CLINICAL GUIDELINE

HELICOBACTER PYLORI INFECTION

(Age < 18 years)

Children's MINNESOTA

Aim: To optimize and standardize the management of *H pylori* infection

Patient with suspected *H pylori* infection:
Does the patient meet <u>any</u> of the following?

1. Strong clinical suspicion of gastric or duodenal ulcers or erosions
   - Symptoms of peptic ulcer disease (PUD) (hematemesis, melena)
   - Persistent gastritis (upper abdominal pain, nausea, vomiting) without improvement on acid suppression
2. Unexplained refractory iron deficiency anemia (IDA) after iron supplementation
3. History of gastric cancer in first degree relative

Yes → Refer to GI as *H pylori* testing may be indicated (see Note 2)

No → H pylori testing ***NOT*** indicated (see Note 1)

Diagnosis of *H pylori* confirmed

No → Evaluate for alternate diagnosis

Yes → STOP → **Primary Care should <u>NOT</u> prescribe antibiotics.** Refer to peds GI if not already done.

- **Peds GI** to determine appropriate treatment regimen (see Note 3). If inpatient, primary team may be asked to prescribe. See page 3-4 for antibiotic regimens and dosing.
- Reiterate to patient/family about importance of adherence to therapy (page 3, note A).

Tolerant of treatment regimen and symptoms improve/stable

No → **Peds GI** to select alternative regimen. See page 3-4.

Yes → **Peds GI** to confirm eradication and communicate follow-up plan

Perform test of cure 6 – 8 weeks after therapy completion (see page 2). Regardless of indication, PPI should be discontinued for ≥ 2 weeks and bismuth/antibiotics for ≥ 4 weeks prior to *H pylori* testing (see page 2 under *Diagnosis*).

Note 1: The primary goal of clinical investigation should be to determine the underlying cause of gastrointestinal (GI) symptoms and not solely the diagnosis of *H. pylori*. See page 2 for more information.
Indications where *H. pylori* testing is **NOT** indicated (unless symptoms of PUD or noted in first box of pathway):

- Short stature or growth failure that has not had other causes worked up
- Chronic immune thrombocytopenia purpura (cITP)
- Initial investigation of management of IDA
- Other GI diseases (e.g., celiac disease, inflammatory bowel disease (IBD), eosinophilic esophagitis)
- Functional abdominal pain, a disorder of gut-brain interaction
  - If presence of alarm symptoms for PUD (e.g., persistent upper abdominal pain, GI blood loss) or uncertainty of clinical relevance, discuss with peds GI.
- Pediatric household members of *H. pylori* positive individuals living in North America or Europe.
- Screening in groups at increased risk of gastric cancer living in North America or Europe, e.g., African Americans, Alaskan Natives, American Indians, Asian Americans, Hispanic Americans, Indigenous Canadians, and immigrants from regions with high incidence of gastric cancer.

Note 2: Diagnosis of *H pylori* should be confirmed with endoscopy and gastric biopsies. For testing related to first degree relative history of gastric cancer, stool antigen is acceptable but should be done through pediatric GI.
For confirmation of eradication, stool antigen can be done through PCP or GI.

Note 3: Prior to selection of antibiotic regimen, an antibiotic exposure history (for any indication) and an allergy history should be performed. If reported penicillin allergy, consider assessing likelihood of true allergy. See Beta-lactam allergy guideline for more information.

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NOTES

Definition[3]

Helicobacter pylori (*H. pylori*) is a Gram-negative, spiral-shaped bacterium that has adapted to survive in the harsh acidic environment of the human stomach. *H. pylori* is categorized by the World Health Organization as a group I (definite) carcinogen because of its causal association with gastric cancer.

Clinical Presentation[1,2,5]

In children, acute *H pylori* infection can result in gastroduodenal inflammation. In children, most *H pylori* infections are believed to be asymptomatic. On occasion, *H pylori* infection can result in acute gastroduodenal inflammation that can manifest as epigastric pain, nausea, vomiting, hematemesis, and guaiac-positive stools. If present these symptoms usually are self-limited. Although all infected people have gastritis, over a lifetime, approximately 10 – 15% will develop peptic ulcer disease and <1% will develop gastric cancers. There are currently no good biomarkers to identify the small number of individuals that will go on to develop more severe sequelae of infection later in life. The risk of peptic disease is low in children, and the risk of severe complications is extremely low in North America and Europe.

There is growing evidence for a possible but unproven protective effect of *H pylori* infection in chronic conditions such as asthma, obesity, and allergies. Atherton & Blaser proposed a biphasic effect of *H pylori* on human health such that *H pylori* may confer benefits to humans early in their life span but later in life *H pylori* has biological costs including peptic ulcers and gastric cancers.

Etiology[1]

Most *H pylori* infections are acquired in the first 8 years of life. The organism can persist in the stomach for years or for life. Infections rates in children are low in resource-abundant, industrialized countries, except in children from lower socioeconomic groups, immigrants from resource-limited countries, and those living in poor hygienic conditions. The precise mode of *H pylori* transmission is unclear. Intrafamilial person-to-person vertical and horizontal transmission (e.g., gastric-oral and fecal-oral) are considered important.

Diagnosis[1,5]

Indications for testing for *H pylori* in children are **not** as broad as for adults, for whom there is stronger evidence for disease associations and lower risk of reinfection following treatment. Also, unlike in adults, noninvasive tests such as the *H pylori* stool antigen test, are **not** routinely recommended for initial diagnosis of *H pylori* in children (page 1, Note 2).

All children who are treated for *H pylori* infection should undergo a **test of cure** with stool antigen test 6 – 8 weeks after completion of therapy and after withholding PPI for at least 2 weeks and bismuth/antibiotics for at least 4 weeks before testing. Standard doses of H_2RAs (e.g., famotidine) or antacids do not affect the accuracy of these tests. H_2RAs should be discontinued 2 days before testing. Resolution or change of symptoms does **not** reliably indicate whether the infection is cleared or not. Serological testing should **not** be used to establish post-treatment status because antibody levels may remain positive for months after successful eradication of *H pylori* infection.

Management

Treatment decisions for *H pylori* should be limited to peds GI. Non-invasive *H pylori* testing or treatment of *H pylori* **without** peds GI consultation is **strongly discouraged** because it may lead to delays in specialist investigation of the underlying cause of GI symptoms and unnecessary antibiotics. For treatment-experienced patients and patients with antibiotic allergies, peds GI will coordinate with peds ID as appropriate.

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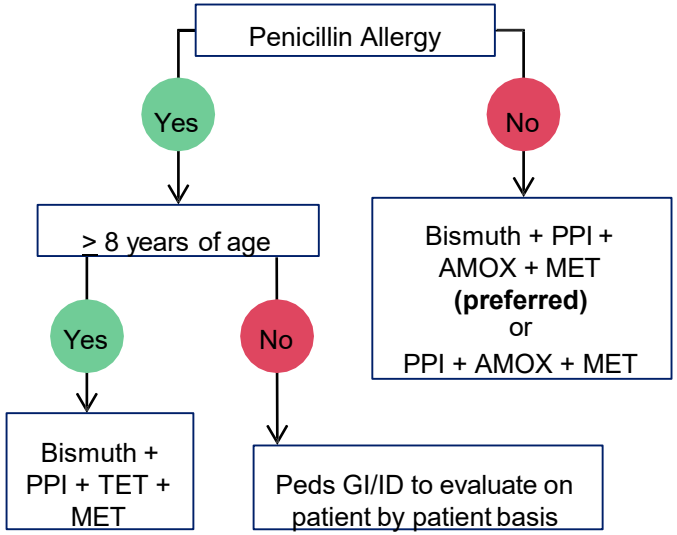
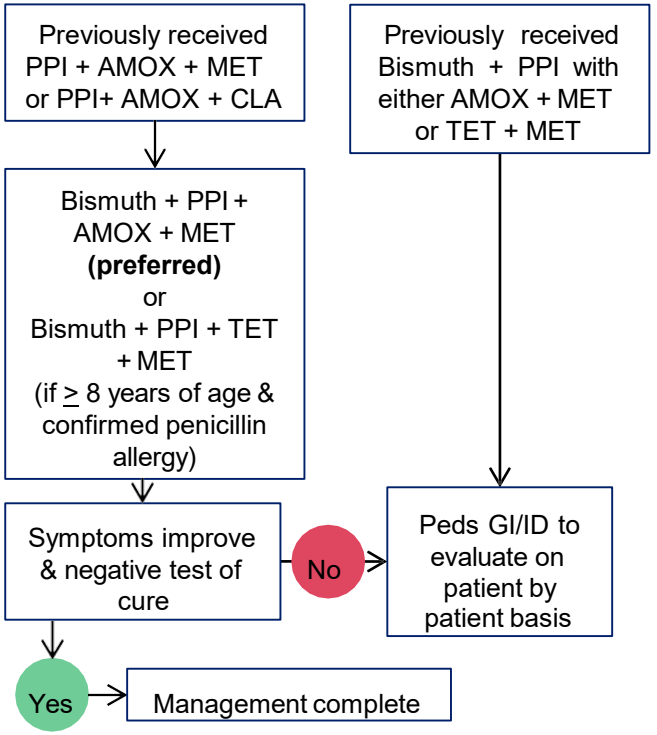
H pylori treatment regimens for children (for use as directed by Pediatric GI and ID only)

See Note A. Dosing on Page 4.

Treatment-naïve and UNKNOWN susceptibilities



Treatment-experienced and UNKNOWN susceptibilities



Abbreviations: PPI = proton pump inhibitor, AMOX = amoxicillin, TET = tetracycline, MET = metronidazole, CLA = clarithromycin

Note A: *H pylori* management considerations

- **Patient adherence**: Adherence to **all** prescribed medication for 14 days is of critical importance. **All** medicines should be started **together.** Engaging the family, setting an alarm, utilizing a phone app can facilitate adherence. Patients and family should be reminded to **call the peds GI clinic** if experiencing medication adverse effects and to avoid caffeine, alcohol, cigarettes, spicy foods, and coffee or tea because these can increase gastric acid and reduce treatment efficacy.
- **Probiotics:** There is **insufficient** evidence on the role of probiotics in improving adherence or tolerability of *H pylori* eradicationregimens.

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Table 1. Oral antibiotic dosing for treatment of H pylori in children (for use as directed by Pediatric GI and ID only)

Medication	Age or Body Weight	Dose	Frequency	Duration
Bismuth subsalicylate	< 10 years of age	262 mg	Four times daily	14 days
	≥ 10 years of age	524 mg	Four times daily	14 days
Esomeprazole* Omeprazole Lansoprazole	15 – 24 kg	20 mg	Twice daily+	14 days
	25 – 34 kg	30 mg	Twice daily+	14 days
	≥ 35 kg	40 mg	Twice daily+	14 days
Amoxicillin	15 – 24 kg	500 mg	Three times daily	14 days
	25 – 34 kg	750 mg	Three times daily	14 days
	≥ 35 kg	1000 mg	Three times daily	14 days
Metronidazole	15 – 24 kg	250 mg	Twice daily	14 days
	25 – 34 kg	375 mg	Twice daily	14 days
	35 – 49 kg	500 mg	Twice daily	14 days
	≥ 50 kg	750 mg	Twice daily	14 days
Tetracycline	≥ 8 years of age	12.5 mg/kg (max 500 mg)	Four times daily	14 days
Clarithromycin	15 – 24 kg	250 mg	Twice daily	14 days
	25 – 34 kg	375 mg	Twice daily	14 days
	≥ 35 kg	500 mg	Twice daily	14 days

* CYP2C19 Genotyping & PPI Dosing: Omeprazole, lansoprazole, and pantoprazole are extensively metabolized by CYP2C19. CYP2C19 genotyping is not required. However, in patients known to be CYP2C19 Ultrarapid or Rapid Metabolizer phenotype, esomeprazole is preferred. If an alternative PPI (i.e., omeprazole or lansoprazole) is selected, it is recommended to increase the dose by 100% for a CYP2C19 Ultrarapid Metabolizer and increase by 50%-100% for a CYP2C19 Rapid Metabolizer.

+ **PPI administration**: PPIs should be taken 30 -60 minutes prior to meals on an empty stomach.

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Patient education: ESPGHAN H pylori patient-parent guide

Helicobacter pylori (H. pylori) in Children - English (PDF)
Helicobacter pylori (H. pylori) in Children - Somali (PDF)
Helicobacter pylori (H. pylori) in Children - Spanish (PDF)

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