



*Oktatás, kutatás,
gyógyítás: 250 éve az
egészség szolgálatában*

Pathology of the oral cavity, salivary gland,
oesophagus, stomach and small intestine

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Research

08/03/2021

Topics

Oral cavity
Salivary glands
Oesophagus
Stomach
Small intestine

Developmental malformation
Inflammation
Tumor



Oral cavity

Developmental malformation

Palatal morphogenesis is sensitive to genetic disturbances or environmental teratogens.

Clefting of lip or palate: common (1/1000 births); often encountered in combined forms, occurring with other anomalies

Cleft lip (cheiloschisis)

Failure of fusion of nasal prominence with the maxillary prominence

Commonly unilateral, rarely bilateral

Feeding is not problem

Cleft palate (palatoschisis)

Non-fusion of the maxillary bone plates □ midline cleft through the soft and/or hard palate

Impairs swallowing and later speech

Combination of cleft lip and cleft palate: cheilognathopalatoschisis



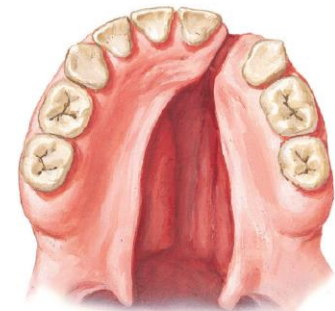
Unilateral cleft lip—partial



Partial cleft of palate



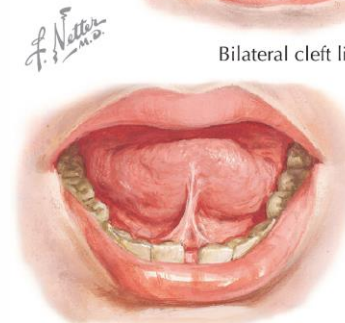
Unilateral cleft of primary palate—complete, involving lip and alveolar ridge



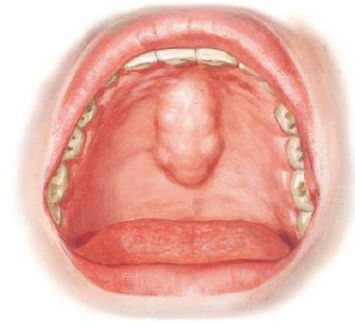
Complete cleft of secondary palate and unilateral cleft of primary palate



Bilateral cleft lip



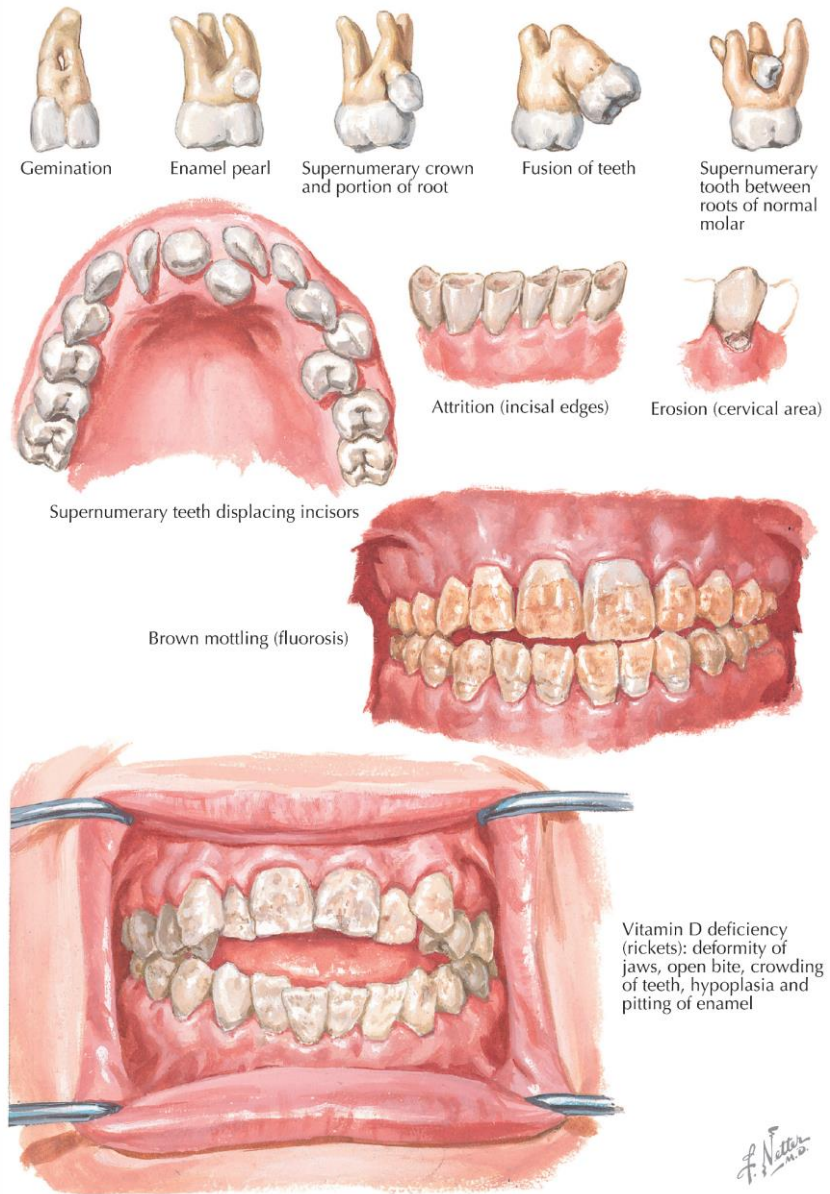
Ankyloglossia—restricted tongue movement from a short lingual frenulum



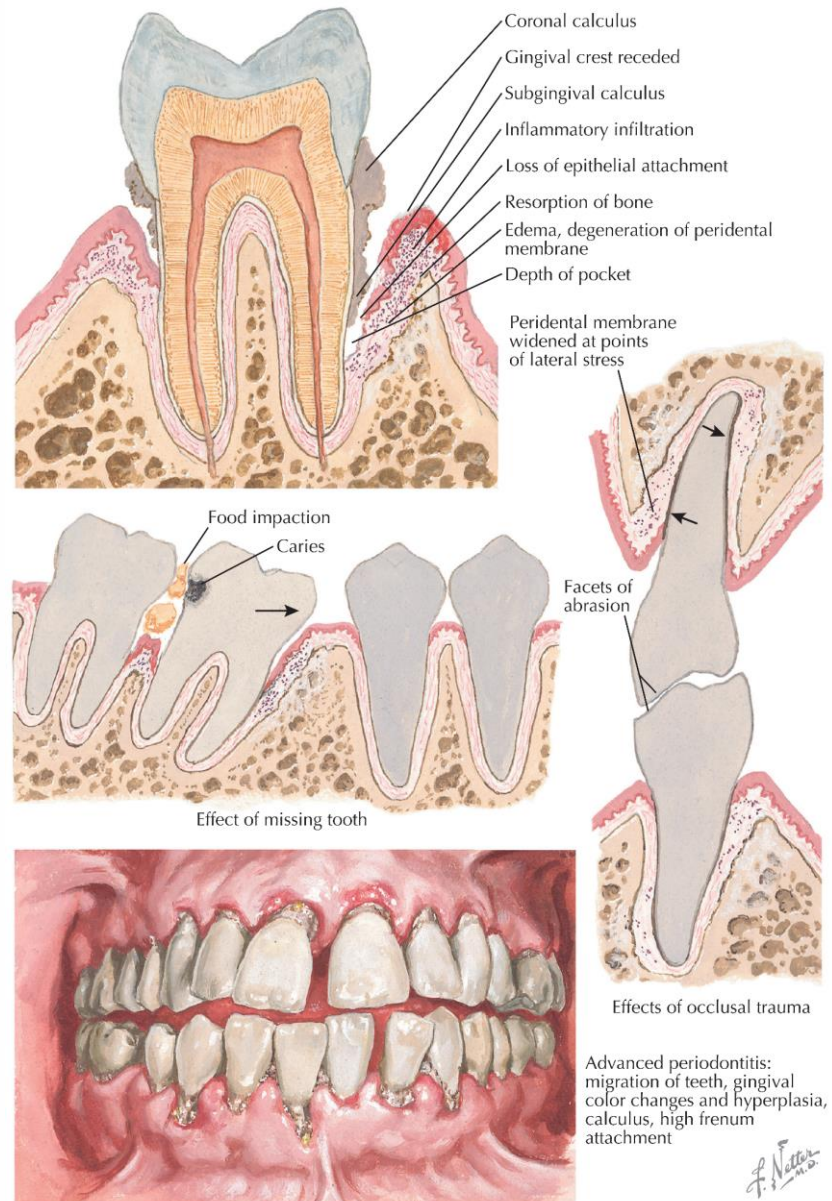
Torus palatinus—bone deposition on palate

Oral cavity

Diseases of the teeth



Oral cavity Inflammation



Oral cavity Inflammation

Dental caries (tooth decay)

Cavities in the tooth where dental plaques accumulate: pits and fissures; cervical part of the tooth; interdental surfaces

Dental plaque: sticky biofilm composed of food debris (sugar), desquamated epithelial cells, salivary glycoproteins and bacteria.

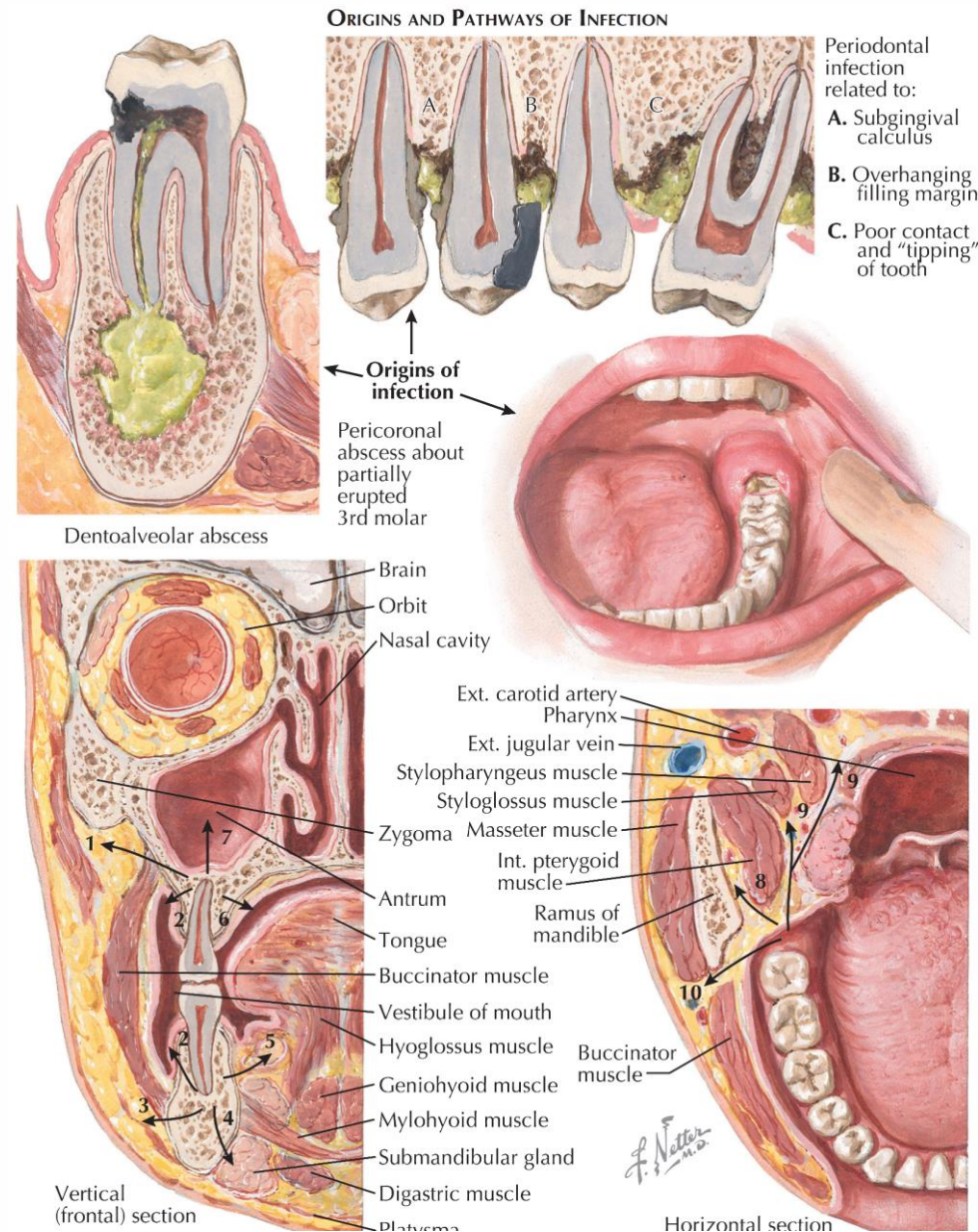
Fermentation of sugar by *Str. mutans*: lactic acid is produced, progressive dissolution of the enamel and dentine minerals

Early complications

Acute purulent pulpitis (severe toothache)

Extension of infection throughout the pulp, necrosis of pulp, loss of tooth

Extension of infection into apical periodontium: acute apical abscess, subperiosteal abscess, osteomyelitis, drainage through the oral mucosa („gumboil”) or to the adjacent facial skin

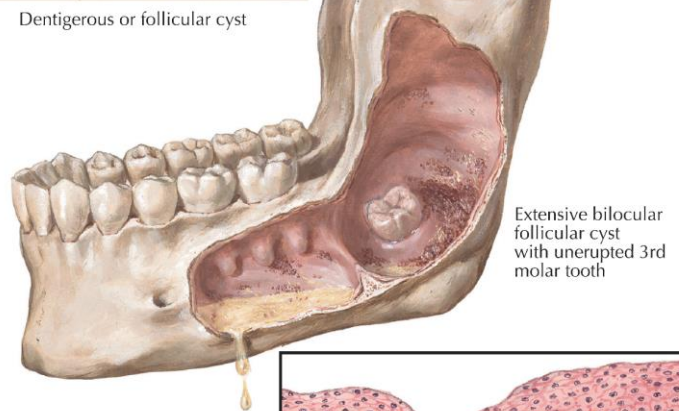
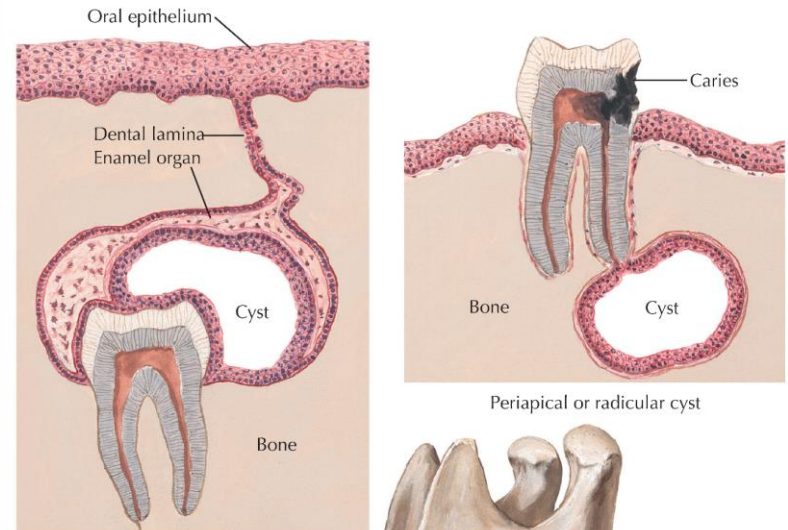


Oral cavity Inflammation

Late complications

Periapical granuloma: necrotic tissue at the apex of the root canal foramen, surrounded by granulation tissue infiltrated by lymphocytes and plasma cells.

Radicular cyst Cystic degeneration and epithelialization of the granuloma



F. Netter M.D.



Oral cavity Inflammation

Stomatitis

Inflammation of the mucosal lining of any of the structures in the mouth, which may involve the cheeks, the gums - gingivitis, the tongue - glossitis, the lips - cheilitis, and roof or floor of the mouth.

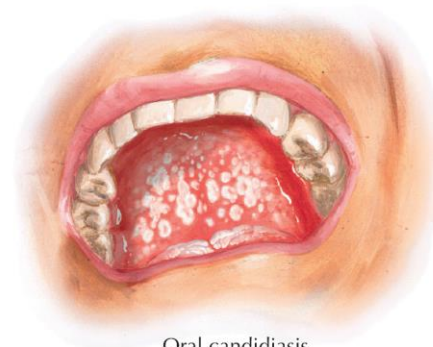


F. Netter M.D.
C. Machado M.D.
F. Palanzo

Herpes simplex



Herpes labialis



Oral candidiasis



Kaposi sarcoma



Oral wart



Necrotizing ulcerative gingivitis

Oral cavity Inflammation

Herpetic stomatitis

Pathogenesis

Causative agent: herpes simplex virus type I (HSV-I).

Primary infection: in children aged 6 months to 5 ys; infected saliva from an adult or another child is the mode of infection.

In adults: latent infection; the virus can be reactivated upon allergies, upper respiratory tract infection, pregnancy, menstruation, etc.

Morphology

Vesicles of mm-s to large bullae, which rupture and ulcerate

Many patients have similar lesions on the lips (herpes labialis, cold sore)

Clinical features

Painful disease, lasts approx. one week, heals spontaneously; tendency to recur



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C. Machado M.D.
F. DalNazo

Herpes simplex



Herpes labialis

Variant: herpetic gingivostomatitis

In children, in association with primary infection

The oral mucosa is swollen, tender, bleeds easily, the vesicles and bullae become ulcerated

Abrupt onset, high fever; tender regional lymph node enlargement

Oral cavity Inflammation

Oral candidiasis (thrush)

Caused by the fungus *Candida albicans*, a normal component of the oral flora.

Disease occurs

- in neonates
- patients receiving broad-spectrum antibiotics
- immunocompromised patients

Morphology

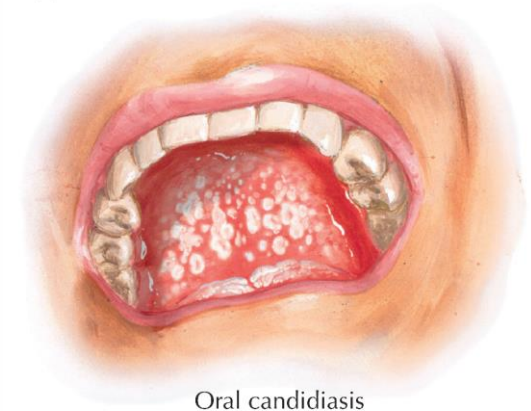
White pseudomembranes on the mucosa consisting of the hyphae of the fungus, enmeshed in a fibrinosopurulent exudate

On the tongue or inner cheeks

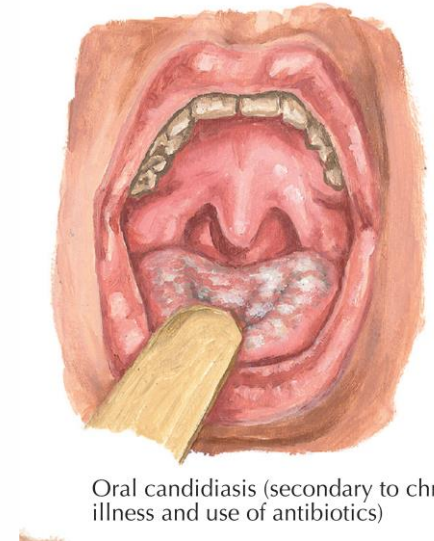
Clinical features

Redness, burning or soreness

M.D.
E. Palanzo



Oral candidiasis



Oral candidiasis (secondary to chronic illness and use of antibiotics)

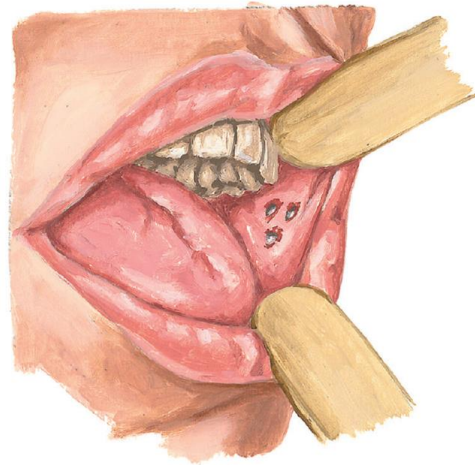
Oral cavity Inflammation

Aphthous stomatitis

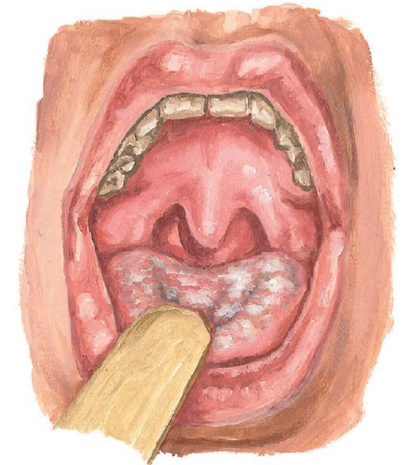
Aphthae are shallow ulcers that occur on movable parts of the mouth (inner surface of the lips, buccal mucosa, or the tongue) and have hemorrhagic rim.

May be associated with:
emotional stress, menstruation
sprue, inflammatory bowel disease
ingestion of certain foods, etc.

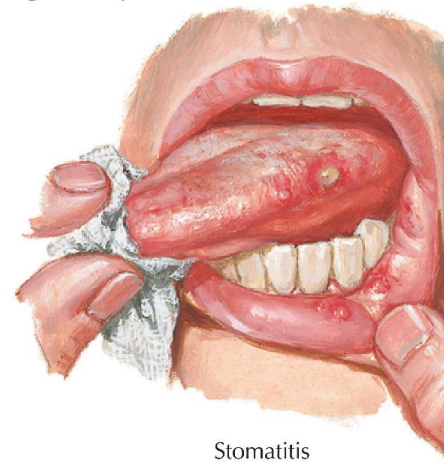
Very common, painful disease;
usually in the first two decades of
life



Aphthous ulcers (occur on buccal mucosa, tongue, and palate)



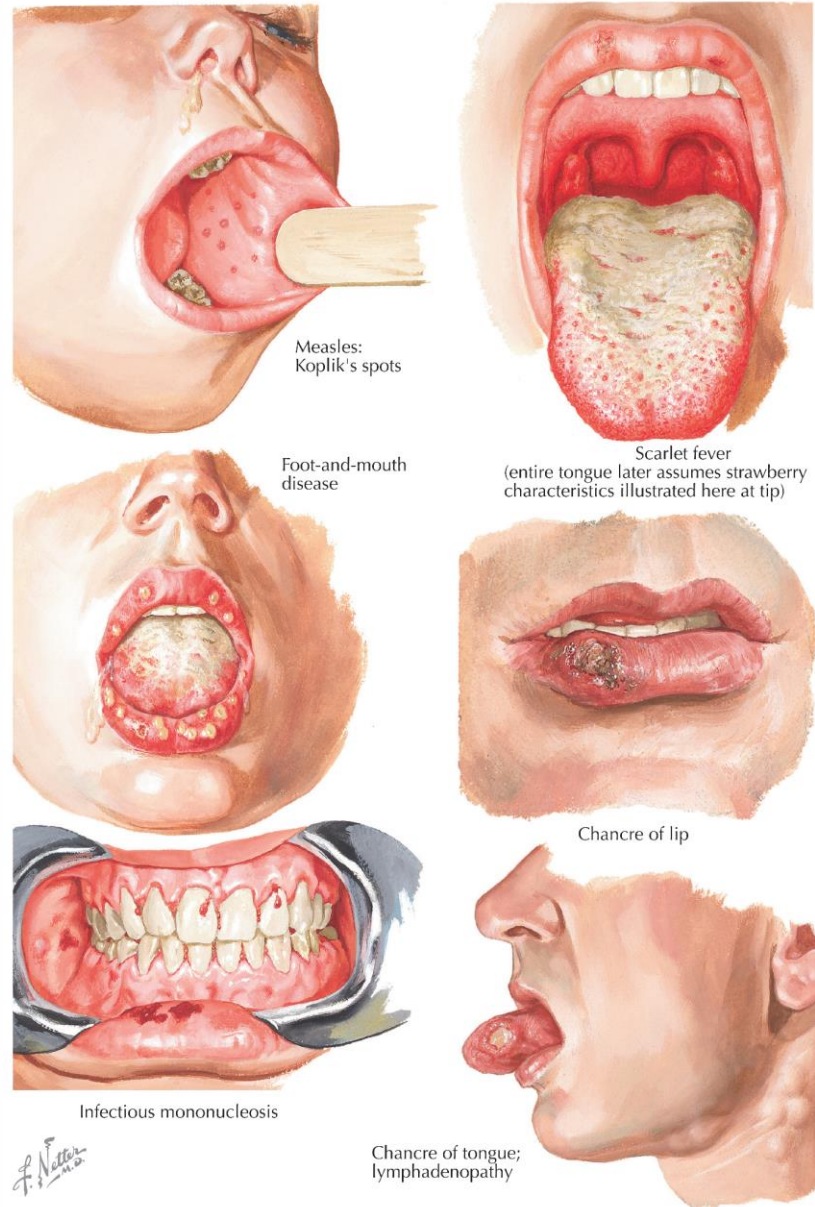
Oral candidiasis (secondary to chronic illness and use of antibiotics)



Stomatitis

J. Netter M.D.
JOHN A. CRAIG, M.D.

Oral cavity Inflammation



Oral cavity Inflammation

Gingivitis

Plaque-associated bacteria + calculus on the tooth surface (tartar), chronic suppurative inflammation in the gingival tissues: the gums are swollen, erythematous, and bleed.

Periodontal pockets (spaces around the teeth, below the gum line) develop; if pus oozes from the pocket is termed **pyorrhea**

Spread to deeper structures, chronic suppurative periodontitis and gingival atrophy

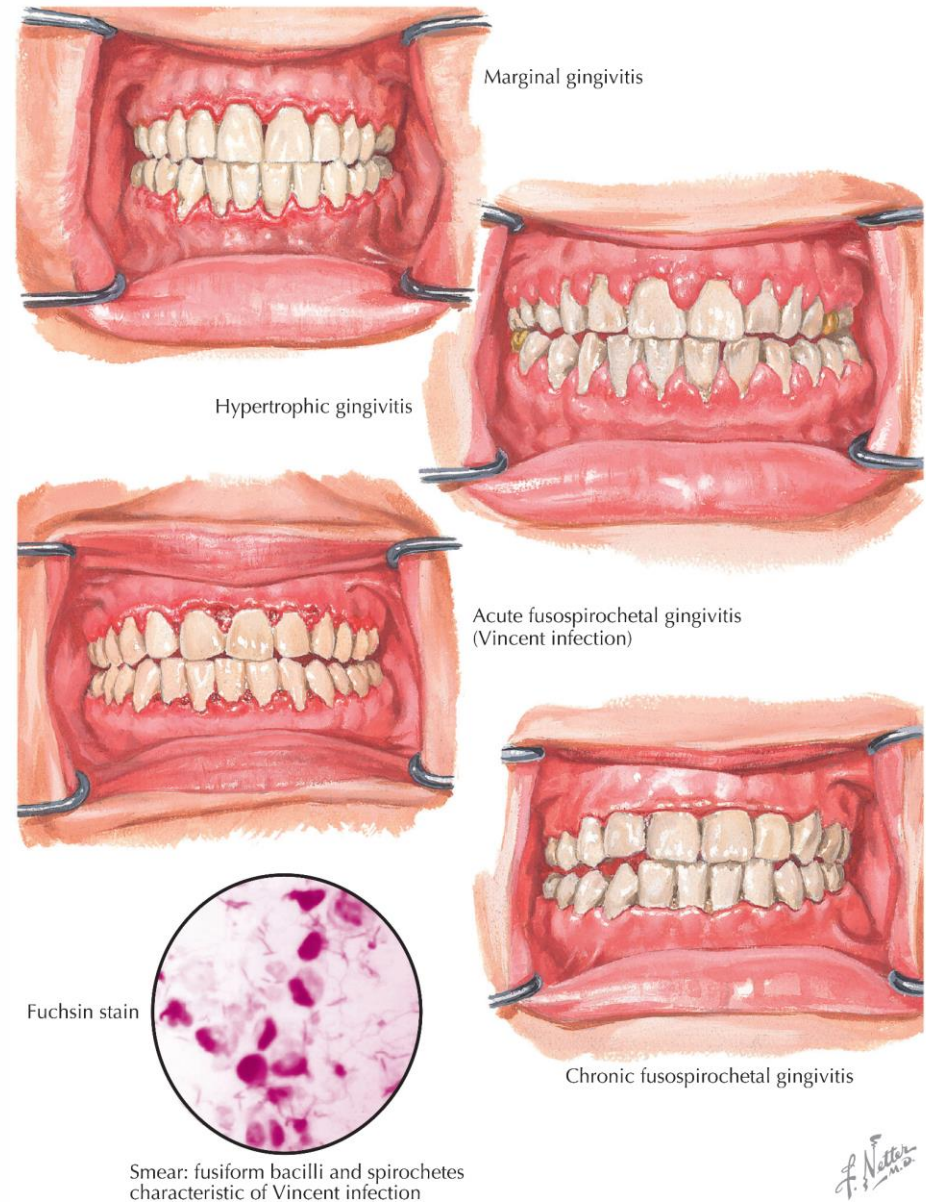
Chronic periodontitis

Gradual destruction of the tooth-supporting tissues and structures (periodontal ligaments, alveolar bone, cementum), loosening and eventual loss of teeth

Odorous breath (foetor ex ore)

Complication of tooth extraction

Str. viridans of the oral flora may enter into the circulation and can cause infective endocarditis



Oral cavity

Tumor

Reactive proliferations

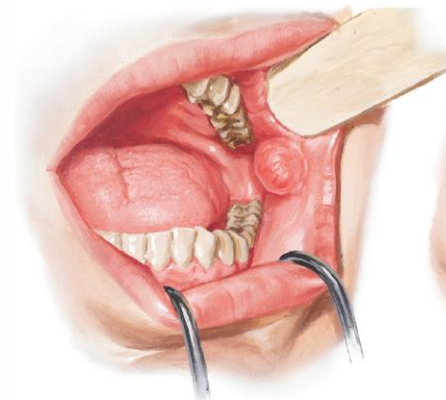
Irritation fibroma

Pedunculated nodule in response to chronic irritation

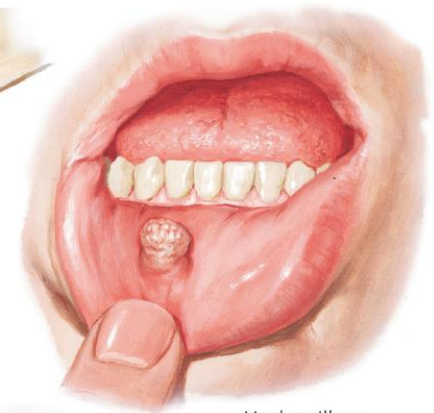
Most often on the buccal mucosa along the bite line

LM: submucosal proliferation of fibroblasts with abundant collagen fiber formation

Excisional biopsy is curative



Fibroma



Hard papilloma

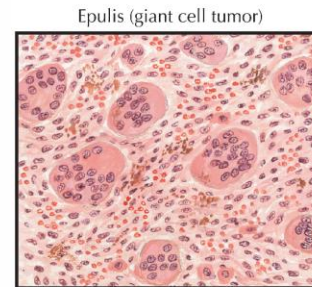
Pyogenic granuloma

Tumorlike polypoid tissue response, often following trauma

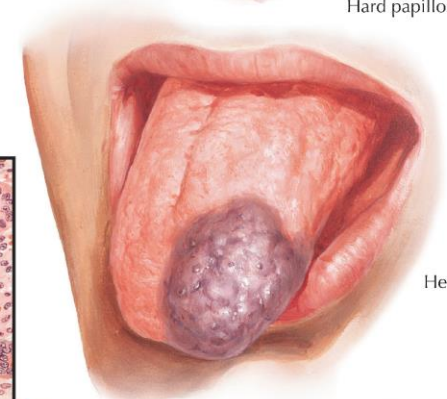
On the buccal gingiva of children, young adults and pregnant women (pregnancy tumor)

LM: richly vascular lesion, the surface is ulcerated

Therapy: excision



Epulis (giant cell tumor)



Hemangioma

Peripheral giant cell granuloma (epulis)

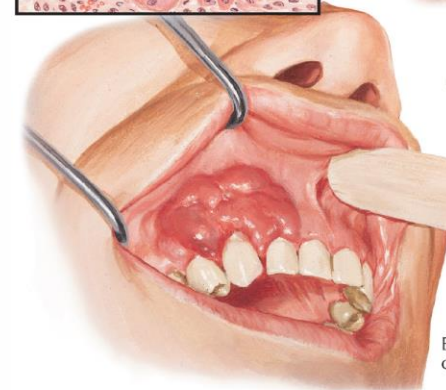
Locally destructive inflammatory lesion of the gingiva (0.5-1.5 cm)

Pushes teeth aside, and may erode alveolar bone

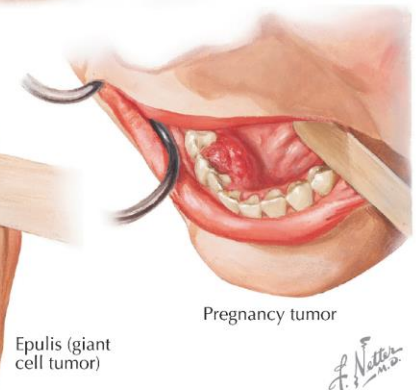
LM: vascularized stroma containing spindle mesenchymal cells, multinucleated giant cells, and fresh and old hemorrhages

Usually in young women

Therapy: excision



Epulis (giant cell tumor)



Pregnancy tumor

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Oral cavity Tumor

Leukoplakia

Clinical term: white plaque (on buccal mucosa, floor of the mouth, tongue or hard palate) which cannot be removed by scraping.

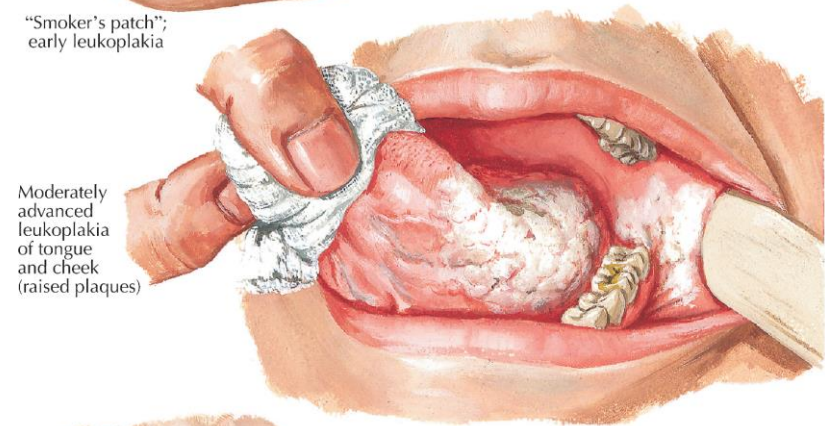
Associated with tobacco use, alcohol, ill-fitting dentures, etc.

LM: 80%: epithelial hyperplasia without atypia; 20%: either dysplasia or cc in situ, or superficially invasive squamous cell cc (SCC)

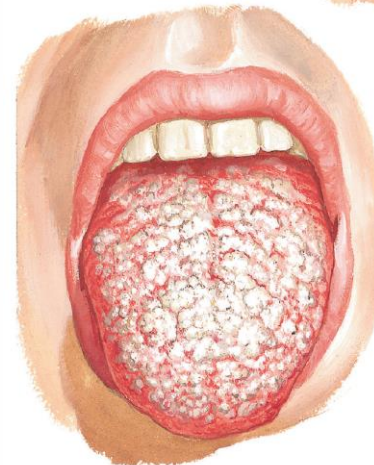


Leukoplakia with beginning dyskeratosis

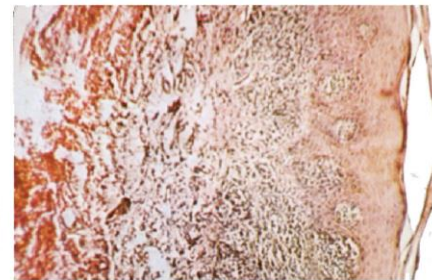
"Smoker's patch";
early leukoplakia



Moderately
advanced
leukoplakia
of tongue
and cheek
(raised plaques)



Advanced leukoplakia of tongue



Lichen planus

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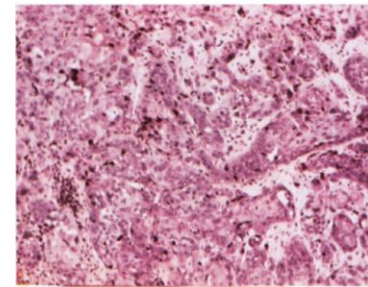
Oral cavity Tumor

Erythroplakia

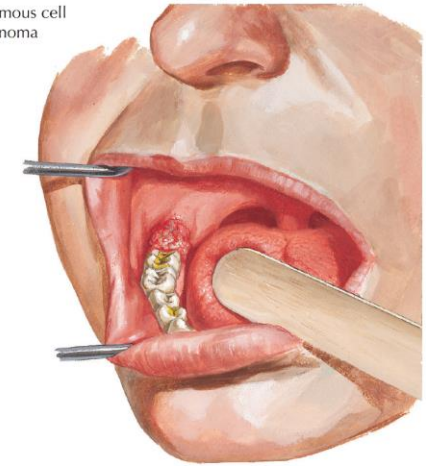
Associated with tobacco use

Superficial erosions with dysplasia, cc in situ, or superficially invasive SCC in 60% to 90% of the cases.

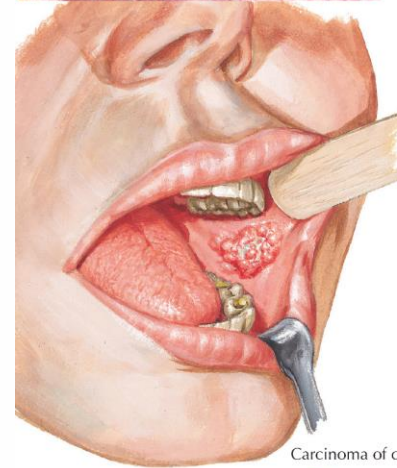
Intense subepithelial inflammatory reaction with vascular dilatation accounts for the red appearance of the lesion.



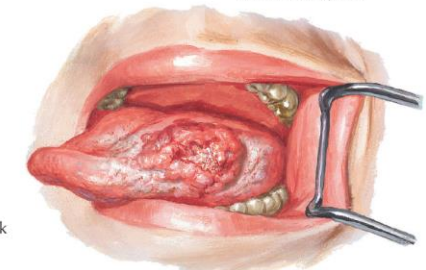
Squamous cell carcinoma



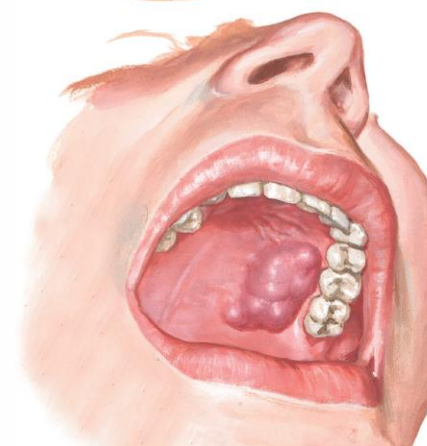
Carcinoma of gingiva (retromolar space)



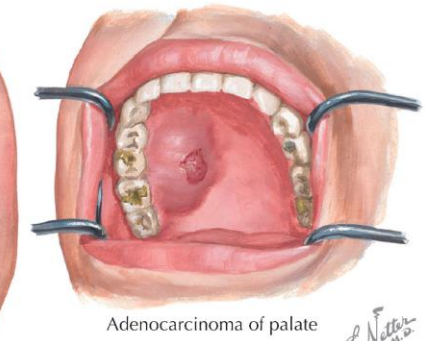
Carcinoma of cheek



Carcinoma of tongue (on leukoplakia)



Lymphosarcoma of palate and gingiva



Adenocarcinoma of palate

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Oral cavity Tumor Squamous cell cancer (SCC)

Frequent neoplasm worldwide; particularly frequent in Hungary

Peak age is 50-60 ys; men are more often affected

Frequent sites: mouth floor, ventral tongue, base of the tongue, soft palate, gingiva, and lower lip

Macro

Early lesions: raised, firm, pearly plaques or irregular verrucal mucosal thickenings; advanced lesions become ulcerated

Lymphatic metastases in submandibular and cervical nodes are common

Hematogeneous metastases: in the lungs

LM

Non-keratinizing squamous cell cc

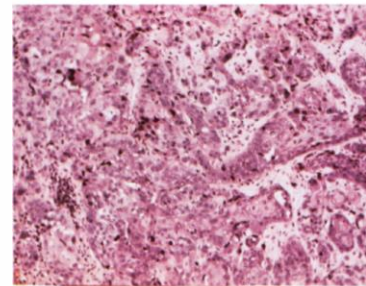
Etiology: infection with HPV-16 serotype

Sites: tonsil, base of tongue

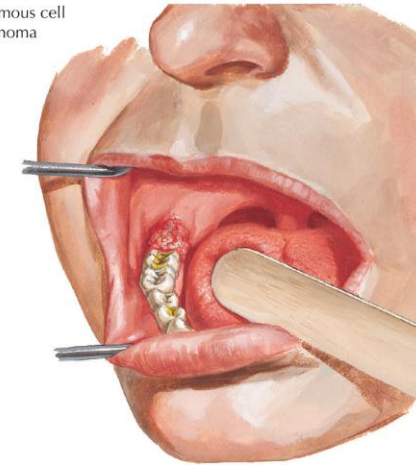
Keratinizing squamous cell cc

Etiology: smoking and alcohol use; in India: chewing of betel quid

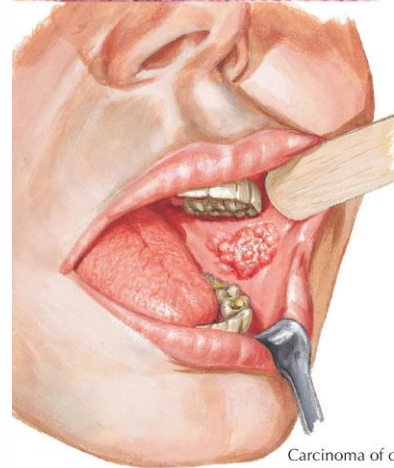
Sites: other than those of the tonsil and base of tongue



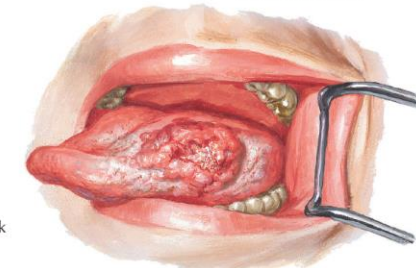
Squamous cell carcinoma



Carcinoma of gingiva (retromolar space)



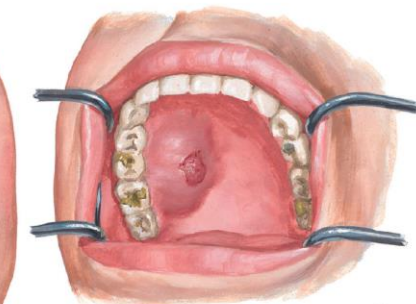
Carcinoma of cheek



Carcinoma of tongue (on leukoplakia)



Lymphosarcoma of palate and gingiva



Adenocarcinoma of palate

F. Netter M.D.



Oral cavity Tumor Squamous cell cancer (SCC)

Clinical features

Early lesions: asymptomatic

Advanced lesions can cause painful and/or difficult swallowing

Prognosis

Depends on tumor stages and the location of the tumor

Lip cancers has the best 5-year survival rate, and the floor of the mouth has the worst

HPV-positive tumors tend to respond better to chemotherapy and/or radiation therapy compared with those with HPV-negative tumors.

HPV associated oropharyngeal carcinoma

Etiology: high-risk (HPV16, HPV18) serotype

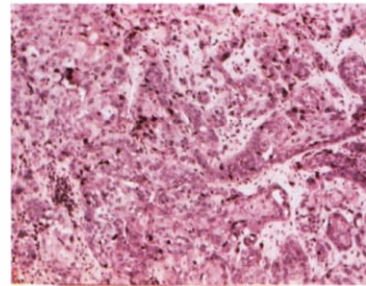
Localisation: oropharyngeal region

Population: Young age, good general condition

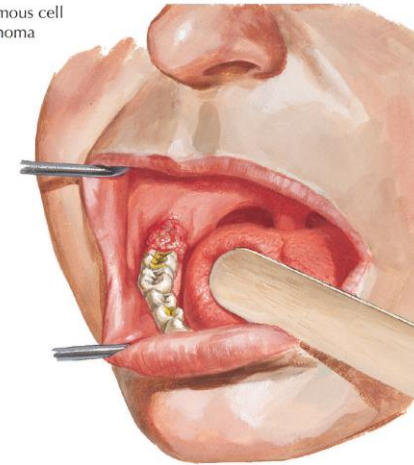
LM: Non-keratinizing squamous cell cc, basaloid morphology, high mitotic rate

IHC: p16 block positivity

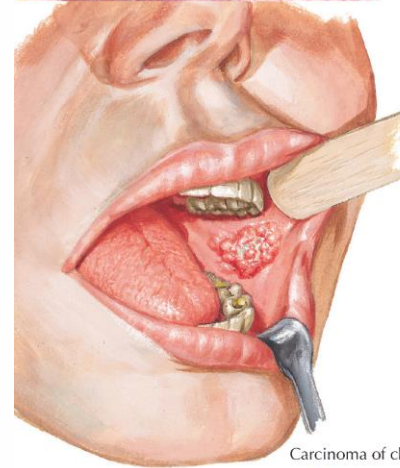
Outcome: Generally good.



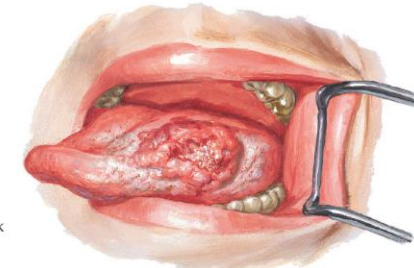
Squamous cell carcinoma



Carcinoma of gingiva (retromolar space)



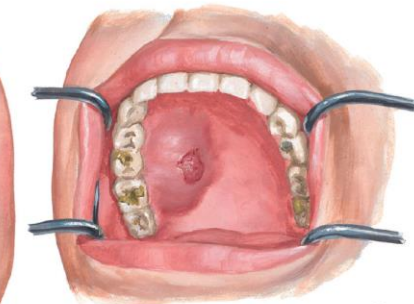
Carcinoma of cheek



Carcinoma of tongue (on leukoplakia)



Lymphosarcoma of palate and gingiva



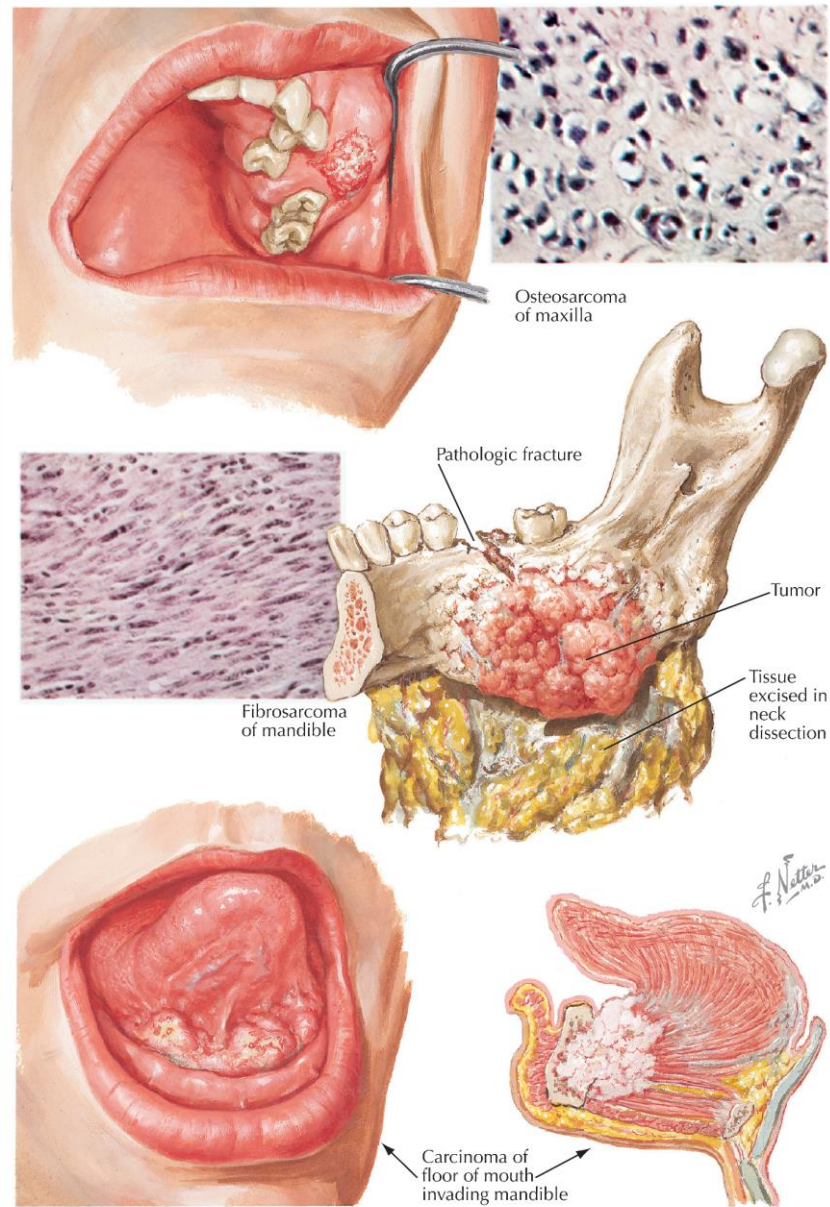
Adenocarcinoma of palate

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Oral cavity Tumor

Bone primarily and secondary tumors.

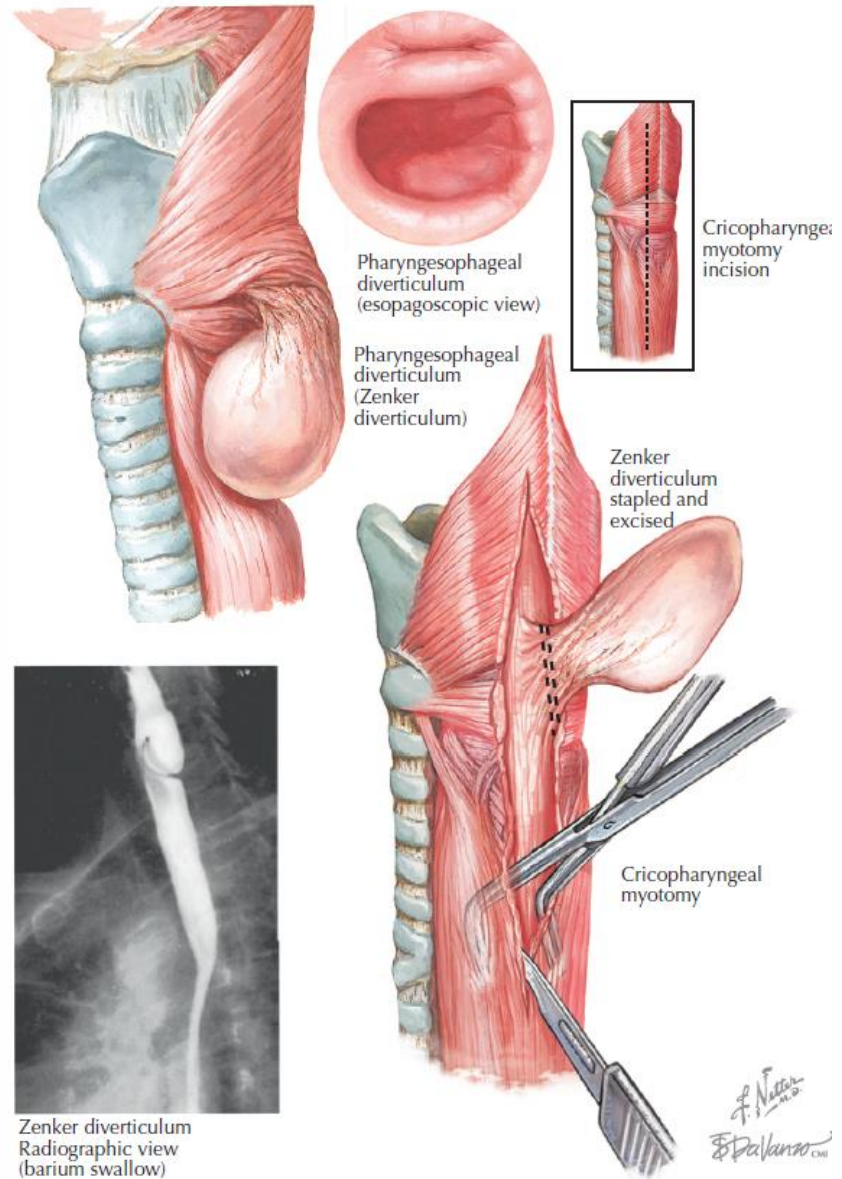


Pharynx

Developmental malformation

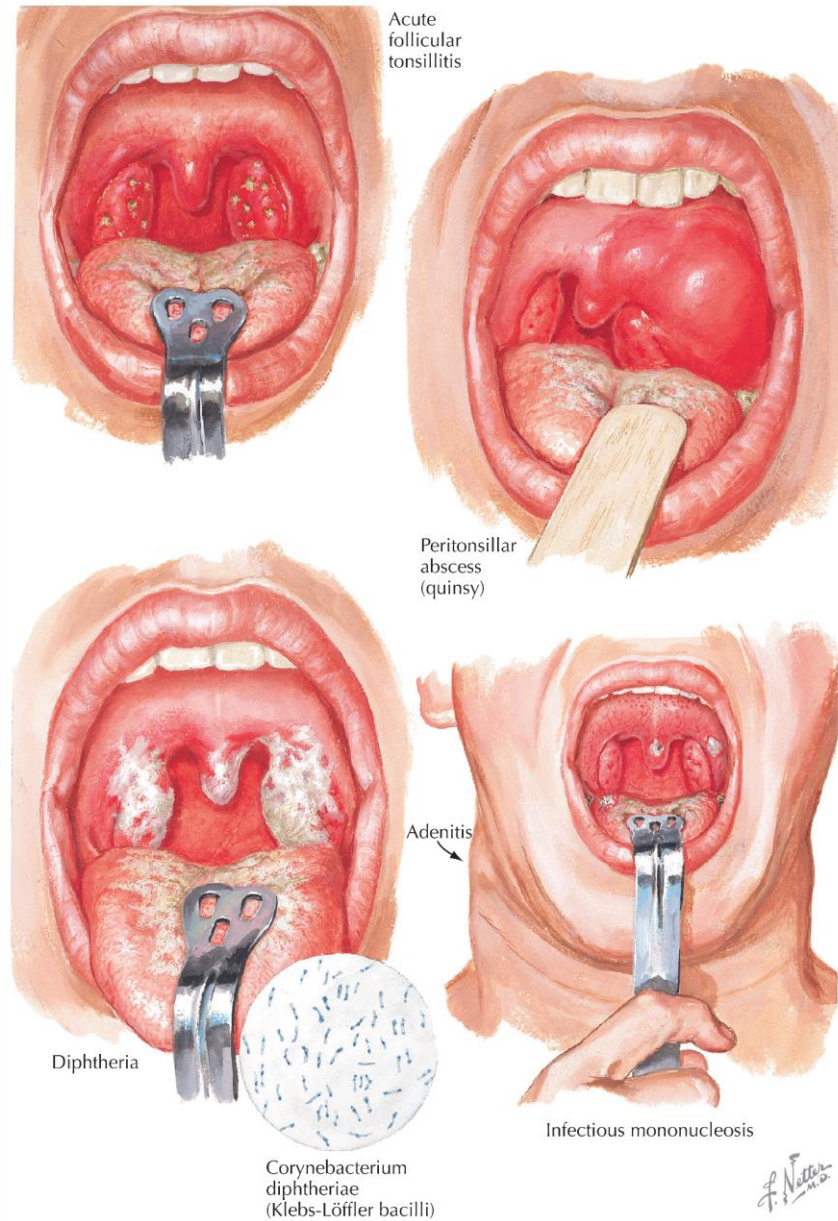
Zenker diverticle

CRICOPHARYNGEAL MYOTOMY AND ESOPHAGEAL DIVERTICULA



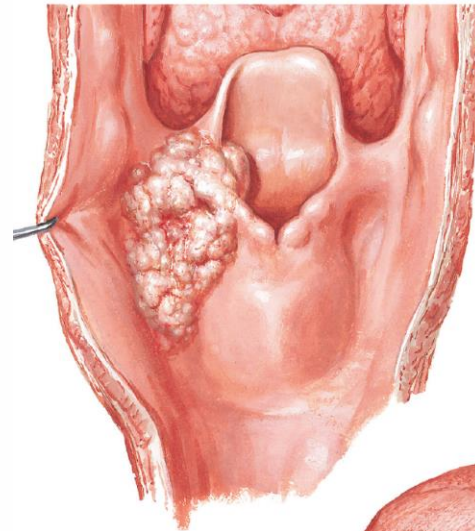
Pharynx Inflammation

Tonsillitis

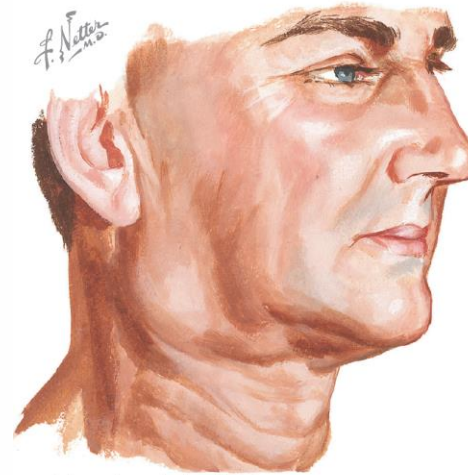


Pharynx Tumor

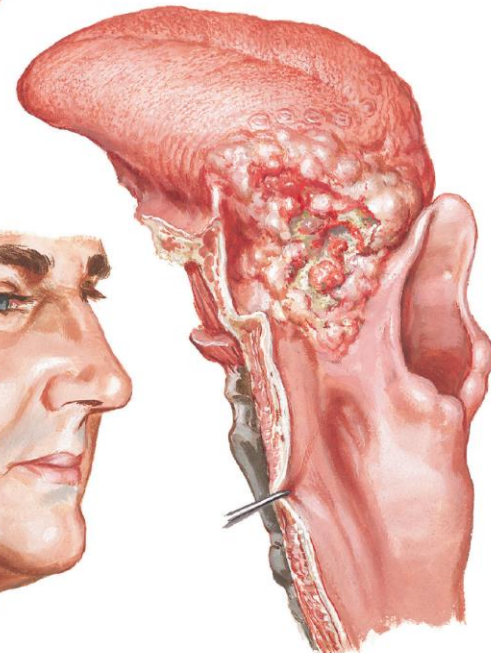
Tumor of base of tongue
Tumor of piriform recess



Carcinoma of piriform recess



Enlarged cervical node (often initial symptom in malignancies of tonsil, fauces, and pharynx)



Carcinoma of root of tongue

Salivary glands Inflammation

Retention cyst

Minor salivary gland duct obstruction,
cystic dilation of the duct

Mucocele

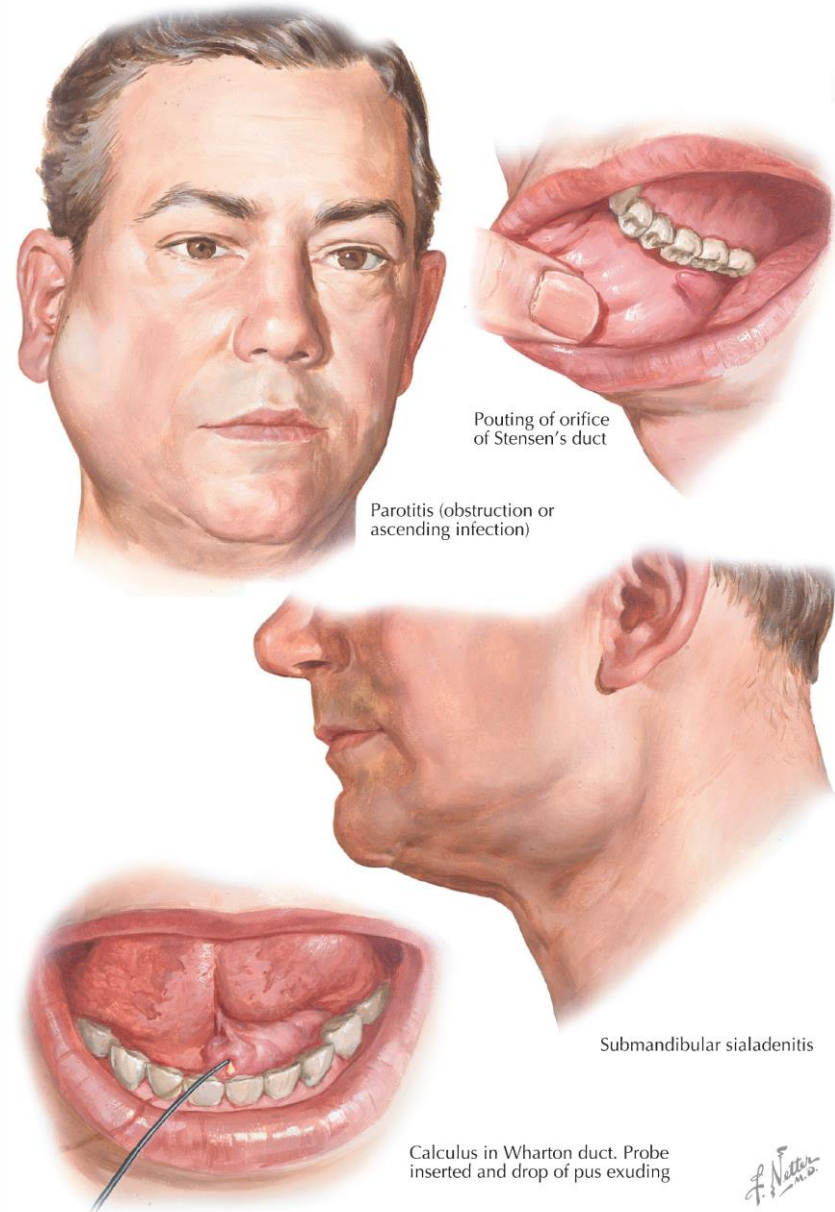
Similar to retention cyst, but the epithelial
lining has been destroyed

LM: pseudocyst containing saliva,
surrounded by inflamed granulation tissue

Sialadenitis

Inflammation of the salivary glands in
response to

- bacterial or viral infection
- autoimmune disease
- ductal occlusion in sialolithiasis



Pouting of orifice
of Stensen's duct

Parotitis (obstruction or
ascending infection)

Submandibular sialadenitis

Calculus in Wharton duct. Probe
inserted and drop of pus exuding

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Salivary glands

Inflammation

Acute purulent sialadenitis

Low salivary flow, dryness of the mouth (**xerostomia**) predisposes to ascending infection by *St. aureus*

Seen in elderly or postoperative states

Painful swelling of the concerned salivary gland, after eating; there may be a purulent discharge

Mumps

Self-limited viral infection; common in children

Diffuse inflammatory enlargement of one or both parotid glands

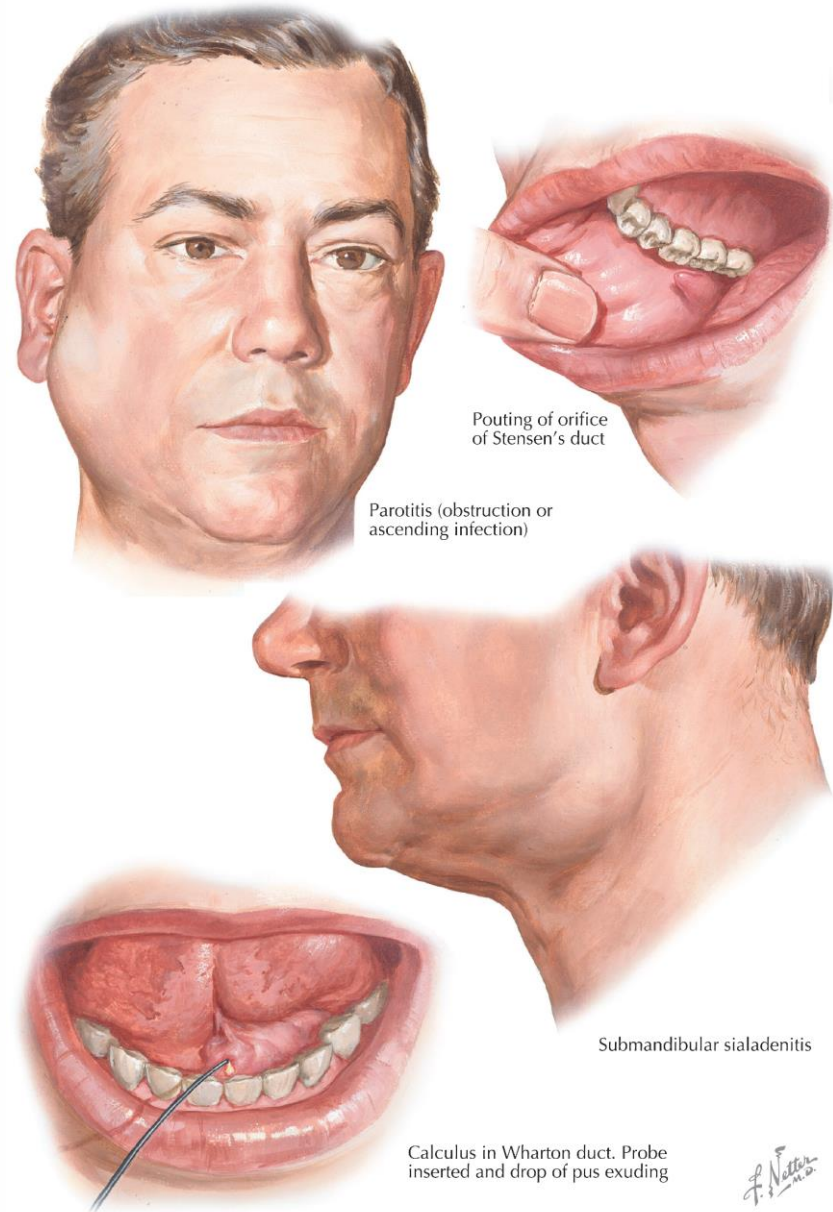
LM: periductal and acinar infiltration of lymphocytes and macrophages

Complications in adults

Pancreatitis

In adolescent and adult males: orchitis (inflammation of the testicles), may result in infertility

Oophoritis (inflammation of the ovaries) is rare



Salivary glands

Inflammation

Sjögren syndrome

Autoimmune-inflammatory destruction of the lacrimal and major and minor salivary glands

May be primary (sicca sy) or secondary in association with rheumatoid arthritis, SLE, or scleroderma

90% of patients are women between ages 35 and 45

Serology

Autoantibodies against ribonucleoproteins SS-A and SS-B

Morphology

Early lesions: intense periductal and perivascular lymphocytic and plasma cell infiltration and proliferation of ducts

Advanced lesions: atrophy of the acini, epi-myoeipithelial islands

Clinical consequences

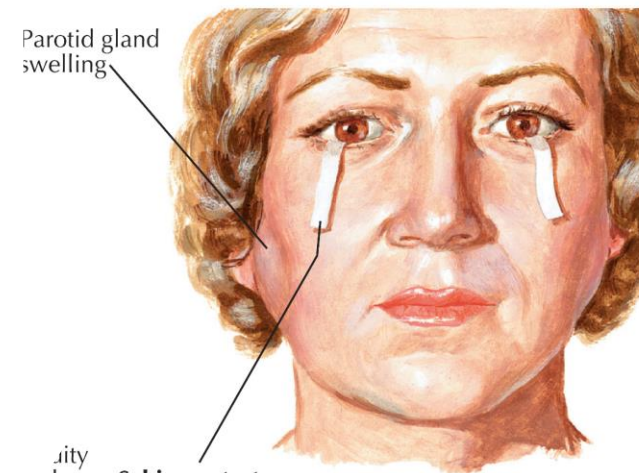
The “sicca syndrome”: lack of tears: xerophthalmia, dry eyes: keratoconjunctivitis sicca; dry mouth: xerostomia; pharyngolaryngitis sicca, rhinitis sicca

The mucosal surfaces become inflamed and ulcerated. Mucosa of GI, respiratory tract, and vagina may also lack mucous secretions.

Risk of developing non-Hodgkin lymphoma in the parotid gland

In one third of patients with primary Sjögren, manifestations of extraglandular disease can be present: chronic tubulointerstitial nephritis with defects in tubular function, pulmonary fibrosis, synovitis

Sjögren syndrome



Parotid gland swelling

Schirmer test
Strips of filter paper inserted behind lower lids. Wetting of 15 mm or more of strip outside of lid = normal; <5 mm = definitely abnormal; 5-15 mm = probably abnormal

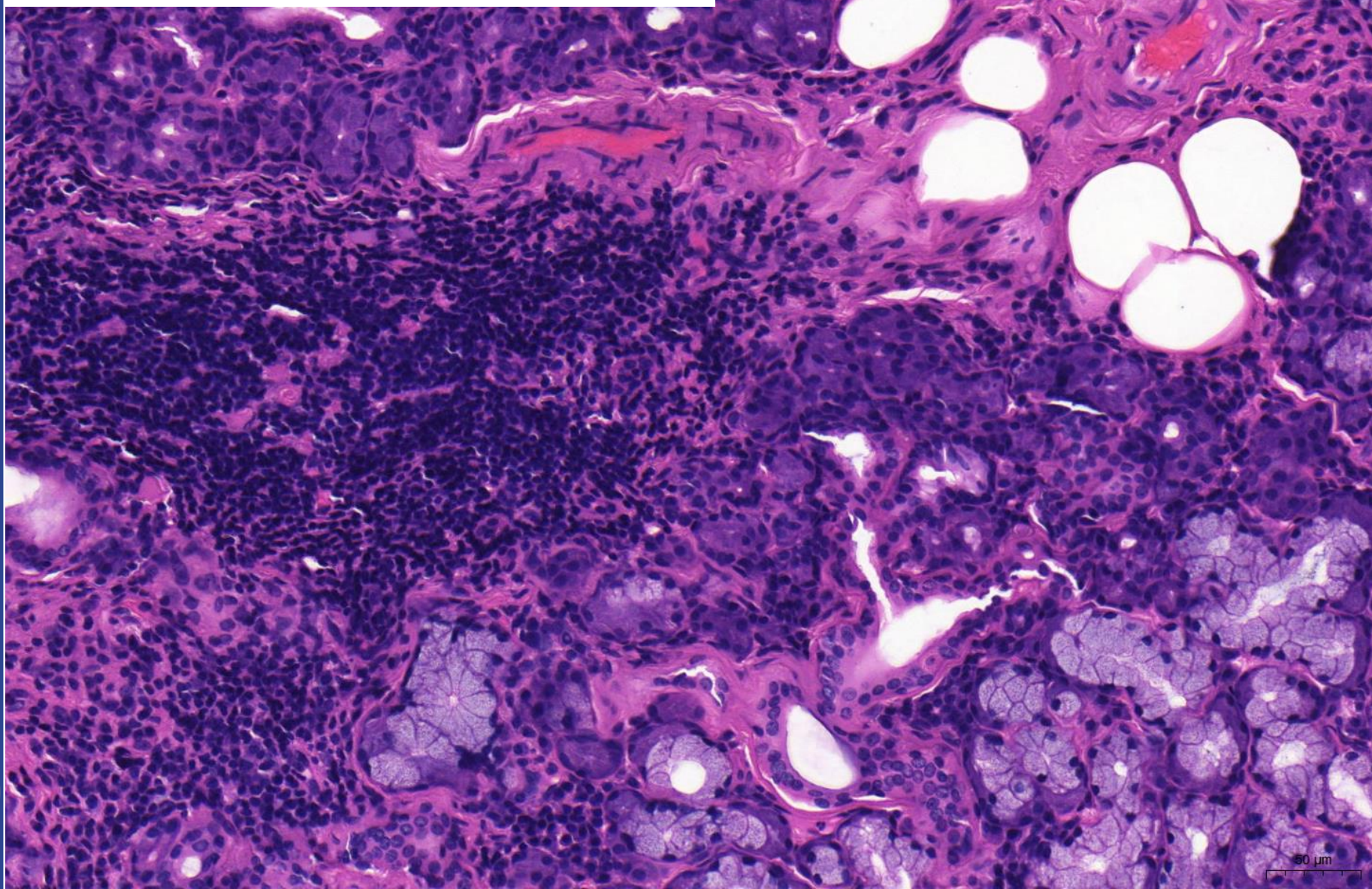
Xerostomia



Calculus in Wharton duct. Probe inserted and drop of pus exuding

Xerostomia and glossitis

Sjögren syndrome in salivary gland



Salivary glands

Tumor

Pleomorphic adenoma (mixed tumor)

Encapsulated; 2-6 cm in diameter

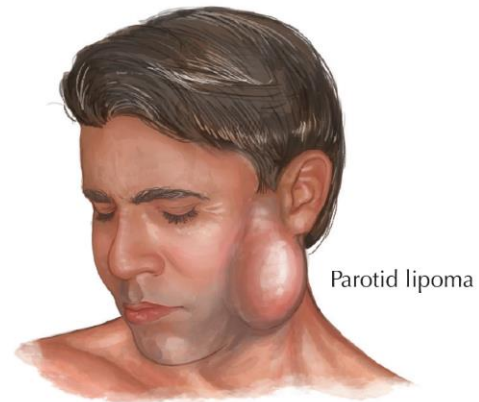
Satellite nodules outside the capsule

LM: A mixture of epithelial and stromal elements; proliferation of myoepithelial and ductal cells; the stroma is myxoid and may contain foci of cartilage

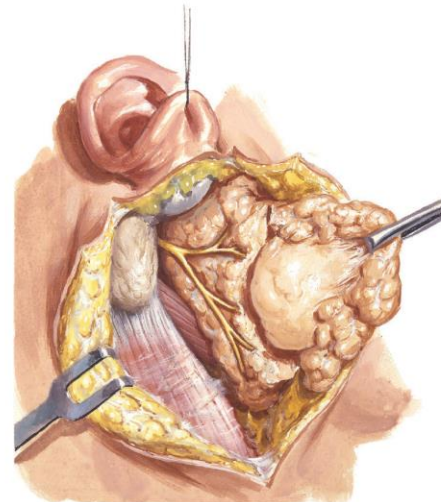
Clinical features

Slow-growing, painless, discrete masses

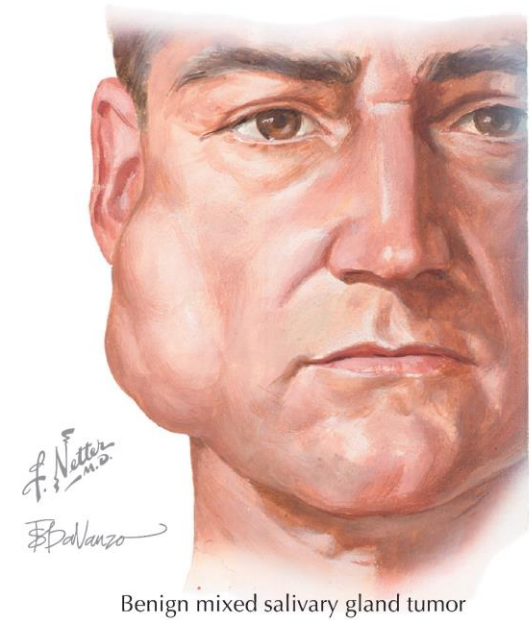
Removal: preservation of the facial nerve is difficult, may recur locally



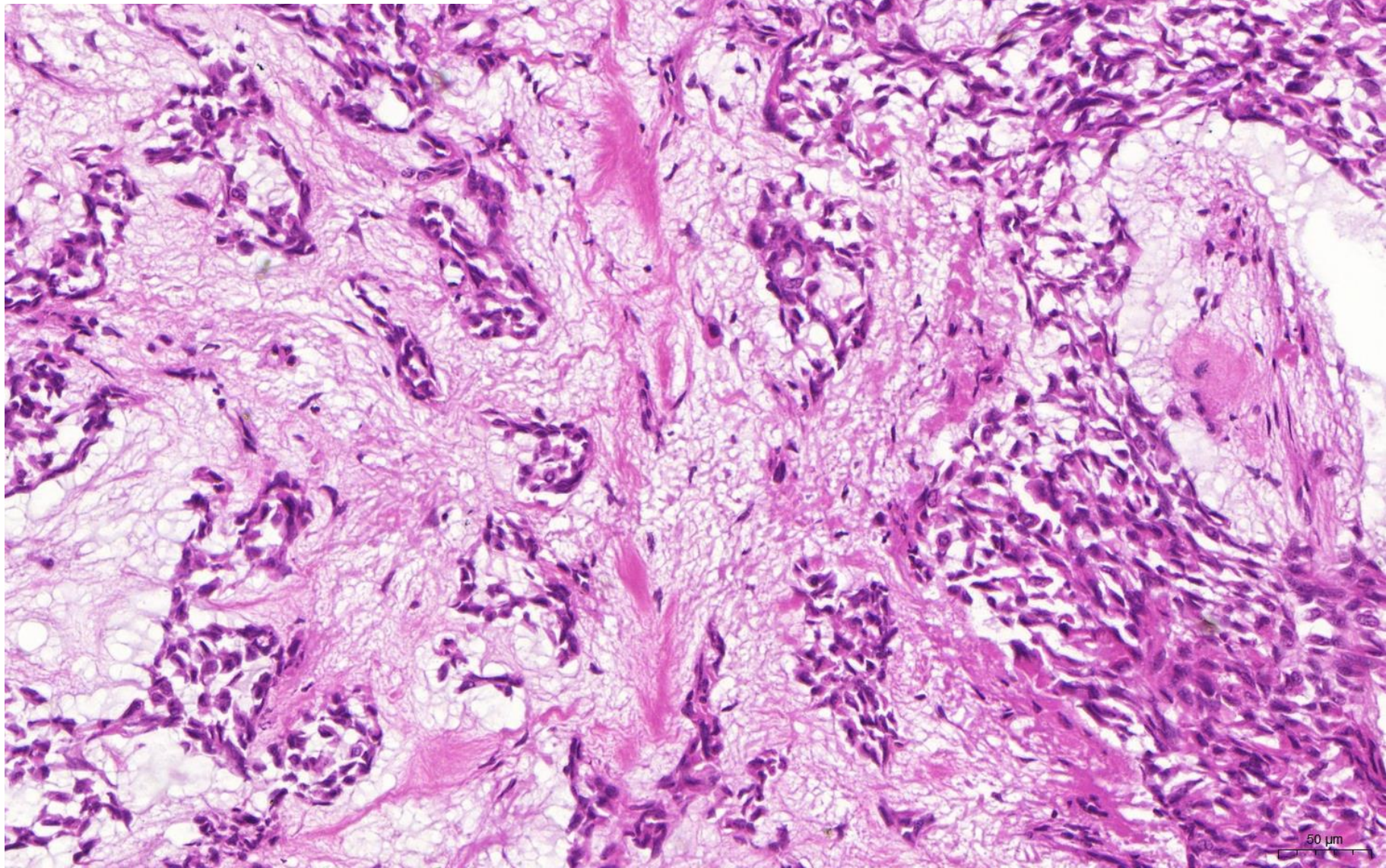
Gross appearance of pleomorphic adenoma



Tumors of parotid gland



Pleomorphic adenoma



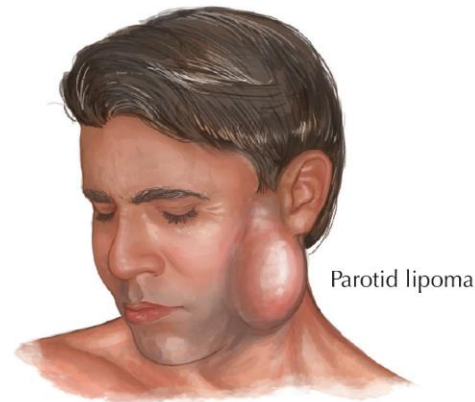
Salivary glands Tumor

Papillary cystadenoma lymphomatosum (Warthin tumor)

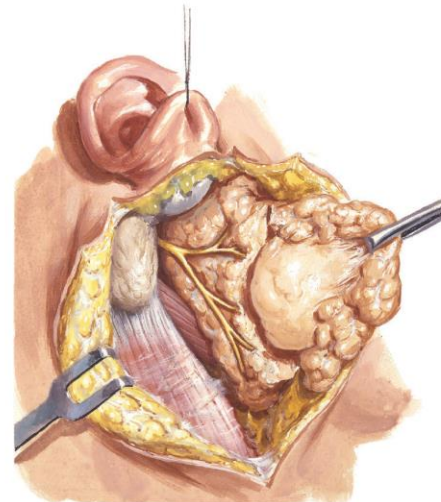
More common in males

Cystic, encapsulated; diameter:
2-5 cm

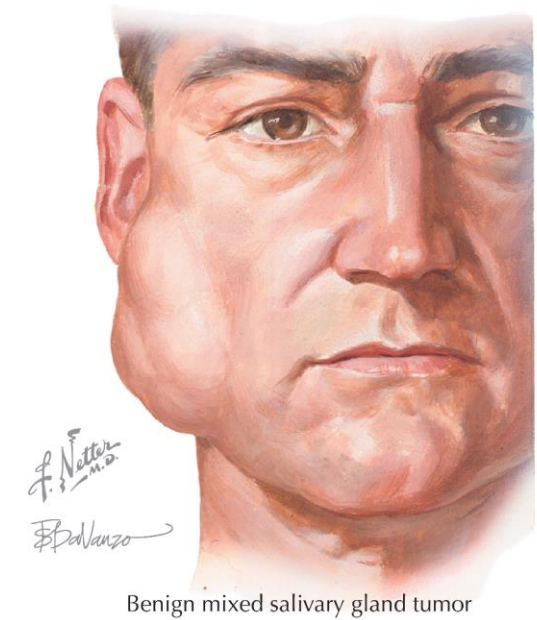
LM: tubular epithelial
parenchyma and lymphoid
stroma; the tubules form
papillary processes, which
localize in dilated cystic spaces.



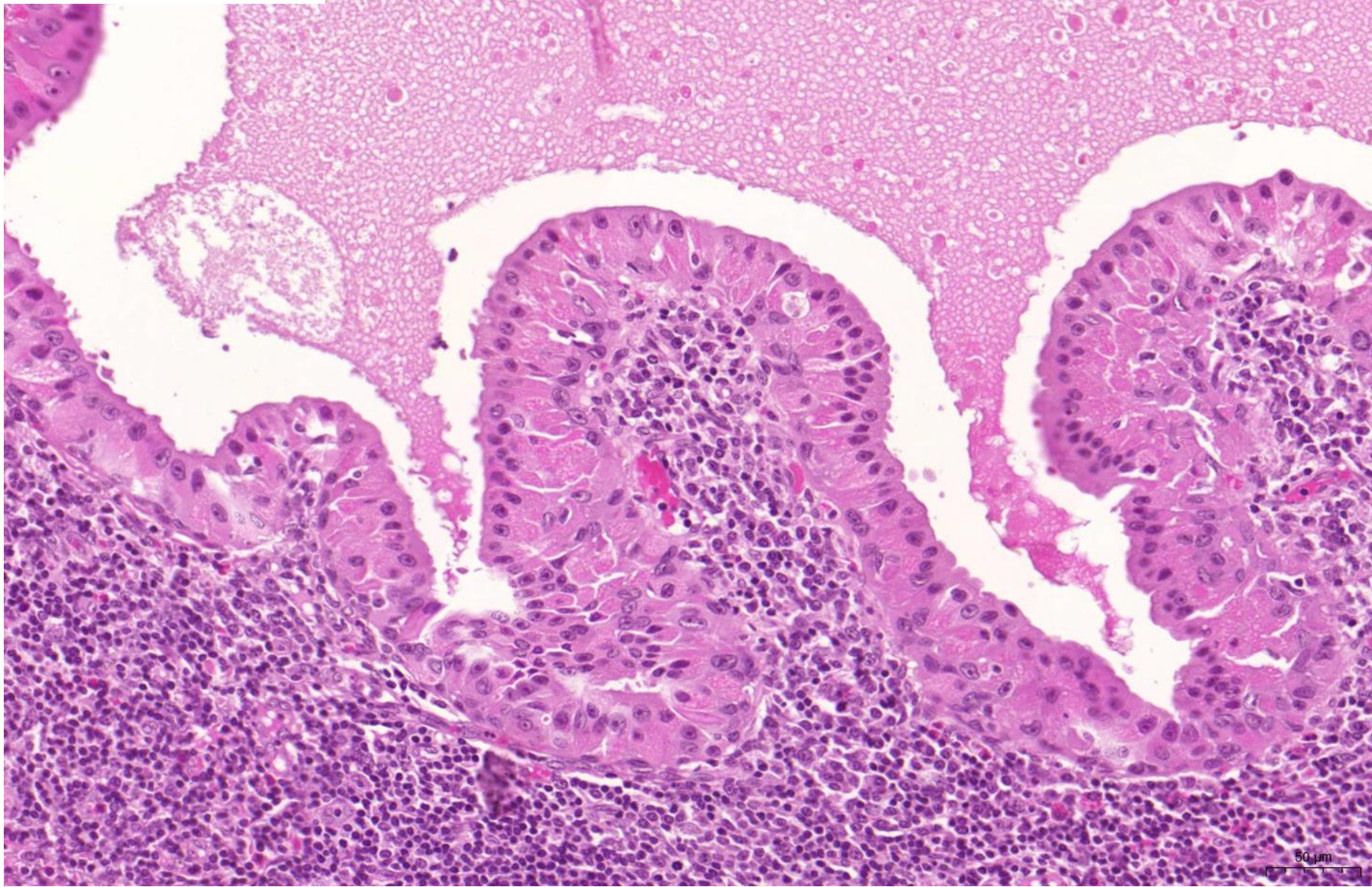
Gross appearance of pleomorphic adenoma



Tumors of parotid gland



Warthin tumor



Salivary glands Tumor

Mucoepidermoid carcinoma

Grows slowly; diameter up to 8 cm

LM: mixtures of squamous cells, mucus-secreting cells, and intermediate cells;

5-y survival rate: low-grade variant 90%; high-grade variant: 40-60%

Adenoid cystic carcinoma

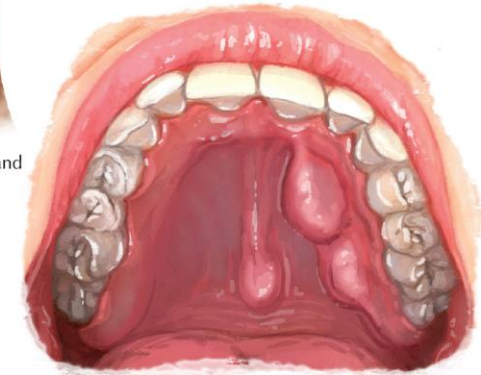
In the minor salivary glands of the palate, with high tendency to infiltrate perineural spaces

LM: the tumor cells form cribriform structures (adenoid), separated by acellular spaces filled excess basement membrane material

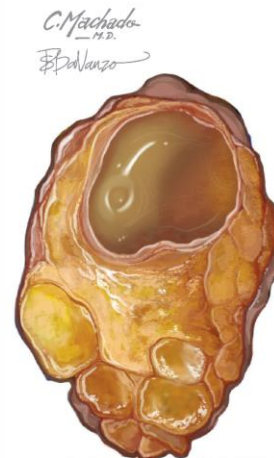
Tendency to develop late, distant metastasis; 5-y survival rate: 60 %



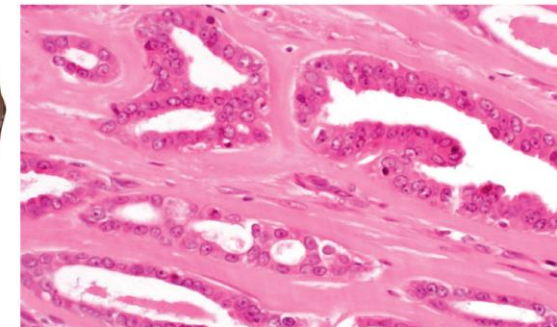
Mucoepidermoid carcinoma in parotid gland



Mucoepidermoid carcinoma on palate



Gross appearance of mucoepidermoid carcinoma



Adenocarcinoma of salivary gland (From Thompson LDR. Head and Neck Pathology: Foundations in Diagnostic Pathology, Elsevier, Philadelphia, 2012.)

Oesophagus

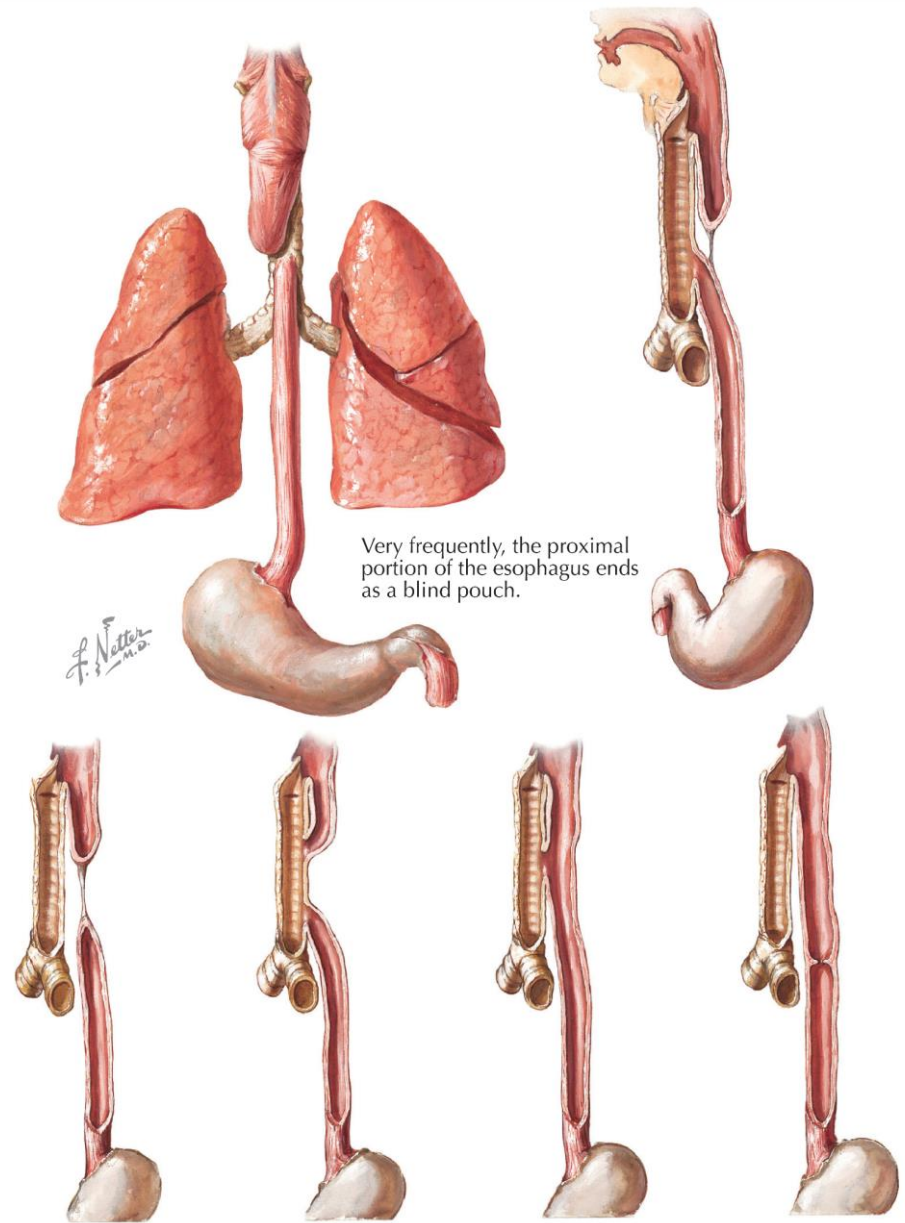
Developmental malformation

Atresia: failure of embryonal canalisation.

Several variants of esophageal atresia exist. Most common: blind upper segment, and fistula between the lower segment and the trachea.

Regurgitation during feeding → lethal aspiration pneumonia soon after birth.

Short atresias may be repaired surgically.

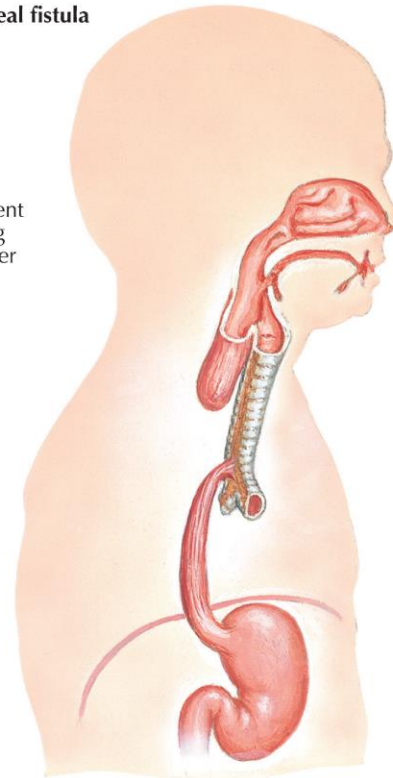


Oesophagus

Developmental malformation

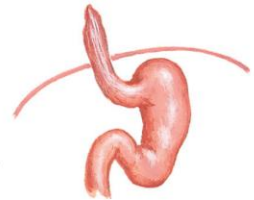
A. Tracheoesophageal fistula

Most common form (90% to 95%) of tracheoesophageal fistula. Upper segment of esophagus ending in blind pouch; lower segment originating from trachea just above bifurcation. The two segments may be connected by a solid cord

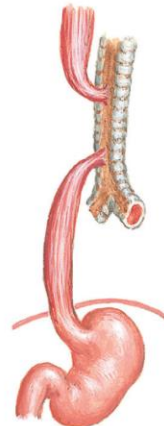


B. Variations of tracheoesophageal fistula and rare anomalies of trachea

Upper segment of esophagus ending in trachea; lower segment of variable length



F. Netter M.D.



C. Double fistula



D. Fistula without esophageal atresia



E. Esophageal atresia without fistula



F. Aplasia of trachea (lethal)

Oesophagus

Developmental malformation

Diverticle

Outpouchings of the wall of the esophagus

Pathogenesis

Traction D. (*pull from outside; e.g., fibrous adhesions*);

Pulsion D. (*push from inside; e.g., high luminal pressure*)

Location

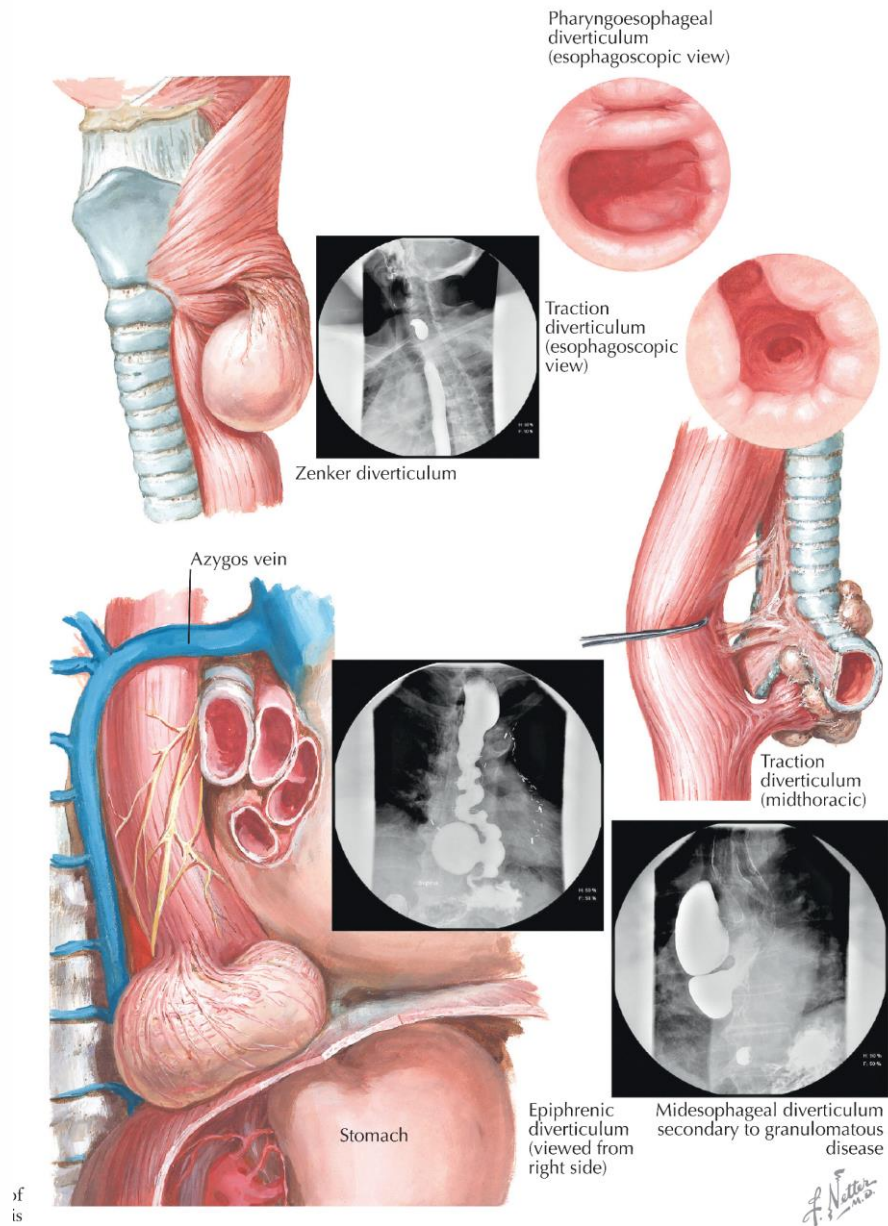
Upper esophagus: Zenker's pulsion D.

Mid esophagus: traction D. due to e.g., scarring of lymph nodes in tuberculosis

Lower oesophagus: epiphrenic pulsion D., associated with diaphragmatic hernia or GERD (Gastro-Esophageal Reflux Disease) or achalasia.

Consequences

May reach several cm-s and may be the site of food accumulation → with nocturnal regurgitation and aspiration during sleep → aspiration pneumonia



Oesophagus

Developmental malformation

Achalasia cardiae

Functional disorder ("failure to relax") characterized by loss of esophageal peristalsis, only partial relaxation of the lower esophageal sphincter (LES) at swallowing, and instead of relaxation, increased resting tone of LES

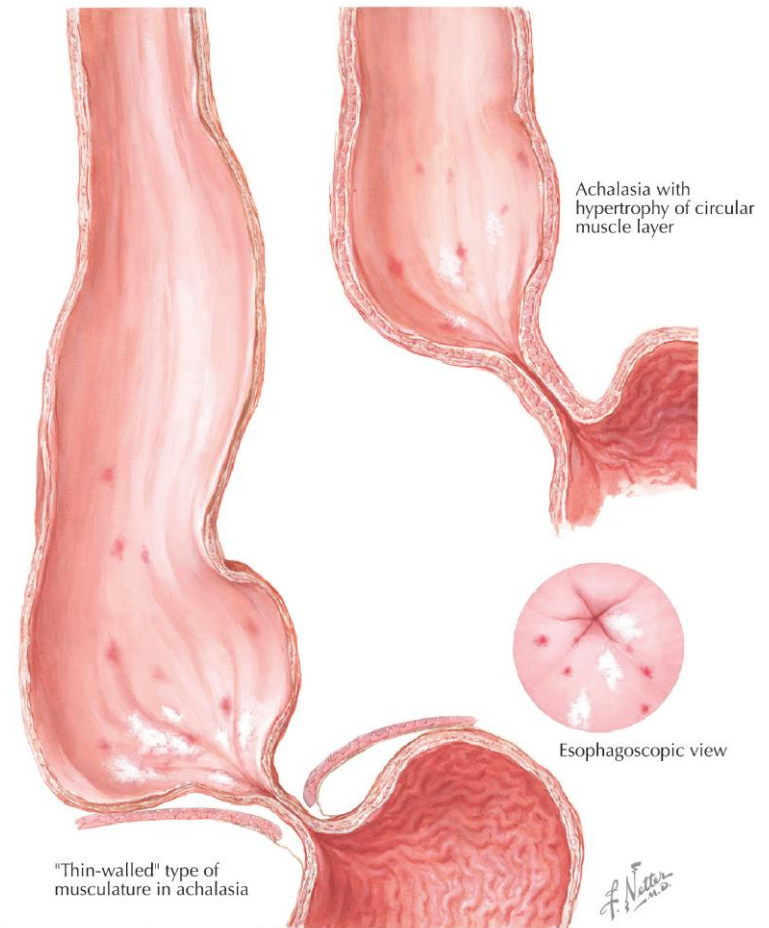
Cause: primary (unknown); secondary: e.g., in diabetic autonomic neuropathy

Consequences

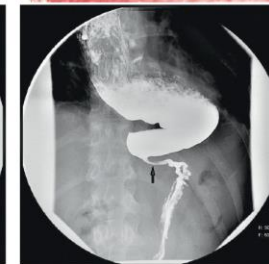
Progressive dilation of the esophagus (megaesophagus) above the LES with inflammation, ulceration and thickening of the mucosal lining

Food regurgitation (nocturnal) → aspiration

Dysplasia may develop and may progress to squamous cell carcinoma



Classic achalasia



Achalasia early sigmoid



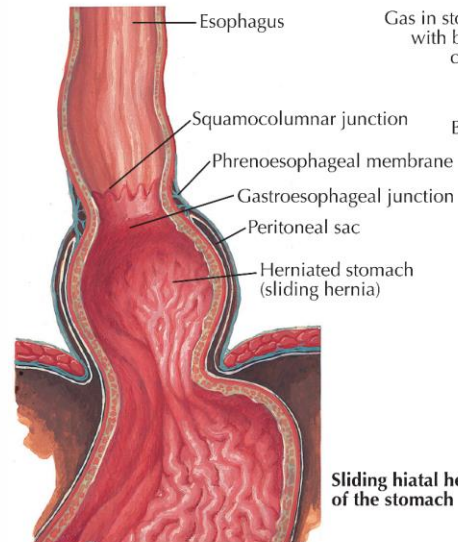
Diffuse esophageal spasm

Oesophagus

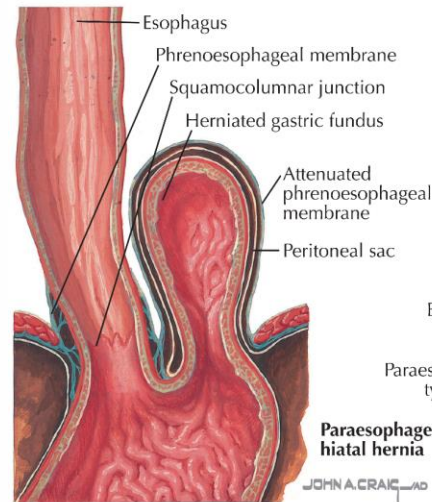
Developmental malformation

Hernia

Abnormal exit of tissue or an organ, such as the bowel, through the wall of the cavity in which it normally resides.

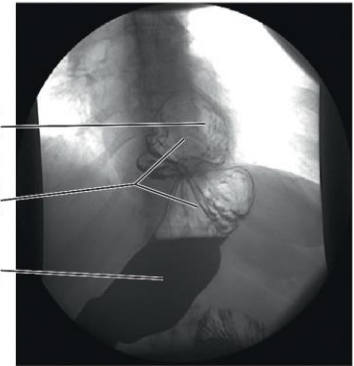


Sliding hiatal hernia of the stomach



Paraesophageal hiatal hernia

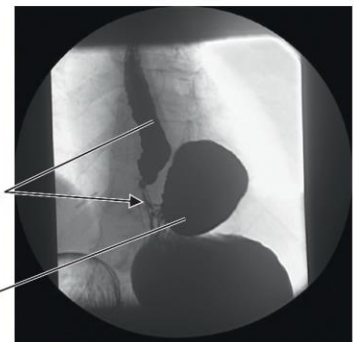
Sliding type hiatal hernia
Gas in stomach with barium coating
Barium



Upper GI fluoroscopy study with double contrast (gas and barium) of a sliding hiatal hernia



Sliding hiatal hernia



Upper GI fluoroscopy study with barium contrast of a paraesophageal hernia

Oesophagus

Developmental malformation

Hiatus hernia (hernia diaphragmatica)

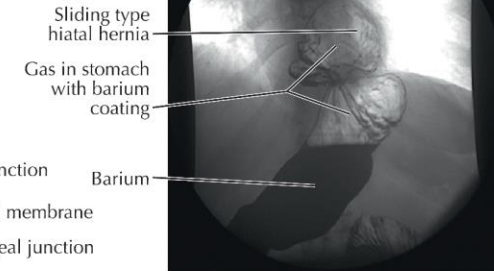
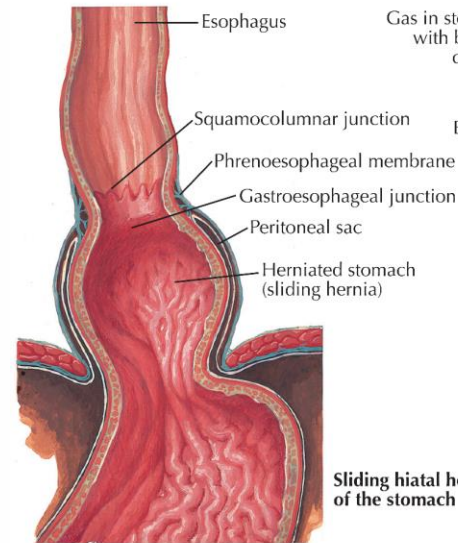
Protrusion of the stomach above the diaphragm through a widened diaphragmatic hiatus; in individuals above 50 ys

Sliding hernia - common: the gastroesophageal junction is pulled into the thorax

Paraesophageal hernia - uncommon: a portion of the stomach rolls up into the thorax

Symptoms

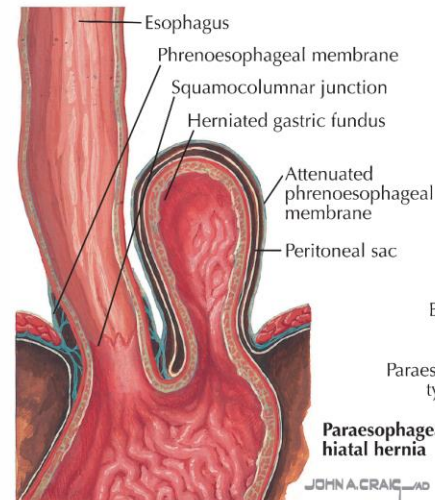
May cause heartburn (a burning sensation behind the sternum) or dysphagia (difficulty in swallowing) or pain on swallowing.



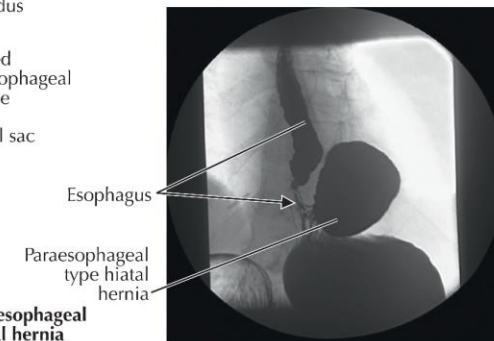
Upper GI fluoroscopy study with double contrast (gas and barium) of a sliding hiatal hernia



Sliding hiatal hernia



Paraesophageal hiatal hernia



Upper GI fluoroscopy study with barium contrast of a paraesophageal hernia

Diaphragm

Developmental malformation

Hiatus hernia (hernia diaphragmatica)

Protrusion of the stomach above the diaphragm through a widened diaphragmatic hiatus; in individuals above 50 ys

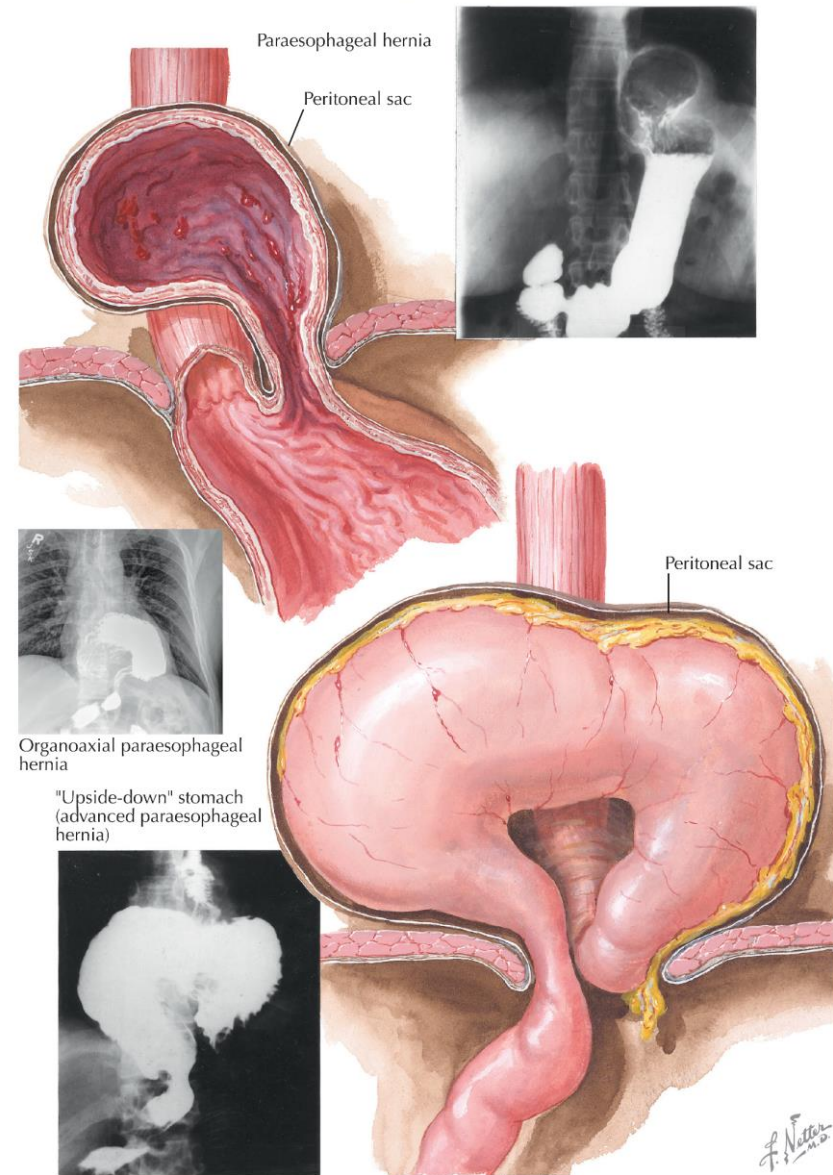
Sliding hernia - common: the gastro-esophageal junction is pulled into the thorax

Paraesophageal hernia - uncommon: a portion of the stomach rolls up into the thorax

Symptoms

May cause heartburn (a burning sensation behind the sternum) or dysphagia (difficulty in swallowing) or pain on swallowing.

PARAESOPHAGEAL HERNIAS



Diaphragm

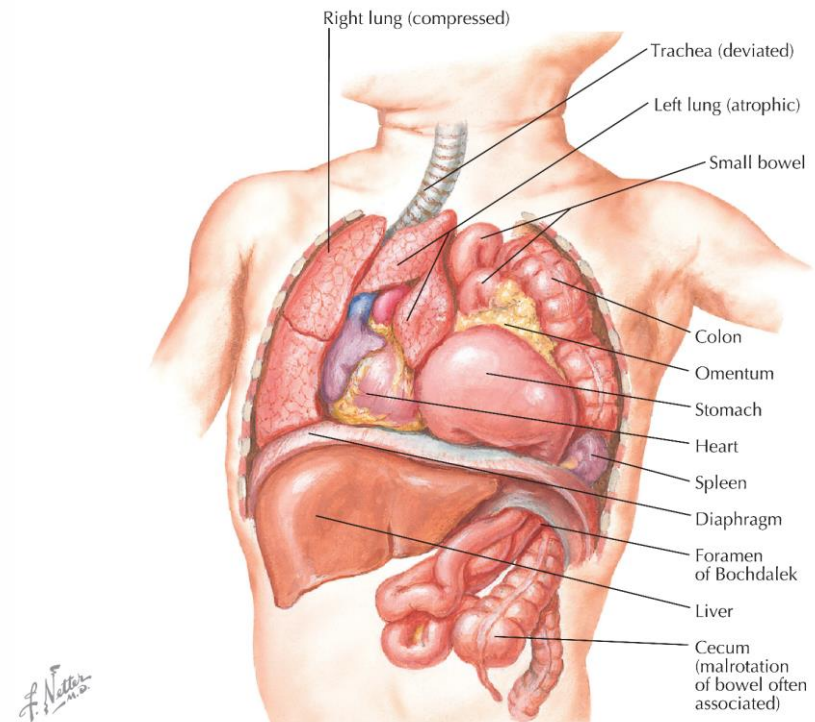
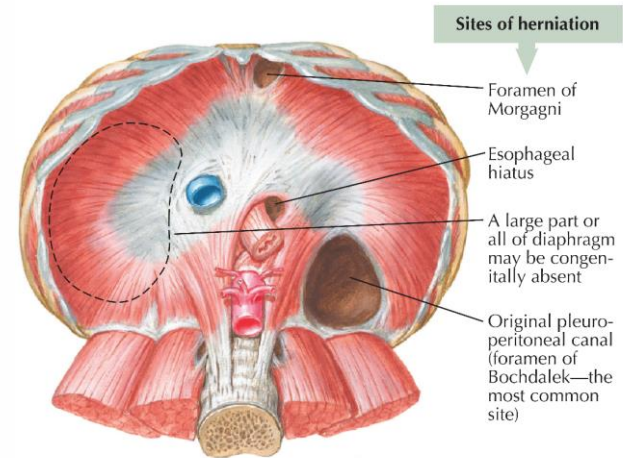
Developmental malformation

Congenital hernia diaphragmatica

A posterolateral defect in the diaphragm, which permits abdominal organs to localize in the thorax.

Dyspnea and cyanosis of the newborn due to the displacement and hypoplasia of lungs.

Large defects are lethal.



Oesophagus Inflammation Oesophagitis

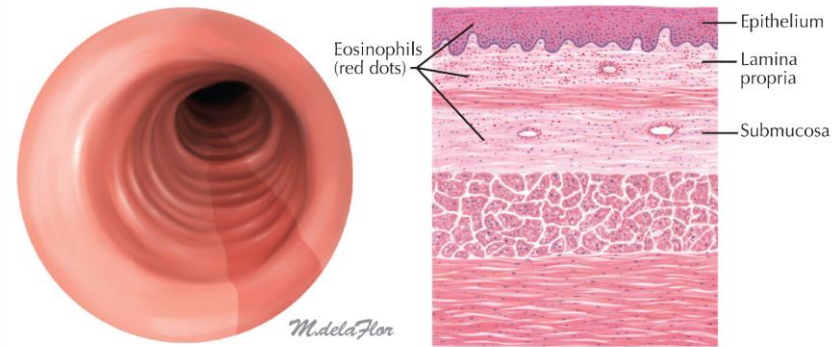
Etiology

Frequent: reflux of gastric juices - GERD
due to incompetence of the LES

Irritation: prolonged gastric intubation,
alcohol, smoking, uremia

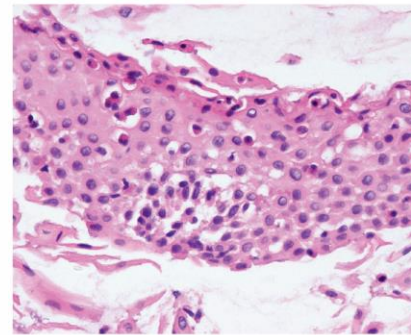
Infections in patients with leukaemias,
lymphomas: viruses (herpes simplex,
cytomegalovirus), fungi (Candida)

Hypersensitivity reaction to food allergens
→ eosinophilic esophagitis

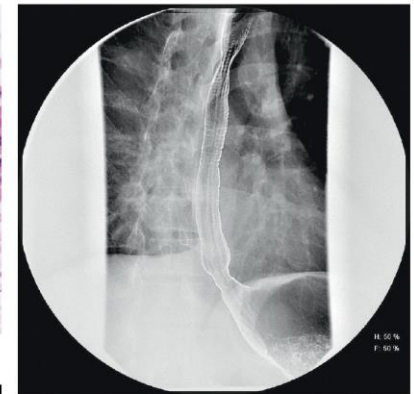


Endoscopic view demonstrates characteristic rings seen in the esophagus with eosinophilic esophagitis

Cross-sectional microscopic view of the esophagus demonstrates the infiltration of all layers of the esophagus with eosinophils. The infiltrate is diagnosed most frequently by endoscopic biopsy so it is seen in the biopsy specimen in the epithelium and lamina propria.



Eosinophilic esophagitis histology



EoE with multiple rings and corrugated appearance



Eosinophilic esophagitis with linear furrows, rings with white exudates

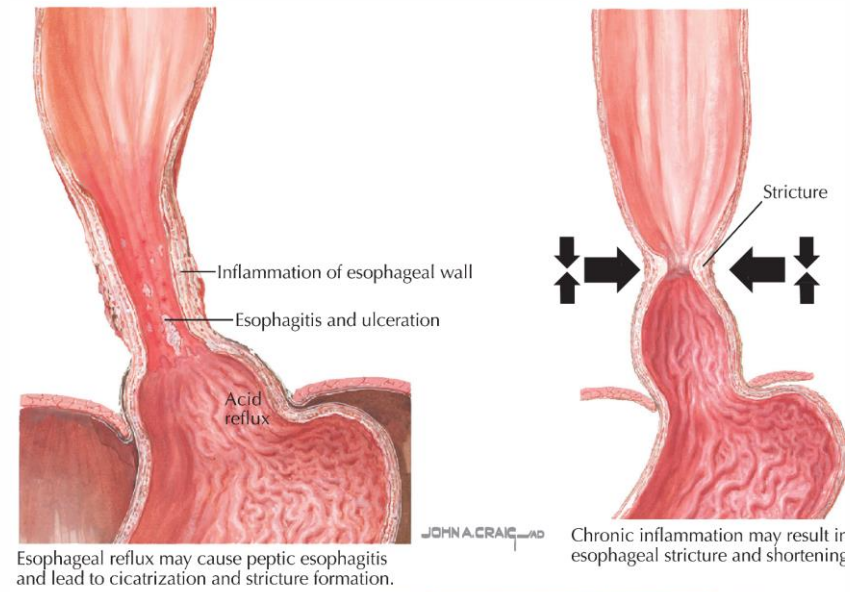
Oesophagus Inflammation GERD

Consequences of GERD

Mucosal injury → severe acute inflammation, necrosis and ulceration with the formation of granulation tissue → eventual fibrosis & stenosis (stricture)

Long-standing reflux → replacement of distal squamous mucosa by metaplastic intestinal epithelium with goblet cells, recognized endoscopically as patches of reddish mucosa extending upward from the gastroesophageal junction, termed Barrett's esophagus

Dysplasia may develop in Barrett's esophagus → risk for esophageal adenocarcinoma



Barium study shows esophageal stricture.



Grade D reflux esophagitis

Los Angeles Classification of Erosive Esophagitis	
Grade A	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds
Grade B	One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds
Grade C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involves less than 75% of the circumference
Grade D	One (or more) mucosal break which involves at least 75% of the esophageal circumference

(From Lundell LR, Dent J, Bennett JR, et al: Endoscopic Assessment of Esophagitis: Clinical and Functional Correlates and Further Validation of the Los Angeles Classification. *Gut* 1999; 45: 172-180).



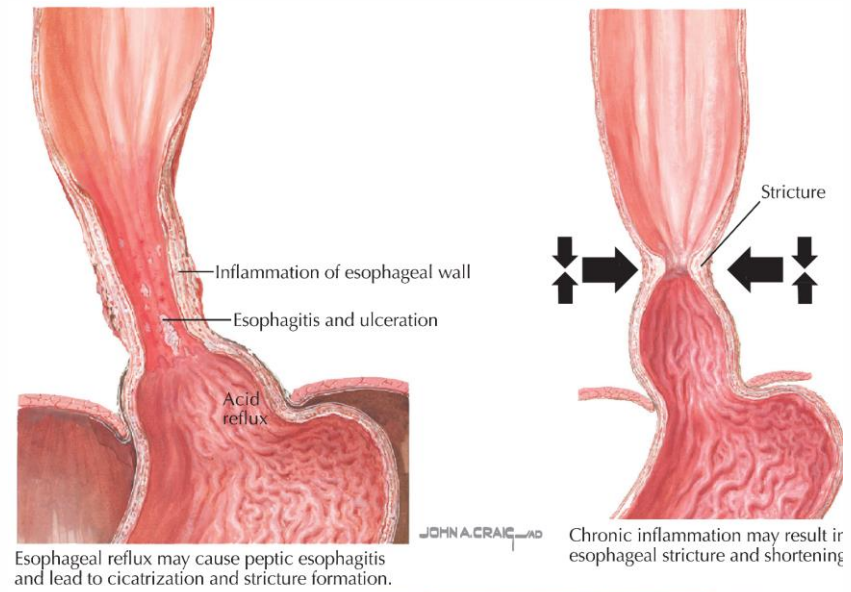
Oesophagus Inflammation GERD

Clinical features of GERD

Heartburn, dysphagia, regurgitation of sour-tasting gastric content

Infrequently: chest pain that may be mistaken for ischemic heart attack

Biopsy evaluation of esophagus mucosa differentiates GERD-induced esophagitis from eosinophilic esophagitis



Barium study shows esophageal stricture.



Grade D reflux esophagitis

Los Angeles Classification of Erosive Esophagitis	
Grade A	One (or more) mucosal break no longer than 5 mm that does not extend between the tops of two mucosal folds
Grade B	One (or more) mucosal break more than 5 mm long that does not extend between the tops of two mucosal folds
Grade C	One (or more) mucosal break that is continuous between the tops of two or more mucosal folds but which involve less than 75% of the circumference
Grade D	One (or more) mucosal break which involves at least 75% of the esophageal circumference

(From Lundell LR, Dent J, Bennett JR, et al: Endoscopic Assessment of Esophagitis: Clinical and Functional Correlates and Further Validation of the Los Angeles Classification. *Gut* 1999; 45: 172-180).

Oesophagus Inflammation

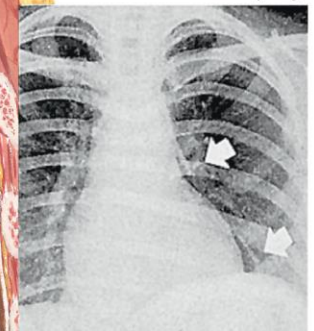
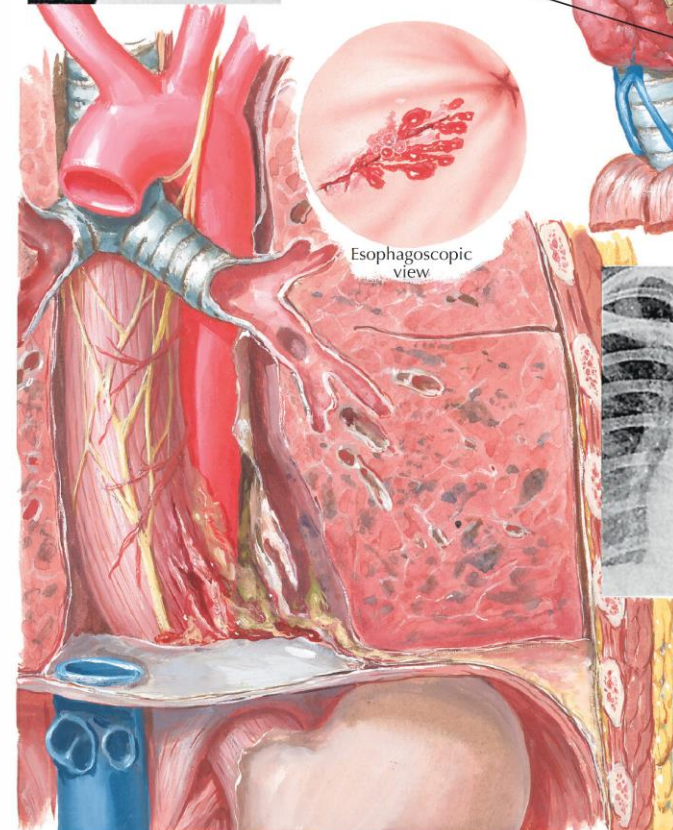
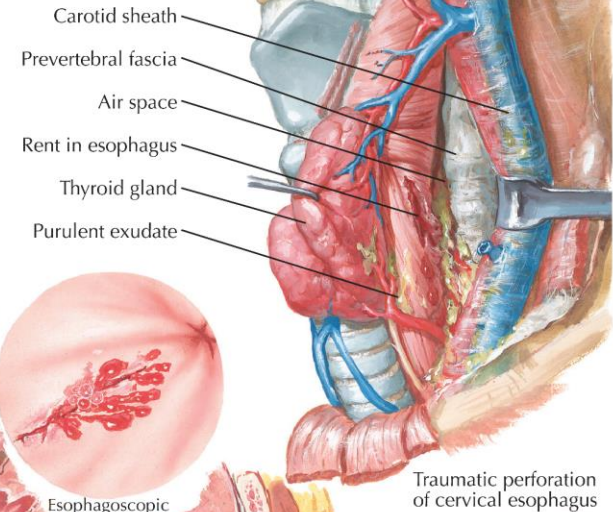
Lacerations / Mallory-Weiss sy

Longitudinal tears at the gastro-oesophageal junction, attributed to excessive vomiting, generally in chronic alcoholics

Complication: bleeding (slight → fatal)

In survivors, healing is generally complete.

Air in interfascial spaces due to perforation of cervical esophagus



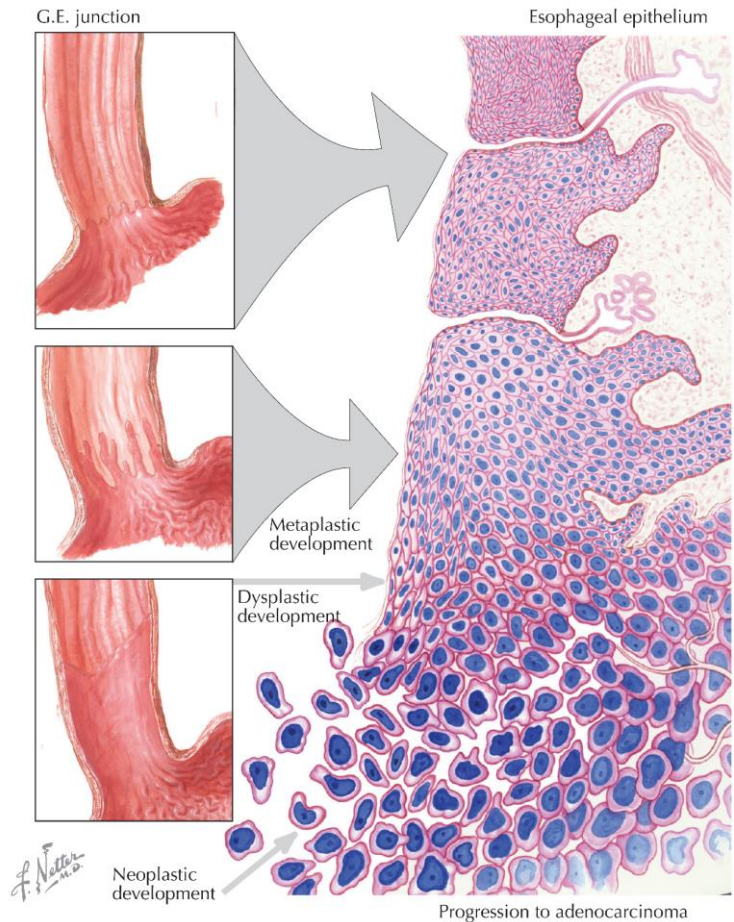
Air in mediastinum due to spontaneous rupture of lower esophagus

Spontaneous rupture of lower esophagus

Oesophagus Tumor

Long-standing reflux → replacement of distal squamous mucosa by metaplastic intestinal epithelium with goblet cells, recognized endoscopically as patches of reddish mucosa extending upward from the gastroesophageal junction, termed Barrett's esophagus

Dysplasia may develop in Barrett's esophagus → risk for esophageal adenocarcinoma



Normal squamocolumnar junction



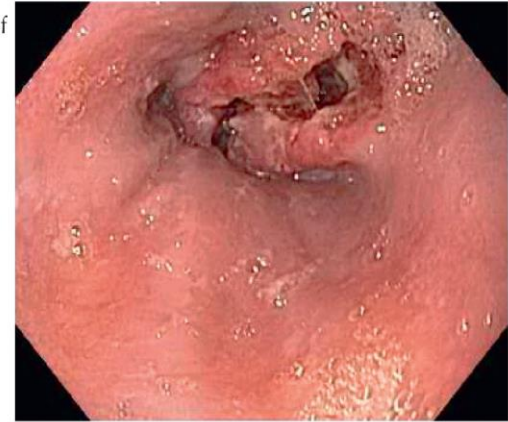
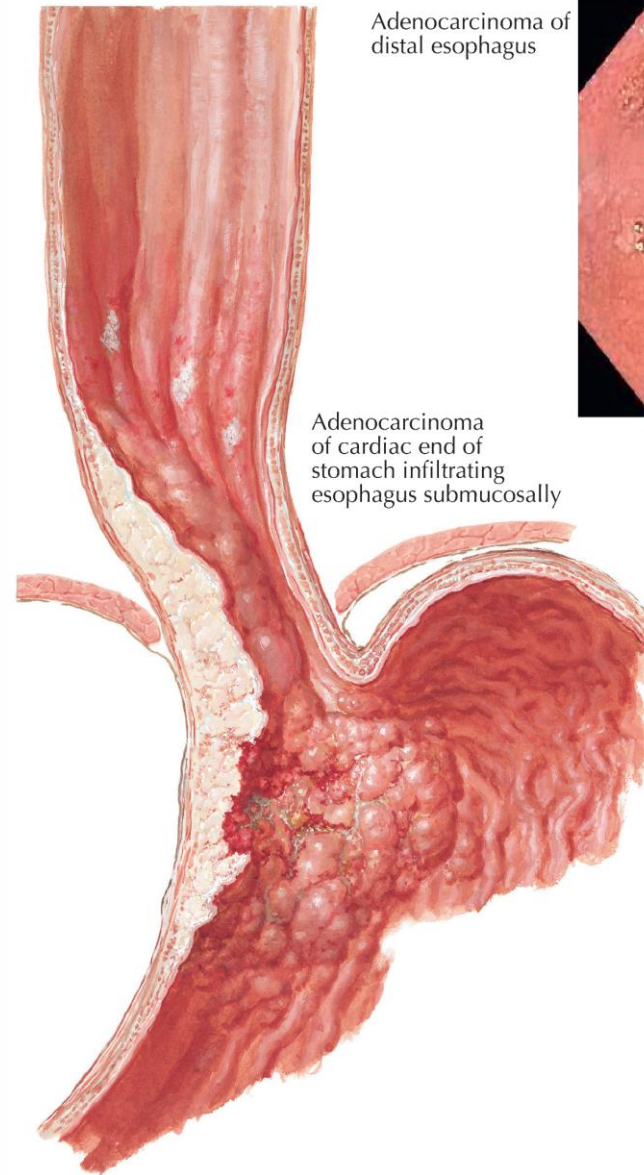
Barrett esophagus

Oesophagus Tumor Adenocarcinoma

In association with Barrett's oesophagus → dysplasia. May invade the adjacent cardia

Gross: similar to SSC, LM: mucin producing adenocarcinoma

Poor prognosis, comparable to SSC



PET scan demonstrating imaging of distal esophageal adenocarcinoma

Oesophagus Tumor Squamous cell carcinoma (SSC)

Usually in males over 50 ys of age

Etiology

Europe, US: smoking & alcohol consumption

Morphology

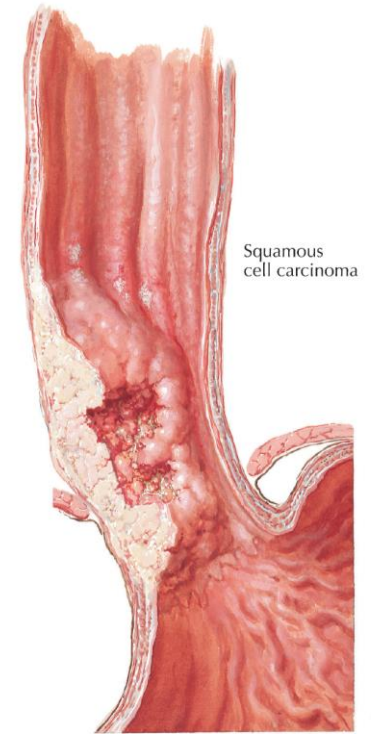
Evolution: dysplasia → cc in situ → invasive cc

Longitudinal and deep extension is enhanced by the rich lymphatic network in the submucosa

Localization: 20% in the upper third, 50% in the middle third, 30% in the lower third.

Gross Polypoid-fungating lesion / Flat, diffusely infiltrative lesion /
Ulcerative-excavating lesion

LM: moderately differentiated SCC



Oesophagus Tumor Laphámrák

Metastases

Lymph node metastasis: upper third: cervical nodes; middle third: mediastinal, paratracheal, and tracheobronchial nodes; lower third: gastric and coeliac nodes.
Hematogeneous metastasis: in the lungs.

Clinical features

Insidious onset, then progressive dysphagia, altering the diet from solid to liquid foods

Complications

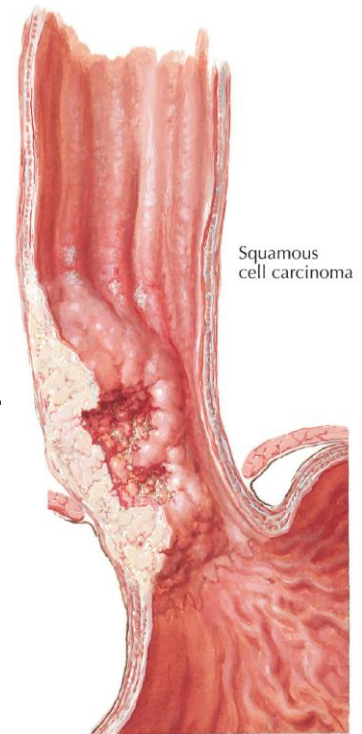
Cancerous esophago-tracheal fistula and aspiration pneumonia

Bleeding

Extreme weight loss because of impaired nutrition and tumor-associated cachexia

Prognosis

If lymph node metastasis is present at the time of surgical resection, the 5-yr-survival rate is 5%.



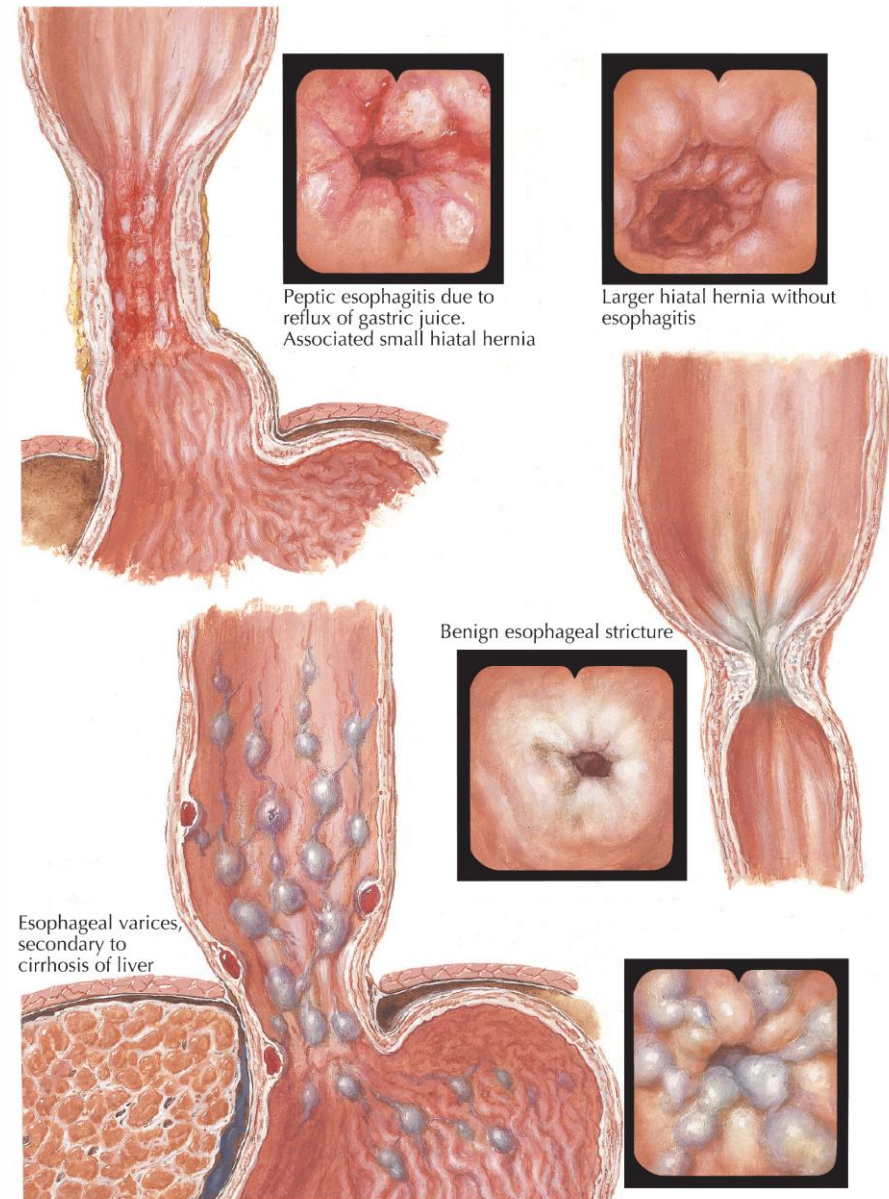
Oesophagus Varices

Esophageal varices

In portal hypertension, the submucosal veins of distal esophagus + upper stomach undergo dilation (portocaval shunt)

Spontaneous rupture through the mucosa → hematemesis, hemorrhagic shock → exsanguination

Autopsy: 2000-3000 ml-s of fresh blood fills the stomach and small bowels



Stomach

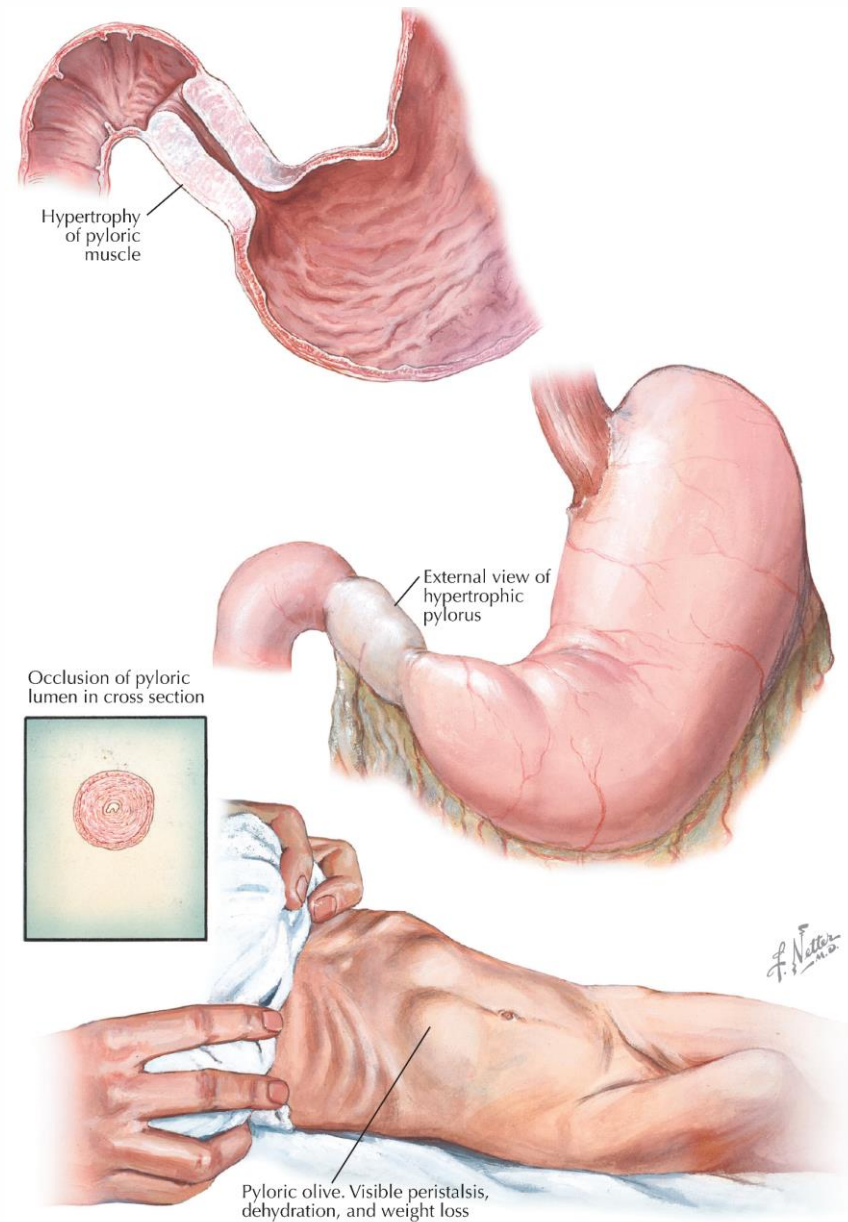
Developmental malformation

Congenitalis pyloric stenosis

Hypertrophy of the pylorus smooth muscle wall; may be palpated through the abdominal wall

Male infants predominate

Nonbilious projectile vomiting from the 2nd week of life; lethal without surgery (pyloromyotomy)



Stomach Inflammation

Stomach mucosa

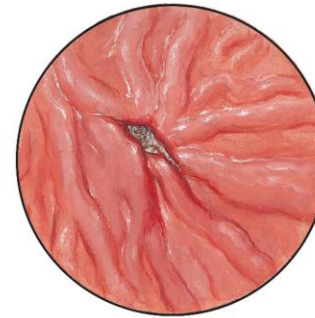
Gastric mucosa is covered by a layer of mucus. The mucosal glands comprise the cardiac glands, the fundic glands in the fundus and body of the stomach, and the pyloric glands in the antrum.

The surface mucous cells and the cardiac and pyloric glands secrete mucus which protects the stomach from self-digestion.

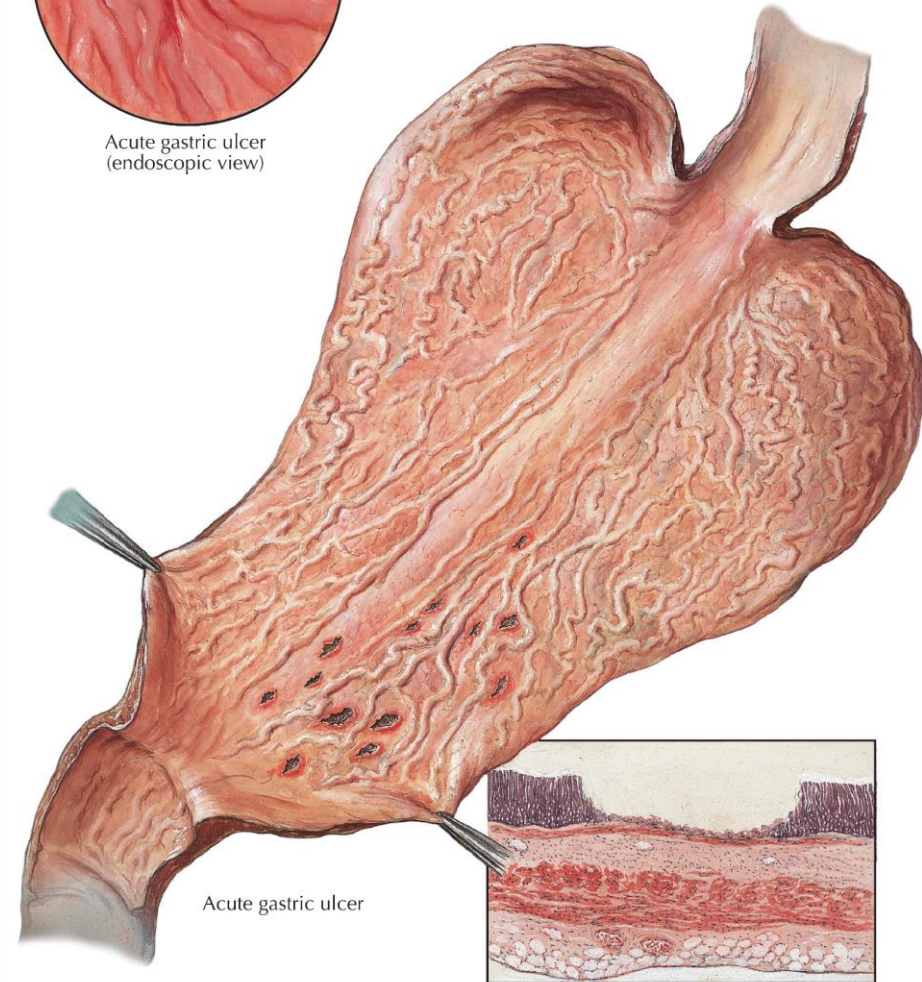
In fundic glands, the chief cells secrete pepsinogen and the parietal cells secrete HCl, bicarbonate, and intrinsic factor. Pyloric gland G cells secrete gastrin. Gastric glands also contain enterochromaffin-like cells which release histamine.

Erosion - circumscribed necrosis-induced defect of mucosa that does not cross the muscularis mucosae

Ulcer - the defect extends beyond the mucosa



Acute gastric ulcer
(endoscopic view)



Acute gastric ulcer

(Hemalum-eosin, $\times 80$)



Stomach

Inflammation

Acute gastritis

Pathogenesis

Common condition induced by acute damage to the gastric mucosa due to alcohol, NSAIDs (nonsteroidal anti-inflammatory drugs, e.g., aspirin) or steroids
stress situations, e.g., severe burns, hypothermia, shock, CNS trauma, etc.
Helicobacter pylori infection

Pathological features

Hemorrhagic-erosive inflammation of gastric mucosa affecting the entire stomach (pangastritis) or the antrum of stomach (antral gastritis)

Mucosal hyperemia, punctate hemorrhages, multiple erosions

Acute ulcers: anywhere in the stomach (rarely in the proximal duodenum); multiple, <1 cm; usually do not penetrate through the muscularis propria layer

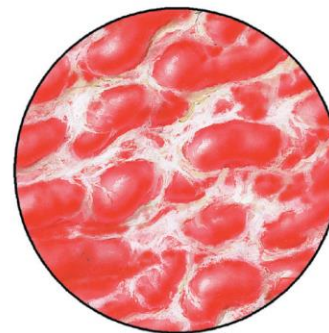
Healing is complete

Clinical features

Epigastric pain, nausea, vomiting

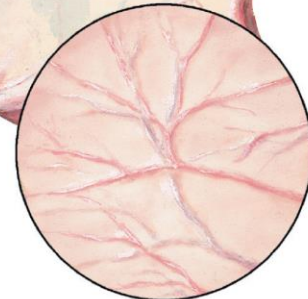
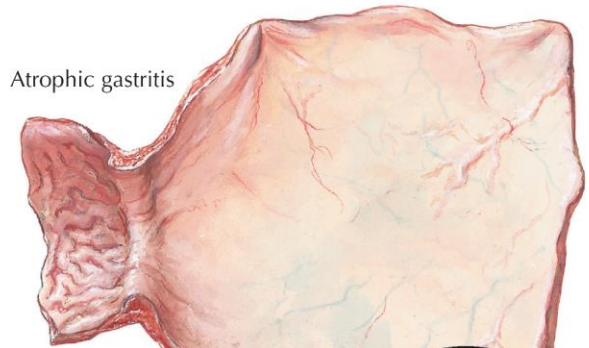
On occasion, massive bleeding with hematemesis and melena ± hemorrhagic shock

Dg.: via endoscopy of stomach



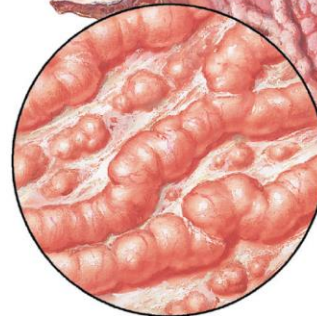
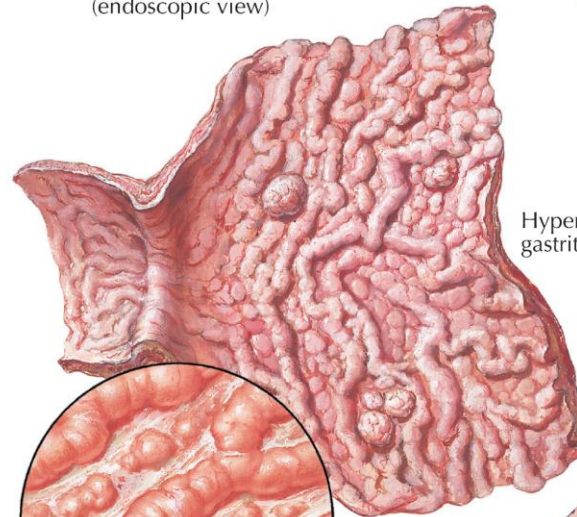
Acute gastritis
(endoscopic view)

Atrophic gastritis



Endoscopic view

Hypertrophic gastritis



Endoscopic view

Erosive (hemorrhagic) gastritis



F. Netter M.D.

Stomach

Inflammation

Chronic gastritis

Autoimmune Metaplastic Atrophic Gastritis (AMAG)
Rare

Pathogenesis

Autoantibodies to the gastric parietal cells. Can be isolated or associated with other autoimmune disorders.

Morphology

Atrophic corpus gastritis: pathologic changes are restricted to the corpus: chronic inflammation of the lamina propria, glandular destruction, mucosal atrophy, intestinal metaplasia

Antrum: G-cell hyperplasia

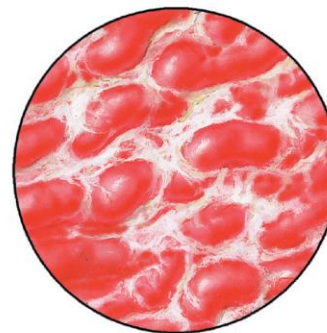
Clinical features

Reduced acid secretion: hypochlorhydria

Hypergastrinemia: response to hypochlorhydria to stimulate HCl production in the vanishing parietal cells

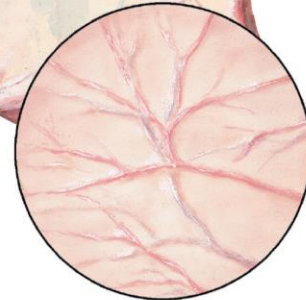
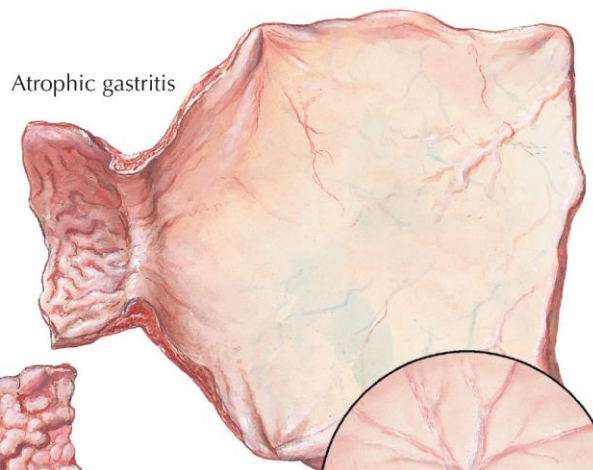
Intrinsic factor is not produced → disturbed vitamin B12 absorption → pernicious anemia

High risk for the development of gastric adenocarcinoma

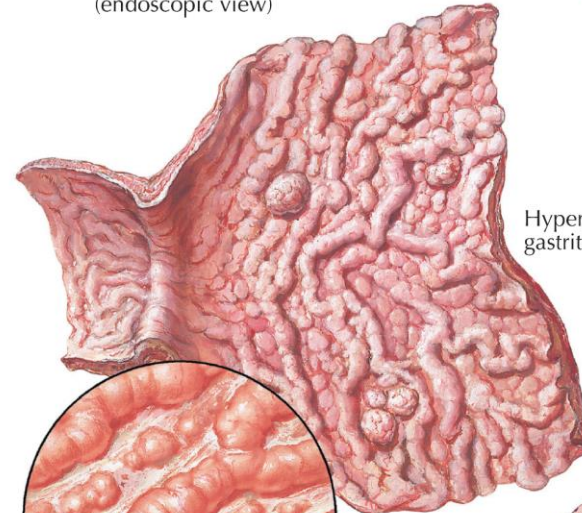


Acute gastritis
(endoscopic view)

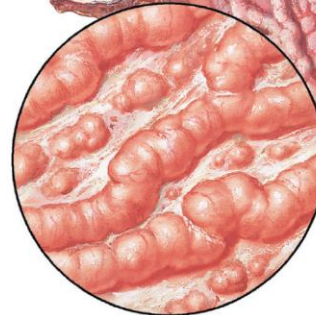
Atrophic gastritis



Endoscopic view



Hypertrophic gastritis



Endoscopic view



Erosive (hemorrhagic) gastritis

F. Netter
M.D.

Stomach Inflammation Chronic peptic ulcer disease

Pathogenesis

Most ulcers are caused by HP infection or NSAID use, both factors disrupt normal mucosal defense and repair, making the mucosa more susceptible to acid and pepsin

Other ulcerogenic effects: smoking, intake of steroids, hypergastrinemia, emotional stress

Duodenal ulcer: Increased production of gastric acid and HP-gastritis. The mechanism by which HP promotes duodenal ulcerogenesis is not known.

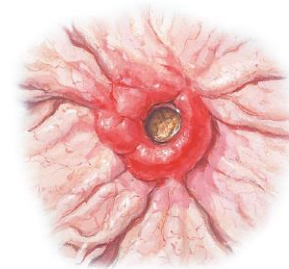
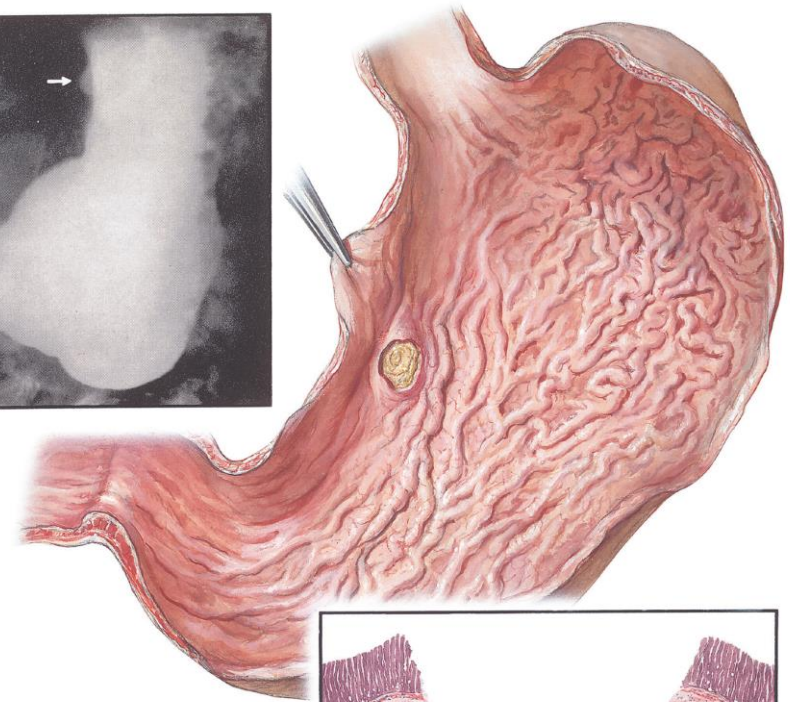
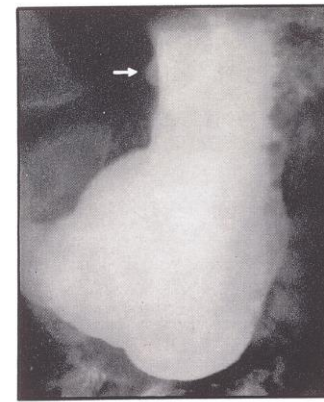
Morphology

Location

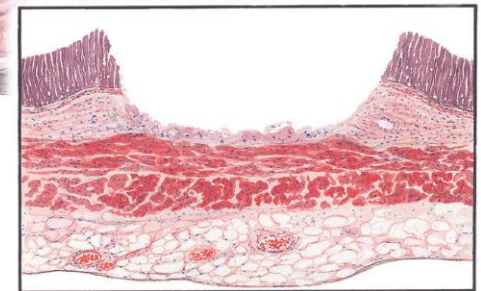
Stomach, usually the antrum and the lesser curvature

Postpyloric duodenum: in the first 2 cm-s distal to the pylorus on the anterior or posterior wall.

Within Barrett's mucosa in esophagus

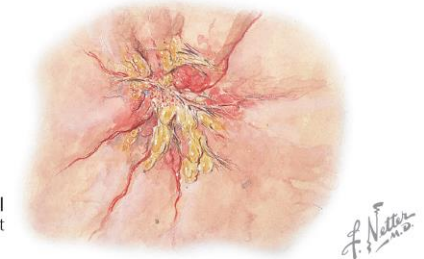


Mucosal aspect



Subacute ulcer

Subacute ulcer with chronic changes



Serosal aspect

Stomach

Inflammation

Chronic peptic ulcer disease

Gross

Single, sharply demarcated round ulcer 1 to 2.5 cm in diameter

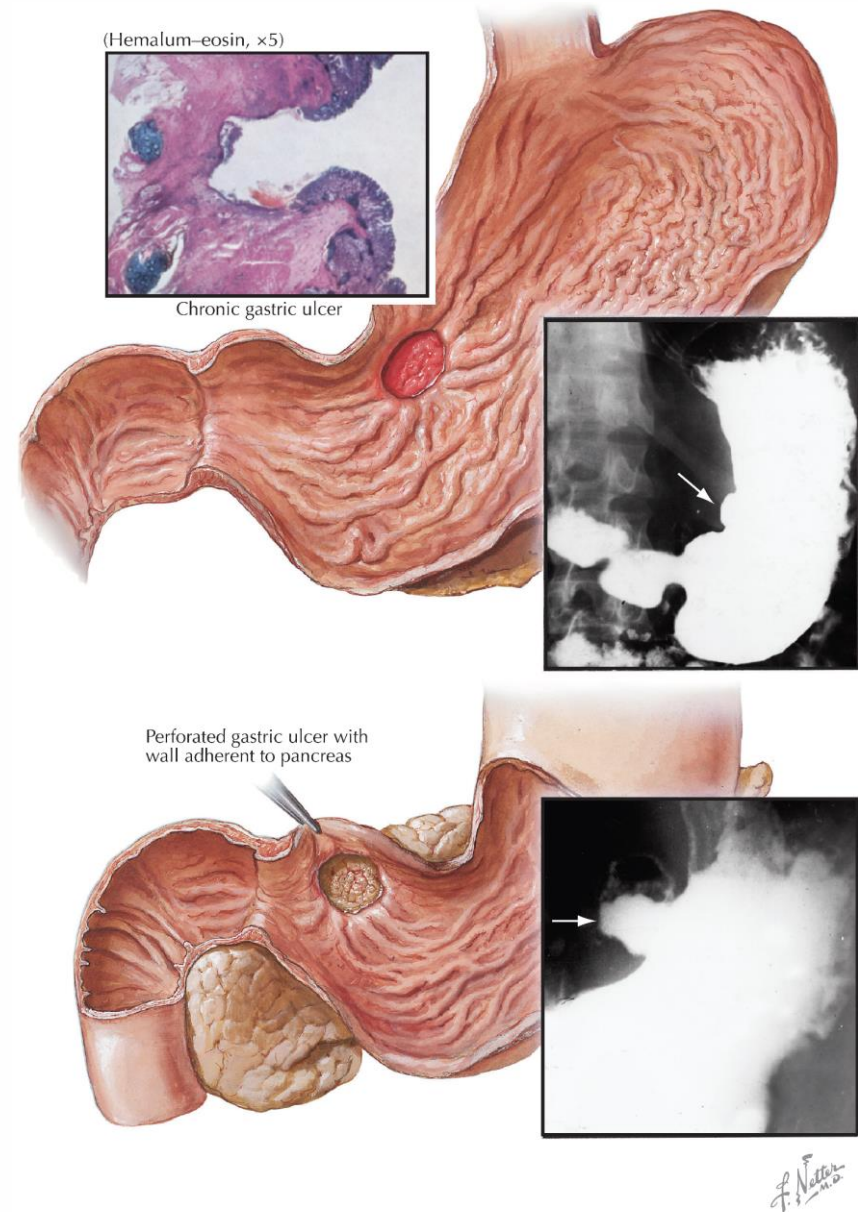
LM

The ulcer has 4 layers starting from the lumen to the muscle wall: 1) cell debris and neutrophils; 2) fibrinoid necrosis; 3) granulation tissue; 4) scar tissue

Healing: epithelium covers the defect, the muscle does not regenerate, fibrosis takes place at the site of the injury.

Clinical features

Epigastric pain relieved by food or antacids



**Stomach
Inflammation
Chronic peptic ulcer disease**

Complications

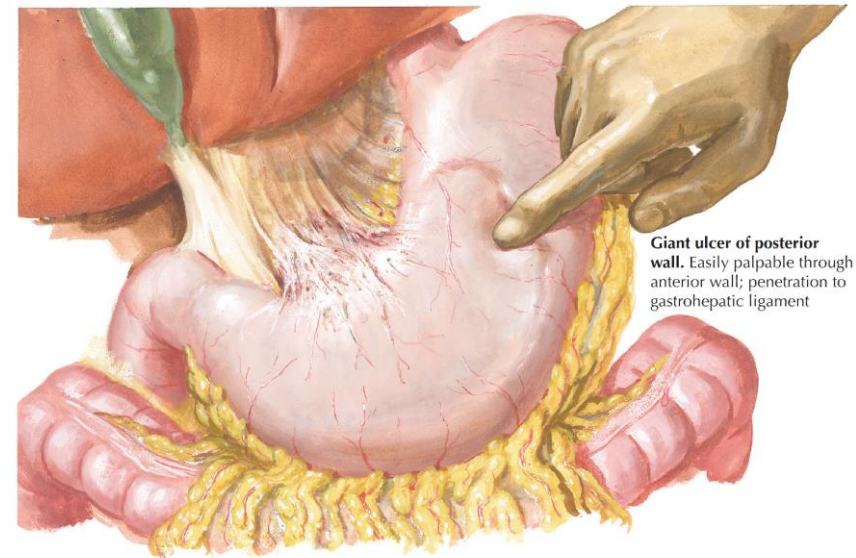
Gastric ulcer

Mild to severe hemorrhage from eroded vessels

Perforation, peritonitis

Pyloric stenosis due to the progressive shrinkage of fibrotic tissue, proximal stomach becomes greatly dilated; persistent vomiting

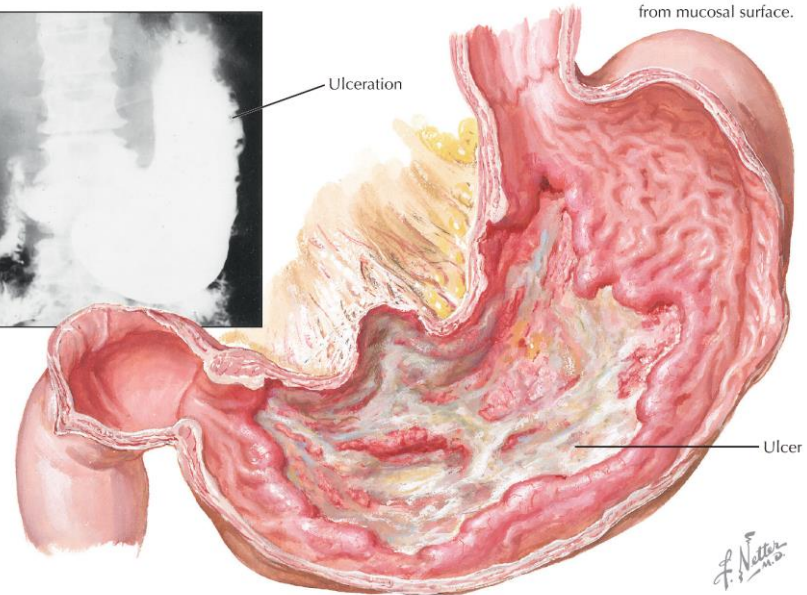
Malignant change



Giant ulcer of posterior wall. Easily palpable through anterior wall; penetration to gastrohepatic ligament



Giant ulcer. Same ulcer viewed from mucosal surface.



F. Netter M.D.

Stomach

Inflammation

Chronic peptic ulcer disease

Complications

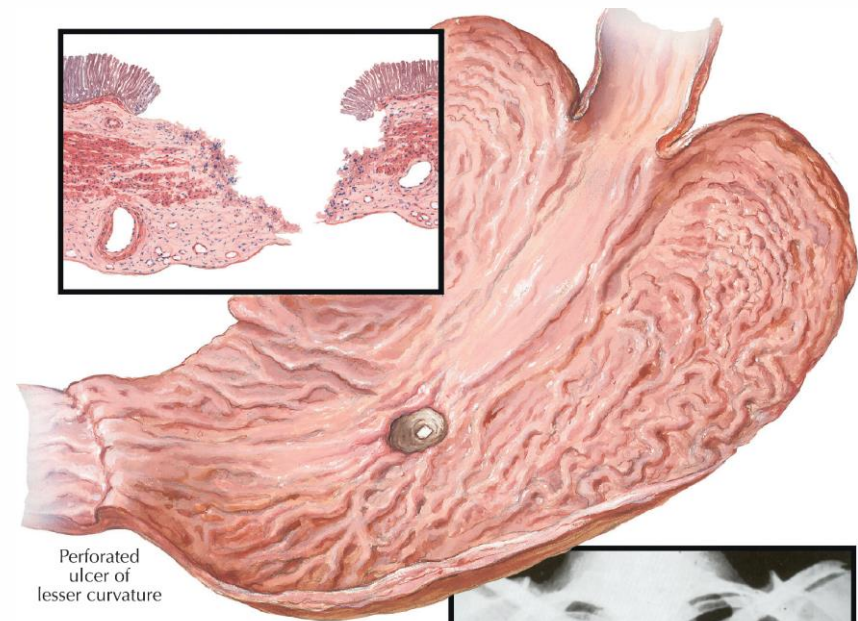
Gastric ulcer

Mild to severe hemorrhage from eroded vessels

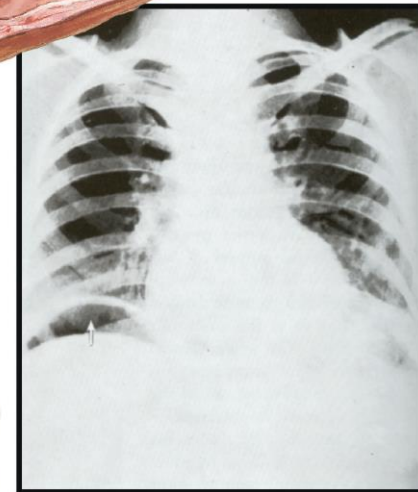
Perforation, peritonitis

Pyloric stenosis due to the progressive shrinkage of fibrotic tissue, proximal stomach becomes greatly dilated; persistent vomiting

Malignant change



Bleeding gastric ulcer



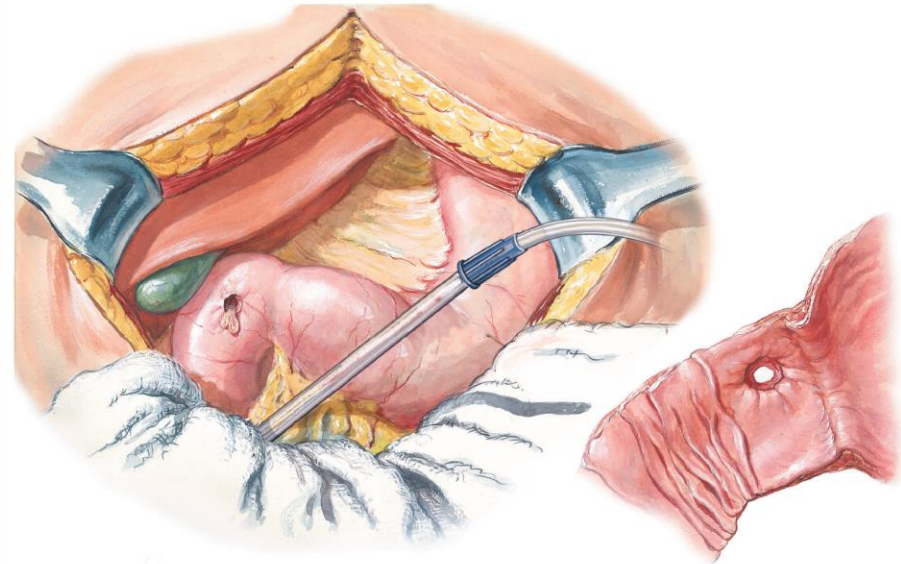
Air under right diaphragm resulting from perforated ulcer

F. Netter M.D.

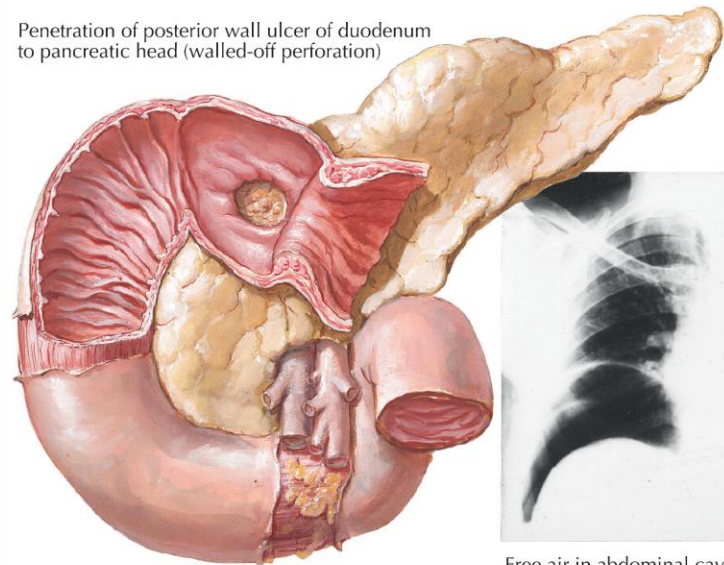
Stomach
Inflammation
Chronic peptic ulcer disease

Duodenal ulcer

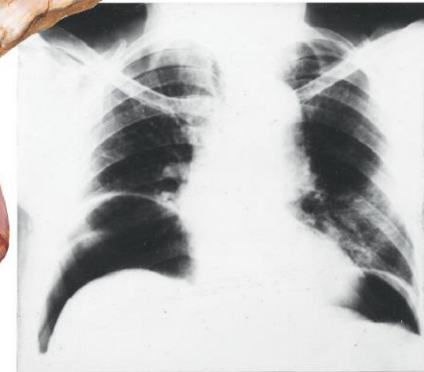
Penetration into the pancreas
Profuse bleeding from erosion of
branches of the superior pancreatico-
duodenal artery, hemorrhagic shock
Perforation, peritonitis
No risk of malignant transformation



Acute perforation of duodenal ulcer of anterior wall

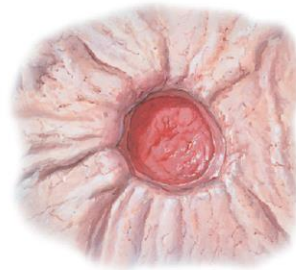


Penetration of posterior wall ulcer of duodenum
to pancreatic head (walled-off perforation)



Free air in abdominal cavity (subphrenic space)
following rupture of duodenal or gastric ulcer

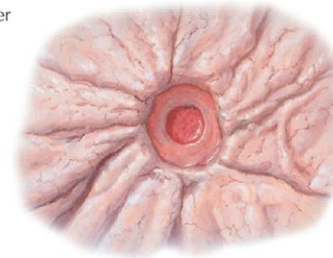
Stomach Inflammation Chronic peptic ulcer disease



Large gastric ulcer



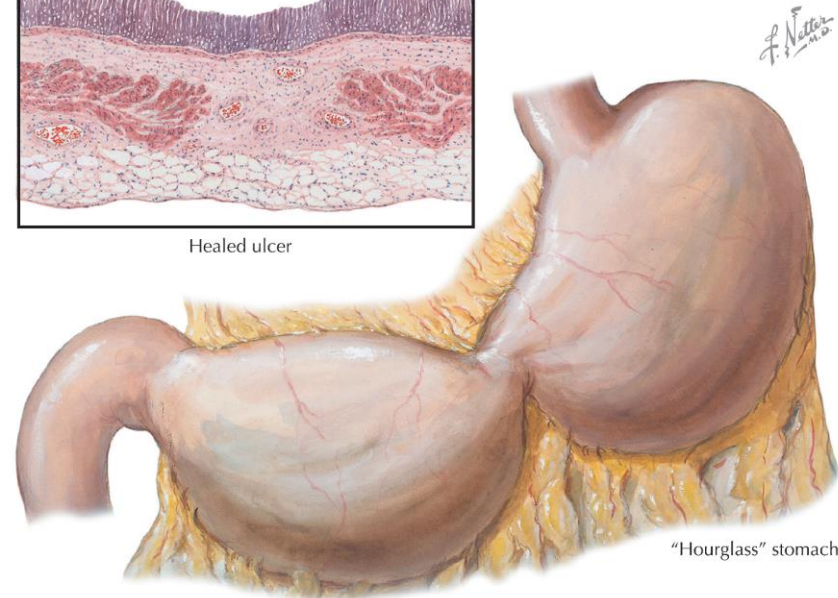
Healed with puckering



Diminution of size with progressive epithelization



Healed ulcer



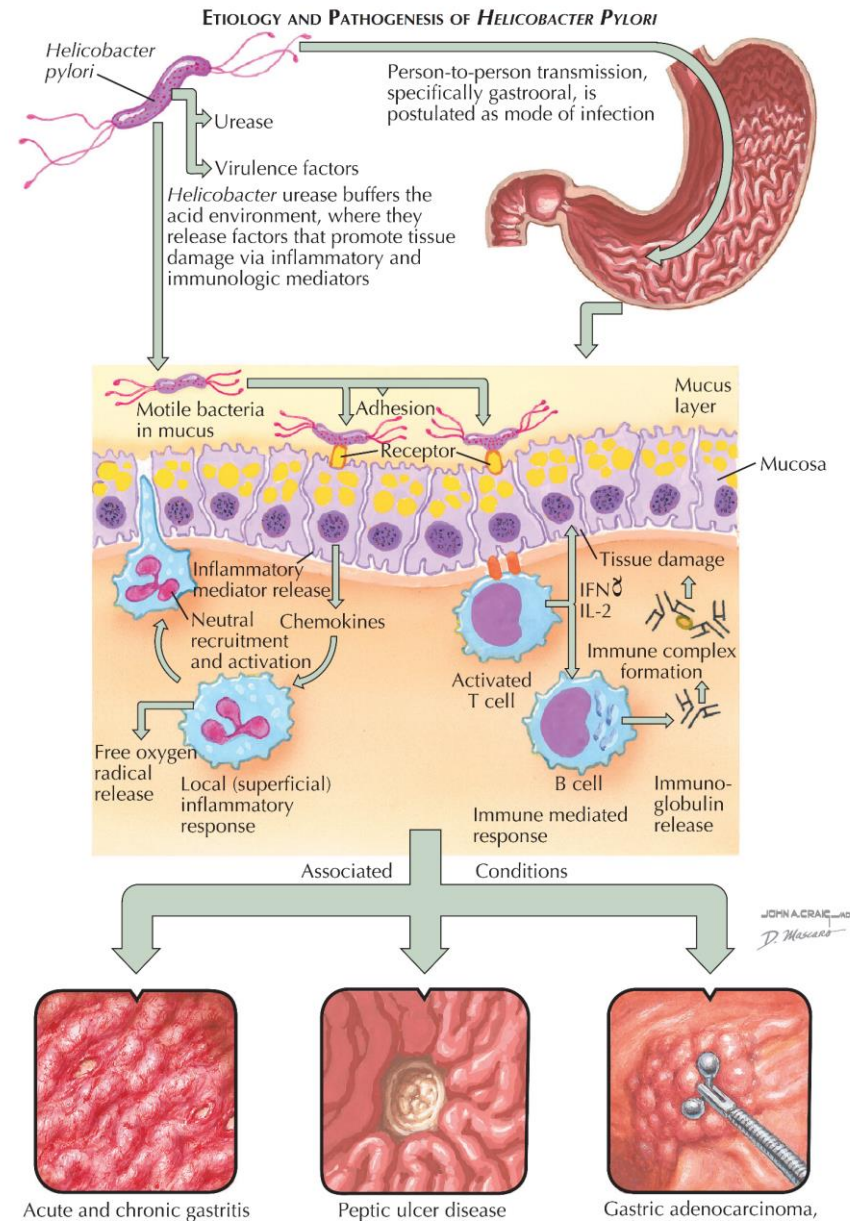
"Hourglass" stomach

Stomach Inflammation Helicobacter pylori-induced gastritis

(„Environmental Metaplastic Atrophic Gastritis”
[EMAG])

Pathogenesis

- HP microbes colonize on the gastric mucosal surface and cause damage to the mucosa
- The bacterium is protected from the acidic gastric juice by its capability to neutralise hydrogen ions by urease and ammonium production



Stomach Inflammation Helicobacter pylori-induced gastritis

Morphology

Chronic active gastritis: lymphocytes and plasma cells infiltrate the lamina propria, and neutrophils infiltrate the glands

Inflammatory changes can lead to

- intestinal metaplasia: replacement of glandular epithelium by columnar absorptive cells and goblet cells
- atrophic gastritis: loss of the gastric glands, endoscopically visible thinning of the mucosa
- dysplasia in the glands, precursor of invasive carcinoma

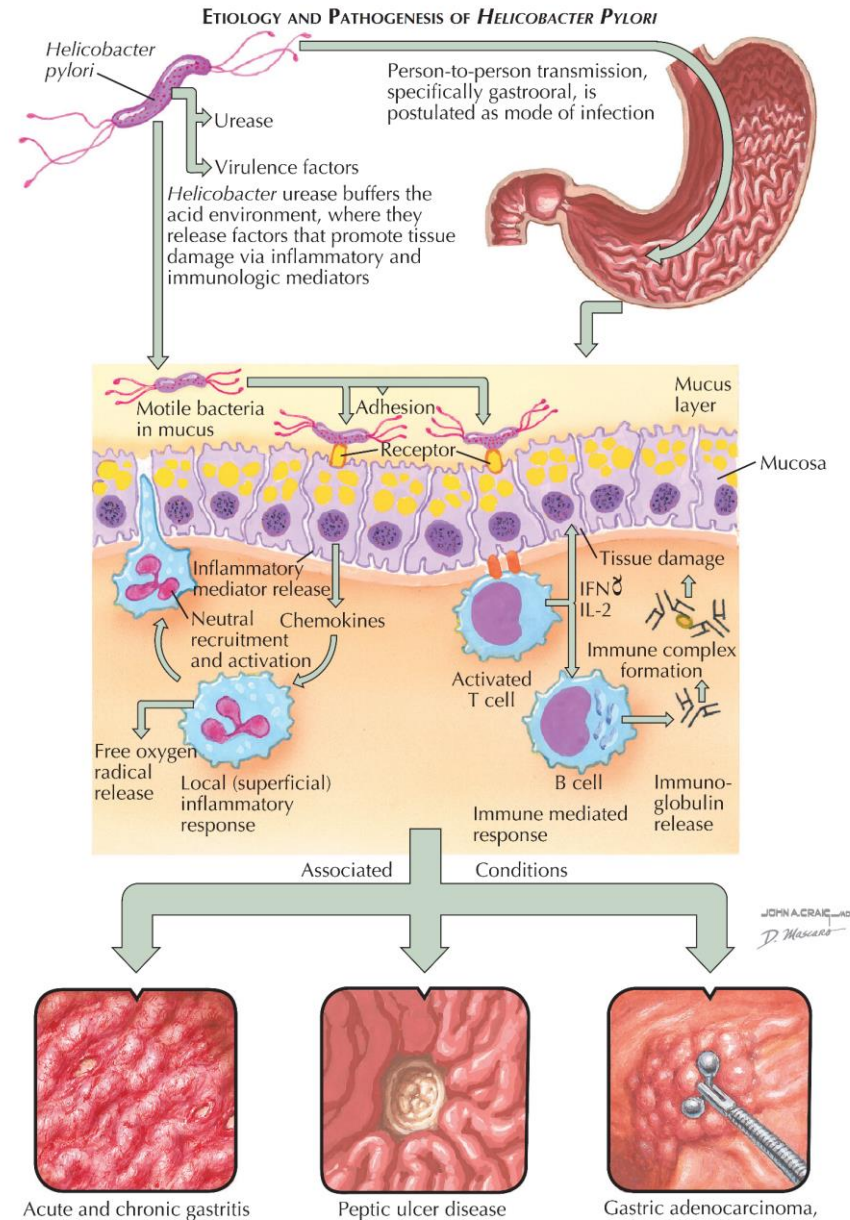
Clinical features

The majority of patients have no symptoms

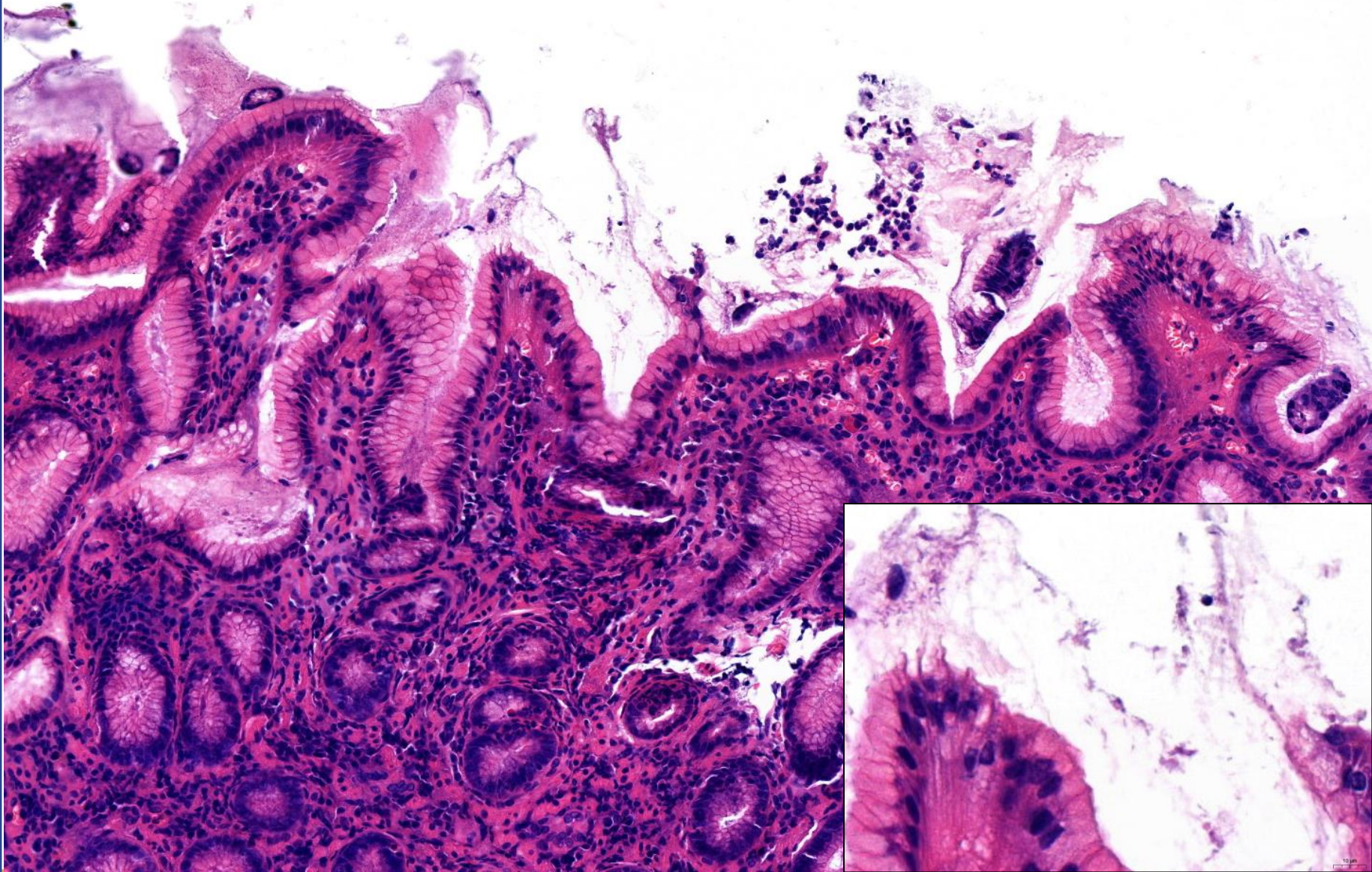
Patients with antral predominant gastritis have high HCl production and frequently develop duodenal peptic ulcer

Patients with multifocal atrophic gastritis have decreased acid production, may develop gastric peptic ulcers and have an increased risk for gastric adenocarcinoma

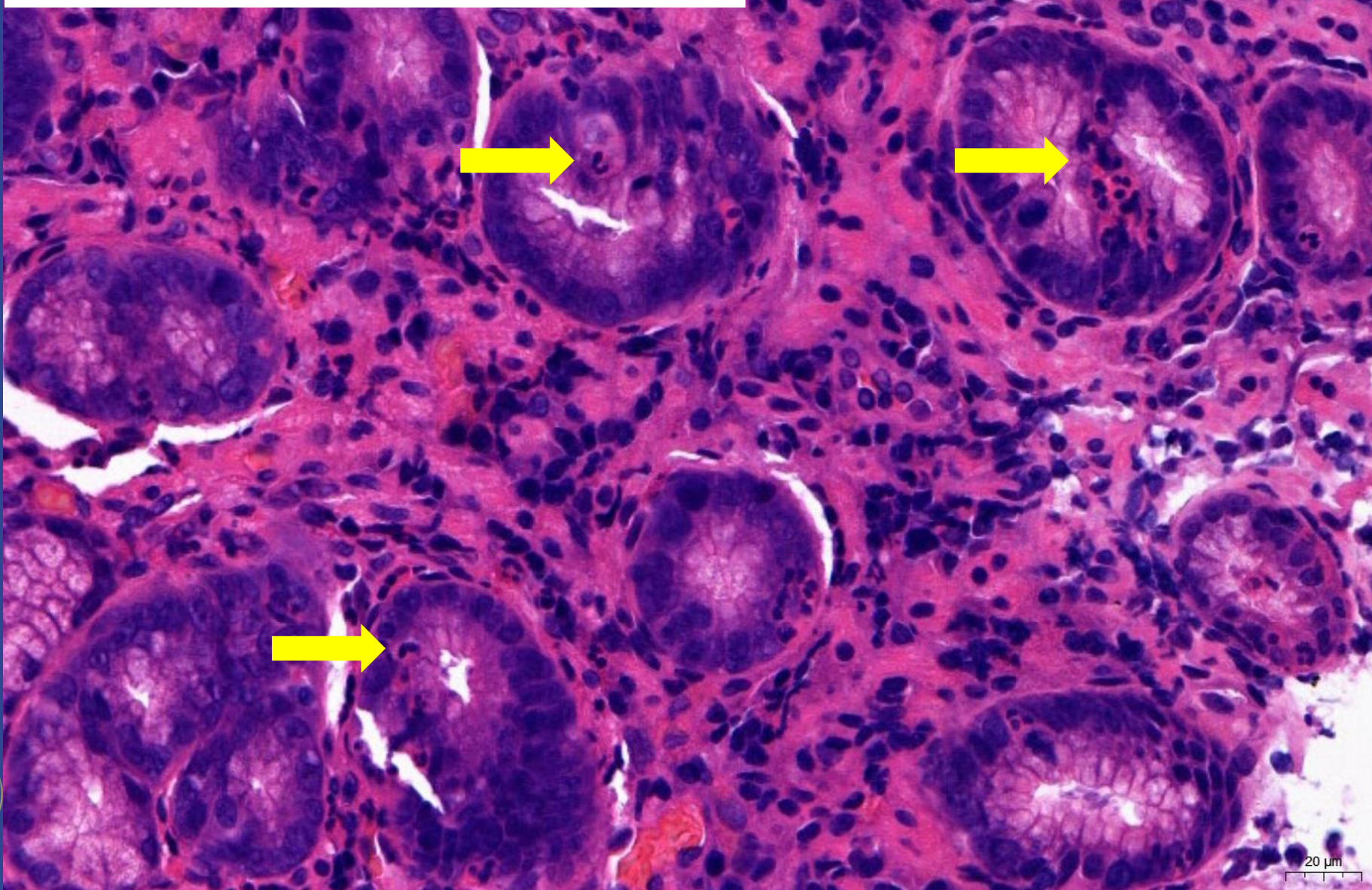
MALT-lymphomas may develop in H. pylori associated gastritis (MALT: Mucosa-Associated Lymphoid Tissue)



Helicobacter pylori-induced gastritis



Helicobacter pylori-induced gastritis



Stomach Tumor Benign

Hyperplastic polyps

Non-neoplastic small, often multiple polyps;
mostly in the antrum

Seen in the setting of chronic gastritis

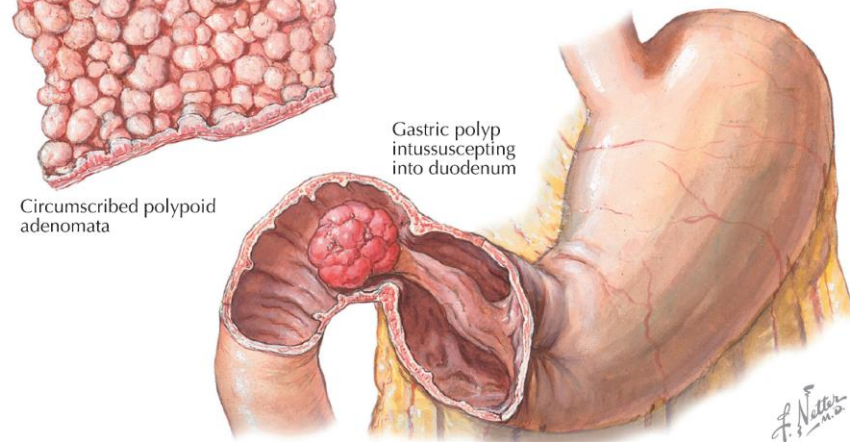
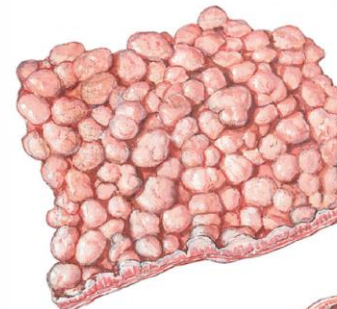
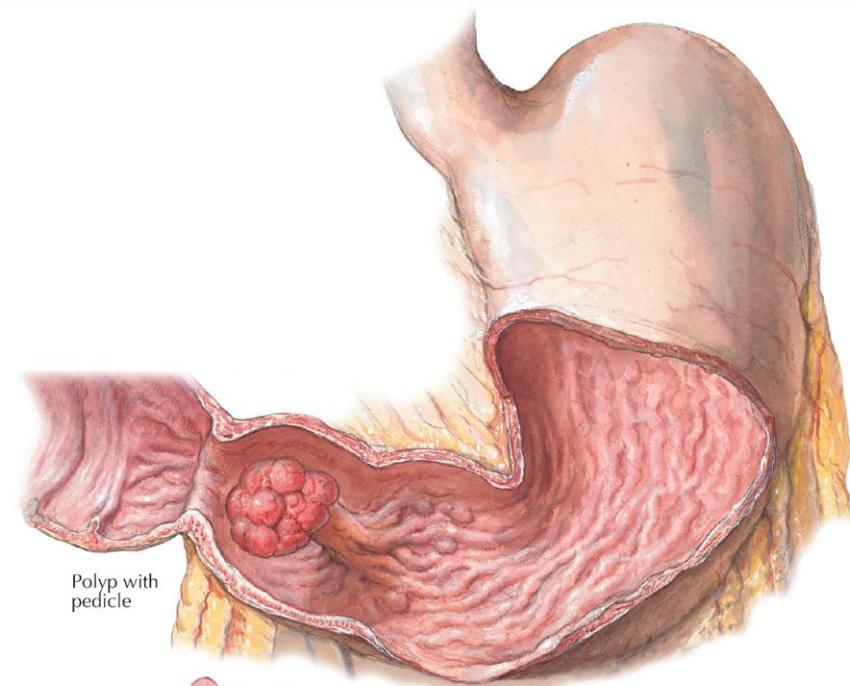
Adenomatous polyps

True neoplasms; strong potential for malignant
change

Gross: solitary, greater than 1 cm; mainly in the
antrum

LM: resemble to colon adenomas

- tubular, villous or tubulovillous architecture
- low grade or high grade dysplasia in the
neoplastic glands



Stomach Tumor

Non-epithelial tumors (rare)

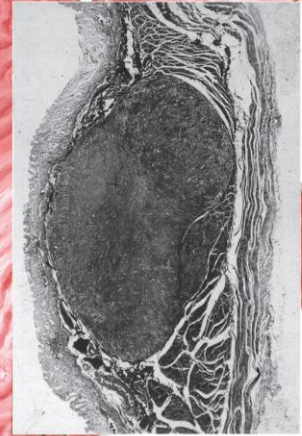
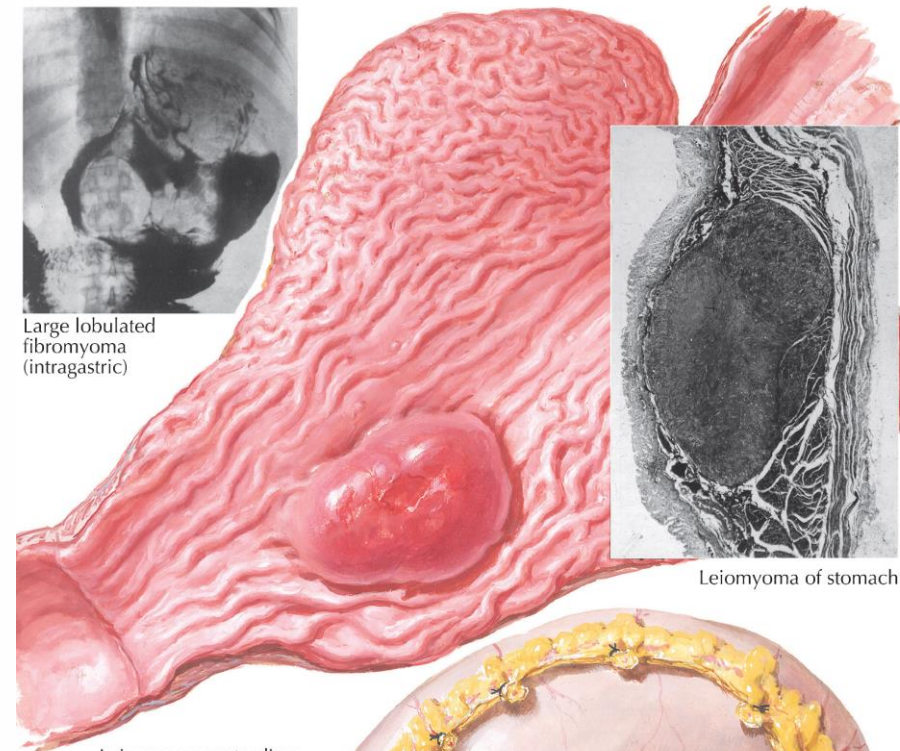
Gastrointestinal stromal tumor (GIST)

Lymphoma

Neuroendocrine tumors

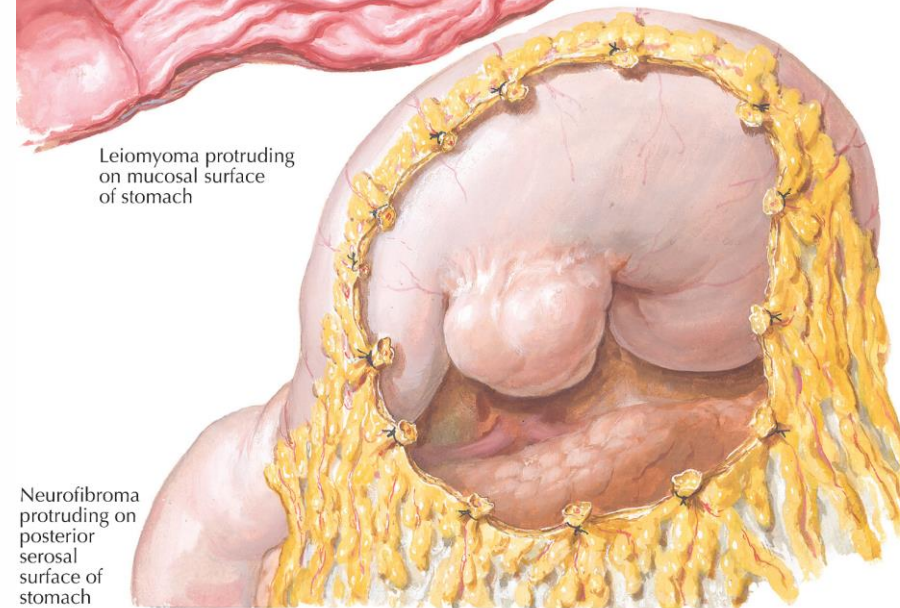


Large lobulated
fibromyoma
(intra-gastric)



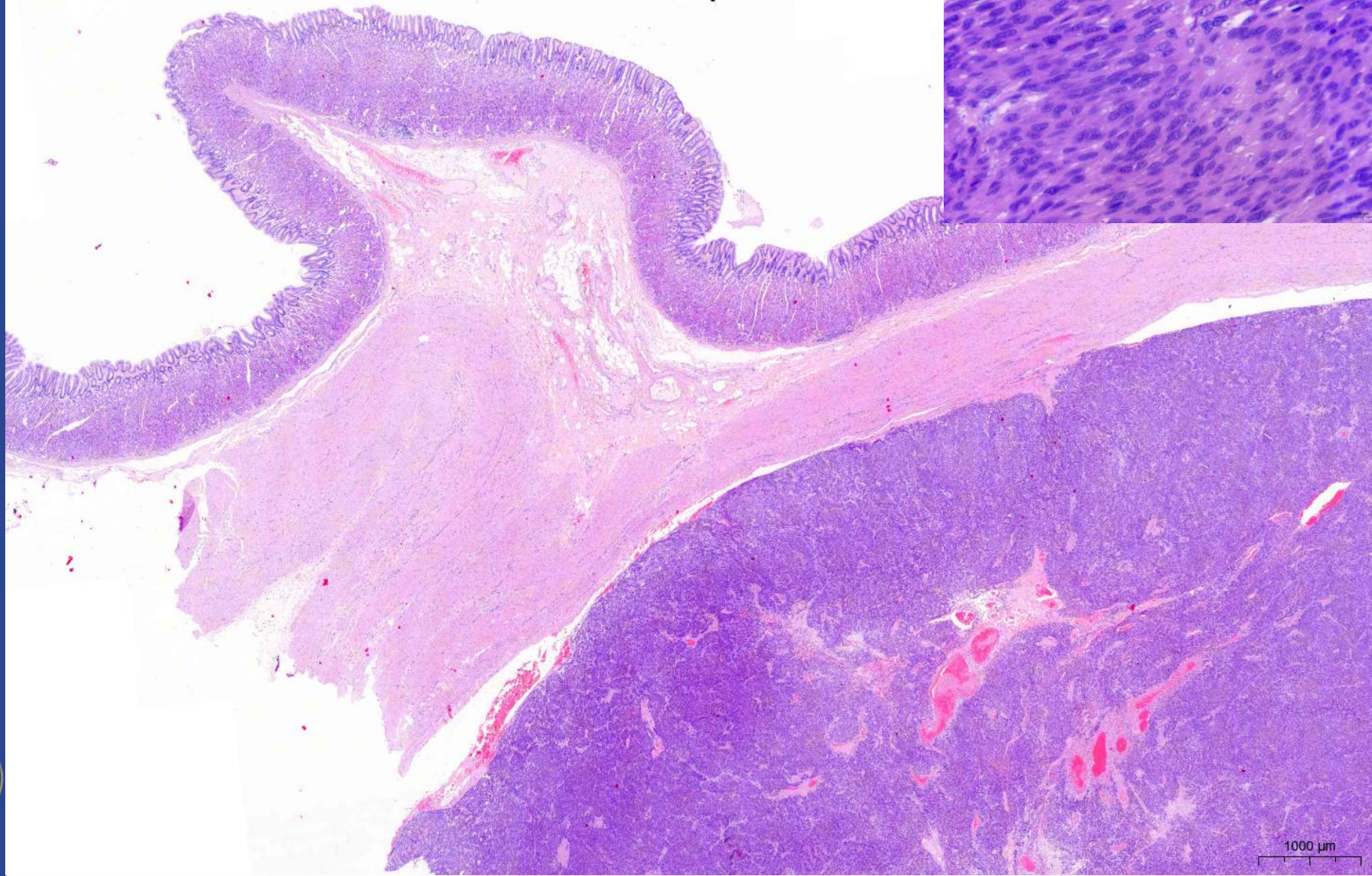
Leiomyoma of stomach

Leiomyoma protruding
on mucosal
surface
of stomach



Neurofibroma
protruding on
posterior
serosal
surface of
stomach

Gastrointestinal stromal tumor (GIST)



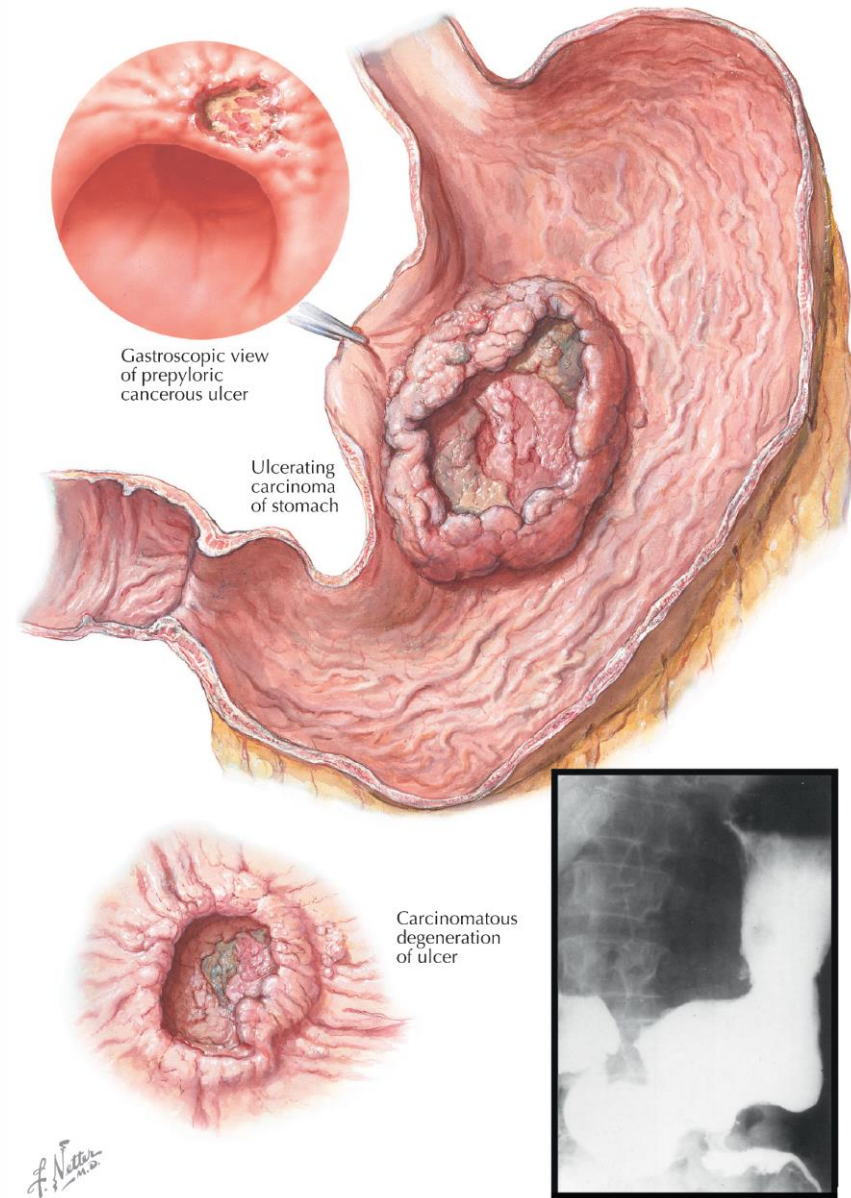
Stomach Tumor Adenocarcinoma

Classification

Lightmicroscopically *intestinal* adenocarcinoma - grossly expansive growth pattern

Lightmicroscopically *diffuse* adenocarcinoma - grossly infiltrative growth pattern

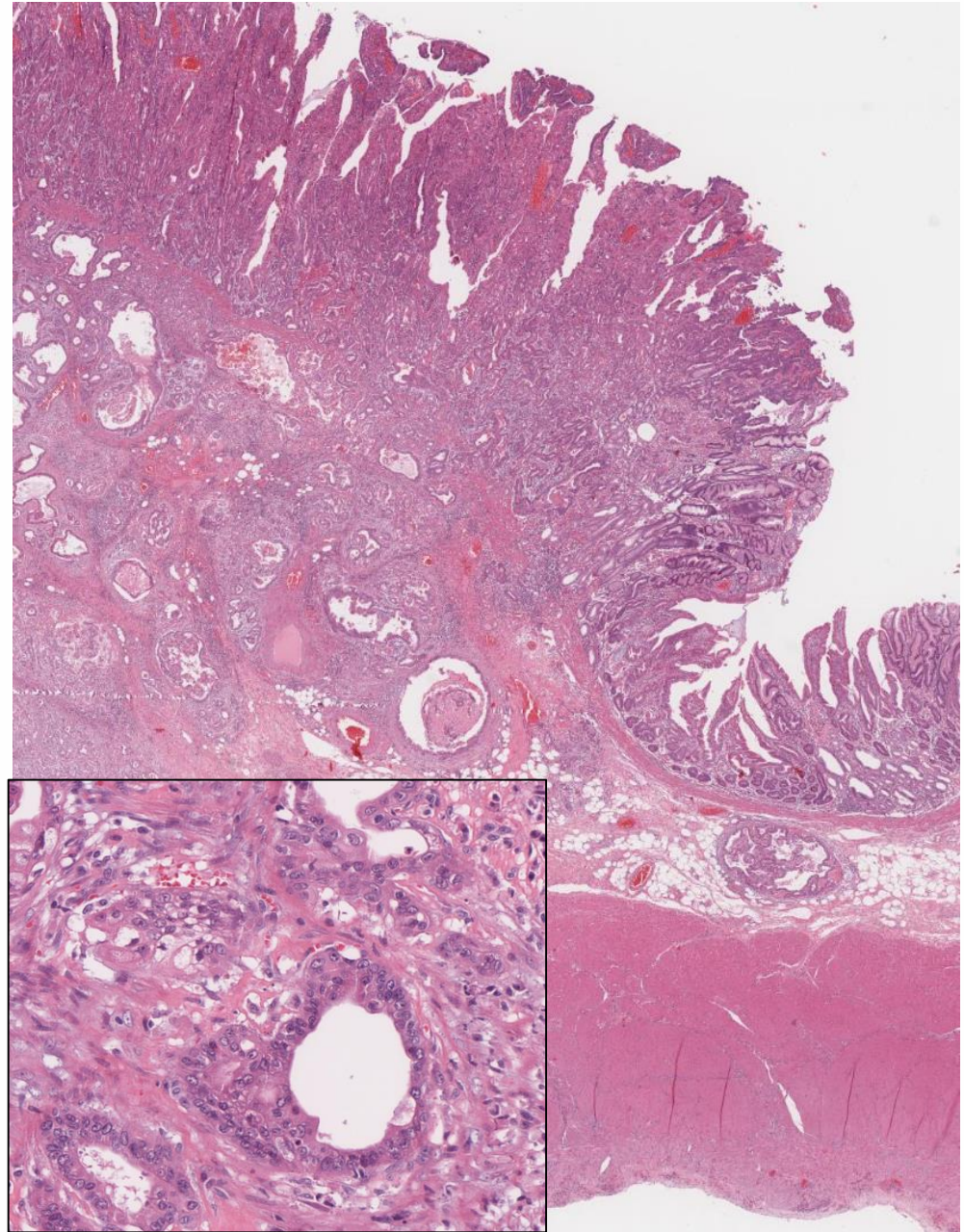
Lightmicroscopically *mixed/indeterminate* adenocarcinoma



Stomach Tumor Adenocarcinoma

Intestinal type: precursors are intestinal metaplasia or adenoma
Similar to adenocarcinoma of the large intestine.

Better prognosis than the diffuse type.



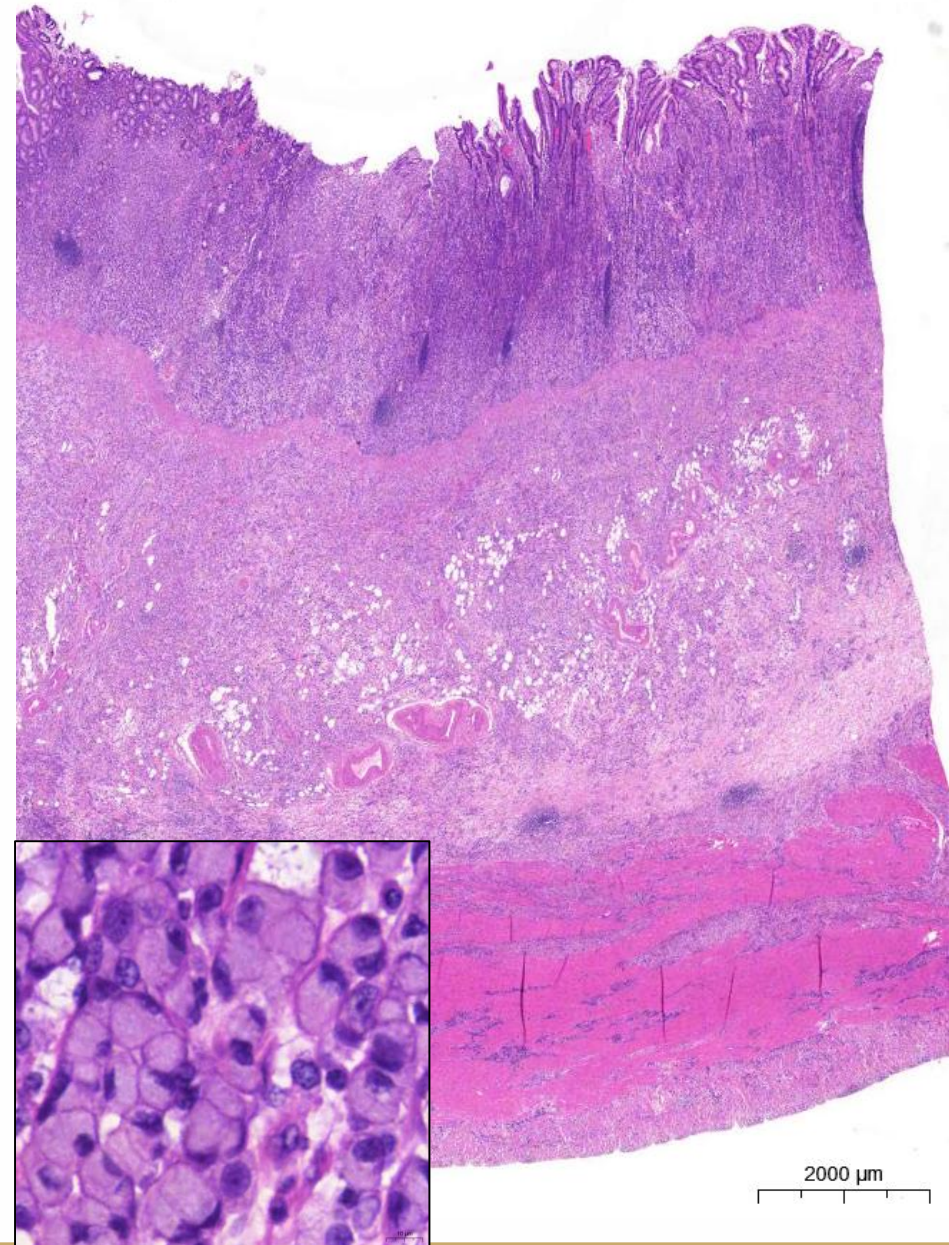
Stomach Tumor Adenocarcinoma

Diffuse type: derived from *gastric mucous cells*

The mucosa and the gastric wall is diffusely infiltrated by scattered, individual tumor cells or small clusters of cells.

Not rarely, mucus secretion produces signet-ring conformation: signet-ring carcinoma. Tumor cells often evoke a strong desmoplastic reaction, linitis plastica.

Highly malignant; poor prognosis.



Stomach Tumor Adenocarcinoma

High incidence in Finland, Russia, Japan, Chorea, and Latin America

Risk factors for *intestinal type*

Environmental factors: HP-gastritis; diet high in smoked and/or salt-preserved foods and low in fruits and vegetables; alcohol consumption (especially beer); smoking

Precancerous lesions: gastric adenomas; chronic autoimmune gastritis

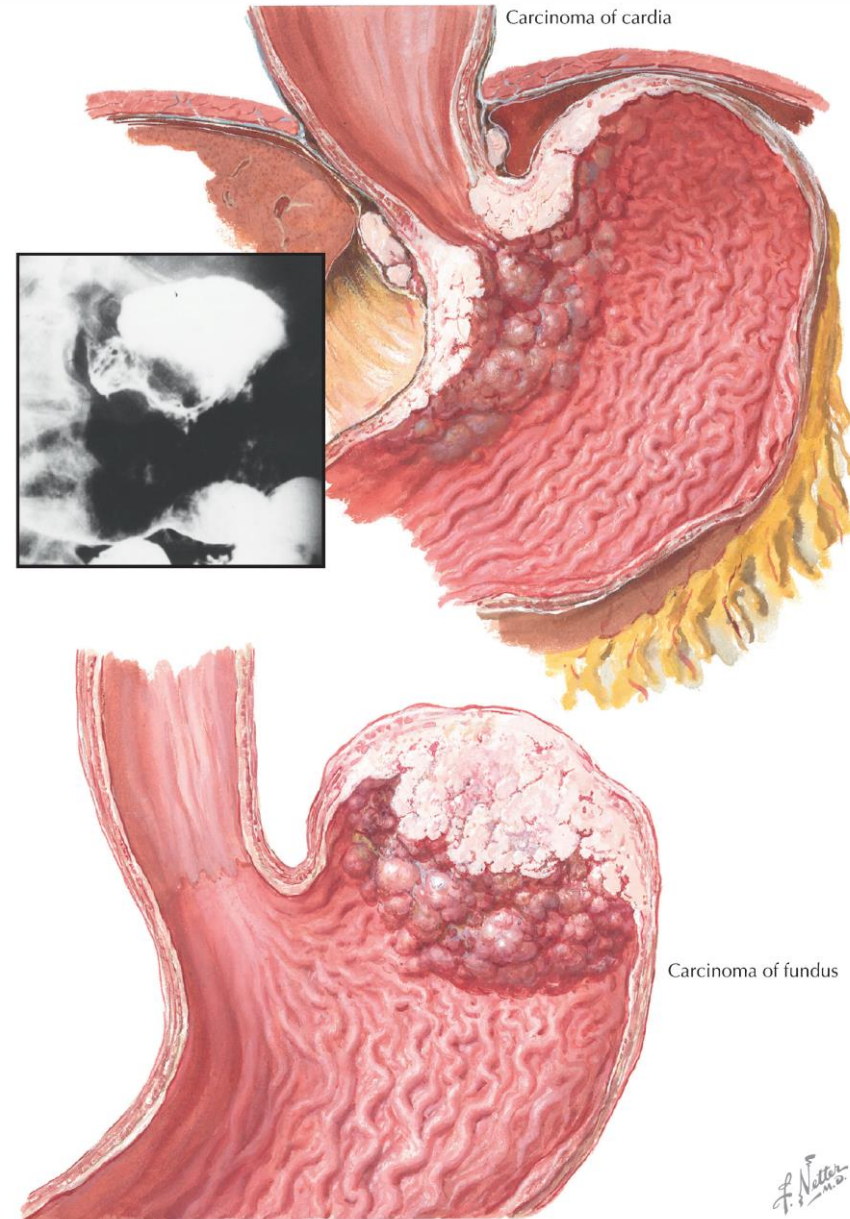
On occasion, oncogenic mutations: HER2, Beta-catenin, APC

Risk factors for *diffuse type*

Not well defined

Germ cell mutation of the epithelial-cadherin gene (CDH1) in hereditary diffuse gastric cancer syndrome (rare)

E-cadherins are found in adherens junctions (zonulae adherentes) to bind cells within epithelial tissues together



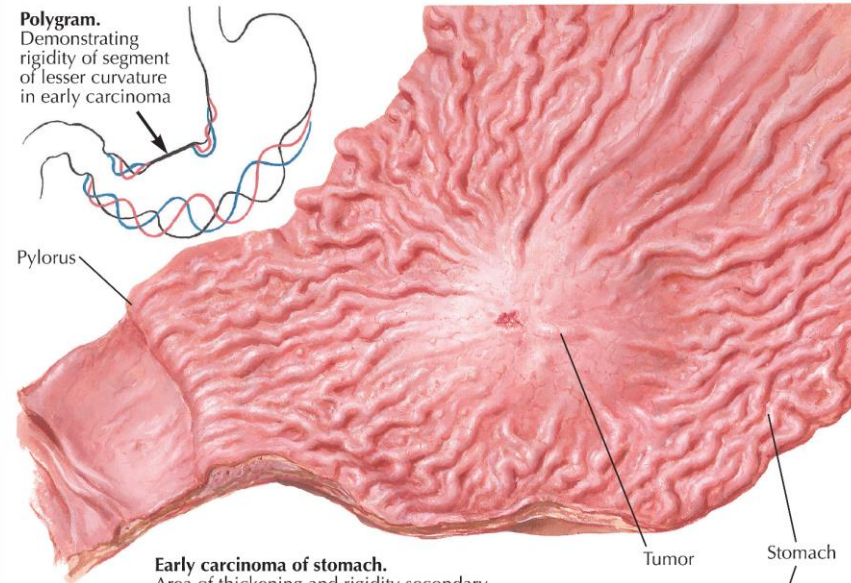
Stomach Tumor Adenocarcinoma

Makro

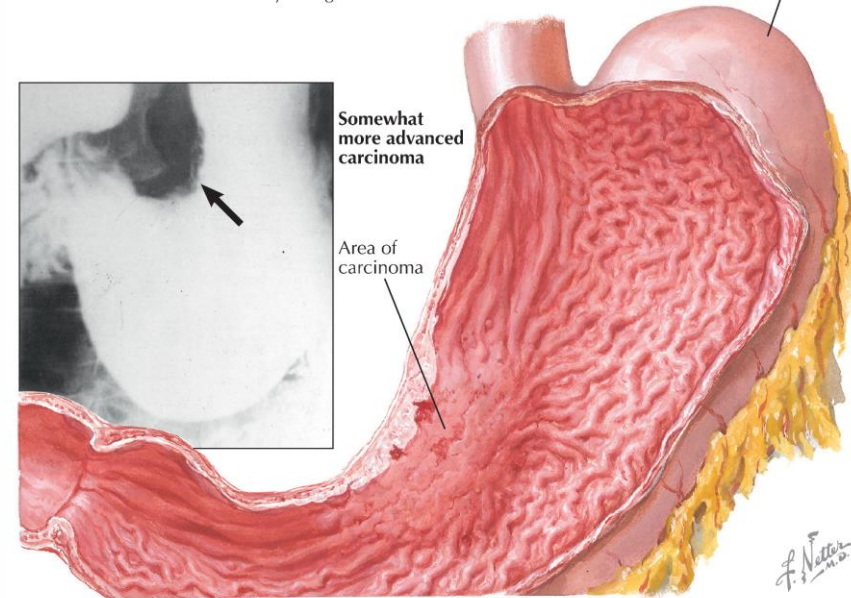
Early stomach tumor

Polypoid (>3 mm) or flat lesion.

Could be missed during endoscopy.



Early carcinoma of stomach.
Area of thickening and rigidity secondary to infiltration by malignant cells



Stomach Tumor Adenocarcinoma

Gross

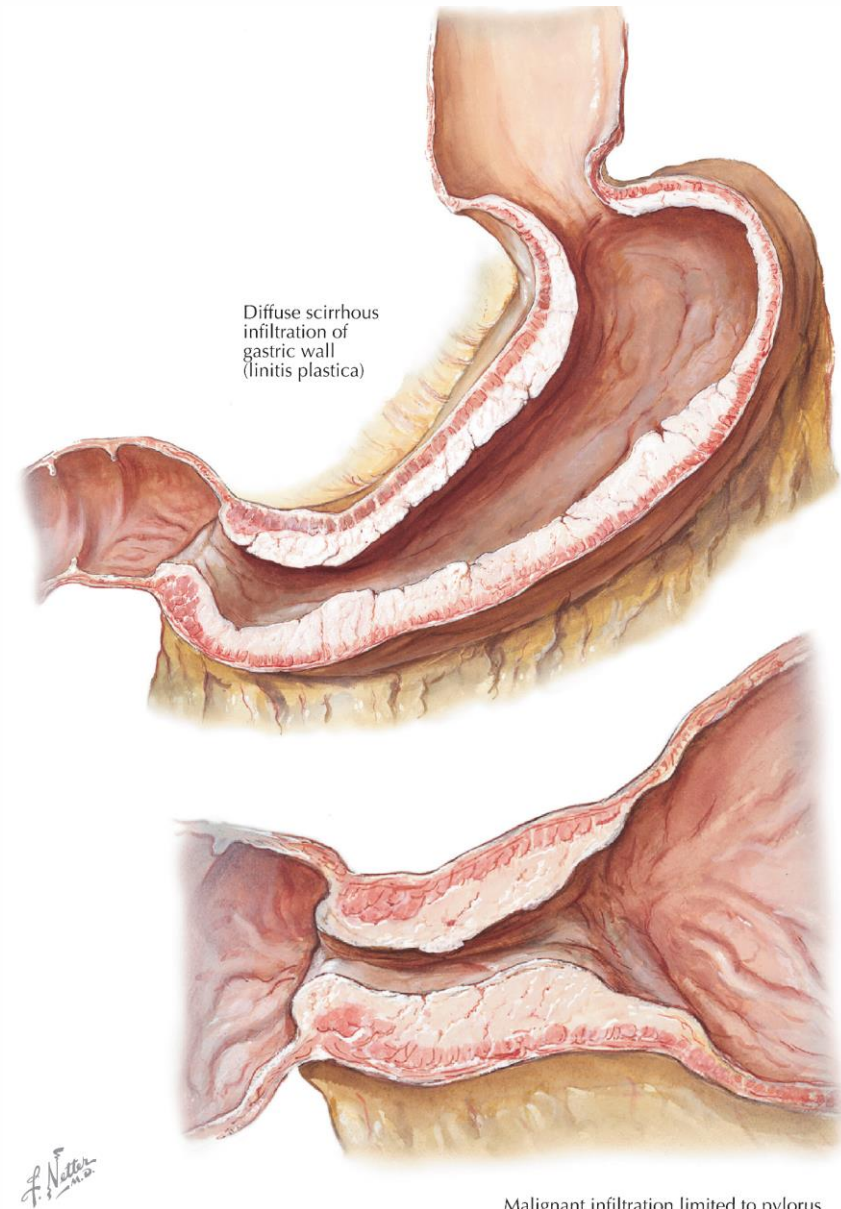
Favoured locations: 50-60 % lesser curvature of the antropyloric region; 25 % - cardia

Macroscopical types:

Expansive: polypoid-fungating

Infiltrative: flat or depressed; no obvious tumour mass is visible on the mucosal surface; however, the gastric wall becomes thickened by the tumorous infiltration; linitis plastica (tube-like alteration of the stomach) in advanced cases

Excavated-ulcerated



Stomach Tumor Adenocarcinoma

Patterns of spread

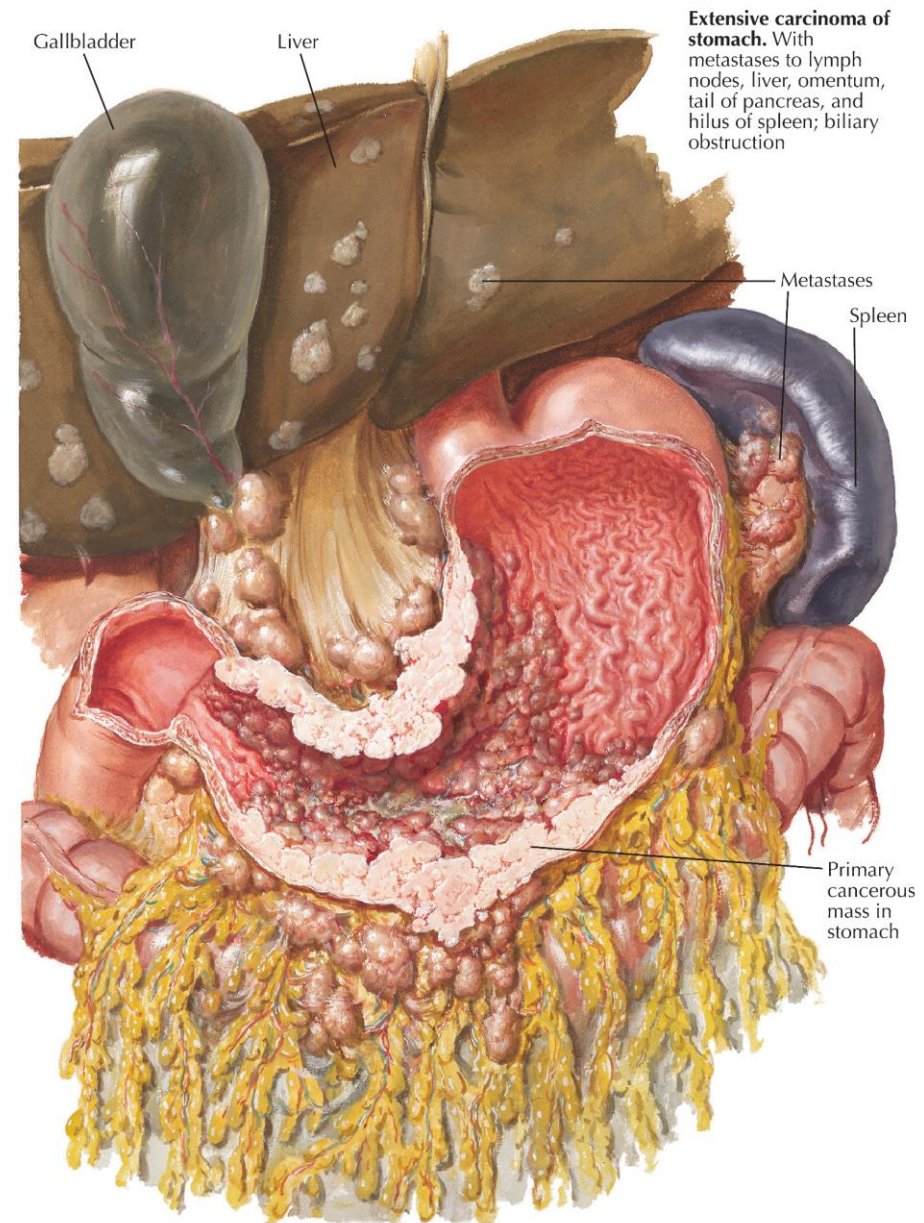
Directly to the serosa; local invasion of the duodenum, pancreas, and retroperitoneum

Peritoneal dissemination: carcinosis of peritoneum

Lymphatic metastases: local lymph nodes; Virchow node: supraclavicular lymph node

Retrograde lymphatic spread: signet-ring carcinoma metastasis to both ovaries (Krukenberg tumor)

Hematogenous metastases: liver



Stomach Tumor Adenocarcinoma

Stage

Early gastric cc

Confines to either the mucosa or submucosa, without or with regional lymph node metastasis.

5-y survival rate: 80-90%.

Advanced gastric cc

Extends into or beyond the tunica muscularis

5-y survival rate: 10%

Clinical features

Early carcinomas

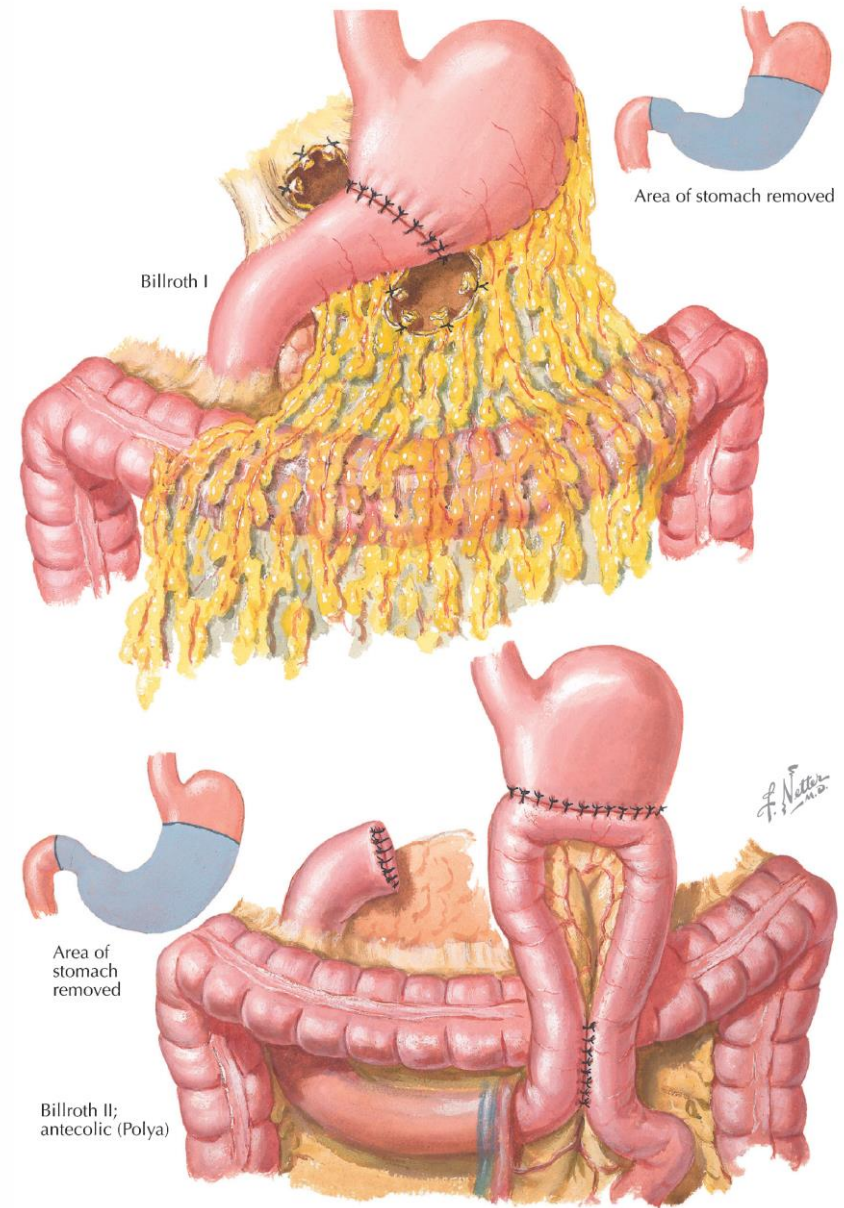
No symptoms

Advanced carcinomas

Pain in the upper abdomen, vomiting, melena

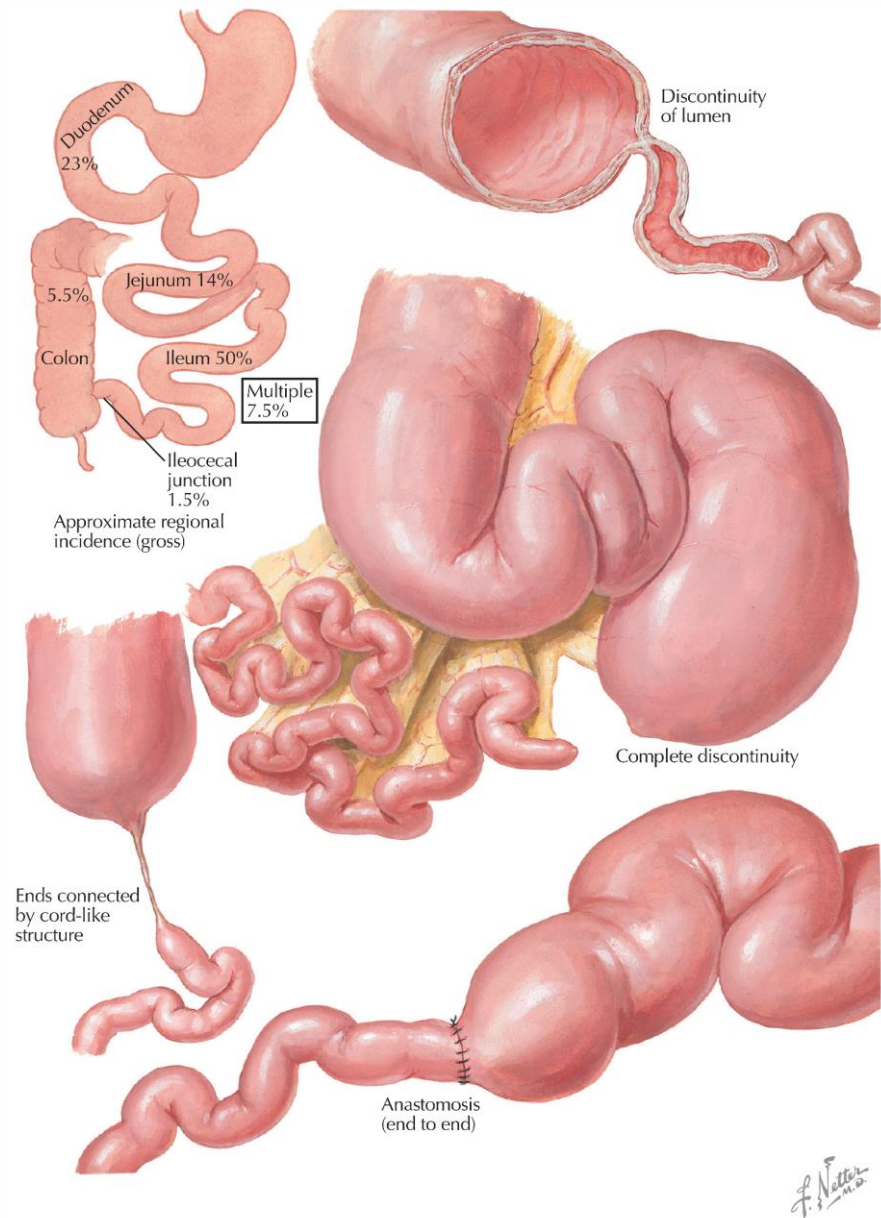
Weight loss, weakness or fatigue associated with anemia

Tumorous ascites



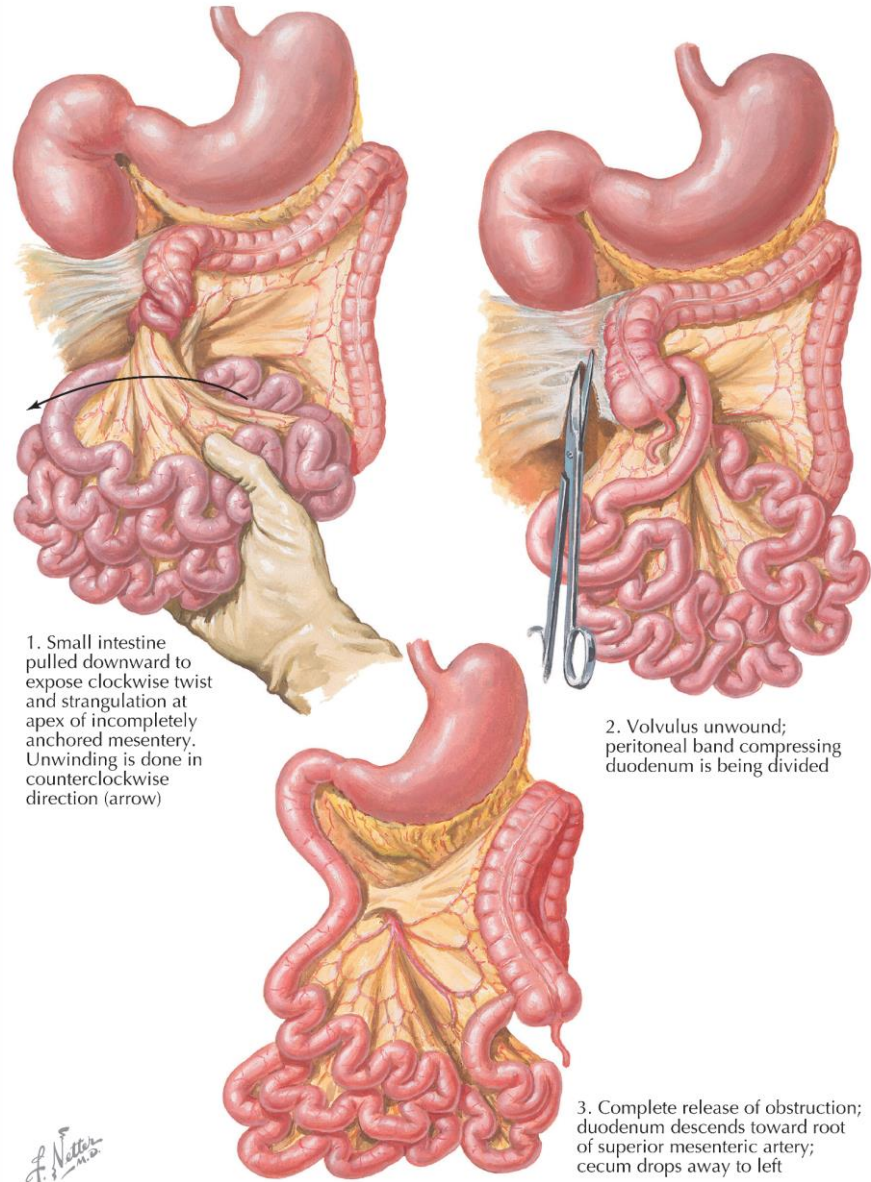
Small intestine

Developmental malformation



Small intestine

Developmental malformation



Small intestine Developmental malformation Hernia

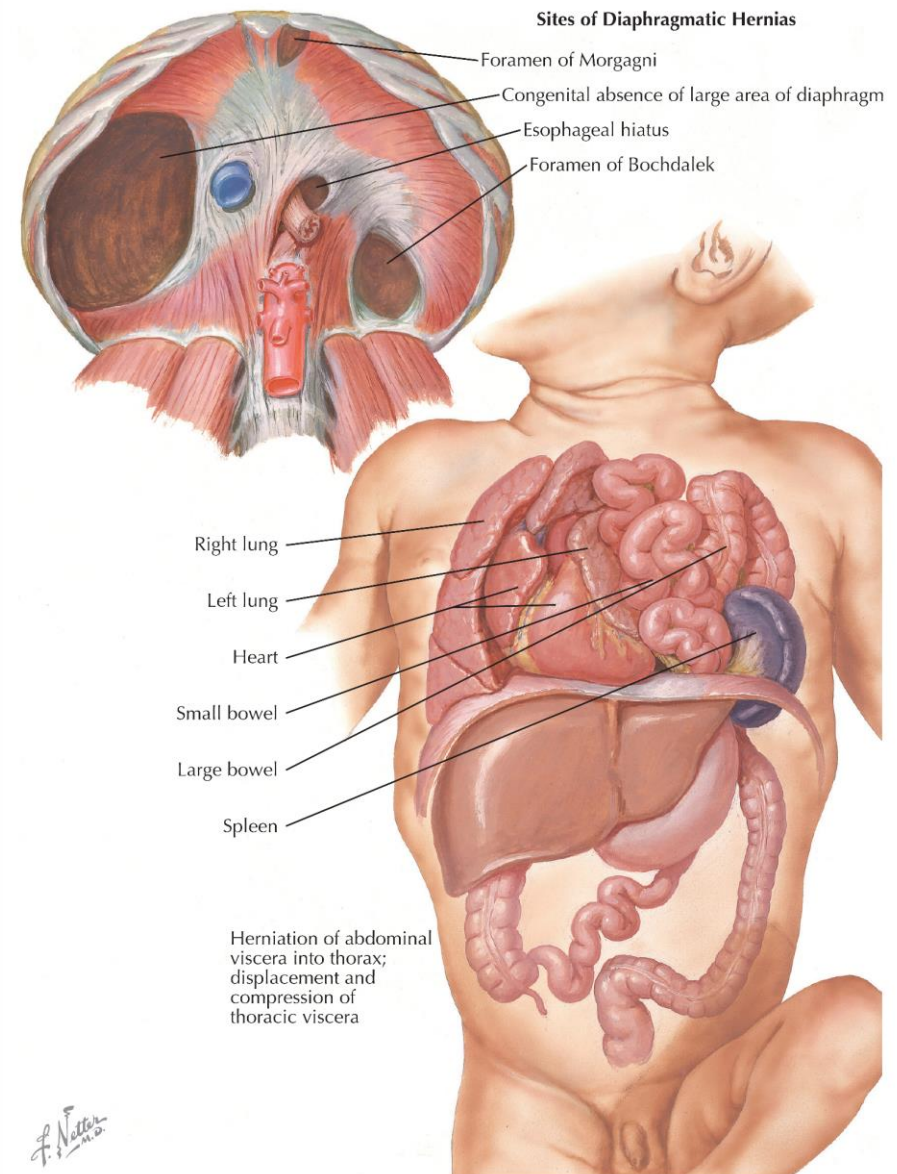
Abnormal exit of tissue or an organ, such as the bowel, through the wall of the cavity in which it normally resides.

Congenital diaphragmatic hernia

A posterolateral defect in the diaphragm, which permits abdominal organs to localize in the thorax.

Dyspnea and cyanosis of the newborn due to the displacement and hypoplasia of lungs.

Large defects are lethal.



Small intestine Hernia

Incarcerated hernia

Hernia: a weakness or defect in the wall of the abdominal cavity permits protrusion of a pouch-like, serosa-lined sac of peritoneum (hernial sac)

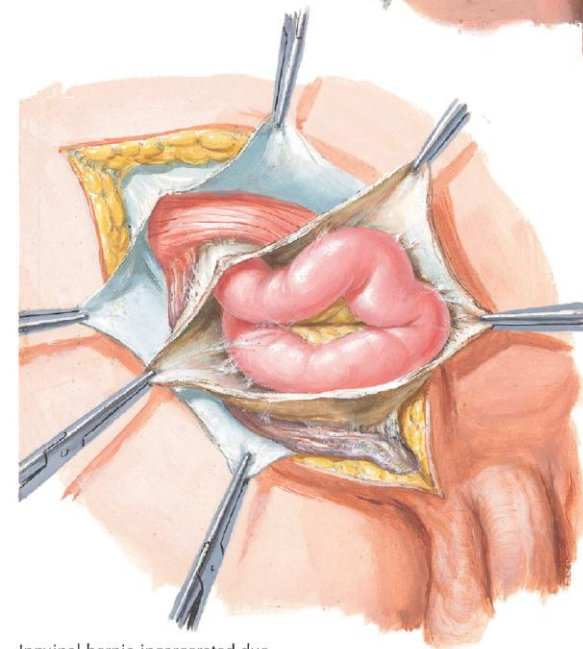
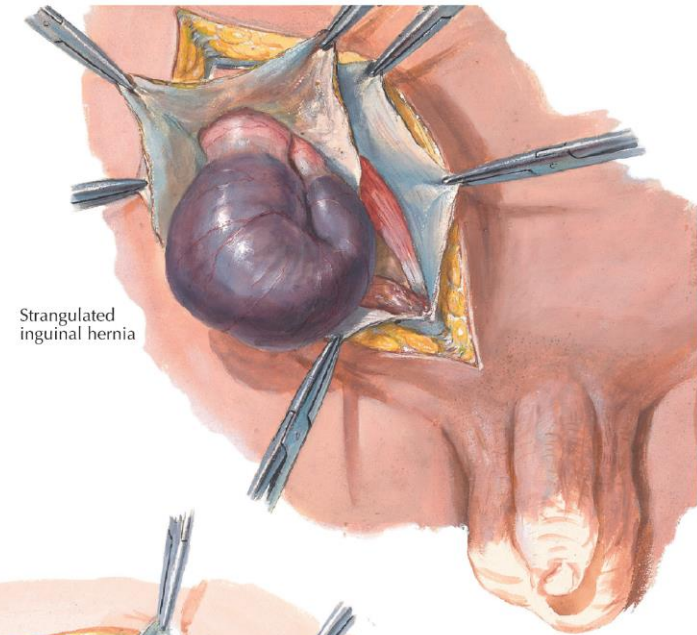
Usual sites:

- inguinal and femoral canals
- umbilicus
- surgical scars

Clinical features

Most hernias are reducible, the herniated contents can be manipulated back into the abdominal cavity

However, bowel loops may become trapped within the hernia sac (incarceration), compromise of lymphatic, venous and, finally, arterial circulation (strangulation), hemorrhagic infarction of the trapped bowel segment



Inguinal hernia incarcerated due to old thickened sac and adhesions

F. Netter M.D.

Small intestine

Disturbance of blood supply

Ischaemic bowel disease

Ischemia causes pathologic changes when the perfusion of the intestines declines below 50% of normal

Ischemia due to occlusion, transmural infarction

Ischemia due to stenosis, mucosal or mural infarction

Occlusive ischemia

The trunk of superior mesenteric artery is occluded by thrombosis over ruptured atheroma (frequent) or embolism

Consequence

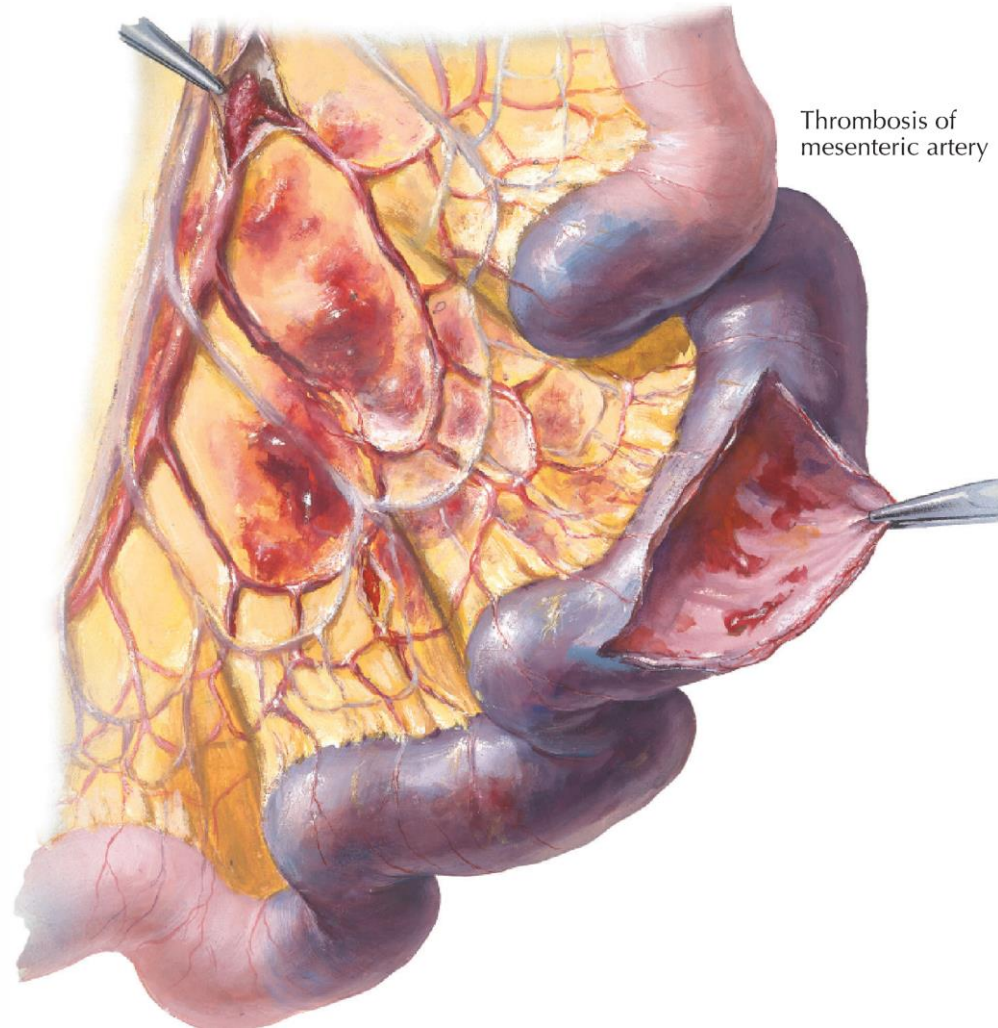
Transmural hemorrhagic infarction of the small bowel (*the necrotic area is reperfused by the blood coming from numerous anastomoses in the intestines*)

Clinical features

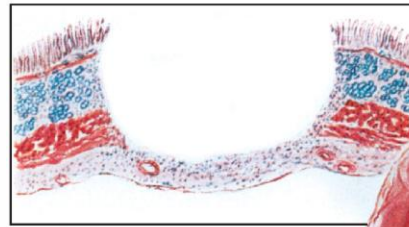
Progressively increasing abdominal pain (thrombosis) or sudden onset of abdominal pain (embolism) + bloody diarrhoea

Shock and vascular collapse within hours

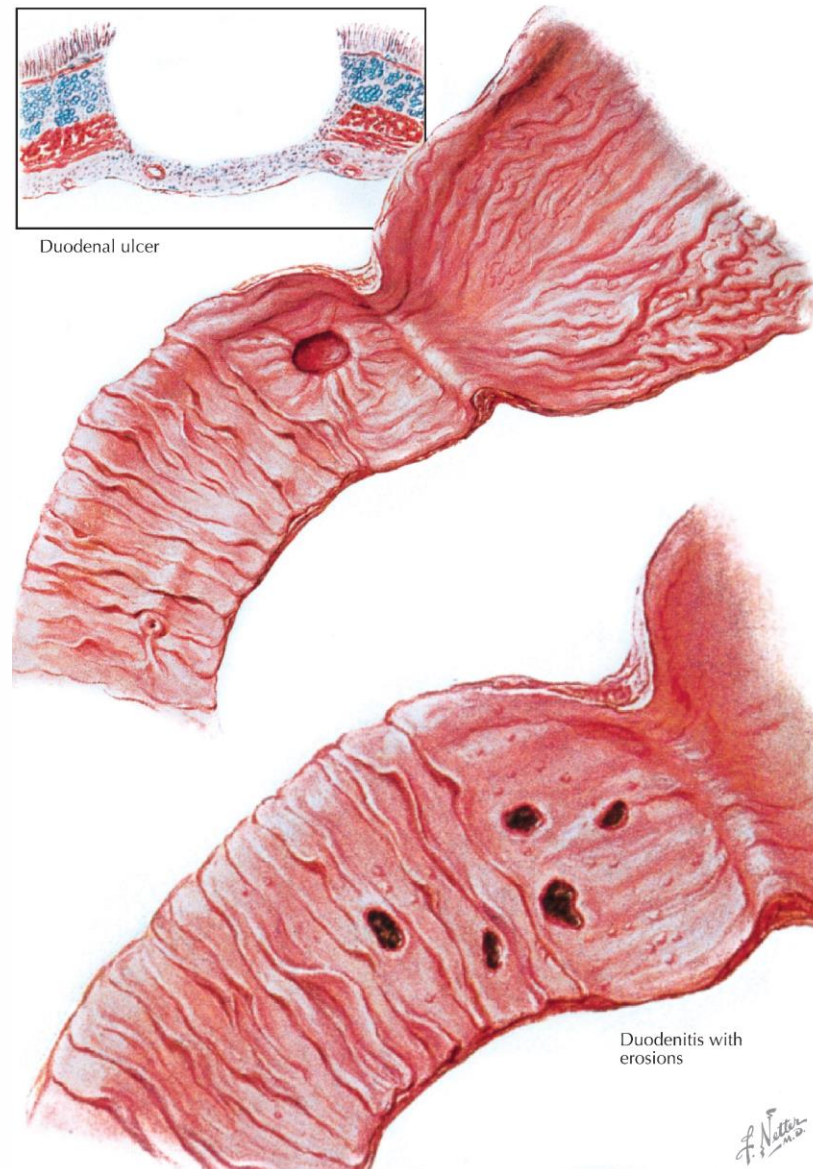
Mortality rate: 90%



Small intestine Inflammation



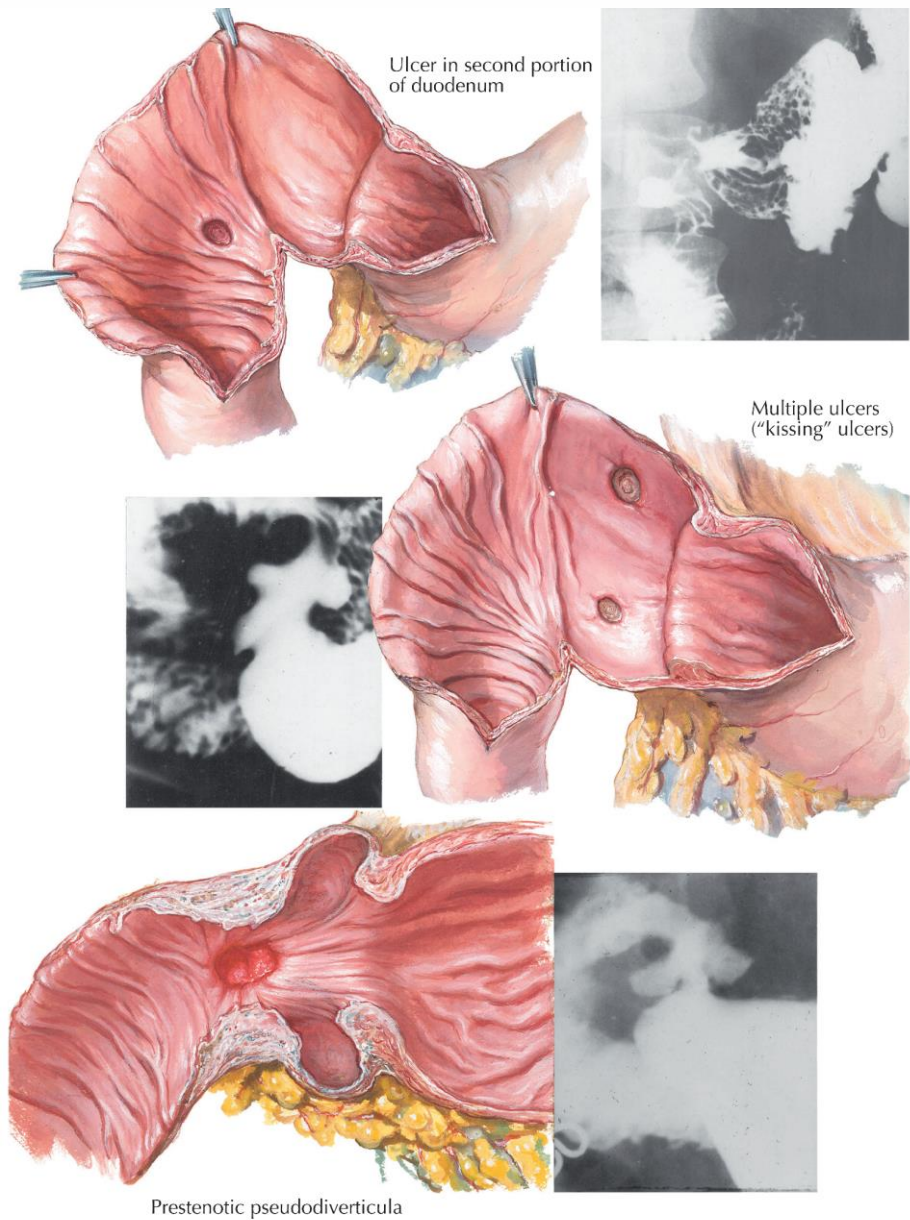
Duodenal ulcer



Duodenitis with
erosions

F. Natter

Small intestine Inflammation



Small intestine Inflammation Coeliacia

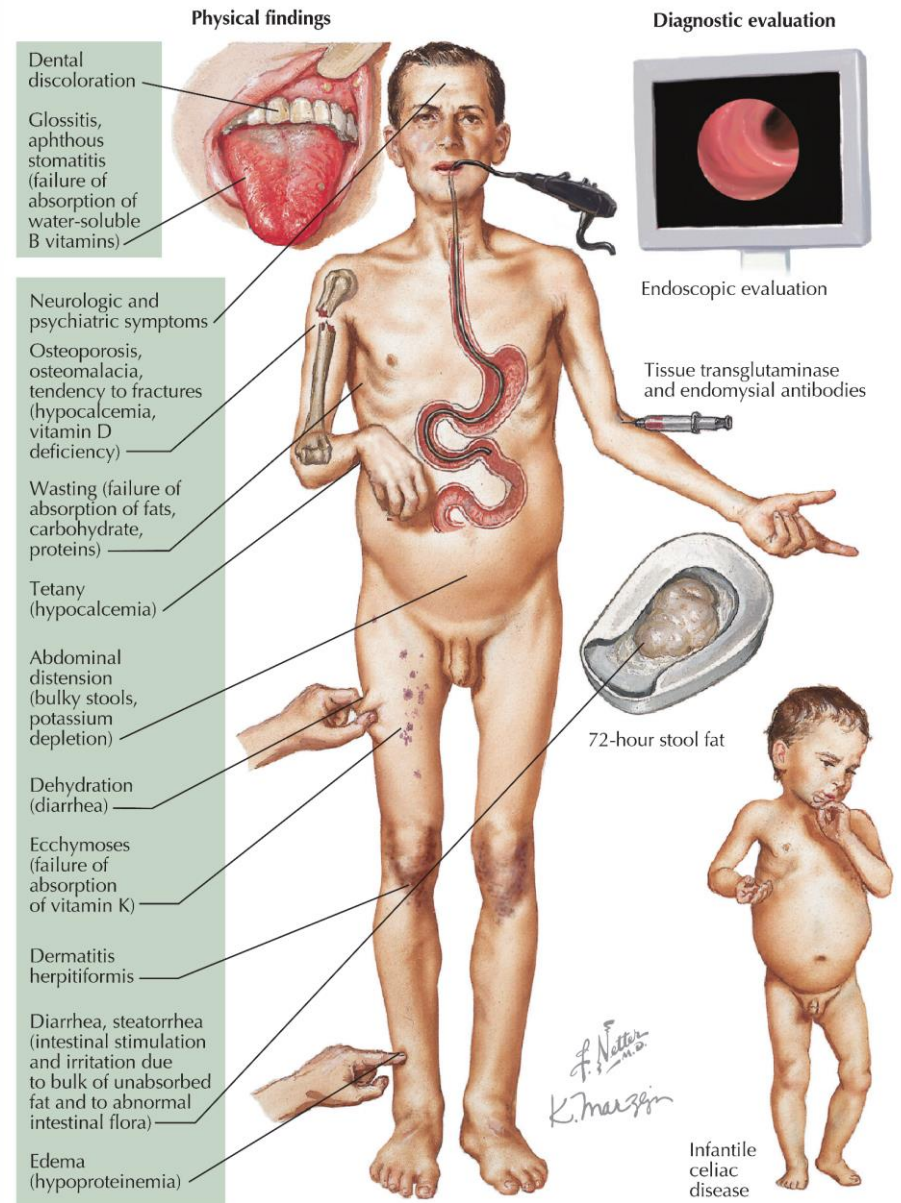
CELIAC DISEASE (SPRUE, GLUTEN-SENSITIVE ENTEROPATHY)

Pathogenesis

- Disease of Caucasians
- Immunologic hypersensitivity to the gliadin component of gluten-containing grains (wheat, rye, oat, and barley)
- Chronic enteritis develops leading to the loss of mucosal and brush border surface area, malabsorption

Clinical features

- Classic form: in infants exposed to solid food, diarrhea, flatulence, failure to thrive, weight loss
- May manifest in middle-aged adults: chronic diarrhea, anemia, bloating, chronic fatigue
- Serology: presence of circulating anti-gliadin antibodies



Small intestine Inflammation Coeliacia

Light microscopy

Increase of intraepithelial CD8+ T-cells;
increase of CD4+ T-cells and plasma cells in
the lamina propria

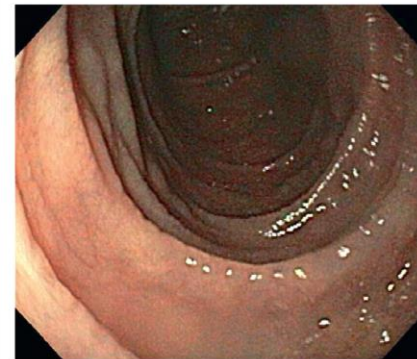
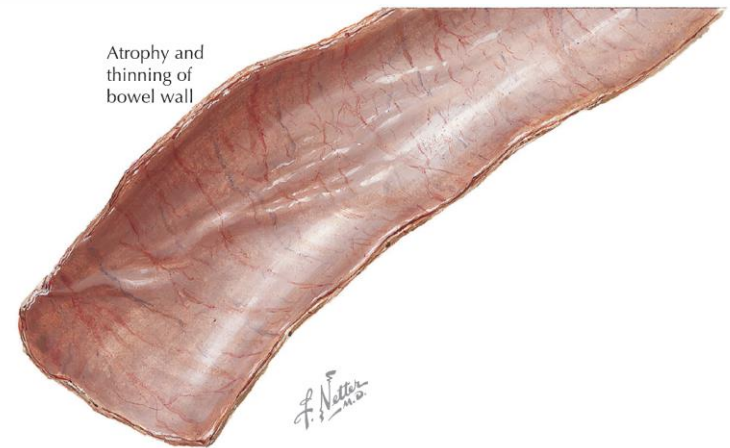
Atrophy of villi with loss of brush

The diagnosis rests on

clinical documentation of malabsorption
biopsy-proven atrophy of small bowel
mucosa

improvement in both symptoms and mucosal
histology on gluten withdrawal from the diet

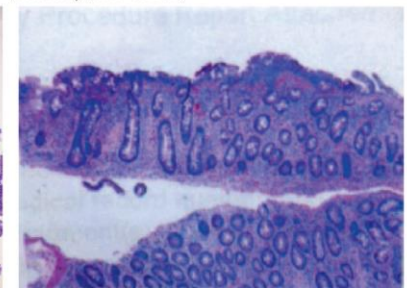
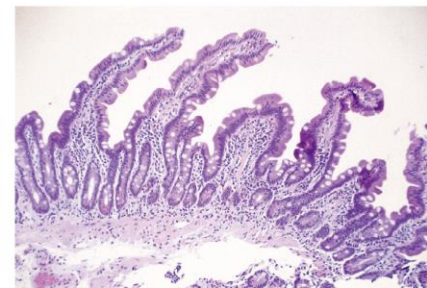
Long-term risk for the development of
enteropathy-associated T-cell lymphoma or
adenocarcinoma of small bowels



Endoscopic image of atrophic mucosa.

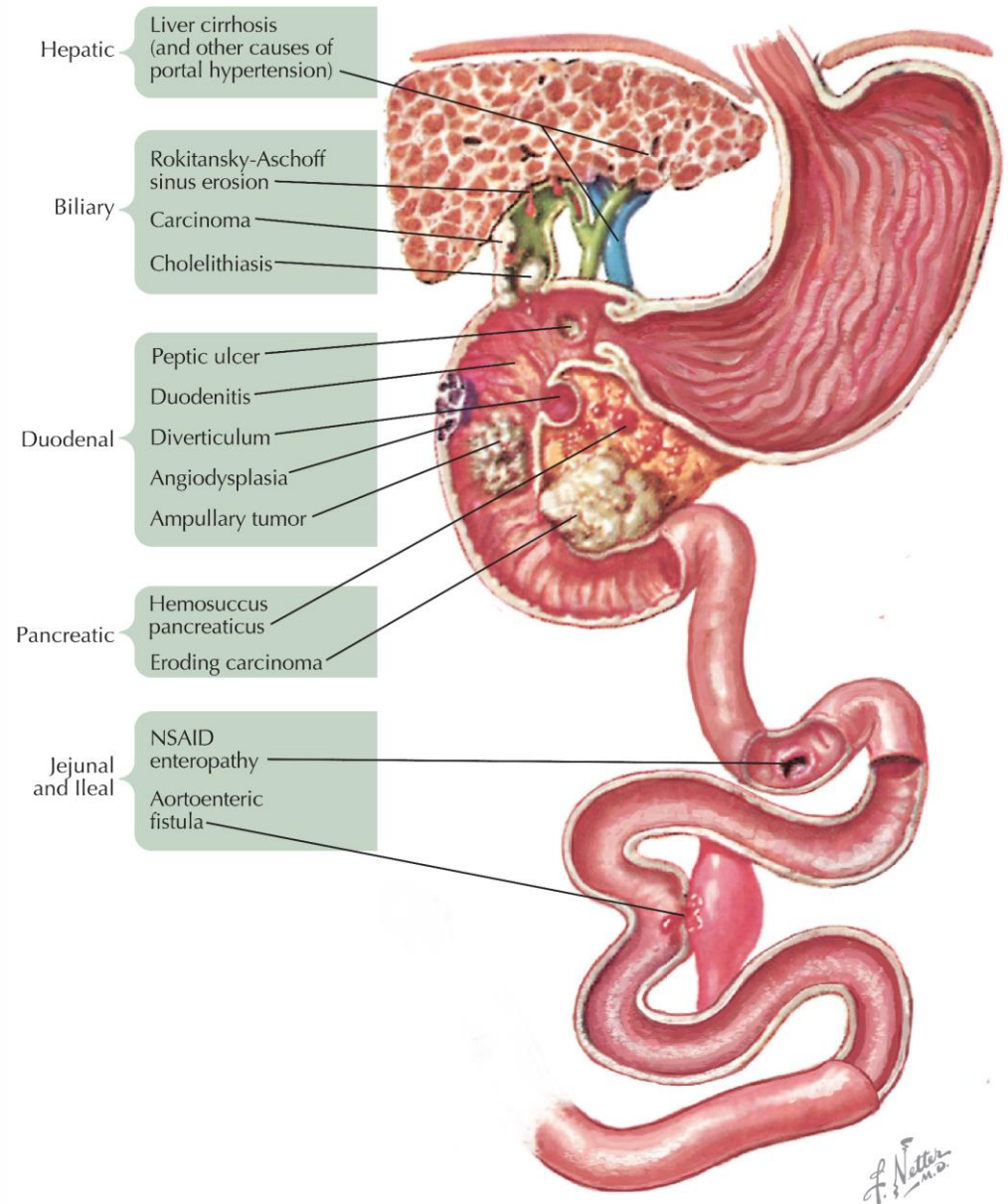


Capsule endoscopic image of scalloping.
(Courtesy Julio C. Bai.)

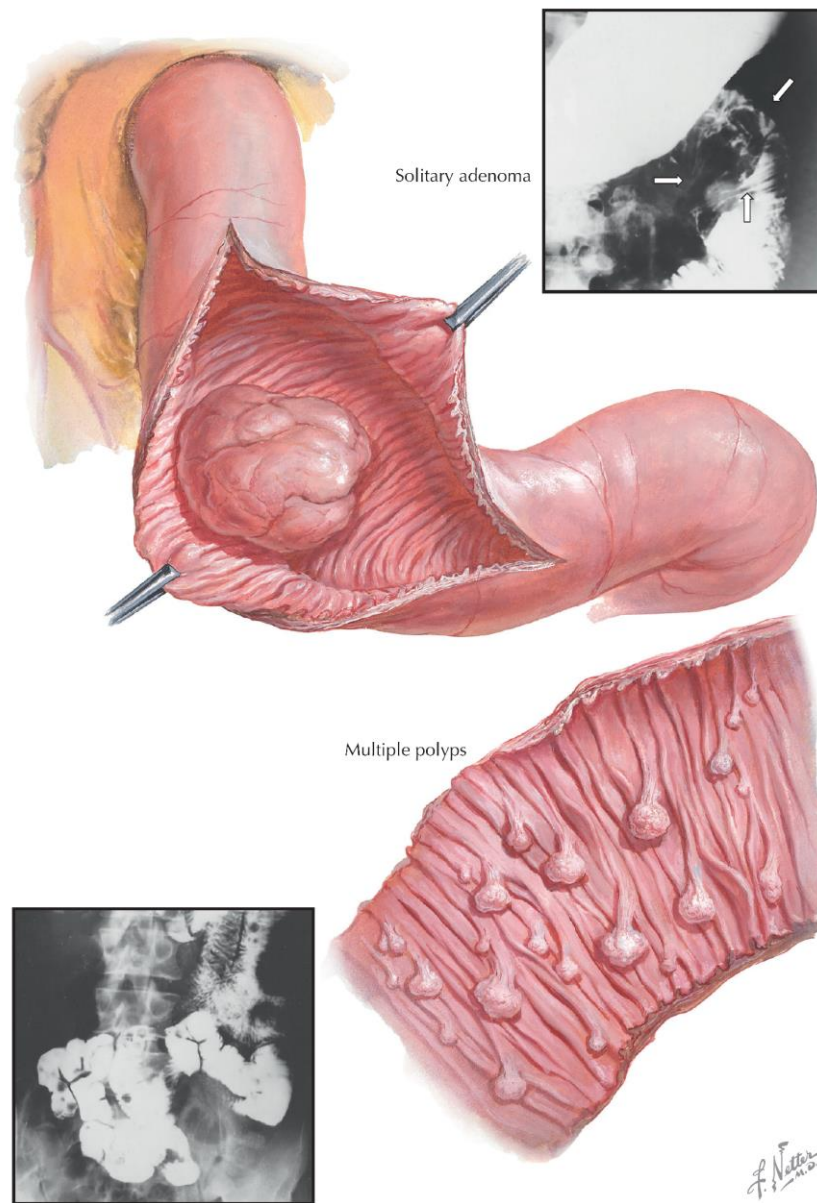


Normal (left) and abnormal (right) intestinal villi. (Left image from Wilcox CM, Munoz-Navas M, Sung JJ. *Atlas of Clinical Gastrointestinal Endoscopy*, Philadelphia, Elsevier, 2012, F4-3.)

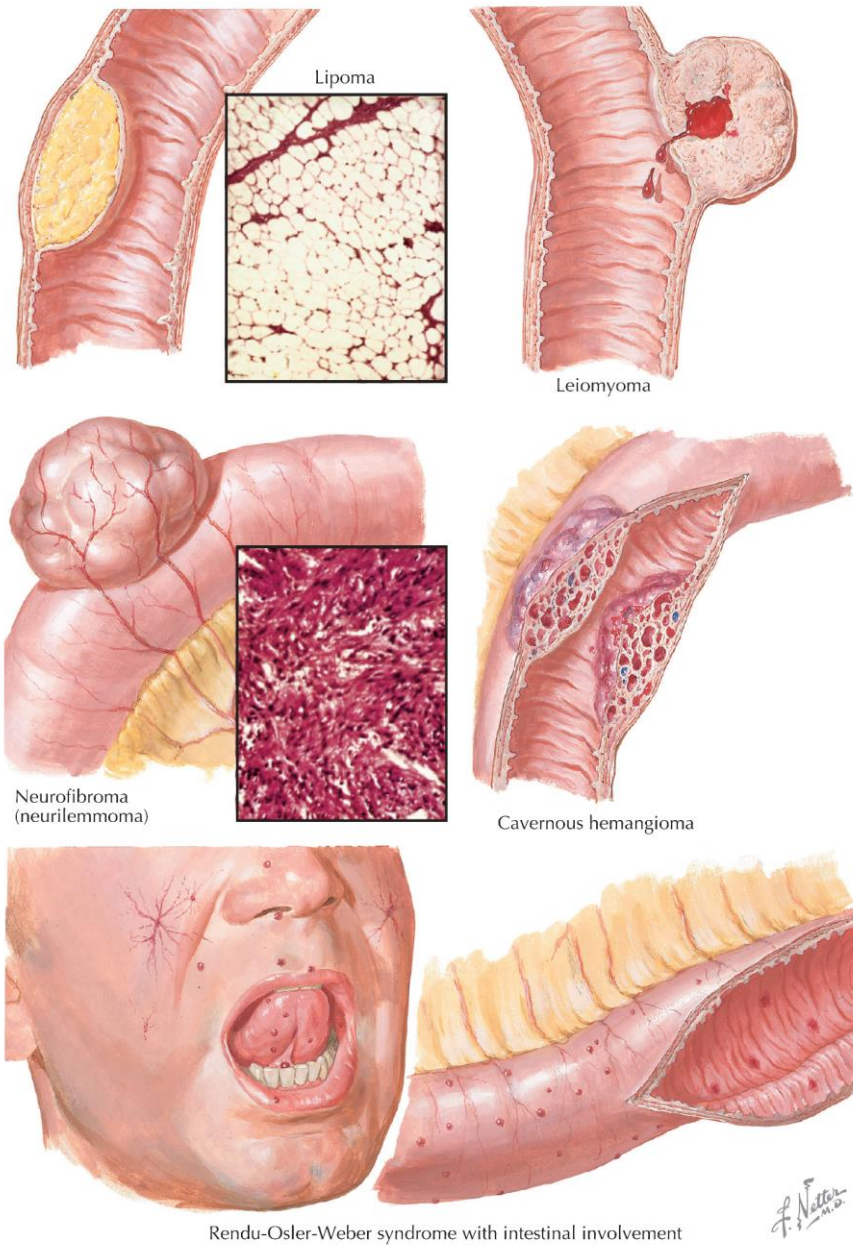
Small intestine Bleeding



Small intestine Tumor

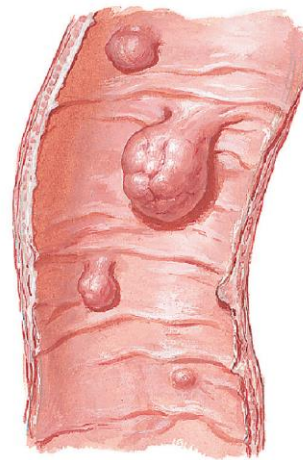


Small intestine Tumor Benign

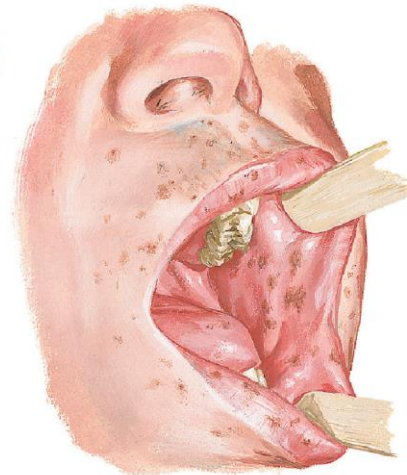


Small intestine Tumor Peutz-Jeghers polyps

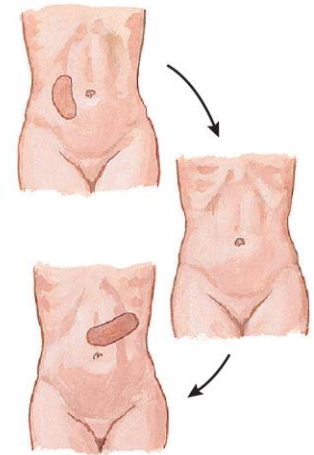
Autosomal-dominant inheritance
Multiple gastrointestinal polyps,
most numerous in the small
intestine; risk of intussusception
Melanotic macules on the lips,
buccal mucosa, palms
Risk of cancer in the lungs,
breast, pancreas, etc.



Polyposis of small intestine



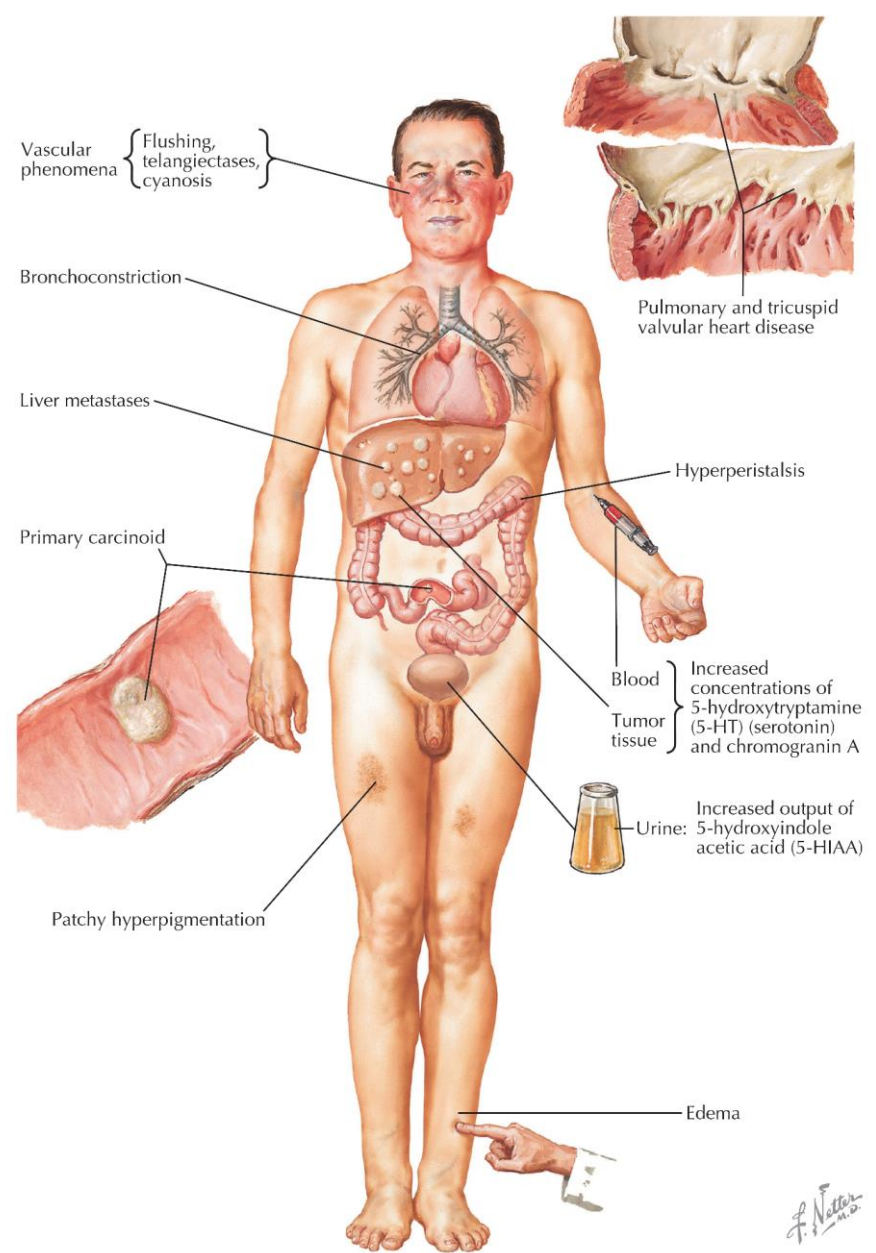
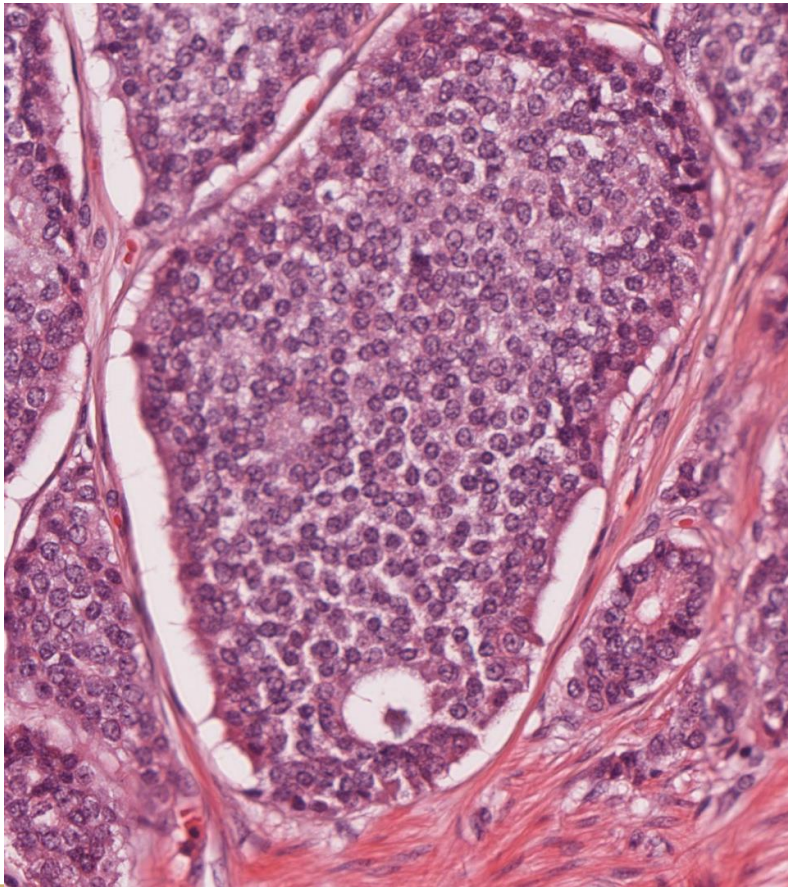
Mucocutaneous pigmentation



Intermittent, migrating mass (due to self-reducing intussusception)

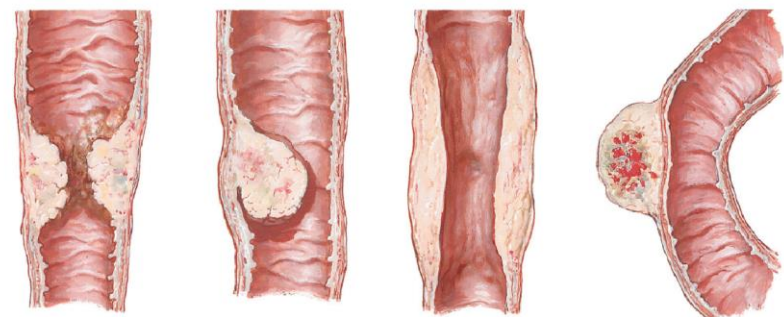
F. Netter M.D.

Small intestine Tumor Neuroendokrin



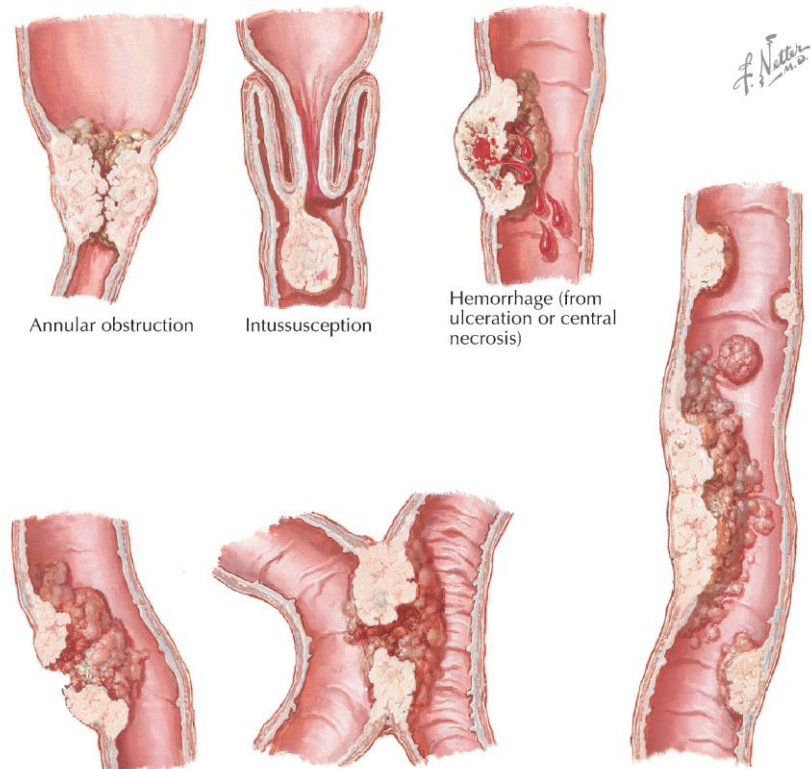
Small intestine Tumor Morphology

Morphologic Types of Growth



Annular (gradual, progressive obstruction)
 Polypoid (sudden obstruction due to intussusception)
 Infiltrating (obstruction due to disturbance of peristalsis)
 Exophytic (obstruction due to kinking or pressure)

Local Consequences



Annular obstruction
 Intussusception
 Hemorrhage (from ulceration or central necrosis)
 Perforation
 Fistula → Malabsorption ← Extensive or multiple



References

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Robbins: Basic pathology (10th edition)

Prof Iványi (Szeged), Dr. Zalatnai (Budapest), Dr. Madaras (Budapest) lecture notes

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