TABLE 188-2 COMMONLY RECOMMENDED TREATMENT REGIMENS FOR *HELICOBACTER PYLORI*

Regimen[a] (Duration)	Drug 1	Drug 2	Drug 3	Drug 4
Regimen 1: OCM (7–14 days)[b]	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Metronidazole (500 mg bid)	—
Regimen 2: OCA (7–14 days)[b]	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Amoxicillin (1 g bid)	—
Regimen 3: OBTM (14 days)[d]	Omeprazole (20 mg bid[c])	Bismuth subsalicylate (2 tabs qid)	Tetracycline HCl (500 mg qid)	Metronidazole (500 mg tid)
Regimen 4[e]: sequential (5 days + 5 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	—	—
	Omeprazole (20 mg bid[c])	Clarithromycin (500 mg bid)	Tinidazole (500 mg bid[g])	—
Regimen 5[f]: concomitant (14 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	Clarithromycin (500 mg bid)	Tinidazole (500 mg bid[g])
Regimen 6[h]: OAL (10 days)	Omeprazole (20 mg bid[c])	Amoxicillin (1 g bid)	Levofloxacin (500 mg bid)	—

[a]The recommended first-line regimens for most of the world are shown in **bold** type. [b]These regimens should be used only for populations in which the prevalence of clarithromycin-resistant strains is known to be <20%. In practice, this restriction limits the regimens' appropriate range mainly to northern Europe. Meta-analyses show that a 14-day course of therapy is slightly superior to a 7-day course. [c]Many authorities and some guidelines recommend doubling this dose of omeprazole, as trials show resultant increased efficacy with some antibiotic combinations. Omeprazole may be replaced with any proton pump inhibitor at an equivalent dosage. [d]Data supporting this regimen come mainly from Europe and are based on the use of bismuth subcitrate (1 tablet qid) and metronidazole (400 mg tid). This is a recommended first-line regimen in most countries and is the recommended second-line regimen in northern Europe. [e]Data supporting this regimen come mainly from Europe. This regimen may be used as an alternative to regimen 3. [f]This regimen may be used as an alternative to regimen 3 or 4. [g]Metronidazole (500 mg bid) may be used as an alternative. [h]Data supporting this regimen come mainly from Europe. It is used as second-line treatment in many countries (particularly where quadruple therapy is used as the first-line regimen) and as third-line treatment in others. This regimen may be less effective where rates of quinolone use are high.

The two most important factors in successful *H. pylori* treatment are the patient's close compliance with the regimen and the use of drugs to which the patient's strain of *H. pylori* has not acquired resistance. Treatment failure following minor lapses in compliance is common and often leads to acquired resistance to metronidazole or clarithromycin. To stress the importance of compliance, written instructions should be given to the patient, and minor side effects of the regimen should be explained. Increasing levels of *H. pylori* resistance to clarithromycin, quinolones, and—to a lesser extent—metronidazole are of growing concern and are thought to be responsible for the reduced efficacy of previously popular clarithromycin-based triple-therapy regimens worldwide. Treatment with these regimens is now virtually confined to certain northern European countries where the use of clarithromycin (or azithromycin) for respiratory infections has not been widespread and resistance rates in *H. pylori* are still low. Strains of *H. pylori* with some degree of in vitro resistance to metronidazole are common but still may be eradicated with metronidazole-containing regimens, which have only slightly reduced efficacy in vivo. Assessment of antibiotic susceptibilities before treatment would be optimal but is not usually undertaken because endoscopy and mucosal biopsy are necessary to obtain *H. pylori* for culture and because most microbiology laboratories are inexperienced in *H. pylori* culture. In the absence of susceptibility information, the patient's history of (even distant) antibiotic use for other conditions should be ascertained; use of the previously administered agent(s) should then be avoided if possible, particularly in the case of clarithromycin (e.g., previous use for upper respiratory infection) and quinolones. If initial *H. pylori* treatment fails, the usual approach is empirical re-treatment with another drug regimen (Table 188-2). The third-line approach should ideally be endoscopy, biopsy, and culture plus treatment based on documented antibiotic sensitivities. However, empirical third-line therapies are often used.

Non-*pylori* gastric helicobacters are treated in the same way as *H. pylori*. However, in the absence of trials, it is unclear whether a positive outcome always represents successful treatment or whether it is sometimes due to natural clearance of the bacteria.

PREVENTION

Carriage of *H. pylori* has considerable public health significance in developed countries, where it is associated with peptic ulcer disease and gastric adenocarcinoma, and in developing countries, where gastric adenocarcinoma may be an even more common cause of cancer death late in life. If mass prevention were contemplated, vaccination would be the most obvious method, and experimental immunization of animals has given promising results. However, given that *H. pylori* has co-evolved with its human host over millennia, preventing or eliminating colonization on a population basis may have biological and clinical costs. For example, lifelong absence of *H. pylori* is a risk factor for GERD complications, including esophageal adenocarcinoma. We have speculated that the disappearance of *H. pylori* may also be associated with an increased risk of other emergent diseases reflecting aspects of the current Western lifestyle, such as childhood-onset asthma and allergy.

189 Infections Due to *Pseudomonas* Species and Related Organisms

Reuben Ramphal

The pseudomonads are a heterogeneous group of gram-negative bacteria that have in common an inability to ferment lactose. Formerly classified in the genus *Pseudomonas*, the members of this group have been assigned to three medically important genera—*Pseudomonas, Burkholderia*, and *Stenotrophomonas*—whose biologic behaviors encompass both similarities and marked differences and whose genetic repertoires differ in many respects. The pathogenicity of most pseudomonads is based on opportunism; the exceptions are the organisms that cause melioidosis (*Burkholderia pseudomallei*) and glanders (*Burkholderia mallei*), which can be considered as primary pathogens.

Pseudomonas aeruginosa, the major pathogen of the group, is a significant cause of infections in hospitalized patients and in patients with cystic fibrosis (CF; Chap. 313). Cytotoxic chemotherapy, mechanical ventilation, and broad-spectrum antibiotic therapy probably paved the way for colonization and infection of increasing numbers of hospitalized patients by this organism. Thus most conditions predisposing to *P. aeruginosa* infections have involved host compromise and/or broad-spectrum antibiotic use. The other members of the genus *Pseudomonas—Pseudomonas putida, Pseudomonas fluorescens*, and *Pseudomonas stutzeri*—infect humans infrequently.

The genus *Burkholderia* comprises more than 40 species, of which *Burkholderia cepacia* is most frequently encountered in Western countries. Like *P. aeruginosa, B. cepacia* is both a nosocomial pathogen and a cause of infection in CF. The other medically important members of this genus are *B. pseudomallei* and *B. mallei,* the etiologic agents of melioidosis and glanders, respectively.

The genus *Stenotrophomonas* contains one species of medical significance, *Stenotrophomonas maltophilia* (previously classified in the genera *Pseudomonas* and *Xanthomonas*). This organism is strictly an opportunist that "overgrows" in the setting of potent broad-spectrum antibiotic use.