Lect.2 Stomach

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STOMACH

- Chronic infection of the gastric mucosa by **H. pylori** is the most common infection worldwide.
- **peptic ulcers** occur in up to 10% of the general population In developed countries.
- **Gastric cancer** is still a significant cause of death, despite its decreasing incidence.

GASTRITIS

- It is a microscopic diagnosis
- It is inflammation of the gastric mucosa"..
- May be acute, with neutrophilic infiltration, or chronic, with lymphocytes and/or plasma cells.

Acute gastritis

- it is transient inflammation may be accompanied by hemorrhage(acute hemorrhagic gastritis) and, sometimes by sloughing (erosions) of the superficial mucosa (acute erosive gastritis).
- **Most common Causes**:

1. a large number of cases have no obvious cause (idiopathic)
2. Heavy use of (NSAIDs) particularly aspirin .
3. Excessive intake of alcohol, heavy smoking
4. Uremia
5. Severe stress (e.g., trauma, burns, surgery)
6. Mechanical trauma (e.g., nasogastric intubation)
7. Distal gastrectomy (reflux of duodenal contents).

Chronic Gastritis

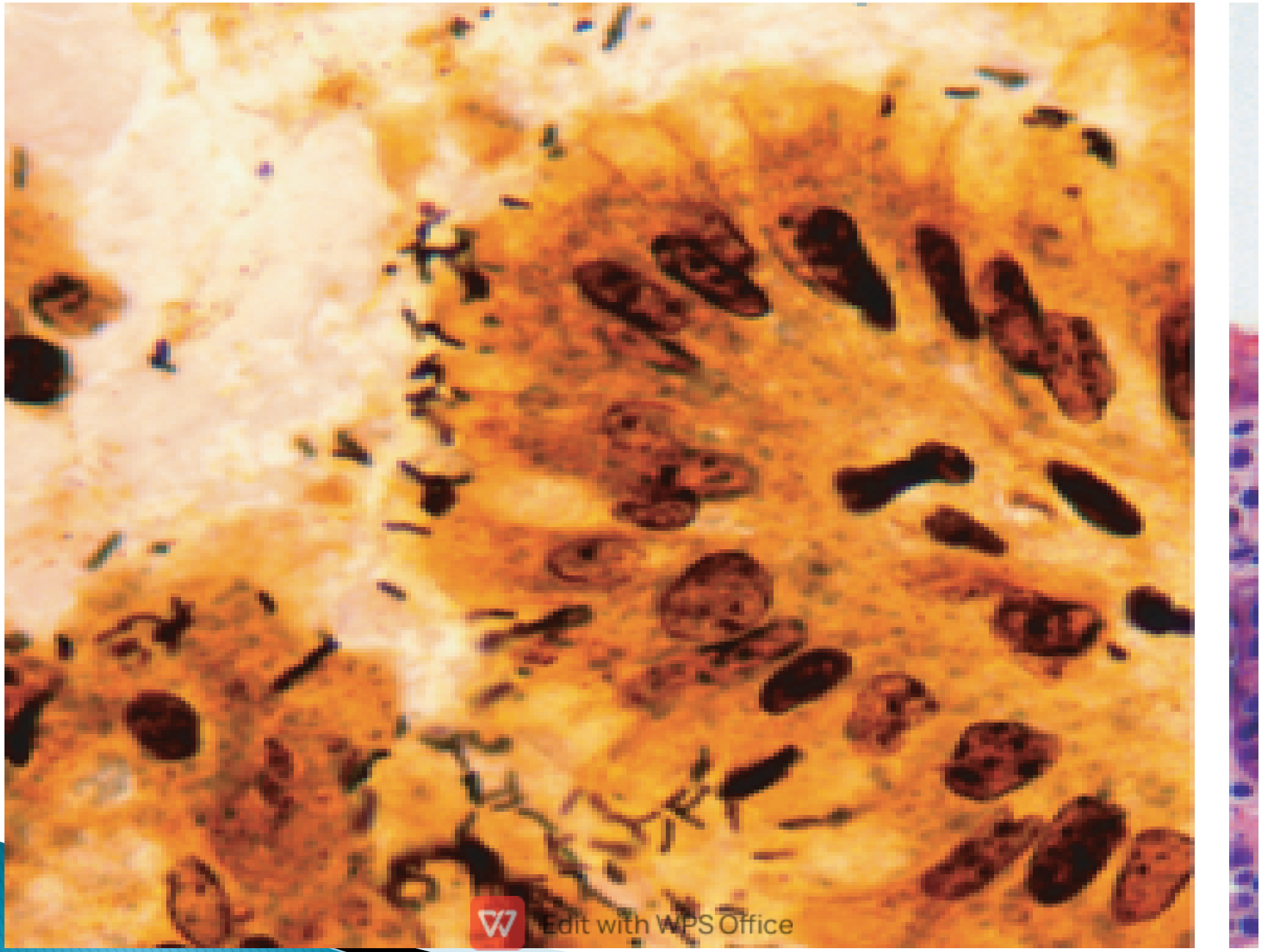
- chronic inflammation of the gastric mucosa that lead to mucosal atrophy and intestinal metaplasia and this changes may progress to dysplasia, which represent the major cause of development of carcinoma.
- **The major cause are**:

1. Chronic infection by H. pylori
2. autoimmune damage
3. Excessive intake of alcohol & heavy smoker
4. Post-antrectomy (due to reflux of bile-containing duodenal secretions)
5. Outlet obstruction, uremia, and other rare causes

H.pylori Infection and Chronic Gastritis

- Infection by H. pylori is the most important cause of chronic gastritis.
- Effective treatment with antibiotics has revolutionized the management of chronic gastritis and peptic ulcer disease
- Those with H. pylori-associated chronic gastritis are **at increased risk** for the development of

1. Peptic ulcer disease
2. Gastric carcinoma
3. Gastric lymphoma



- The bacteria cause gastritis by stimulating production of pro-inflammatory cytokines as well as by directly damaging epithelial cells by the liberation of toxins & degrading enzymes e.g. vacuolating toxin (VacA), urease, proteases and phospholipases.

- Gastritis occurs in two patterns:

1. Antral-predominant gastritis with high acid production and elevated risk for duodenal ulcer
2. Pan gastritis with low acid secretion and higher risk for adenocarcinoma

Diagnosis of H. pylori.

1. Noninvasive tests including
   a. Serologic test for antibodies
   b. Stool culture for bacterial detection
   c. Urea breath test: based on the generation of ammonia by bacterial urease.
2. Invasive tests (through gastroscopy):
   detection of H. pylori in gastric biopsy tissue samples
   a. visualization of the bacteria in histologic sections with special stains.
   b. bacterial culture of the biopsy
   c. bacterial DNA detection by the polymerase chain reaction

Autoimmune gastritis

- About 10% of chronic gastritis are autoimmune in nature, results from the presence of autoantibodies to components of parietal cells, including the acid-producing enzyme H+/K+-ATPase, gastrin receptor, and intrinsic factor.
- Gland destruction and mucosal atrophy lead to loss of acid production (hypo- or achlorhydria).
- In the most severe cases, production of intrinsic factor is also impaired, leading to pernicious anemia.
- Affected patients have a significant risk for developing gastric carcinoma and endocrine tumors (carcinoid tumor).

Pathological features of chronic gastritis

- Autoimmune gastritis is characterized by diffuse mucosal damage of the body-fundic mucosa, with sparing of antral region (Corpus-predominant gastritis)
- Environmental gastritis due to environmental cause such as H. pylori infection it is usually affect antral mucosa (antral gastritis) or both antral and body-fundic mucosa (pangastritis)
  .

Gross (endoscopic) features

- The mucosa of the affected regions is usually hyperemic and has coarser than normal.
- With long-standing disease, the mucosa may become thinned and flattened because of atrophy.

Microscopic features :

- The mucosa is infiltrated by lymphocytes & plasma cells.
- lymphocytes are frequently presented as aggregates i. e. follicles, some with germinal centers.
- Neutrophils may or may not be present.

characteristic histologic features are;

- Intestinal metaplasia: the mucosa partially replaced by metaplastic columnar cells and goblet cells of intestinal morphology; these may display flat or villous arrangement. If the columnar cells are absorptive (with ciliated border) is termed complete, otherwise it is incomplete.

- Atrophy: marked loss of the mucosal glands,such as parietal cells may be absent in the autoimmune form.

- Dysplasia:occure with long-standing chronic gastritis, may become so severe as to constitute in situ carcinoma. It occurs in both autoimmune and H. pylori- associated chronic gastritis.

- H. pylori, the organism lies in the superficial mucosa on the surface and within the gastric pits. They do not invade the mucosa. These bacteria are most easily demonstrated with silver or Giemsa stains.

PEPTIC ULCER DISEASE

- An ulcer is defined as "a breach in the mucosa of the alimentary tract that extends into the submucosa or deeper." Although they may occur anywhere in the alimentary tract, they are most common in the duodenum and stomach.

- Ulcers have to be distinguished from erosions. The latter is limited to the mucosa and does not extend into the submucosa.

Pathogenesis of peptic ulcers

- Produced by an imbalance between gastro-duodenal **mucosal defenses** and the damaging forces, particularly of gastric acid and pepsin.
- **Hyperacidity** is not necessary; only a minority of patients with duodenal ulcers has hyperacidity, and it is even less common in those with gastric ulcers.
- **H. pylori infection** is a important factor in the pathogenesis of peptic ulcer. It is present in all patients with duodenal ulcers and in about 70% of those with gastric ulcers. Antibiotic treatment of the infection promotes healing of ulcers and prevents their recurrence.

Effect of H.pylori in mucosal defenses :

- 1. Stimulate inflammatory and immune responses lead
- to increased production of **pro-inflammatory cytokines** cause activation of neutrophils with their damaging properties.
- 2. Several bacterial products cause epithelial cell injury such as a vacuolating toxin called VacA ,urease, proteases and phospholipases.
- gastric acid secretion and duodenal bicarbonate
- production, thus reducing luminal pH with its damaging effects on the duodenal mucosa.
- 4. Thrombotic occlusion of surface capillaries is enhanced by abacterial platelet-activating factor may lead to mucosal damage.

Risk factor of peptic ulceration:

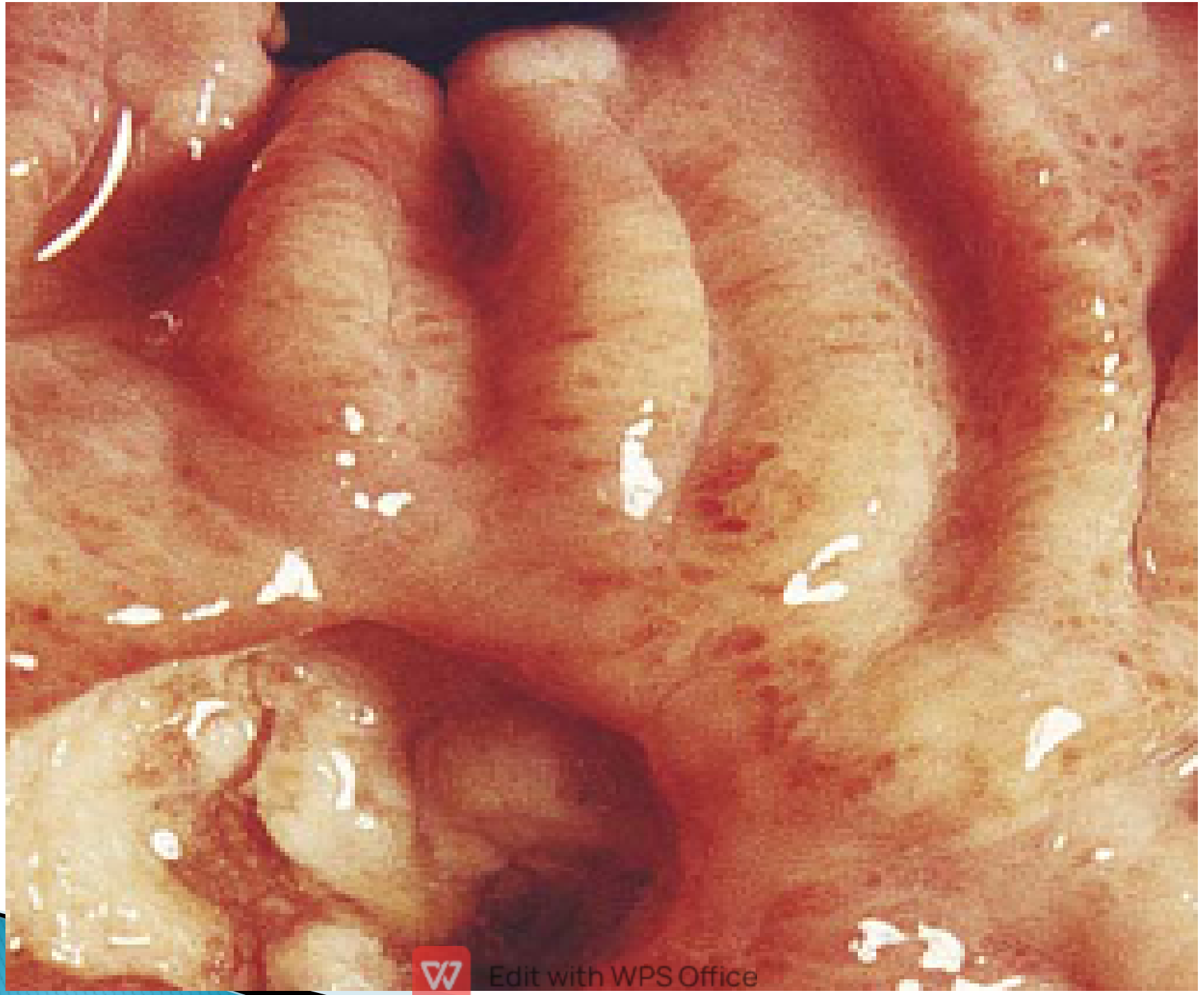
1. **Gastric hyperacidity**:as in Zollinger-Ellison syndrome, in which there are multiple peptic ulcerations in the stomach, duodenum, and even jejunum. This is due to excess gastrin secretion by a gastrinoma.
2. **Chronic use of NSAIDs**: this suppresses mucosal prostaglandin synthesis; aspirin also is a direct irritant.
3. **Smoking**: this impairs mucosal blood flow and healing of ulcer.
4 **Corticosteroids**: usually with large dose and frequent use

5. **diseases** that increase risk of duodenal ulcer:
   a. alcoholic cirrhosis
   b. chronic obstructive pulmonary disease
   c. chronic renal failure and hyperparathyroidis lead to hypercalcemia stimulating gastrin production and acid secretion.
6. **psychological stress** seems to be important contributing factors

Gross features

1. The vast majority of peptic ulcers are located in the first part of the duodenum or in the stomach, in a ratio of about 4: 1.
2. 50% of peptic ulcers less than 2 cm but about 10% are more than 4 cm.
3. The classic peptic ulcer is a round to oval with sharply demarcated crater. The margins are usually level with the surrounding mucosa or only slightly elevated. Heaping-up of these margins is rare in the benign ulcer but is characteristic of the malignant ones.

4. Peptic ulcers penetrate the wall to a variable extent.
5. The base of a peptic ulcer is smooth and clean, owing to peptic digestion of any exudate that may form. Sometimes, thrombosed or patent blood vessels (the source of life threatening hemorrhage) are evident at the base of the ulcer.
6. Ulcer-related scarring may involve the entire thickness of the gastric wall; crinkle of the surrounding mucosa creates mucosal folds that radiate from the crater in spoke-like fashion. This is different from malignant ulcers where there is flattening of the mucosal folds.



Microscopic features:

In **active ulcers** *four zones* are recognized

1. The base and walls have a superficial thin layer of necrotic fibrinoid necrosis.
2. Beneath this layer is a zone of predominantly neutrophilic inflammatory infiltrate.
3. Deeper still, there is granulation tissue infiltrated with inflammatory cells. This rests on
4. Fibrous or collagenous scar.

The complications of peptic ulcer disease are

1. **Bleeding** is the most frequent complication (20%).
2. **Perforation** is much less frequent (5% of patients) but much more serious being fatal in 60% of patients.
3. **Obstruction** (from edema or scarring)occurs in2%
4. **Malignant transformation** does not occur with duodenal ulcers and is extremely rare with gastric ulcers.

Acute Gastric Ulceration

Focal, acutely developing gastric mucosal defects are a well-known complication of

1. NSAIDs
2. Severe stress (stress ulcers) they usually occur in proximal duodenum
3. Sepsis
4. Raised intracranial pressure or intracranial surgery; may produce gastric, duodenal, and esophageal ulcers & called Cushing ulcers, which carry a high incidence of perforation.

Gross features

:

1. small (less than 1 cm) and circular.
2. The ulcer base is frequently stained a dark brown by the acid digestion of blood.
3. They differ from chronic peptic ulcers by the following:
   - They are found anywhere in the stomach, and are often multiple
   - The margins and base of the ulcers are not indurated
   - The related mucosal folds are normal (chronic peptic ulcer, which show overlap on the ulcer)

Microscopically

1. There is focal loss of the mucosa & at least part of the submucosa
2. There is no chronic gastritis or scarring.
3. Healing with complete re-epithelialization occurs after the causative factor is removed.

tumors

BENIGN TUMORS

Gastric polyps

- The term **polyp** is applied to any nodule or mass that projects above the level of the surrounding mucosa of GIT. They are uncommon and classified as non-neoplastic or neoplastic.
- Hyperplastic polyps (the most frequent; 90%) are small, sessile and multiple in about 25% of cases. There is hyperplasia of the surface epithelium and cystically dilated glandular tissue.

- Adenomatous polyp (adenoma) (10% of polypoid lesions):They contain proliferative dysplastic epithelium and hence have malignant potential. They are usually single, and may grow up to 4 cm in size before detection.
- Up to **40% of gastric adenomas** contain a focus of carcinoma; and may present in 30% with adjacent carcinoma that is why histologic examination of all gastric polyps is essential.

cancer

CANCERS OF THE STOMACH

- Carcinoma is the most important and the most common (90%) of malignant tumors of the stomach. Next in order of frequency are lymphomas (5%)
- Two subtypes of carcinoma:
- intestinal
- diffuse.

Pathogenesis

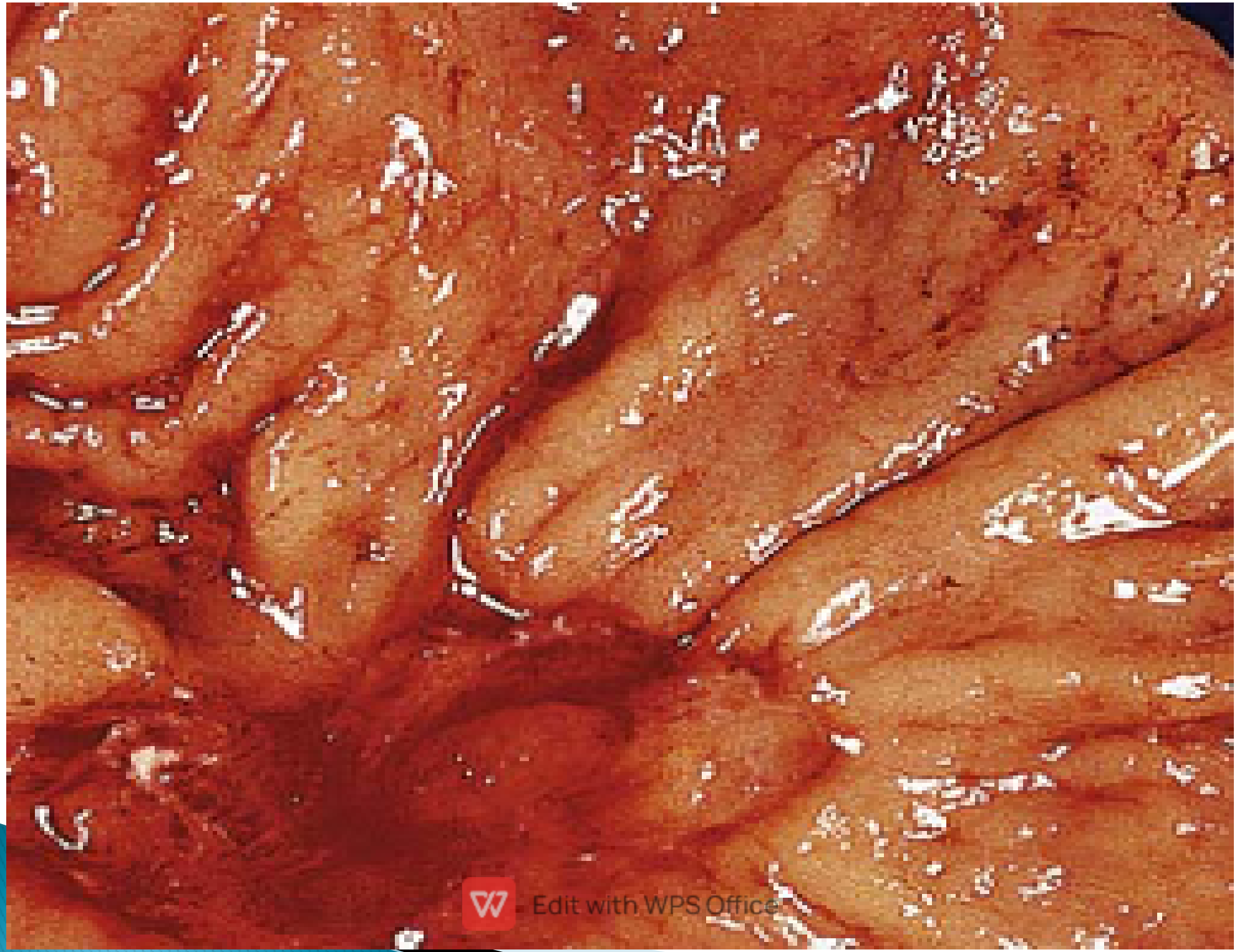
1. Helicobacter pylori Infection: this generally increases the risk five- fold. Long-standing mucosal inflammation is associated with damage of epithelial cells, which leads to compensatory epithelial cell proliferation lead to increase risk of genomic mutation. Since most individuals infected with H. pylori do not develop cancer, other factors must be involved in carcinogenesis.

2. Adenomatous polyps:
3. Environmental factors: The diet is suspected to be a primary factor. Consumption of preserved and salted foods; water contamination with nitrates all these increase risk while the intake of green, leafy vegetables and citrus fruits, which contain antioxidants such as vitamin C, vitamin E seems to play a protective role.
4. Autoimmune gastritis, like H. pylori infection, increases the risk of gastric cancer.

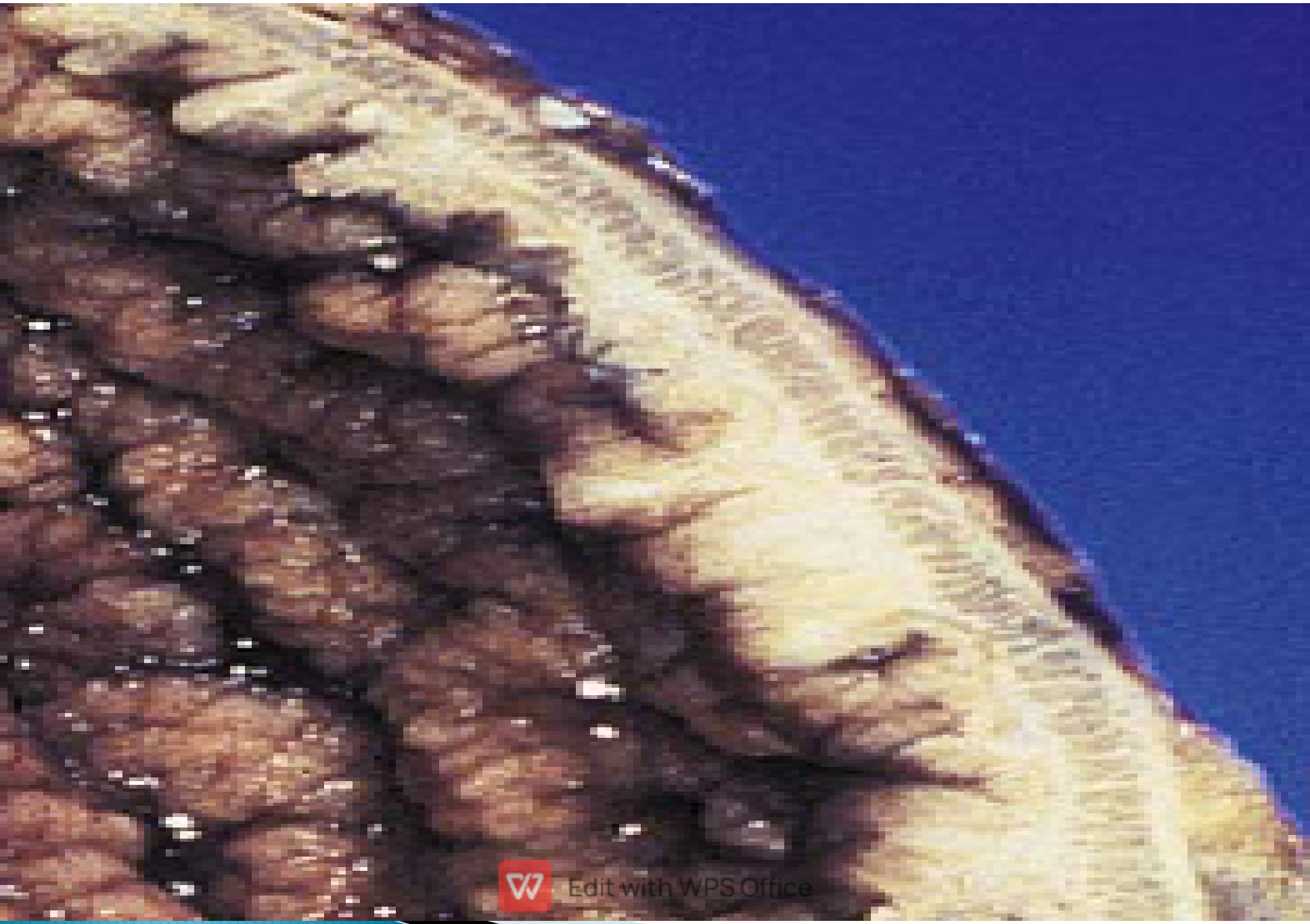
Gross features

- The most common location of gastric carcinomas is the pyloric antrum (50%). A favored location is the lesser curvature.
- Depth of invasion is the most important determinant of prognosis(early or advance stage)
- The three macroscopic growth patterns of gastric carcinoma, which may be evident at both the early and advanced stages, are:

1. Fungating (exophytic)
2. Flat or depressed
3. Ulcerative (excavated).



- Fungating tumors are readily identified by radiography and endoscopy in contrast to flat (depressed) malignancy.
- Ulcerative cancers may closely mimic chronic peptic ulcers.
- In advanced cases, there are heaped-up, beaded margins and necrotic bases.
- The neoplastic tissue extends into the surrounding mucosa and wall; this leads to flattening of the mucosa surrounding the ulcer.

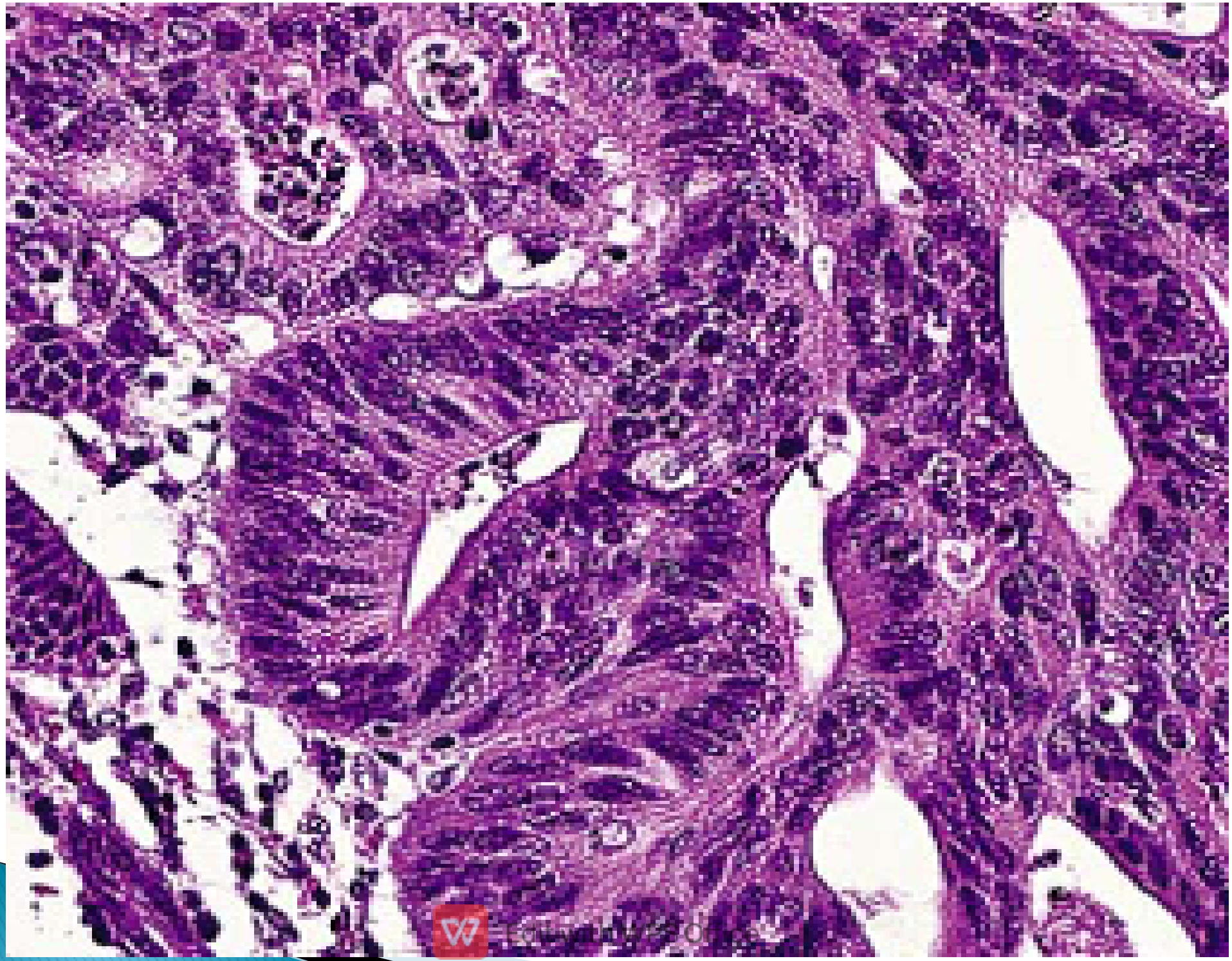


Microscopic features

- There are two main microscopic type of gastric carcinoma; intestinal and diffuse.

- The intestinal variant is composed of neoplastic glands with mucin in their lumina.

- The diffuse variant is composed of mucus-containing cells, which do not form glands, but infiltrate the mucosa and wall as scattered individual and small clusters of cells. In this variant, mucin formation expands the malignant cells and pushes the nucleus to the periphery, creating"signet ring" morphology.



- Infiltrative tumors often evoke a strong desmoplastic reaction (fibrosis), in which the scattered cells are embedded; the fibrosis creates local rigidity of the wall.

- Whatever the microscopic type, all gastric carcinomas eventually penetrate the wall to involve the serosa and spread to regional and more distant lymph nodes.

Gastric Lymphomas

- represent 5% of all gastric malignancies. However, the stomach is the most common site for extra-nodal lymphoma (20%).
- Nearly all primary gastric lymphomas are B-cell type and of mucosa-associated lymphoid tissue (MALT lymphomas).
- The majority of gastric lymphomas (>80%) are associated with chronic gastritis and H. pylori infection.
- Generally, the prognosis of gastric lymphoma is better than carcinoma.

Gastrointestinal Stromal Tumors (GISTs)

- these are thought to originate from the interstitial cells of Cajal (normally control gastrointestinal peristalsis).
- 95% of GISTs stain with antibodies against c-KIT (CD117).
- The tumor can protrude into the lumen or extrude on the serosal side of the gastric wall.
- Microscopically, the tumor can exhibit spindle cells, plump "epithelioid" cells, or a mixture of both.
- Most of the tumors are quite cellular but mitotic activity is variable.