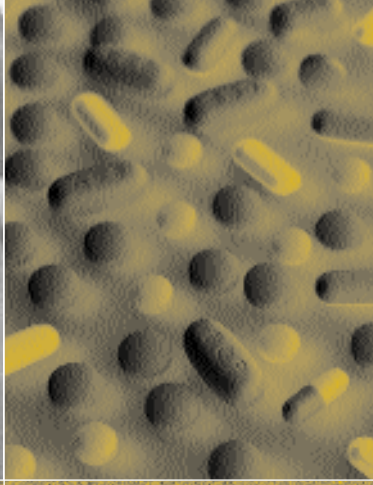

Protocol for Diagnosis and Treatment of PEPTIC ULCER IN ADULTS

American International Health Alliance

Protocol for Diagnosis and Treatment of Peptic Ulcer in Adults

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The guideline on management of peptic ulcer was developed by Marta Lebedeva, MD, head, Department of Internal Medicine, Donetsk City Hospital #25, who made significant contributions to the process and, indeed, to the final product.

The guideline is intended for health care professionals, including family physicians, nurses, and others involved in the organization and delivery of health services to provide practical and evidence-based information about etiology, diagnosis, management and prevention of peptic ulcer disease in adults.

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Protocol for Diagnosis and Treatment of Peptic Ulcer in Adults

The following Protocol for diagnosis and treatment of gastric and duodenal ulcer in adults was developed in Family Practice Center, Donetsk City Hospital #25.*

This Protocol may be used by general practitioners, family doctors, and nurses.

The Protocol includes:

1. ICD definition
2. List of evaluation procedures: laboratory tests and instrumental procedures
3. List of supplementary or complementary evaluation
4. Treatment
5. Diagnostic algorithm

* *Developed March 29, 2002 by Marta Lebedeva, Head of Department of Medicine at DCH # 25*

Protocol implementation goal:

1. To provide patient with high quality treatment meeting up-to-date standards of care
2. To reduce time spent by the patient at FPC
3. To decrease the recurrence rate and to prevent overuse of antacids

ETIOLOGY:

Causes of peptic ulcer:

1. Use of non-steroid anti-inflammatory drugs (NSAID)
2. Bacterium Helicobacter pylori. (Helicobacter pylori can also be detected in the absence of ulcer symptoms.) All duodenal ulcer cases as well as 2/3 of gastric ulcer cases are thought to be associated with Helicobacter pylori.
3. Other causes (benign and malignant tumors)

I. Diseases

1. Gastric ulcer, including peptic ulcer of the pyloric and other parts of the stomach (CODE K-25)

2. Duodenal ulcer, including peptic ulcer of all parts of the duodenum (CODE K-26)

3. Gastrojejunal ulcer, including peptic ulcer of gastric anastomoses, afferent and efferent intestinal loops, gastroenterostomy excluding the primary intestinal ulcer (CODE K-28)

Complaints in case of uncomplicated ulcer:

- Aching, burning localized pain in epigastrium (peptic ulcer diagnosis is confirmed in less than 50% of the patients with the mentioned complaints)

- Antacids alleviate pain

- Nocturnal pain (midnight–3 A.M.) or during intervals between meals (pain from hunger). This is the leading complaint for 2/3 of patients with duodenal ulcer and 1/3 of patients with gastric ulcer. However the same complaint is predominate in 1/3 of patients with dyspepsia not associated with ulcer.

- Belching as a dominating symptom is characteristic for esophageal reflux, but not for the peptic ulcer.

Signs of the complicated ulcer:

- Gastrointestinal bleeding (melena, hematemesis, positive fecal blood test). The most common complications encountered in 15-20% of cases.
- Obstruction (vomiting preceded by nausea).
- Penetration, perforated ulcer (acute abdominal pain).
- Gastric cancer (weight loss, loss of appetite). Chances for development of gastric cancer increase with age. Patients older than 45 with recent onset of complaints require early consultation by gastroenterologist.

II. Laboratory Tests

Title	Frequency
1. CBC should be repeated in case of abnormalities revealed	Once in 10 days (for treatment monitoring)
2. Blood type	Once
3. Rh-factor	Once
4. Feces for occult blood	Once
5. Urinalysis	Once
6. Iron in blood serum	Once
7. Reticulocyte count	Once
8. Blood sugar	Once
9. Histological and cytological evaluation of biopsy sample if endoscopy was conducted	Once
10. Urease test	Once*

**This test is performed to detect active infection. Its specificity and sensitivity exceed 90%. May be also used to diagnose successful eradication of Helicobacter pylori.*

Antibiotics and bismuth medications should be discontinued at least four weeks before the test. Ranitidin and other histamine receptors blockers should be discontinued at least seven days prior to the procedure. The test should be conducted no earlier than six hours after the last meal.

This test is not recommended in case of the prior partial gastrectomy related to gastric cancer, prolonged use of proton pump inhibitors (Omeprasol, etc.) and severe esophageal reflux and prolonged use of NSAID irrespective of the fact whether the ulcer has developed or not.

Other non-invasive HP diagnostic tests include ELISA–serology testing for identification of IgG antibodies (sensitivity -90-93%, specificity -95-96%) it is not recommended as the confirmation test for eradication; fecal test for identification of HP antigen (sensitivity - 95-98%, specificity- 92-95%); may be used to confirm successful eradication.

III. Instrumental Evaluation

1. Ultrasonography of liver, biliary tract and duodenum: **Once**
2. Esophagogastroduodenoscopy with targeted biopsy and brush cytology: **twice (if indicated) prior and after treatment**

Indications for endoscopy.

Despite the fact that currently endoscopy is considered "the golden standard" for HP detection, in uncomplicated cases of dyspepsia in patients younger than 45 years of age, non-invasive diagnostic modalities are recommended (C level of recommendations). Indications for endoscopy include:

- above-mentioned complaints alongside with
  - disphagia
  - recurrent vomiting
  - anemia
  - weight loss more than 10% of weight
  - signs of gastrointestinal bleeding
  - family history of gastric cancer
- first onset of symptoms in patients older than 45 years of age
- if your regional statistics show that gastric cancer rate is rather high for the younger age

group, then age qualification for endoscopy testing should be lower
- patient refractory to treatment with complaints persisting two weeks after eradication therapy or patients with new complaints
- negative result of the Helicobacter pylori detection test

IV. Additional Evaluation and Consultation of Gastroenterologist

An additional evaluation should be performed if malignant ulcer is suspected, in case of complications of comorbidities or in case of treatment failure. If in two weeks following the completion of therapy there are no results, one should exclude other causes of peptic ulcers.

V. Treatment

Goal: HP eradication, healing of ulcers, prevention of recurrences and complications of ulcer.

DRUG TREATMENT OF GASTRODUODENAL ULCERS ASSOCIATED WITH HP.

HP eradication regimen includes use of antibiotics and antacids (level A recommendations). Prolonged antacid use for treatment of ulcers caused by HP is not recommended (level B recommendations). Successful HP eradication decreases the recurrence rate from 90% to less than 5% a year.

1. Seven day regimen: May be taken 10-14 days, however, there is no data available to show the benefits of a 10- to 14-day regimen as compared to a seven-day regimen

(See chart on next page.)

- **Omeprasol (Losek, Omez)** from other analogues currently recommended is Lansoprasol (Zoton) 20 mg bid or 30 mg bid (in the morning and in the evening before the meal, no later than 8 P.M. with mandatory 12-hour interval); capsule should be swallowed, not chewed
- **Klarythromicin (Klacide)** 250 mg bid
- **Metronidazole (Trikhopole and other analogues)** 500 mg bid at the end of the meal. The drug should not be taken with alcohol; metallic taste and/or dark urine are possible.

Eradication rate 87-91%.

- **Omeprasol (Losek, Omez)** from other analogues currently recommended is Lansoprasol (Zoton) 20 mg bid or 30 mg bid (in the morning and in the evening before the meal, no later than 8 P.M. with mandatory 12-hour interval); capsule should be swallowed, not chewed
- **Klarythromicin (Klacide)** 250 mg bid
- **Amoxicillin** 1g bid at the end of the meal. Amoxicillin is recommended in case of prior Metronidazole failure. Metronidazole is recommended for use in case of hypersensitivity to penicillin.

Eradication rate 80-90%.

- **Omeprasol (Losek and analogues)** 20 mg bid (in the morning and in the evening, no later than 8 P.M. with mandatory 12-hour interval)
- **Amoxicillin (Flemoksyn Solutab, Kchikoniil and other analogues)** 1 g/bid at the end of the meal
- **Metronidazole (Trikhopole and other analogues)** 500 mg bid at the end of the meal.

Eradication rate 77-83%.

- **Pylorid (Ranitidin Bismuth Citrate)** 400 mg bid at the end of the meal
- **Klarythromycin (Klacide)** 250 mg/bid or tetracycline 500 mg four times a day or Amoxicillin 1000 mg/bid
- **Metronidazole (Trikhopole and other analogues)** 500 mg bid during the meal

Eradication rate 78-83%.

- **Omeprasol (Losek and analogues** 20 mg/bid (in the morning and in the evening, no later than 8 P.M. with mandatory 12-hour interval)
- **Colloid Subcitrate of Bysmuth (Ventrisol, Denol and other analogues)** 240 mg/bid 30 minutes before the meal (breakfast or supper) or 120 mg/q.i.d (first three doses should be taken 30 minutes before breakfast or dinner, or supper. The last two – after the meal before going to bed). With this medication the tongue and the feces may develop dark color; half an hour before and after taking the medication it is not recommended to drink milk; it should be used with caution in patients hypersensitive to aspirin; in case of tinnutis the medication should be discontinued
- **Metronidazole** 250 mg/qid after the meal or Tinidazole – 500 mg/bid after the meal
- **Tetracyclin or amoxicillin** 500 mg/qid after the meal

Eradication rate in tetracyclin regimen 88-90%, in amoxicillin regimen 80-86%

2. Two-week regimens

- **Ranitidin (Zantak and other analogies)** 150 mg/bid or Famotidin (Gastrosydyn, Kvamatel, Ulfamyd) 20 mg/bid in the morning and in the evening (no later than 8 P.M.) with mandatory 12-hour interval;
- **Potassium salt of bismuth citrate – gastrostat** 120 mg/qid before the meal
- **Metronidazole** 250 mg/qid after meal
- **Tetracyclin hydrochloride** 250 mg /qid after meals. Tetracyclin should not be used with dairy products, antacids and medications containing iron; photosensitization in the sun and a rash may develop

Eradication rate 80%

- **Potassium salt of bismuth citrate – gastrostat** 120 mg/qid before the meal
- **Metronidazole** 250 mg/qid after meal
- **Tetracyclin hydrochloride** 250 mg/qid after meals

Eradication rate 75%

Comments:

- Resistance may develop in regimens with Metronidazole and Klarythromycin
- Smoking hinders healing of ulcers and is associated with increased recurrence rate
- In absence of symptoms, diagnostic procedures to confirm successful eradication may be omitted. In case of complicated ulcer, endoscopy is indicated to confirm the success of the therapy.

Refractory ulcer.

The most common causes of refractory and recurrent ulcer include 1) ineffective eradication therapy; 2) unidentified use of NSAID and poor compliance with medications regimens, incomplete healing of large ulcers, Zollinger-Ellison syndrome and malignant neoplasms. Should the first stage of

therapy fail, a second stage of eradication therapy with other antibiotics is recommended; term of the therapy: 14 days. Treatment success in the case of gastric and gastrojejunal ulcers is monitored endoscopically in eight weeks; in the case of complicated duodenal ulcer; in 4 weeks. Use of serology testing to confirm eradication of HP is not justified, since antibody titer remains elevated even in the absence of HP.

TREATMENT OF ULCERS CAUSED BY NSAID

NSAID use should be discontinued. Acetaminophen is as effective as NSAID in treatment of mild/severe arthritis. Routine HP evaluation of patients complaining of dyspepsia for NSAID is currently not recommended. In those cases when NSAID cannot be discontinued a 20 mg, single dose for four weeks of Omeprasol (or its analogues) is recommended. Clinical trials have shown that percentage of healing reaches 75-80% for an eight-week treatment.

If NSAID can be discontinued, ranitidin (or its analogues) is recommended: 150 mg/bid for 8 weeks.

To prevent peptic ulcer development in patients taking NSAID with associated risk factors (history of peptic ulcer or gastric bleeding, older than 75, history of cardiovascular problems), a simultaneous prescription of Misoprostole 200 mg/three times a day is recommended.

To prevent gastric and duodenal ulcer recurrence and their complications:

1. Prophylactic therapy "on demand"—stipulating administration of one of antacids (Ranitidin, Famotidin, Omeprasol) in a daily dose for 2-3 days, and then one half of the dose for two weeks in case of onset of symptoms characteristic for the exacerbation of ulcer—is recommended. If the symptoms of the exacerbation disappear, the therapy is discontinued. If they persist, EFGDS and other evaluation procedures envisaged by this protocol are indicated.

2. Continuous supportive therapy (for a month or even years) with half the dose of antacid. For example, one should take every evening: 150 mg of Ranitidin or 20 mg Famotidine (gastrosidin, kvamatel, ulfamide). Indications for this type of therapy include:

   - complications of ulcer (ulcer-related bleeding or perforated ulcer)
   - concurrent ulcerative -erosive esophageal reflux
   - patients 60+ with annual recurrences of ulcer, despite adequate therapy

VI. Treatment of Gastro-duodenal Ulcers Not Associated with HP.

To exclude or reduce smoking and alcohol use as well as NSAID use, one of the following drug combinations and regimens is used:

1. **Ranitidin (Zantak and other analogues)** 300 mg a day, single dose at 7–8 P.M. and antacid (Maaloks, Remagel, Gastrin gel, etc.) as symptomatic medication

2. **Famotidin (Gastrosidin, Kvamatel, Ulfamid)** 40 mg a day at 7–8 P.M. and antacid (Maaloks, Remagel, Gastrin gel, etc.) as symptomatic medication

3. **Sukralfat (Venter, Sukrat gel)** 4 g a day; more often 1 g 30 min. before the meal and in the evening two hours after the meal for four weeks, then 2 g a day for eight weeks.

For the treatment of refractory duodenal ulcers not associated with HP, maximal dose of proton pump inhibitors is recommended (Omeprasol, etc.). Concurrent use of proton pump inhibitors (PPI) and 2nd type histamine receptors blockers (HRB) is not recommended due to the potential

decrease in the PPI effectiveness of. In cases of ulcers refractory to HRB-2, PPI is recommended (level A).

Recommendation levels:

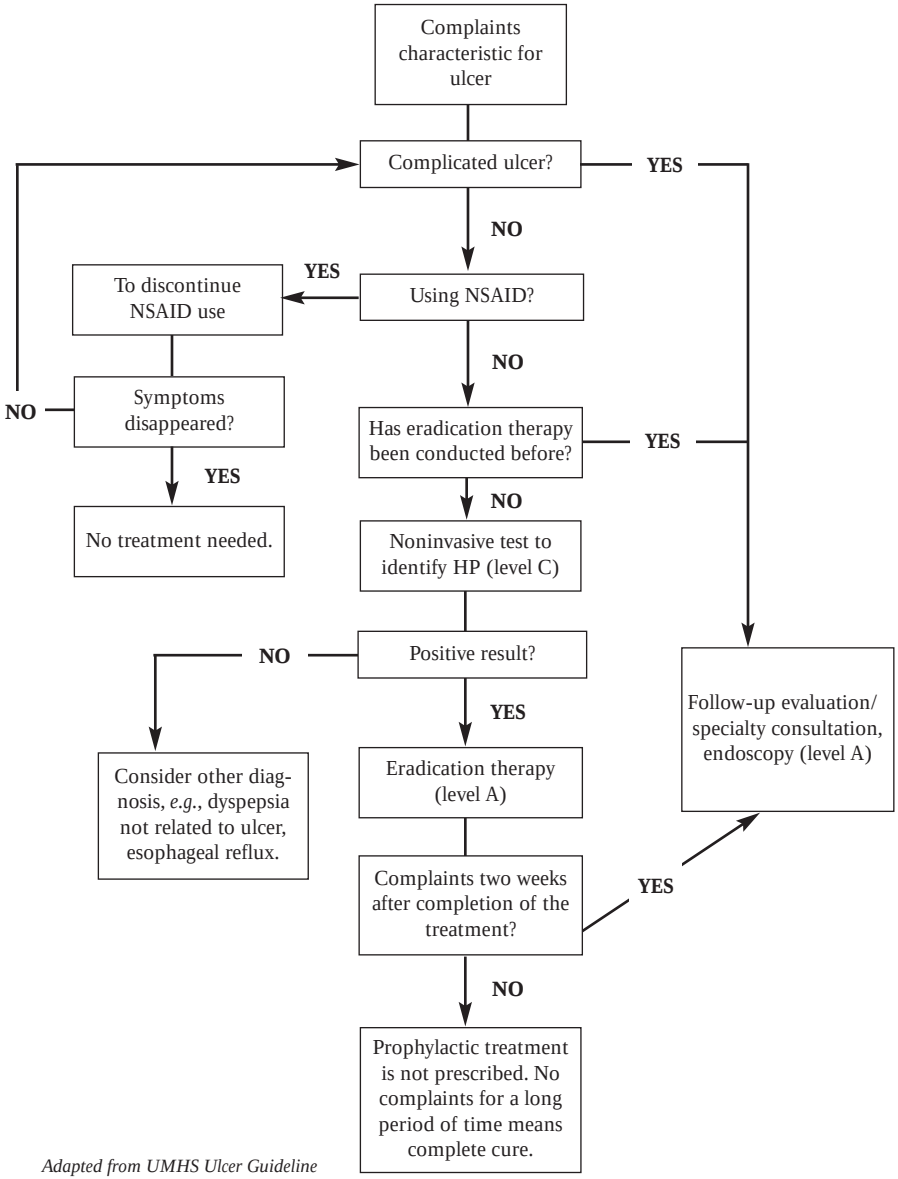
A Randomized clinical trials or meta-analysis with statistically valid results

B Randomized clinical trials or meta-analysis in which clinical outcome is possible but not valid

C Non-randomized clinical trials, the physician makes his own decision

D Recommendations of panel, results of separate clinical observations

DIAGNOSTIC ALGORITHM



Adapted from UMHS Ulcer Guideline

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