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Material

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PEPTIC ULCERS Peptic ulcers are the areas of degeneration and necrosis of gastrointestinal mucosa exposed to acid-peptic secretions. Though they can occur at any level of the alimentary tract that is exposed to hydrochloric acid and pepsin, they occur most commonly (98-99%) in either the duodenum or the stomach in the ratio of 4:1. Each of the two main types may be acute or chronic.

A, Chronic atrophic gastritis (right) contrasted with normal pyloric mucosa (left). There is marked gastric atrophy with disappearance of gastric glands and appearance of goblet cells (intestinal metaplasia). B, Photomicrograph showing chronic atrophic gastritis with intestinal metaplasia.

Acute Peptic (Stress) Ulcers Acute peptic ulcers or stress ulcers are multiple, small mucosal erosions, seen most commonly in the stomach but occasionally involving the duodenum. ETIOLOGY. These ulcers occur following severe stress. The causes are as follows: i) Psychological stress ii) Physiological stress as in the following: Shock Severe trauma Septicaemia Extensive burns (Curling's ulcers in the posterior aspect of the first part of the duodenum). Intracranial lesions (Cushing's ulcers developing from hyperacidity following excessive vagal stimulation). Drug intake (e.g. aspirin, steroids, butazolidine, indomethacin). Local irritants (e.g. alcohol, smoking, coffee etc).

PATHOGENESIS. It is not clear how the mucosal erosions occur in stress ulcers because actual hypersecretion of gastric acid is demonstrable in only Cushing's ulcers occurring from intracranial conditions such as due to brain trauma, intracranial surgery and brain tumours. In all other etiologic factors, gastric acid secretion is normal or below normal. In these conditions, the possible hypotheses for genesis of stress ulcers are as under: 1. Ischaemic hypoxic injury to the mucosal cells. 2.

Depletion of the gastric mucus 'barrier' rendering the mucosa susceptible to attack by acid-peptic secretions.

MORPHOLOGIC FEATURES. Grossly, acute stress ulcers are multiple (more than three ulcers in 75% of cases). They are more common anywhere in the stomach, followed in decreasing frequency by occurrence in the first part of duodenum. They may be oval or circular in shape, usually less than 1 cm in diameter. Microscopically, the stress ulcers are shallow and do not invade the muscular layer. The margins and base may show some inflammatory reaction depending upon the duration of the ulcers. These ulcers commonly heal by complete re-epithelialisation without leaving any scars. Complications such as haemorrhage and perforation may occur.

Chronic Peptic Ulcers (Gastric and Duodenal Ulcers) If not specified, chronic peptic ulcers would mean gastric and duodenal ulcers, the two major forms of 'peptic ulcer disease' of the upper GI tract in which the acid-pepsin secretions are implicated in their pathogenesis. Peptic ulcers are common in the present-day life of the industrialised and civilised world. Gastric and duodenal ulcers represent two distinct diseases as far as their etiology, pathogenesis and clinical features are concerned. However, morphological findings in both are similar and quite diagnostic. The features of gastric

and duodenal peptic ulcers are described together below while their contrasting features are presented. INCIDENCE. Peptic ulcers are more frequent in middle-aged adults. The peak incidence for duodenal ulcer is 5th decade, while for gastric ulcer it is a decade later (6th decade). Duodenal as well as gastric ulcers are more common in males than in females. Duodenal ulcer is almost four times more common than gastric ulcer; the overall incidence of gastroduodenal ulcers being approximately 10% of the male population. ETIOLOGY. The immediate

cause of peptic ulcer disease is disturbance in normal protective mucosal 'barrier' by acidpepsin, resulting in digestion of the mucosa. However, in contrast to duodenal ulcers, the patients of gastric ulcer have low-to-normal gastric acid secretions, though true achlorhydria in response to stimulants never occurs in benign gastric ulcer. Besides, 10-20% patients of gastric ulcer may have coexistent duodenal ulcer as well. Thus, the etiology of peptic ulcers possibly may not be explained on the basis of a single factor but is multifactorial. These factors are discussed below but the first two—H. pylori gastritis and NSAIDs-induced injury are considered most important. 1. Helicobacter pylori gastritis. About 15-20% cases infected with H. pylori in the antrum develop duodenal ulcer in their life time while gastric colonisation by H. pylori never develops ulceration and remain asymptomatic. H. pylori can be identified in mucosal samples by histologic examination, culture and serology. 2. NSAIDs-induced mucosal injury. Non-steroidal antiinflammatory drugs are most commonly used medications in the developed countries and are responsible for direct toxicity, endothelial damage and epithelial injury to both gastric as well as duodenal mucosa. 3. Acid-pepsin secretions. There is conclusive evidence that some level of acid-pepsin secretion is essential for the development of duodenal as well as gastric ulcer. Peptic ulcers never occur in association with pernicious anaemia in which there are no acid and pepsin-secreting parietal and chief cells respectively. 4. Gastritis. Some degree of gastritis is always present in the region of gastric ulcer, though it is not clear whether it is the cause or the effect of ulcer. Besides, the population distribution pattern of gastric ulcer is similar to that of chronic gastritis. 5. Other local irritants. Pyloric antrum and lesser curvature of the stomach are the sites most exposed for longer periods to local irritants and thus are the common sites for occurrence of gastric ulcers. Some of the local irritating substances implicated in

the etiology of peptic ulcers are heavily spiced foods, alcohol, cigarette smoking, unbuffered aspirin. 6. Dietary factors. Nutritional deficiencies have been regarded as etiologic factors in peptic ulcers e.g. occurrence of gastric ulcer in poor socioeconomic strata, higher incidence of duodenal ulcer in parts of South India. However, malnutrition does not appear to have any causative role in peptic ulceration in European countries and the U.S.

7. Psychological factors. Psychological stress, anxiety, fatigue and ulcer-type personality may exacerbate as well as predispose to peptic ulcer disease. 8. Genetic factors. People with blood group O appear to be more prone to develop peptic ulcers than those with other blood groups. Genetic influences appear to have greater role in duodenal ulcers as evidenced by their occurrence in families, monozygotic twins and association with HLA-B5 antigen. 9. Hormonal factors. Secretion of certain hormones by tumours is associated with peptic ulceration e.g. elaboration of gastrin by islet-cell tumour in Zollinger-Ellison syndrome, endocrine secretions in hyperplasia and adenomas of parathyroid glands, adrenal cortex and anterior pituitary. 10. Miscellaneous. Duodenal ulcers have been observed to occur in association with various other conditions such as

alcoholic cirrhosis, chronic renal failure, hyperparathyroidism, chronic obstructive pulmonary disease, and chronic pancreatitis.

PATHOGENESIS. Although the role of various etiologic factors just described is well known in ulcerogenesis, two most important factors in peptic ulcer are as under: Exposure of mucosa to gastric acid and pepsin secretion. Strong etiologic association with H. pylori infection. There are distinct differences in the pathogenetic mechanisms involved in duodenal and gastric ulcers as under: Duodenal ulcer. There is conclusive evidence to support the role of high acid-pepsin secretions

in the causation of duodenal ulcers. Besides this, a few other noteworthy features in the pathogenesis of duodenal ulcers are as follows:

Distinguishing Features of Two Major Forms of Peptic Ulcers. Feature Duodenal Ulcer Gastric Ulcer

1. Incidence i) Four times more common than gastric ulcers Less common than duodenal ulcers

ii) Usual age 25-50 years Usually beyond 6th decade

iii) More common in males than in females (4:1) More common in males than in females (3.5:1)

2. Etiology Most commonly as a result of H. pylori infection Gastric colonisation with H. pylori asymptomatic Other factors—hypersecretion of acid-pepsin, but higher chances of development of duodenal ulcer. association with alcoholic cirrhosis, tobacco, Disruption of mucus barrier most important factor. hyperparathyroidism, chronic pancreatitis, Association with gastritis, bile reflux, drugs, blood group O, genetic factors alcohol, tobacco

3. Pathogenesis i) Mucosal digestion from hyperacidity most Usually normal-to-low acid levels; hyperacidity significant factor if present is due to high serum gastrin

ii) Protective gastric mucus barrier may be damaged Damage to mucus barrier significant factor

4. Pathologic changes i) Most common in the first part of duodenum Most common along the lesser curvature and pyloric antrum

ii) Often solitary, 1-2.5 cm in size, round to oval, Grossly similar to duodenal ulcer punched out

iii) Histologically, composed of 4 layers—necrotic, Histologically, indistinguishable from superficial exudative, granulation tissue and duodenal ulcer cicatrisation

5. Complications Commonly haemorrhage, perforation, Perforation, haemorrhage and at times sometimes obstruction; malignant obstruction; malignant transformation in transformation never occurs less than 1% cases

6. Clinical features i) Pain-food-relief pattern Food-pain pattern

ii) Night pain common No night pain

iii) No vomiting Vomiting common

iv) Melaena more common than haematemesis Haematemesis more common

v) No loss of weight Significant loss of weight

vi) No particular choice of diet Patients choose bland diet devoid of fried foods, curries etc.

vii) Deep tenderness in the right hypochondrium Deep tenderness in the midline in epigastrium

viii) Marked seasonal variation No seasonal variation

ix) Occurs more commonly in people at greater stress More often in labouring groups

1. There is generally hypersecretion of gastric acid into the fasting stomach at night which takes place under the influence of vagal stimulation. There is high basal as well as maximal acid output (BAO and MAO) in response to various stimuli. 2. Patients of duodenal ulcer have rapid emptying of the stomach so that the food which normally buffers and neutralises the gastric acid, passes down into the small

intestine, leaving the duodenal mucosa exposed to the aggressive action of gastric acid. 3. Helicobacter gastritis caused by H. pylori is seen in 95-100% cases of duodenal ulcers. The underlying mechanisms are as under: i) Gastric mucosal defense is broken by bacterial elaboration of urease, protease, catalase and phospholipase. ii) Host factors: H. pylori-infected mucosal epithelium releases proinflammatory cytokines such as IL-1, IL-6, IL-8 and tumour necrosis factor-α, all of which incite intense inflammatory reaction. iii) Bacterial factors: Epithelial injury is also induced by cytotoxin-associated gene protein (CagA), while vacuolating cytotoxin (VacA) induces elaboration of cytokines. Gastric ulcer. The pathogenesis of gastric ulcer is mainly explained on the basis of impaired gastric mucosal defenses against acid-pepsin secretions. Some other features in the pathogenesis of gastric ulcer are as follows: 1. Hyperacidity may occur in gastric ulcer due to increased serum gastrin levels in response to ingested food in an atonic stomach. 2 However, many patients of gastric ulcer have low-tonormal gastric acid levels. Ulcerogenesis in such patients is explained on the basis of damaging influence of other factors such as gastritis, bile reflux, cigarette smoke etc. 3. The normally protective gastric mucus 'barrier' against acid-pepsin is deranged in gastric ulcer. There is depletion in the quantity as well as quality of gastric mucus. One of the mechanisms for its depletion is colonisation of the gastric mucosa by H. pylori seen in 75-80% patients of gastric ulcer.

MORPHOLOGIC FEATURES. Gross and microscopic changes in gastric and duodenal ulcers are similar and quite characteristic. Gastric ulcers are found predominantly along the lesser curvature in the region of pyloric antrum, more commonly on the posterior than the anterior wall. Most duodenal ulcers are found in the first part of the duodenum, usually immediate post-pyloric, more commonly on the anterior than

the posterior wall. Uncommon locations include ulcer in the cardia, marginal ulcer and in the Meckel's diverticulum. Grossly, typical peptic ulcers are commonly solitary (80%), small (1-2.5 cm in diameter), round to oval and characteristically 'punched out'. Benign ulcers usually have flat margins in level with the surrounding mucosa. The mucosal folds converge towards the ulcer. The ulcers may vary in depth from being superficial (confined to mucosa) to deep ulcers (penetrating into the muscular layer) (Fig. 20.12). In about 10-20% of cases, gastric and

duodenal ulcers are coexistent. Vast majority of the peptic ulcers are benign. Chronic duodenal ulcer never turns malignant, while chronic gastric ulcer may develop carcinoma in less than 1% of cases. Malignant gastric ulcers are larger, bowl-shaped with elevated and indurated mucosa at the margin (Fig. 20.13). Microscopically, chronic peptic ulcers have 4 histological zones. From within outside, these are as under 1. Necrotic zone—lies in the floor of the ulcer and is composed of fibrinous exudate containing necrotic debris and a few leucocytes. 2. Superficial exudative zone—lies underneath the necrotic zone. The tissue elements here show coagulative necrosis giving eosinophilic, smudgy appearance with nuclear debris. 3. Granulation tissue zone—is seen merging into the necrotic zone. It is composed of nonspecific inflammatory infiltrate and proliferating capillaries. 4. Zone of cicatrisation—is seen merging into thick layer of granulation tissue. It is composed of dense fibrocollagenic scar tissue over which granulation tissue rests. Thrombosed or sclerotic arteries may cross the ulcer which on erosion may result in haemorrhage.

COMPLICATIONS. Acute and subacute peptic ulcers usually heal without leaving any visible scar. However, healing of chronic, larger and deeper ulcers may result in complications. These are as follows: 1. Obstruction. Development of fibrous scar at or near the pylorus results in pyloric

stenosis. In the case of healed duodenal ulcer, it causes duodenal stenosis. Healed ulcers along the lesser curvatures may produce 'hourglass' deformity due to fibrosis and contraction. 2. Haemorrhage. Minor bleeding by erosion of small blood vessels in the base of an ulcer occurs in all the ulcers and can be detected by testing the stool for occult blood. Chronic blood loss may result in iron deficiency anaemia. Severe bleeding may cause 'coffee ground' vomitus or melaena. A penetrating chronic ulcer may erode a major artery (e.g. left gastric, gastroduodenal or splenic artery) and cause a massive and severe hematemesis and sometimes death. 3. Perforation. A perforated peptic ulcer is an acute abdominal emergency. Perforation occurs more commonly in chronic duodenal ulcers than chronic gastric ulcers. Following sequelae may result:

i) On perforation the contents escape into the lesser sac or into the peritoneal cavity, causing acute peritonitis. ii) Air escapes from the stomach and lies between the liver and the diaphragm giving the characteristic radiological appearance of air under the diaphragm. iii) Subphrenic abscess between the liver and the diaphragm may develop due to infection. iv) Perforation may extend to involve the adjacent organs e.g. the liver and pancreas. 4. Malignant transformation. The dictum 'cancers ulcerate but ulcers rarely cancerate' holds true for most peptic ulcers. A chronic duodenal ulcer never turns malignant, while less than 1% of chronic gastric ulcers may transform into carcinoma. CLINICAL FEATURES. Peptic ulcers are remitting and relapsing lesions. Their chronic and recurrent behaviour is summed up the saying: 'once a peptic ulcer patient, always a peptic ulcer patient.' The two major forms of chronic peptic ulcers show variations in clinical features which are as follows: 1. Age. The peak incidence of duodenal ulcer is in 5th decade while that for gastric ulcer is a decade later. 2.

People at risk. Duodenal ulcer occurs more commonly in people faced with more stress and strain of life (e.g. executives, leaders), while gastric ulcer is seen more often in labouring groups. 3. Periodicity. The attacks in gastric ulcers last from 2-6 weeks, with interval of freedom from 1-6 months. The attacks of duodenal ulcer, are classically worsened by 'work, worry and weather.' 4. Pain. In gastric ulcer, epigastric pain occurs immediately or within 2 hours after food and never occurs at night. In duodenal ulcer, pain is severe, occurs late at night ('hunger pain') and is usually relieved by food.

5. Vomiting. Vomiting which relieves the pain is a conspicuous feature in patients of gastric ulcer. Duodenal ulcer patients rarely have vomiting but instead get heart-burn (retrosternal pain) and 'water brash' (burning fluid into the mouth). 6. Haematemesis and melaena. Haematemesis and melaena occur in gastric ulcers in the ratio of 60:40, while in duodenal ulcers in the ratio of 40:60. Both may occur together more commonly in duodenal ulcer than in gastric ulcer patients. 7. Appetite. The gastric ulcer patients, though have good appetite but are afraid to eat, while duodenal ulcer patients have very good appetite. 8. Diet. Patients of gastric ulcer commonly get used to a bland diet consisting of milk, eggs etc and avoid taking fried foods, curries and heavily spiced foods. In contrast, duodenal ulcer patients usually take all kinds of diets. 9. Weight. Loss of weight is a common finding in gastric ulcer patients while patients of duodenal ulcer tend to gain weight due to frequent ingestion of milk to avoid pain. 10. Deep tenderness. Deep tenderness is demonstrable in both types of peptic ulcers. In the case of gastric ulcer it is in the midline of the epigastrium, while in the duodenal ulcer it is in the right hypochondrium.