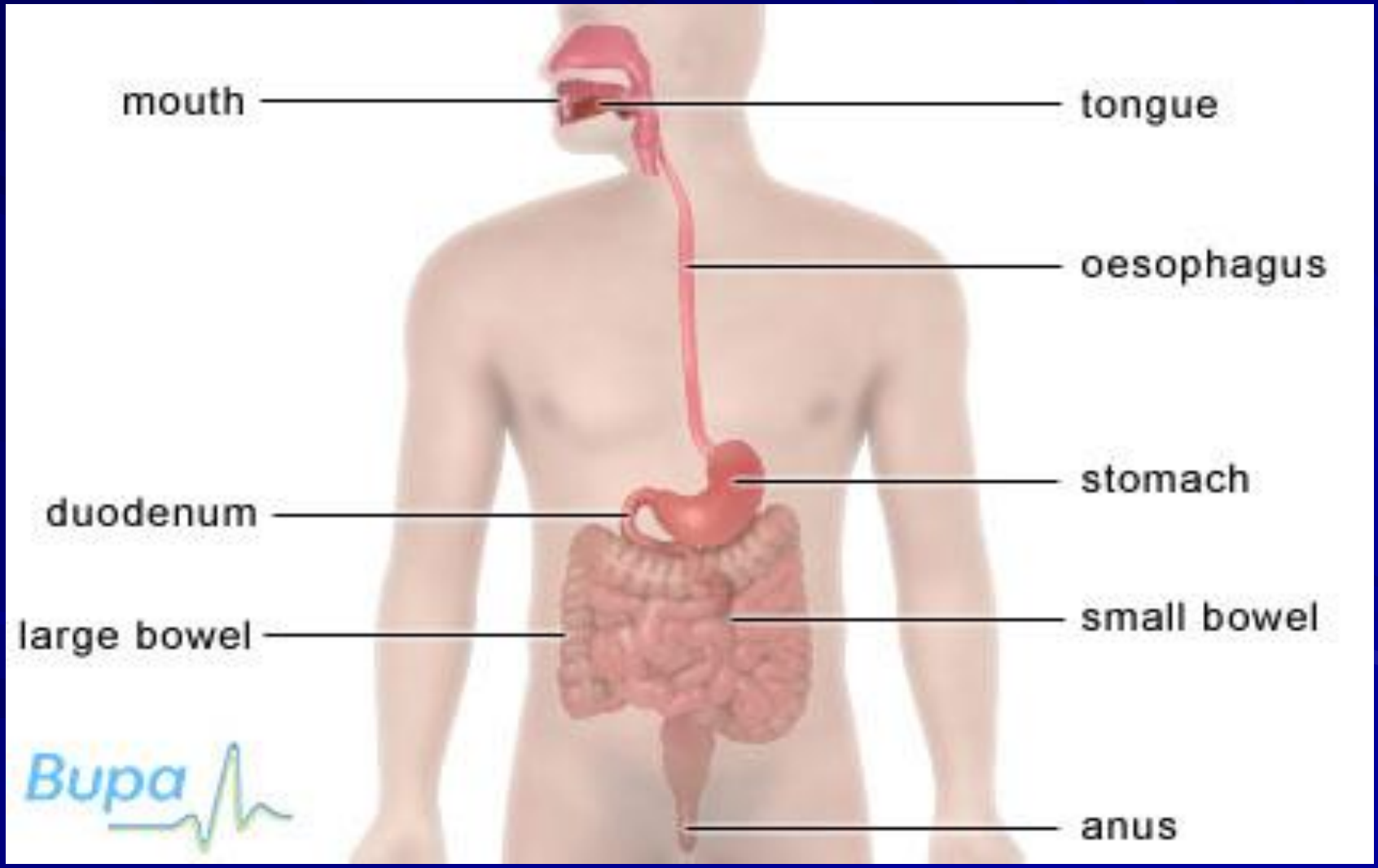
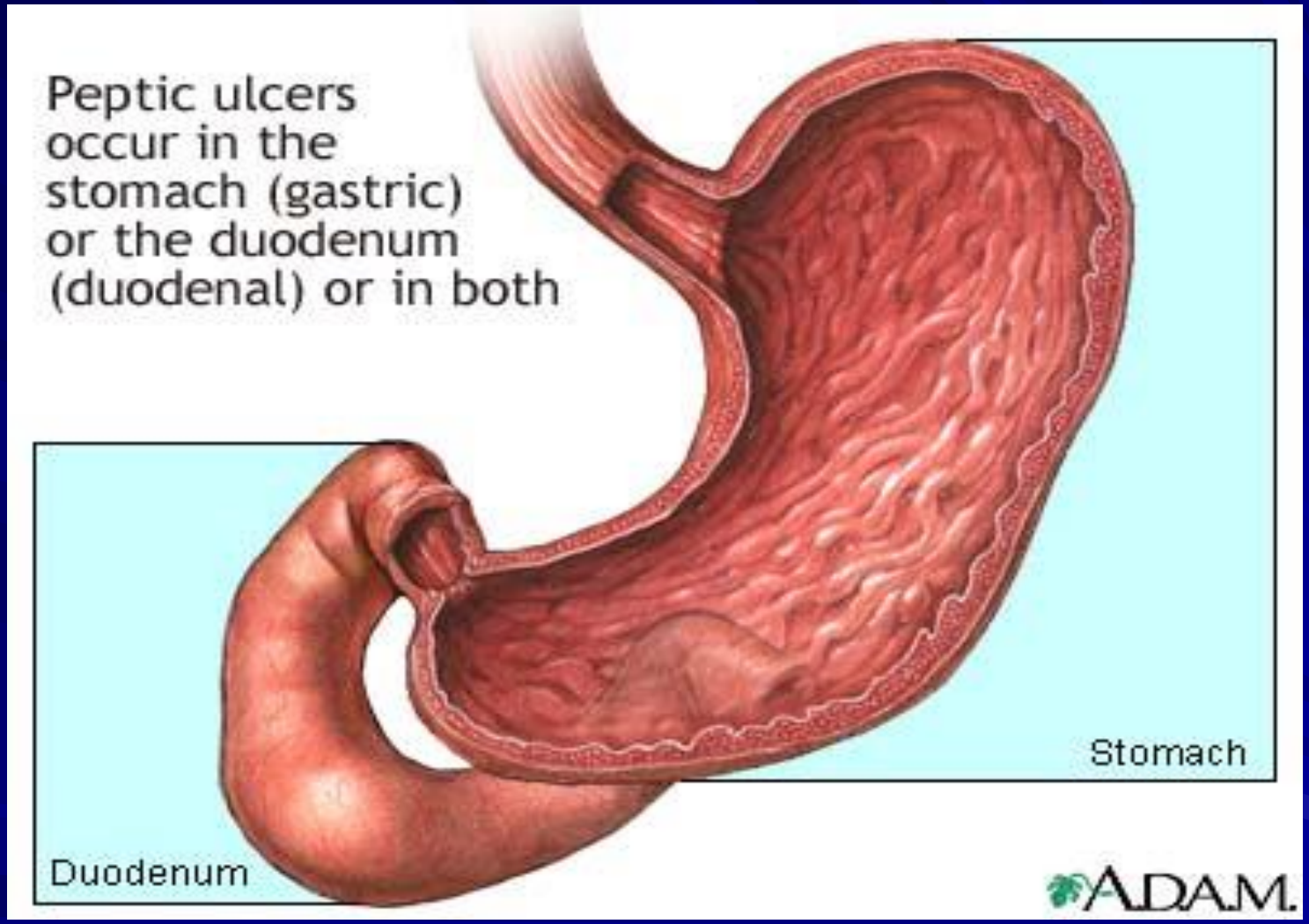
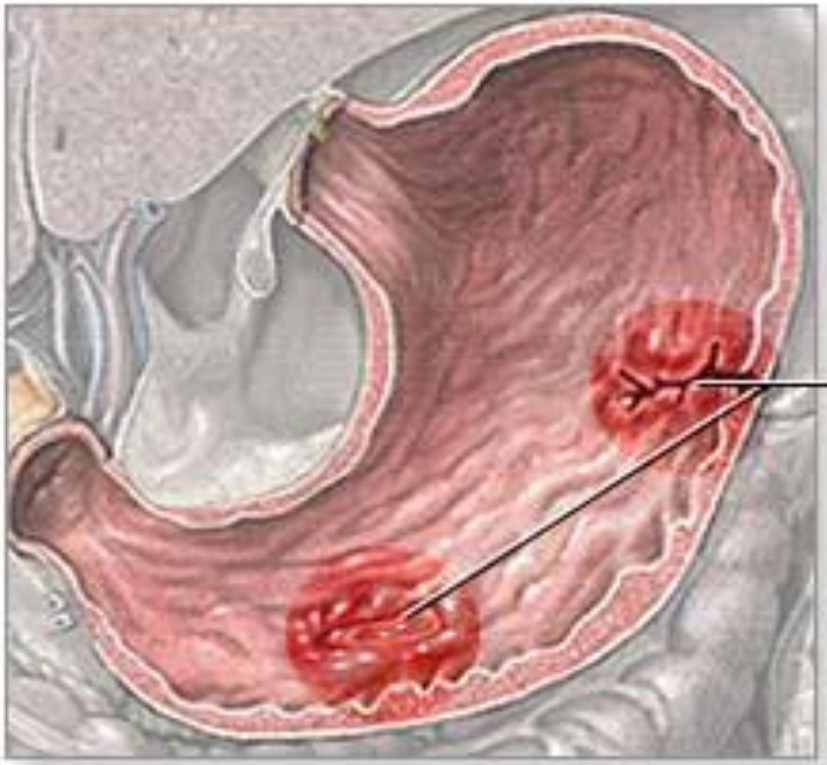
PEPTIC ULCER, PUD




Peptic ulcers occur in the stomach (gastric) or the duodenum (duodenal) or in both
Stomach
Duodenum
A.D.A.M.



A.D.A.M.

Definistion

- A peptic ulcer is an open sore or raw area in the lining of the stomach (gastric) or the upper part of the small intestine (duodenal).
- **An ulcer is a crater-like lesion on the skin or mucous membrane caused by an: inflammatory, infectious, or malignant condition .**

- Ulcers of the small intestine are known as ***duodenal ulcers.*** Duodenal ulcers affect about ***1 in 10 people*** at some point in their lives, usually between the ***ages*** of ***45 and 65.***
- **Stomach ulcers are less common**, and usually affect people aged ***over 65.***

- ***Causes***
- **The following are the most important causes of peptic ulcers:**
- **The most common cause is infection of the stomach with:**
- ***1).*** **bacteria called *Helicobacter pylori* or *H. pylori*. This infection is quite common; about half of the world's population is infected. These bacteria cause the stomach to make too much acid, which damages the lining of the stomach or duodenum and can cause the ulcer.**

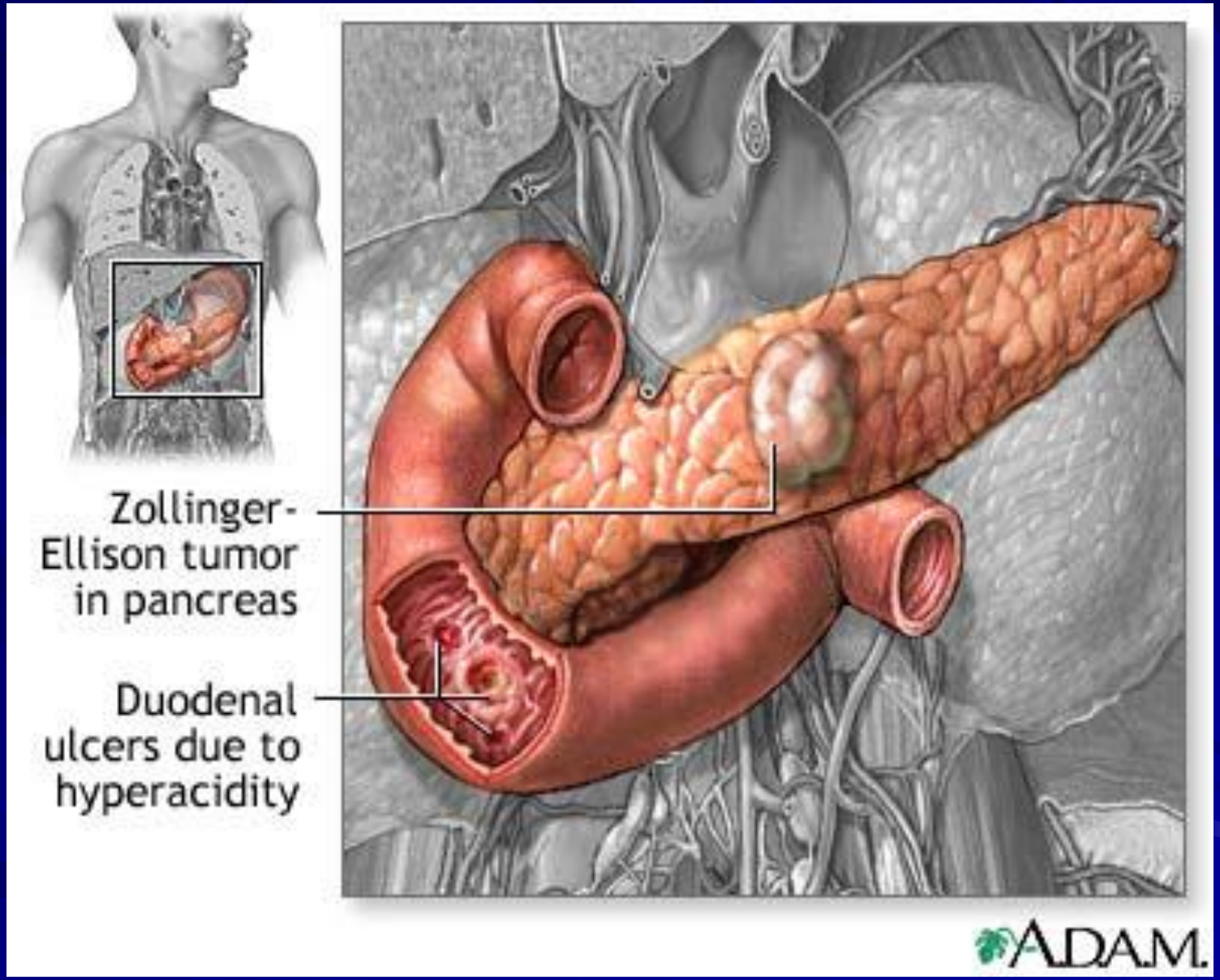
- ***2).*** **Non-steroidal anti-inflammatory drugs (NSAIDs),** can cause peptic ulcers. Examples : **aspirin, ibuprofen, naproxen and diclofenac.** However most people can take these safely.

- ***3).*** **Smoking and drinking excessive alcohol.**

- ***4)***. **Stress** is widely thought to cause ulcers, but this **has not been proven**. It could be that **people under lots of stress are more likely to smoke and drink too much.**

- ***5).*** **Zollinger-Ellison syndrome** egral A . tnuoma**of excess acid is produced in** response to the overproduction of the **hormone gastrin** si nrut ni hcihw ،**caused by** ***tumors*** eht no ***pancreas or duodenum*** . eb tsum ،tnangilam yllausu era sromut esehT ot desserppus noitcudorp dica dna devomer .sreclu eht fo ecnerrucer eht eveiler

- ***6).*** Coffee, tea, cola beverages, beer, and spices **may cause dyspepsia** ***but do not increase PUD risk?.***


Zollinger-
Ellison tumor
in pancreas
Duodenal
ulcers due to
hyperacidity
A.D.A.M.

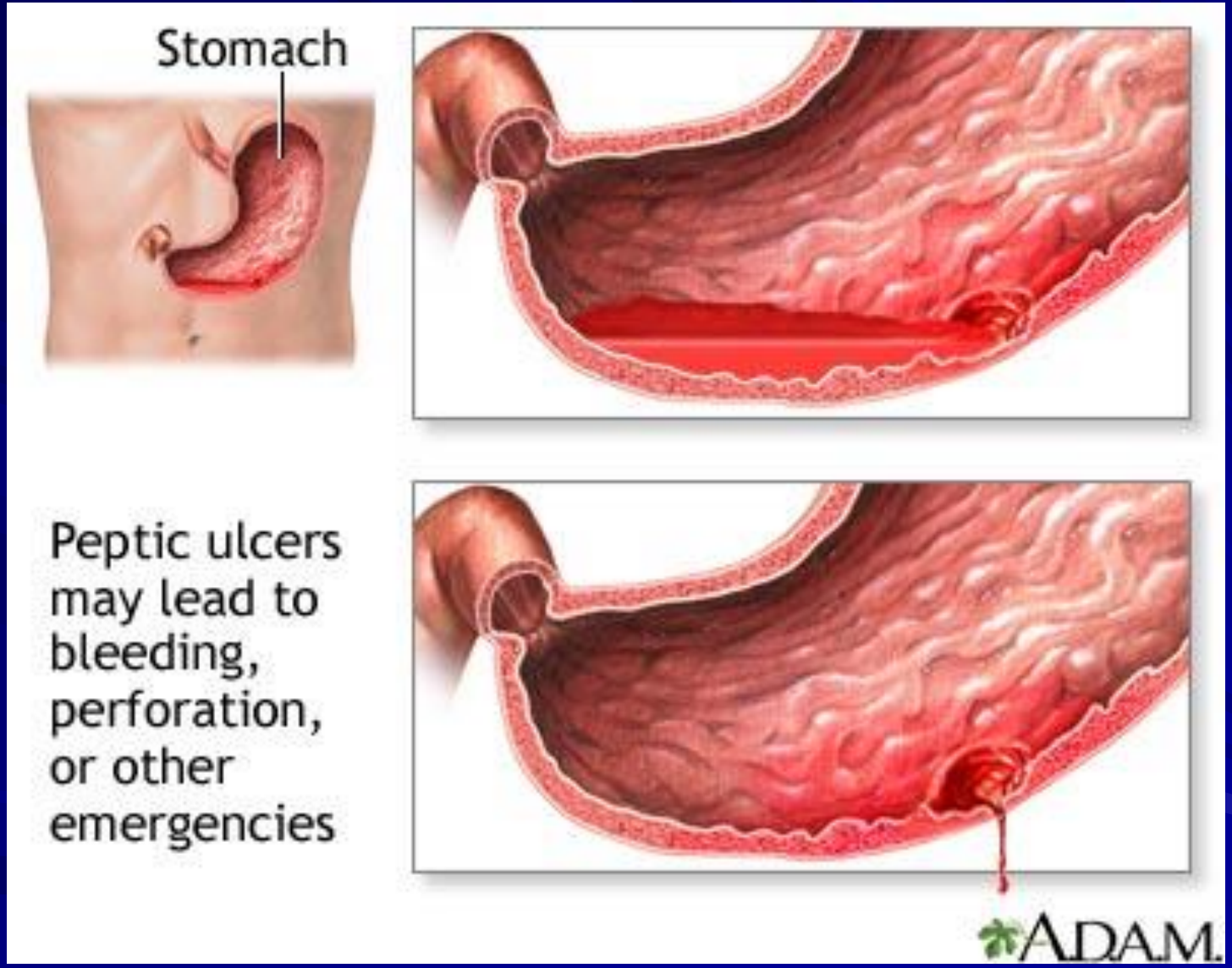
- ***Symptoms***
- **Some people** with a peptic ulcer **have no symptoms.** However, many people have **upper abdominal pain** usually just below the breastbone (sternum). **Feel a pain in a back**. The pain usually comes on an hour or two after eating and can be relieved by more food or antacid medicine. It may also **wake you at night especially between 12 am and 3 am.**

- ***Other symptoms may include*:**
- belching : تَجَشُّؤ
- heartburn
- general discomfort in the abdomen
- bloating or fullness after eating
- feeling sick
- vomiting
- difficulty swallowing
- lost weight without trying to do
- a reduced appetite
- seen blood in a vomit or bowel movements

Complications

- **Possible** complications include the following **:**

- **Bleeding**
- Occasionally ulcers can cause the lining of the stomach or duodenum to bleed.
- A bleeding ulcer will give symptoms that include**:**
- vomit containing dark brown bits of clotted blood (with an appearance like ground coffee)


Stomach
Peptic ulcers may lead to bleeding, perforation, or other emergencies
A.D.A.M.

- blood in the faeces (usually dark red) black, tarry faeces.

- **Anaemia : Chronic iron deficiency**
- If the bleeding from the ulcer is slow, you might not get blood in your vomit or faeces. However, you may develop anemia.

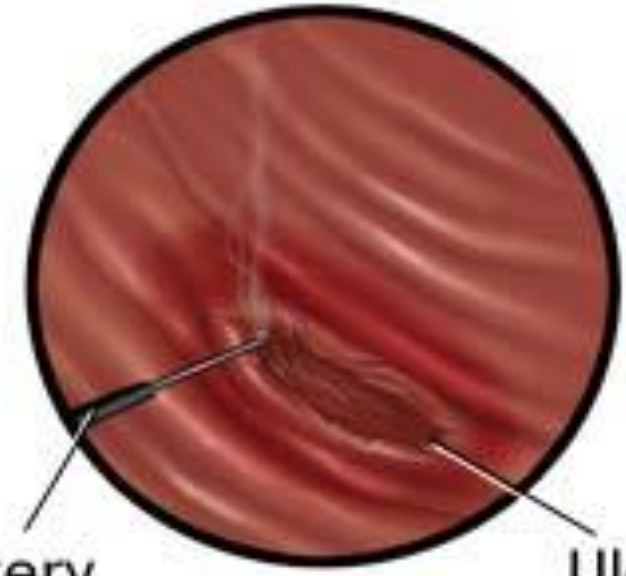
- **Perforation**
- Rarely, the ulcer may erode very deeply into the wall of the stomach or duodenum, leaving a hole into the abdomen. **This causes severe pain and needs emergency surgery.**

- **Diagnosis**
- The tests to diagnose, are.
- ***H. pylori tests:***
  - Testing for *H. pylori :* ***breath***
  - (**breath**) *urea* $\longrightarrow$ $Co_2 + NH_3$ *(90%)*
  - (**stool**) test. H pylori **antigen** (90%)
  - (**blood)** : anti H pylori **IgG antibodies**
  - (# Active or previous infection).

- **If an anti-ulcer proton pump inhibitor (PPI) is used, the breath and faeces test won't be accurate until two weeks after stopping the medicine.**

- ***Endoscopy***
- The endoscopy is the only way to be certain whether you have a peptic ulcer.

View of a duodenal ulcer through the endoscope



A.D.A.M.

- A flexible, tube-like instrument called a **gastroscope** is passed through the mouth and into the stomach, usually under sedation in hospital. The procedure usually **lasts a few minutes.**

- **With the instrument :**
- looking the lining of the stomach, and
- can take a sample of stomach lining or a biopsy for laboratory, or
- **directly tested for *H. pylori*.**

- **Treatment: Drugs**
- **Three major landmarks for peptic ulcer disease**
- **1) The first : *H2 Receptor Antagonists*** (H2RA) of
- which the first was cimitidine.
- Ranitidine, Famotidine , Nizatidine **Lavoltidine**
- **Structural : analogues to histamine**
- **Blockage : histamine receptor**
- ⟶ decreasing Hcl secretion
- **Preventing conversion of pepsinogene to pepsin (acid PH medium).**

- **Tmax = 1 – 3 hr**
- ***Elimination = Kidneys***
- **Dose adjustment (renal failures)**
- Evening Dose Administration (PH low)
- **ADR** : Diarrhea, Headache, confusion
- **Drug – interaction :**
- Cimitidine : **Reduction Cl int (oxidation) of :**
  - Theophylline = Cl reduced (40%), Toxicity
  - Phenytoin + bezodiazepines = Met reduced
  - **itraconazole + Ketoconazole = Abs reduced**
  - ***Css aver Warfarin increase***
- ***Proffered (over PPI) in pregnancy***

- ***Bismuth Chelate*** (Safe form of bismuth)
- Cytoprotective properties
- Toxic to H pylori (ranitidine + bismuth chelate +
- 2 antibiotics) leads to 90% efficacy H pylori.

- **ADR :**
- **Accumulation in impairment renal**, nausea,
- vomiting, ***dark faces, black end langue.***

- ***Sucralfate : Al sucrose octasulphate***
- Mechanism : Stimulation of bicarbonate
- Stimulation of mucus secretion
- Stimulation of prostanoid, eg :
- (prostaglandin, thromboxane, prostacyclins)

- PH < 4 : it form sticky viscid gel, adheres to ulcer surface
- Dose = 2 gr twice daily .
- ADR = risk Al toxicity (long terms)
- **Caution in renal impairment**
- **Interactions = reducing absorption some drugs:**
- Antifungal agents, azole, (itraconazole, ketoconazole)
- (ciprofloxacin, lomefloxacin, moxifloxacin, norfloxacin, ofloxacin, sparfloxacin)
- Phosphate supplements (oral). interval = 2 hr

- **2)** The second **:** **proton pump inhibitors**
- **(PPI)** of which **omeprazole** was the first.
- Lansoprazole, Pantoprazole, Esomeprazole,
- Rabeprazole, Binzinidazole,
- Pro-drug: converted to drug, which binds to PP
- Site of action : Secretory canaliculus
- Dosage forms : enteric coating
- Half-life : 1 – 2 hr
- Duration of action : 45 - 50 hr
- Dosing intervals : 24 hr

- Effectives : 30 min before a meal
- **(Ideal = 30 – 60 min before first meal)**
- **Elimination : Hepatic (80%) conjugation**
- **ADR** : Diarrhea – headache, abdominal pain,
- change in intestinal PH + Bacterial over growth
- Long term : Respiratory tract infection **(clos diff)**

- **Drug interaction :**
- **Omeprazole inhibit Cyp450 : 2C9 – 2C19**
- ***Lansoprazole : induce Cyp 450 : 1A2***
- **PPI > H2RA : Efficacy**

- **3)** The third was the discovery that **H pylori** is associated with much peptic ulcer disease, and with this came the rationale for **eradication** of the organism. As a result of these innovations, the need for surgery for peptic ulcer has been dramatically reduced.
- **H pylori infection** is associated with about 95% of duodenal ulcers and 80% of gastric ulcers. The remainder are mainly **related** to **NSAIDs**. **Bisphosphonates** and **corticosteroids** may also be implicated.

Contraindications

- Many of the drugs used in the management of peptic ulcer disease carry a warning that **they *should not be used in pregnancy* or whilst *breast feeding*.**
- The exception is **misoprostol**, a **prostaglandin analogue**, ***that should be avoided in pregnancy*** as it may **cause abortion.**
- If H pylori eradication is used, it may be necessary to avoid a certain antibiotic if the patient is allergic. For example, **amoxicillin** may be replaced by either **tetracycline** or **metronidazole.**

- **Indications**
- Symptomatic management of **ulcer dyspepsia** and **non – ulcer dyspepsia**
- **1)**. Healing of gastric or duodenal ulcers
- **2)**. Eradication of Helicobacter pylori
- **3)**. Healing of ulcers related to drugs. This is usually the **NSAIDs** and in some cases it may be desirable to continue the drug and to give something to heal the ulcers.

- **Caution**
- Beware of the possibility of failing to diagnose **gastric malignancy**.
- **PPIs are metabolised mostly in the liver.**
- **In liver disease, do not exceed the following doses:**
  - 20 mg daily for **omeprazole, Pantoprazole, and esomeprazole;**
  - 30 mg daily for **lansoprazol**
  - There are no data on the use of **rabeprazol** in people with severe hepatic impairment so the manufacturer advises caution.(20 mg daily)

- **Omeprazole and esomeprazole may interfere with *warfarin* monitoring.**

- **If metronidazole is used, remember to warn the patient to avoid alcohol.**

- **Initiation of treatment**
- **Management** is not just pharmacological but **should include attention** to **lifestyle**. This may include **:**
- **stopping smoking,**
- **more regular meals,**
- **ceasing excessive alcohol consumption** and
- **possibly stopping drugs that may be contributing to the problem.**

- **Choice of treatment**
- ***Antacids*** are cheap, simple and may be all **that is required for *relief* of occasional *symptoms*.**
- ***H2RAs*** provide a **swift** and effective means of acid suppression and can be used intermittently to achieve control of symptoms.
- ***PPIs*** are more prolonged in action, produce more profound acid suppression.

- ***Misoprostol*** tends to be **used to heal NSAID associated ulcers.**

- Using a **prostaglandin analogue** to heal ulcers antagonism, **tend to cause diarrhoea too** and may be unacceptable. ***Proprietary combinations of NSAID with misoprostol are available.***

- Attempts should be made to eradicate Helicobacter pylori whenever it is found, whether the diagnosis is duodenal ulcer, gastric ulcer, **NSAID induced ulcer or even non-ulcer dyspepsia.**

- **Symptomatic relief**
- *Simple* ***antacids*** will usually give symptomatic *relief of fairly short duration*. However, such relief is very non-specific and **should not be taken as indicative of peptic ulcer disease.**
- Heartburn may also occur in this condition although it is more typical of **gastro-oesophageal reflux disease**. **An antacid alginate mixture is usually preferred for reflux.**

- More profound and prolonged acid suppression may be achieved with a **H2RA or, better still, a PPI.**

- **Clinical Knowledge Summaries**
- recommend that if an **ulcer is proven** but **H pylori testing is negative**, then ***acid suppression*** **at full dose should be offered for 1 or 2 months.** **A lower maintainance dose** may be **continued after.** The ***full course*** should be taken as there is little correlation between the relief of symptoms and the healing of ulcers **and if medication is stopped too soon the ulcer will relapse.**

Helicobacter pylori eradication

The following is based on the recommendations of NICE:

omeprazole 20mg •

- amoxicillin 1000mg
- Clarithromycin 500mg, **all** twice daily for 21days.
-

An alternative regimen with a similar eradication rate of around 90% is:

- omeprazole 20mg
- clarithromycin 250mg
- metronidazole 400mg, again **all** twice daily for 21days.

- It is common practice to **use 4 drugs** for a repeated attempt. The antibiotics can be changed and chelated bismuth may be used. ***A typical quadruple therapy would be:***
- ***PPI twice** a day*
- ***Bismuth chelate** 120 mg **4 times** a day*
- ***metronidazole** 400 mg **3 times** a day*
- ***Oxytetracycline** 500 mg **4 times** a day, all for 21days.*
- Reinforce the importance of compliance as it is not easy to take so many tablets so many times a day, **even for just a week**.

- **Ulcers associated with NSAIDs**
- **If a drug is thought to be the cause of peptic ulceration, it is sensible to stop the drug or change it to another with a lower risk. There may be times when it is desirable to continue that drug. An old person may need treatment for arthritis to maintain mobility or aspirin may be required in cardiovascular disease. It is often possible to heal the ulcer without stopping the offending drug and a maintenance dose is continued to prevent relapse.**

- **Clinical Knowledge Summaries** recommend that **omeprazole 20 mg daily** is ***preferable*** to **ranitidine 150 mg twice daily** as the respective rates of healing are **80%** and **63%.**

- H2RAs are slow to heal the ulcers if the offending drug is not stopped and so, under these conditions, a ***PPI is preferred.***

- **H pylori eradication is no more effective than omeprazole alone** to heal ulcers, ***but*** **if the *infection is present*, then *eradication will reduce the rate of relapse.***

- **Monitoring**
- Patients should be reviewed at the end of a course of treatment, especially H pylori eradication, to confirm a satisfactory outcome.

- ***Repeat endoscopy may be required for*** **:**
- **Failure to eradicate symptoms** in a duodenal ulcer.
- **Failure to have eradicated H pylori.**

- Follow up of a gastric ulcer requires repeat endoscopy to confirm healing at 6 to 8 weeks along with confirmation of eradication of H pylori.

- **If a gastric ulcer persists, referral to secondary care is required.**

- If it is **healed** but **symptoms persist**, a **course of acid suppression for a limited duration may be in order**, **but if symptoms persist, referral is necessary.**