children) Who To Test and When to Treat

- Recurrent abdominal pain is not an indication to test for *H. pylori* infection
- *H. pylori* testing is not required in patients with newly diagnosed gastroesophageal reflux disease; in whom proton pump therapy is to be initiated
  - When long-term treatment with a PPI is planned, *H. pylori* infection eradication can be considered

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011 53(2):230-243

Extra-Gastric Disease Associated with *H. pylori* Infection

H. pylori Infection and Blood Disorders: Summary

- A number of mechanisms for iron deficiency with or without of anemia have been described which provided evidence for biological plausibility
- *H. pylori* eradication studies demonstrated evidence supporting cause-effect i.e., *H. pylori* infection and iron deficiency
  - Further long-term *H. pylori* eradication follow up studies (> 1 year) are needed with assessment of iron deficiency and anemia
- ITP is an acquired bleeding disorder
  - autoantibodies bind to the platelets surface resulting in platelet destruction in the reticuloendothelial system
- *H. pylori* infection appears to have higher prevalence rates in patients with chronic ITP compared to those without ITP
- Eradication of *H. pylori* results in normalization of platelet populations in up to 60% of patients with chronic ITP

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011 53(2):230-243

H. pylori Infection and Extra Gastric Disease

- There is currently insufficient evidence that *H. pylori* infection is causally related to:
  - Otitis media
  - Upper respiratory tract infections
  - Periodontal disease
  - Sudden infant death syndrome (SIDS)
  - Coronary artery disease; atherosclerosis
- Growing body of evidence that *H. pylori* is a causal factor leading to:
  - Short stature, poor growth velocity
- Continued controversial associations/causations:
  - Asthma, allergy
  - Inflammatory Bowel Disease

Kodama M et al Helicobacter 2007; 12: 36-42
Emilia G et al Am J Med 2005;118:420-421
Franceschi F et al. Best Prac Res Clin Gastroenterol 2007;21(2):325-334
Franchini M et al. Helicobacter 2004;9:342-348

Diagnosis of *H. pylori* Infection

Diagnosis of *H. pylori* Infection Children

- The primary goal for clinical investigation of gastrointestinal symptoms is to
  - determine the underlying cause of the symptoms and…
  - not solely the presence of *H. pylori* infection

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

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When To Test in Children

- If endoscopy is performed for the diagnosis of persistent abdominal symptoms
  - testing for *H. pylori* should be considered
- When *H. pylori* infection is detected by histopathology in the absence of peptic ulcer disease
  - *H. pylori* treatment can be considered
- If a history of gastric cancer exists in primary relatives
  - testing for *H. pylori* in the child is suggested

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011 53(2):230-243

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Invasive Methods for Diagnosis

- Validated tissue-based (invasive) diagnostic tests for *H. pylori* infection that can be used for clinical decision making in BOTH adults and children
  - Histology with appropriate staining
  - Rapid urease test
  - Primary Culture
    - Includes antibiotic susceptibility testing
  - FISH (controversial)
  - PCR and Real Time PCR (controversial)

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

Gold B et al J Pediatr Gastroenterol Nutr 2000;31(5):490-497
Drumm B et al J Pediatr Gastroenterol Nutr 2000;30(2):207-213
Crone J and Gold BD. Helicobacter 2004;9(supp 1):49-56

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Invasive Methods for Diagnosis Children and Adults

- For the diagnosis of *H. pylori* infection during EGD…
  - it is recommended to obtain gastric biopsies (antrum, incisura and corpus) for histopathology according to the updated Sydney classification
- It is recommended not to perform biopsy based and non-invasive tests (UBT, stool test) for at least…
  - 2 weeks after stopping PPI therapy and
  - within 4 weeks after stopping antibiotics
- Culture and PCR are primary means for antibiotic susceptibility profiles
  - Neither is widely available for clinical use

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

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Non-Invasive Methods for Diagnosis in Children and Adults

- Validated non-invasive diagnostic tests for *H. pylori* infection before antibiotic therapy, and, used for clinical decisions must detect active infection
  - 13C-urea breath test
  - Stool antigen tests (monoclonal, polyclonal)
- Tests based on the detection of antibodies (IgG, IgA) against *H. pylori* are NOT reliable for use in the clinical setting
  - serum, whole blood, urine and saliva
- Antibody testing is inexpensive and widely available but has poor predictive value in
  - Populations with low *H. pylori* prevalence
  - Bleeding ulcers, gastric atrophy, MALT lymphoma
  - Recent or current use of PPIs and antibiotics

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243
Gold B et al J Pediatr Gastroenterol Nutr 2000;31(5):490-497
Drumm B et al J Pediatr Gastroenterol Nutr 2000;30(2):207-213
Crone J and Gold BD. Helicobacter 2004 9Issue 1):49-56

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Methods to Determine *H. pylori* Eradication in Adults and Children

- UBT is the most reliable non-endoscopic test to document eradication success (i.e., test for cure)
- Monoclonal fecal antigen test provides another non-endoscopic means of establishing *H. pylori* cure after eradication
- Testing for eradication appears to be most accurate if performed *at least* 4 - 6 weeks after the completion of antibiotic therapy

Jones NL et al Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243
Chey WD et al Am J Gastroenterol 2007;102:1808-1825
Malfertheiner P et al Gut 2007; Jan 17

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Treatment of *H. pylori* Infection

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Recommended Eradication Therapy Regimens for *H. pylori*-Infected Children

First line eradication regimens (twice daily for 10-14 days)

- Option 1
  - PPI + Amoxicillin + Imidazole (e.g. Metronidazole, Tinidazole)
- Option 2
  - PPI + Amoxicillin + Clarithromycin
- Option 3
  - Bismuth salts + Amoxicillin + Imidazole
- Option 4
  - Sequential Therapy: PPI+Amoxicillin (5 d), then PPI+Imidazole+ Clarithromycin (5 d)

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Jones NL et al. Canadian J Gastroenterol 2005;19(7):399-408
Koletzko, S., et al. J Pediatr Gastroenterol Nutr 2011;53(2): 230-243.

Sequential Therapy for *H. pylori* Infection Eradication

Sequential Therapy

PPI BID + Amoxicillin BID — **X 5 days**

PPI BID + Clarithromycin BID + Imidazole BID (Tinidazole; Metronidazole) — **X 5 days**

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Koletzko, S., et al. J Pediatr Gastroenterol Nutr 2011;53(2): 230-243.

H. pylori eradication
Duration of Therapy and Post-Therapy

- It is recommended that the duration of triple therapy is 7 – 14 days
- Costs, compliance and adverse effects (e.g. antimicrobial resistance of the patient) should be taken into account when choosing the eradication regimen
- A reliable non-invasive test for eradication is recommended at least 4-8 weeks following completion of therapy

Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

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Case Continues

- **Symptoms persist; mild and intermittent**
- **Follow up UBT and endoscopy at 3 months**
  - **UBT: negative**
  - **EGD: erosion healing, nodularity almost gone;**
    - **Histology: mild esophagitis, gastritis, and no evidence of infection**
- **But….symptoms return 6 months later;**
  - **Nausea, regurgitation and epigastric pain**

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What would you do now?

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The Growing Concern Regards Antibiotic Resistant *H. pylori*

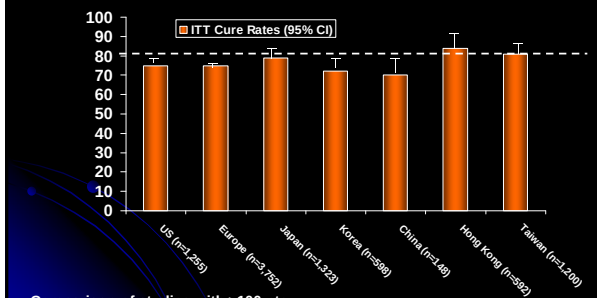
Approach to Therapy

Treatment Strategies and Antibiotic Resistance

- Surveillance of antibiotic resistance rate of *H. pylori* strains in children and adolescents is recommended in different countries, specific populations and geographic areas where…
  - High rates of infection exist and
  - High rates of resistant strains are likely
- Antibiotic susceptibility testing for clarithromycin is recommended prior to initial clarithromycin-based triple therapy in
  - areas/population with known high resistance rate (>20%) of *H. pylori* strains in children
- World wide cure rates of PPI + amoxicillin + clarithromycin now in "*unacceptable range* (<80%)"
  - Assumption: patients are infected with resistant strains

Graham DY et al. Nat Clin Pract Gastroenterol Hepatol 2008;5(4):1-11
Jones NL et al. Canadian J Gastroenterol 2005;19(7):399-408
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

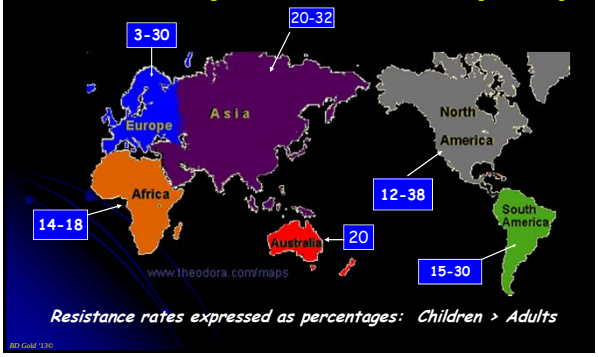
Treatment Strategies and Antibiotic Resistance



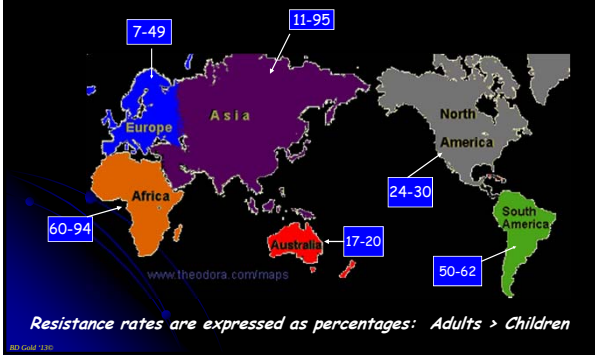
Comparison of studies with >100 pts employing PPI + amox + clari

Graham DY et al. Nat Clin Pract Gastroenterol Hepatol 2008;5(4):1-11
Graham DY et al Helicobacter 2007;12:275-278

H. pylori Treatment: Clarithromycin Resistance (2012)



H. pylori Treatment: Metronidazole Resistance (2012)



Clarithromycin Resistance is High in *H. pylori*-infected Children

Multicenter study in 14 European Countries

	Prior 1st tx. n=1037	Post tx. n=196	All n=1233
Amoxicillin (1094)	0.6%	0.6%	0.6%
Metronidazole (1216)	23%	35%	25%
Clarithromycin (1181)	20%	42%	24%
DR (1181)	5%	15%	7%

S. Koletzko et al Gut 2006;55:1711-16

Risk Factors: Carithromycin Resistance

		OR	adj.OR	95%CI	p
Sex	female	1	1		
	male	1.62	1.58	[1.12-2.24]	0.01
Age	>12 y	1	1		
	6-12 y	1.38	1.21	[0.81-1.78]	0.35
	<6 y	2.03	1.82	[1.10-3.03]	0.02
Center	NWE-Europe	1	1		
	South-Europe	2.29	2.25	[1.53-3.30]	<0.001

Boys, children <6 y and children living in South-Europe have an increased risk to harbor a CLA-resistant strain

S. Koletzko et al Gut 2006;55:1711-16

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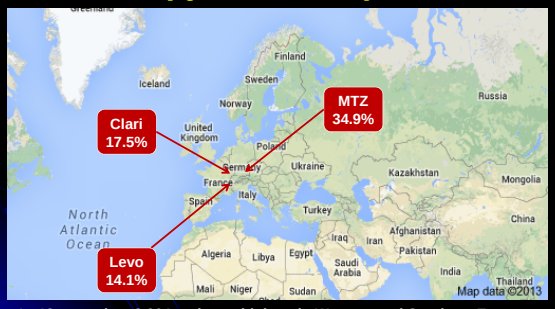
Antimicrobial Resistance of *H. pylori:* Europe 2013



- 18 countries; 2,204 patients; highest in Western and Southern Europe
- High rate of clari resistance prohibits first line empiric use in Hp therapy

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Reasons for *H. pylori* Treatment Failure

- **Inadequate treatment of the primary infection**
  - Compliance
- **Reinfection by other family members**
  - Transmission of H. pylori within a family appears to be the predominant mode of contamination
- **Resistant infecting H. pylori strains**
- **Resistance rates (highest to lowest)**
  - Metronidazole
  - Clarithromycin
  - Quinolones (Levofloxacin, Ciprofloxacin)
  - Tetracycline
  - Amoxicillin

Moya, D. A. and K. D. Crissinger Curr Gastroenterol Rep 2012;14(3): 236-242
Koletzko S, Gold BD et al J Pediatr Gastroenterol Nutr; 2011; 53(2):230-243

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Case Outcome

- **Performed repeat upper endoscopy**
  - **Macroscopic: antral nodularity, gastric erosions**
  - **Microscopic: antral predominant gastritis; *H. pylori* positive by silver stain; rapid urease test positive**
  - **Biopsies sent for primary culture and resistance testing by Agar Dilution**
- ***H. pylori* strains grow and found resistant to both clarithromycin and metronidazole**
- **PPI-based quadruple triple therapy with amoxicillin and levofloxacin + peptobismol initiated for 4 weeks (PPI continued for 8 weeks)**
- **Follow up endoscopy and biopsy at 6 months;**
  - **Biopsies negative for *H. pylori* by histology and primary culture as well as urease test**
  - **Histology improved but not absent**

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Recommended Salvage Therapies for Eradication of Resistant *H. pylori*

Salvage therapies should be employed for 2 weeks minimum

- Option 1
  - PPI + Amoxicillin + Imidazole (e.g. Metronidazole, Tinidazole) + Bismuth salts
    - 2 week and 4 week options employed; longer is better
- Option 2
  - PPI + Amoxicillin + Quinolone (e.g. Levofloxacin) x 4 weeks
- Option 3
  - PPI + Bismuth salts + Amoxicillin + Tetracycline
    - 2 week and 4 week options employed
- **Note: directly observed therapy yeilds best results; not feasible in practice**

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H. pylori infection in 2013: Summary

- **No multicenter randomized controlled trials evaluating efficacy of different regimens and new antimicrobial agents for *H. pylori* eradication in childhood**
- **Reduction in eradication rates has the potential of creating a public health problem with refractory *H. pylori* infection**
  - **Could infection transmission be successfully interrupted?**
- **New/Novel therapies showing promise**
  - **Probiotics: adjuvant to traditional therapy; reduce side-effects, increase efficacy**
  - **Green tea catechins (epigallocatechin gallate); Pronase, N-acetyl cysteine**
  - **Furazolidone; nitazoxinide; levofloxacin**
  - **Vaccines…is there really a future for enteric infection vaccination?**
- **Antibiotic resistance is still a main factor affecting the outcome of *H. pylori* treatment**
  - ***H. pylori* strains isolated from children - higher clarithromycin resistance (16 – 24%) than adults**
  - **Imidazole resistance (e.g., metronidazole) generally lower in *H. pylori* isolates from children compared to adults**
  - **Emerging resistance observed for amoxicillin, tetracycline and quinolones**

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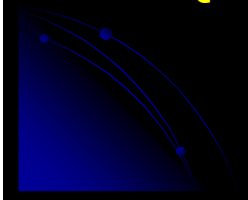
Thanks for your kind attention!

Questions?



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