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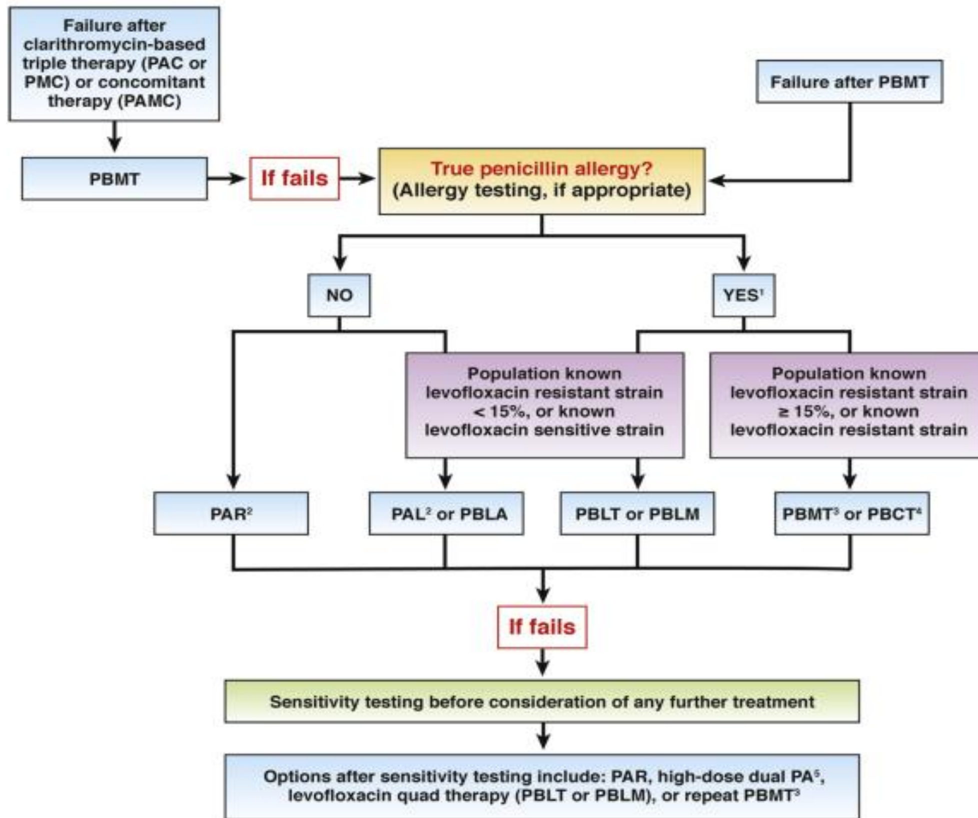
AGA Clinical Practice Update on the Management of Refractory *Helicobacter pylori* infection: Expert Review

By Cindy Ye

The Definition

- Persistently positive **non-serologic** H. Pylori test results (breath, stool, or gastroscopy based-test)
- **≥ 4 weeks** after 1 or more completed course of first-line H. pylori treatment.
- **Must be off PPI for 2 weeks.**



[1]Limited evidence guiding therapy in individuals with true penicillin allergy

[2]With high-dose or high-potency PPI, amoxicillin 750 mg TID

[3]High-dose metronidazole (1.5–2g divided)

[4]Only if clarithromycin sensitive strain

[5]High-dose dual PA = amoxicillin 2–3g daily in 3–4 divided doses + high-dose PPI BID. PA in place of PAR may be considered, although one study from the US demonstrated superiority of PAR compared to PA as first-line treatment (Graham et al. 2020); however, this has not been directly compared in refractory *H pylori* treatment.

P, PPI; C, Clarithromycin; A, Amoxicillin; M, Metronidazole; B, Bismuth; T, Tetracycline; R, Rifabutin; L, Levofloxacin

The Causes

- **Antibiotic resistance** (i.e. prior antibiotic exposure to levofloxacin)
- **Non-adherence** (i.e. insufficient acid suppression)
- Host genetics (i.e. genes that affect intragastric pH such as CYP2C19)
- Non-genetics (i.e. smoking leads to more treatment failure)
- H. pylori strain diversity

The Best Practices

- Attempt to **identify the causes and review the antibiotic exposure** (i.e., if any treatment with macrolides or fluoroquinolones, then avoid clarithromycin and levofloxacin-based regimens) (BPA # 1 and 2).
- To avoid non-adherence, explain rationale to patients to increase compliance (BPA #3).
- **If bismuth quadruple therapy fails**, select between levofloxacin- or rifabutin-based triple-therapy regimens with high-dose dual PPI and amoxicillin or alternative bismuth-containing quadruple therapy (BPA #4).
- Give **high dose metronidazole** in divided doses with bismuth to improve eradication (BPA #5).
- **If PCN allergy**, unless anaphylaxis, consider allergy testing to delist PCN as an allergy, and then give amoxicillin if able (BPA #6).
- Use **high dose, more potent PPIs**, PPIs not metabolized by CYP2C19, or potassium-competitive acid blockers, and consider longer treatment times with **14 days** instead of 7 days (BPA #7 and #8) .
- In certain populations such as elderly, consider shared decision making in order to optimize risk versus benefits (BPA #9).
- **If treatment fails ≥ 2 times**, consider H. pylori susceptibility testing (BPA #10).

Shah SC et al. AGA Clinical Practice Update on The Management of Refractory Helicobacter pylori Infection: Expert Review. Gastroenterology. 2021 Jan 29.