DISORDERS OF GIT:

Pathophysiology of oral cavity
Dysphagia. Gastroesophageal reflux.

Jan Živný
Ústav patologické fyziologie
1. LF UK
jzivny@LF1.cuni.cz

Outline

- Functions of GIT
- General manifestation of GIT disorders
- Pathophysiology of oral cavity
  - Salivary gland
  - Periodontium
  - Oral mucosa
  - Teeth
- Manifestation of systemic diseases in oral cavity
- Dysphagia
- Oesophagus
  - Structural diseases
  - Motility diseases
    - GERD

Function of GIT

- Water and nutrient uptake
  - Motility
  - Secretion
  - Digestion
  - Resorption
- Endocrine function
- Defense function
  - pathogens
  - toxins

GIT defense mechanism

- Integrity of oral mucosa is protected by:
  - Barrier function
    - Mucosa integrity (growth factors, prostaglandins, buffer systems), bacteria colonization..
  - Innate defence mechanisms
    - mucins, lysozyme, lactoferine, lactoperoxidase, antimicrobial peptides – histatin, defensins..., protease inhibitors...
  - Adaptive defense mechanisms
    - immune cells, secretory S-IgA, IgG, IgM

General manifestation of upper GIT disorders

- oral, pharyngeal, chest, and abdominal pain

- Nausea and vomiting
- dysphagia (difficulty with swallowing)
- bleeding

- Some diseases of GIT may progress for a relatively long period without clinical manifestation

Complications of GIT disorders

- acute
  - dehydration
  - bleeding
  - sepsis
- chronic
  - malnutrition
  - deficiencies (vitamins, minerals, ...)
  - obstructions - partial or full occlusions
    - caused by
      - edema
      - tumor
      - strincure

Pathophysiology of oral cavity

Salivary gland

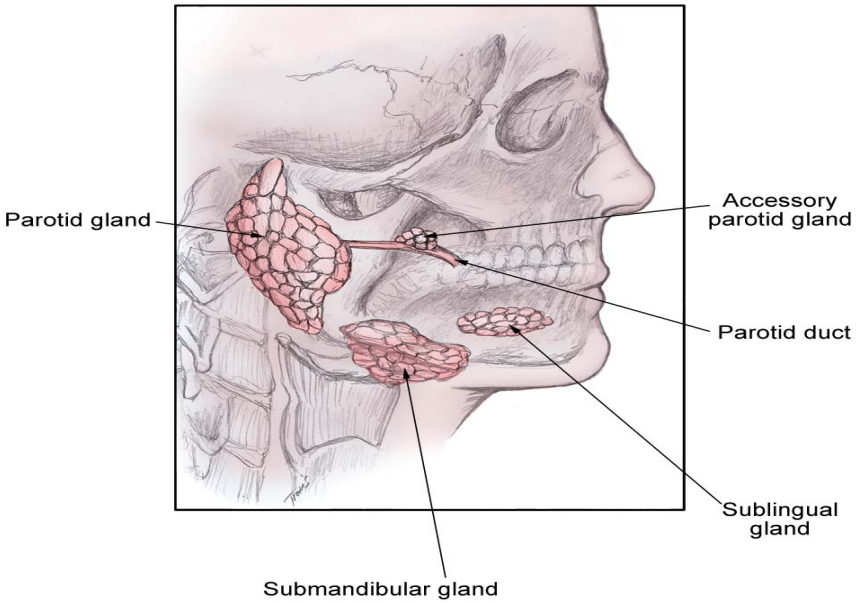
Periodontium

Oral mucosa

Teeth

Pathophysiology of salivary gland disorders

Saliva



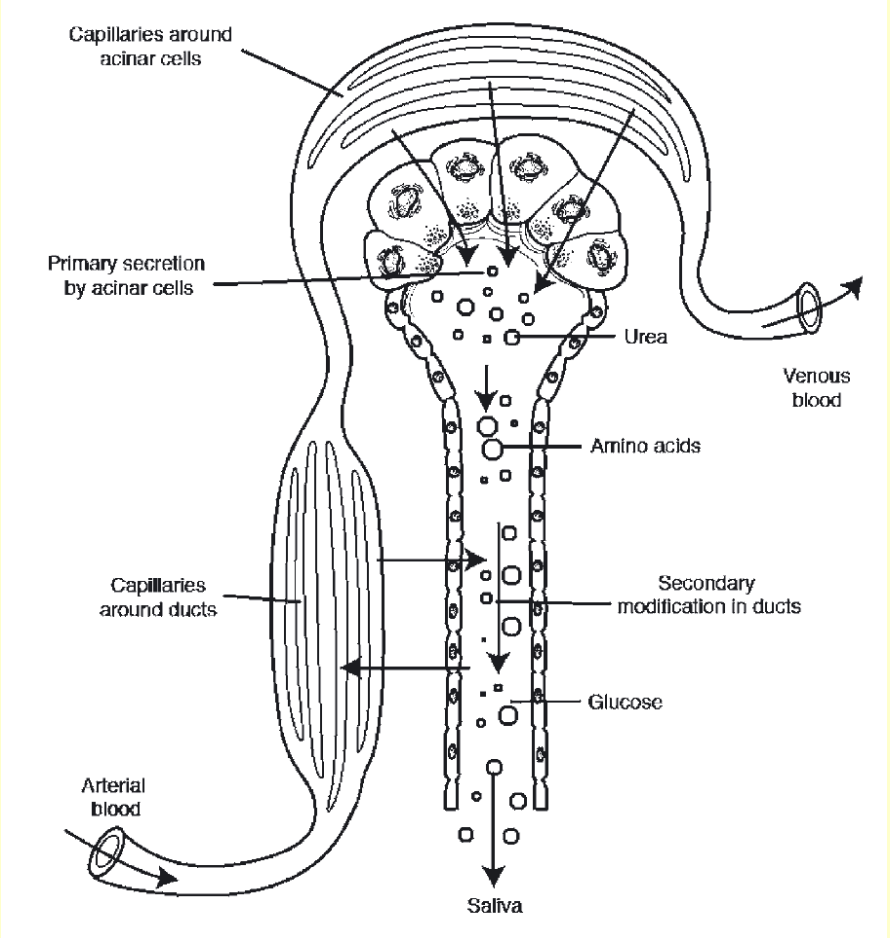
750 – 1000 mL / day

Sources:

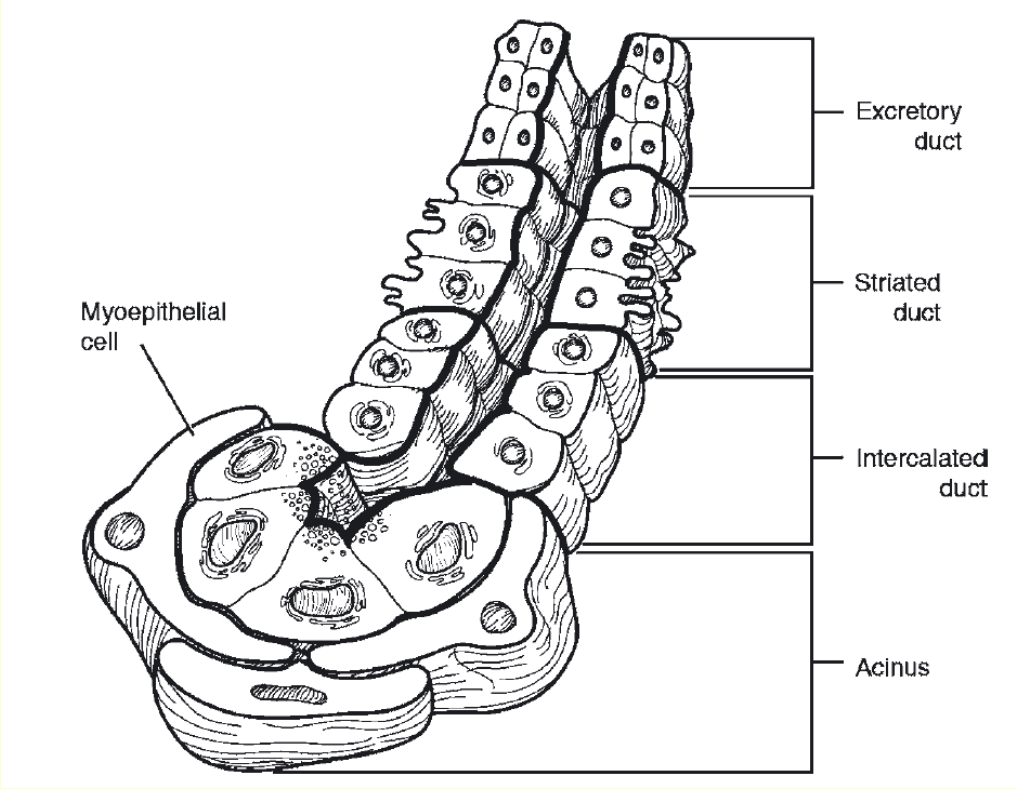
- parotid gland (~40 %)
- submandibular gland (~40 %)
- sublingual gland (~10%)
- minor salivary glands (~10%)
- crevicular fluid (~ 0.5%)

Salivary glands

- Are exocrine glands which consist of individual acini (lobules)
- Saliva
  - Ultrafiltrate of plasma
  - Primary secretion by acinar cells (secretory granules)
  - Secondary modification in ducts (hypoosmolar saliva)



Salivary glands



- Classification of acini and salivary glands:
  - mucinose
  - serose (e.g. parotid gl.)
  - mixed

Myoepithelial cells between acinar cells and basal membrane are able to contract and squeeze out saliva.

Regulation of saliva secreation - inervation

- Parasympathetic nerves (acetylcholine - muscarin receptor)
  - inervation of large salivary glands
  - increase production of watery saliva with low concentration of amylases
- Sympathetic nerves (beta-adreneric)
  - production of viscose saliva with high concentration of minerals and organic substances (amylase, mucin)
  - contraction of acinar and ductal myoepithelial cells

Daily production: ~ 1 L

Gl. parotis produce ~ 70% of stimulated secretion

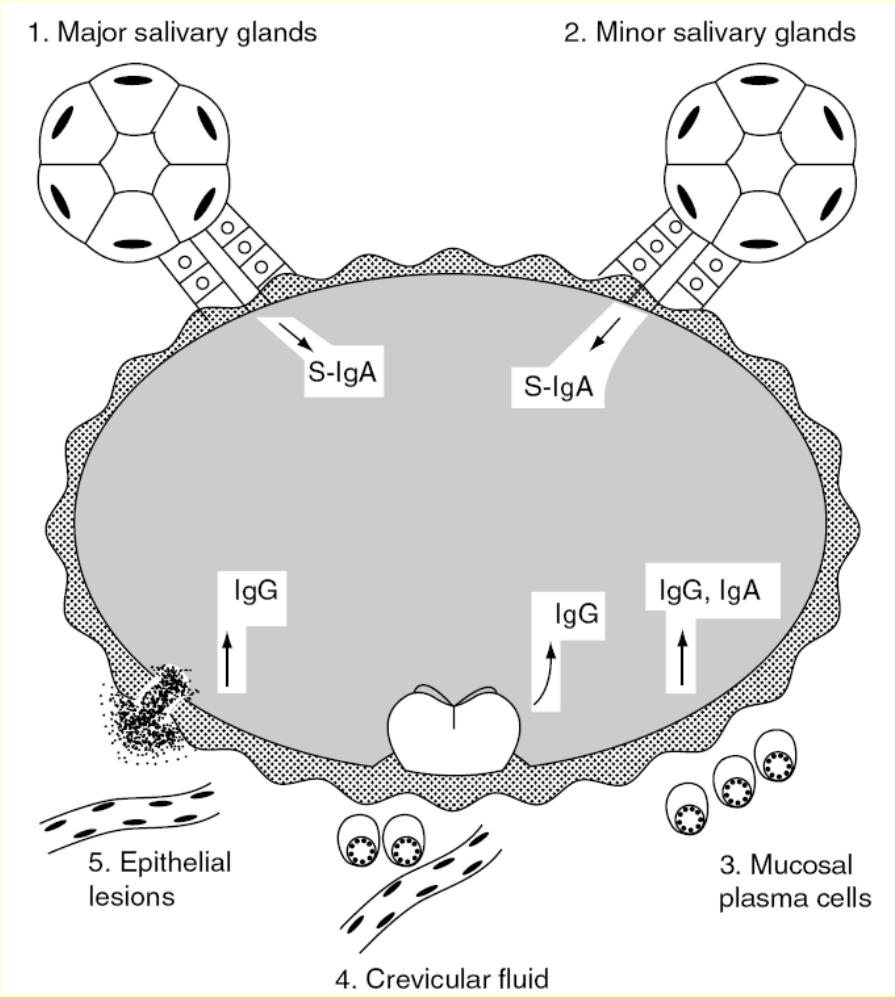
Saliva

Essential for the maintenance of healthy mucosa

Composition of saliva

- Water
- Anorganic components
  - HCO_3^-, I^-, K^+, Cl^-, Na^+, Ca^{2+}, phosphates, etc.
- Organic components
  - mucin
  - enzymes (alpha-amylases, lipases)
  - Antimicrobial substances (e.g. lysozyme, lactoperoxidase, lactoferrin, defensins, IgA, IgG, IgM...)

Sources of Immunoglobulin in oral cavity



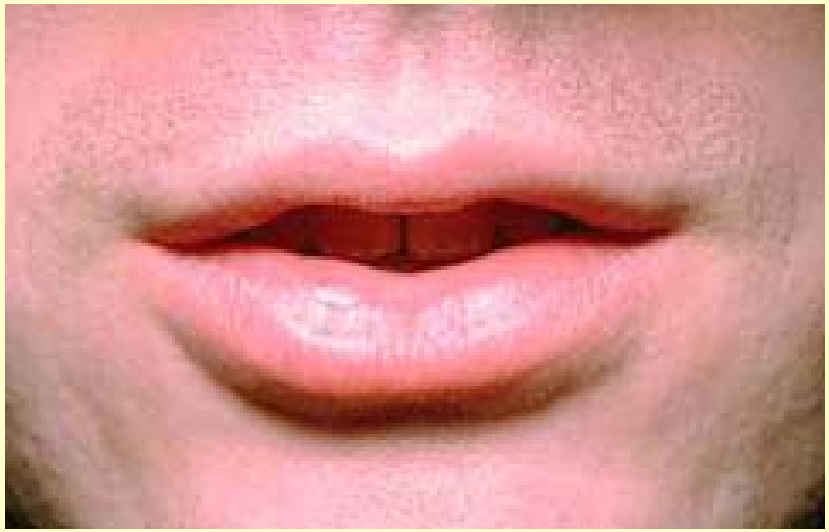
Saliva contains ~ 10^8 bacteria / mL (> 25 000 species)

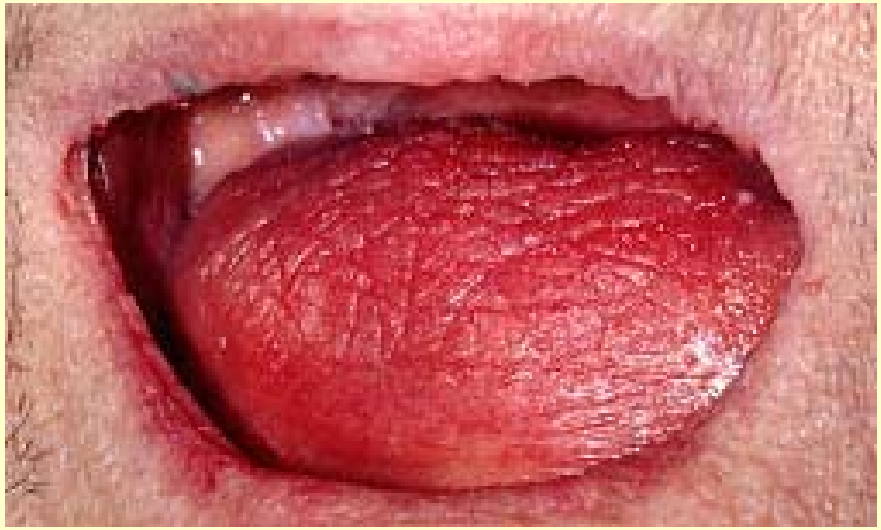
The importance of saliva

- Moistening food and facilitate swallowing
  - water, mucin
- oral hygiene
  - Enzymes (amylase) break down food residues
  - Water - washing away food debris
- Support the creation of voice
  - mucin, water
- Protection of the mucosa and dental enamel
  - mechanical (mucin, water)
  - innate and adaptive immunity (antimicrobial molecules, antibodies, cells)
  - Remineralization of tooth enamel
  - Control of pH in the oral cavity (buffer capacity)

Xerostomia

dry mouth





Decreased saliva production by 50% and more

Causes of xerostomia

- **Medication**
  - anticholinergics
  - alpha and beta blockers
  - calcium channel blockers
  - diuretics
- **Inflammatory and infectious diseases**
  - Sjögren's syndrome
  - Chronic parotitis
  - HIV / AIDS
  - Radiation therapy to the head and neck
- **Dehydration**
- **Obstruction of the salivary glands outlets**
- **Other causes** (e.g. Diabetes mellitus)

Complications of xerostomia

- Inflammation
  - Mucositis (lichen planus, aphthous stomatitis), periodontal disease
- Burning mouth sy (oral dysestesia)
- Malnutrition
  - difficulty swallowing
  - burning sensation
- Psychologic status of the patient
  - difficulty speaking
  - constant sore throat
- Infections
  - dental caries, periodontal infection,tooth loss

Ptyalism

- Hypersalivation

- Causes:
  - Excessive production
  - Decreased or affected clearance

Excessive production of saliva

- Pregnancy (Ptyalism Gravidarum)
- GIT causes
  - Stomach diseases (dilatation, irritation, gastritis, ulcerations), GERD, pancreatitis, liver diseases
- Medication and intoxication
  - Clozapine (antipsychotikum), Pilocarpin (parasympathomimetic alkaloid), Intoxication with mercury, arsenic, copperí, iodides, bromides
- Localized oral infections and lesions
    - Aphtose stomatitis, Oral chemical burns, Dental caries, Chicken-pox, Tuberculosis ...
- Increased consumption of carbohydrates (saccharides)

Decreased or affected clearance of saliva

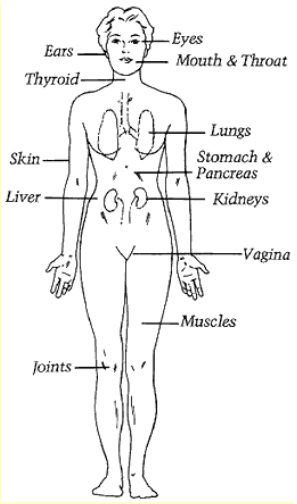
- Infectins
  - tonsilitis, retropharyngeal or peritonsilar absces, epiglotitis, mumps
- Damage to the jaw
  - fractures,, temporomandibular ankylosis, sarcoma)
- Neuromuscular diseases
  - e.g. Myastenia gravis, N. hypoglossus paralysis, botulism, Mental retardation, Cerebrovascular damage.
- Other
  - Radiotherapy, Macroglosia

Salivary gland diseases

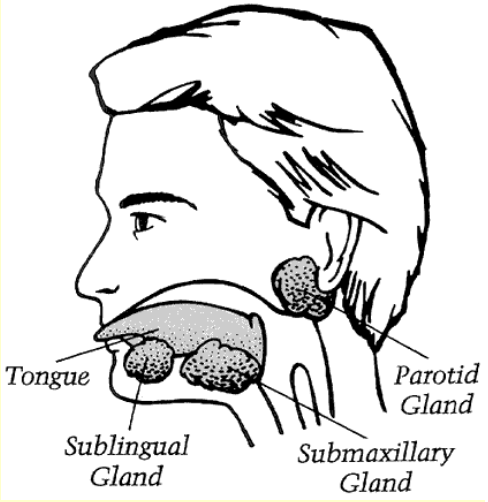
Salivary gland diseases

- **Inflammatory diseases**
  - Autoimmunity (Sjögren sy)
  - Infectious
  - Other noninfectious inflammations (irritation, irradiation, chemotherapy)
- **Sialolithiasis**
- **Sialoadenosis**
- **Tumors**

Sjögren sy (SS)



- Chronic inflammatory autoimmune disorder
- Systemic
- **Exocrine glands are affected**
- Manifestation:
  - dryness of the mouth, eyes, and other mucousal membranes



- middle-aged women

Etiology of Sjögren sy

- Multifactorial disease
- Genetic factors and environmental factors
- Infections – EBV, retroviruses, HCV
- Predisposition HLA-DR3

Among the frequent autoimmune diseses with F : M ~ 9:1)

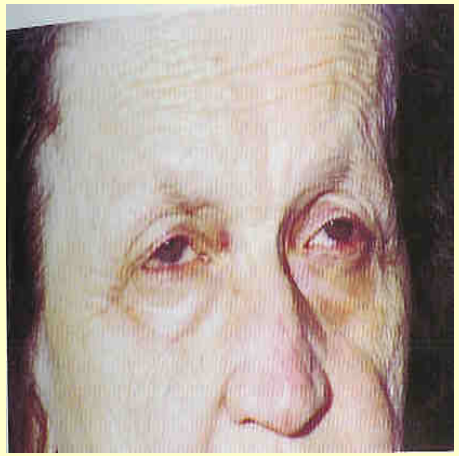
Patophysiology of SS

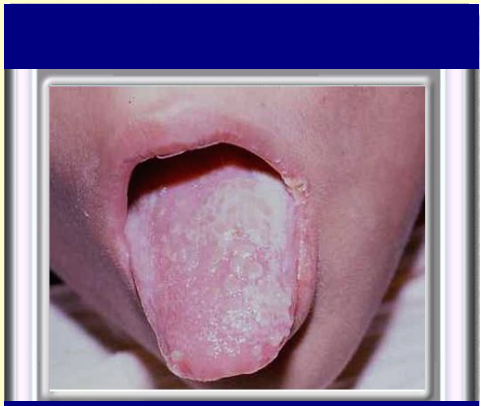
- Salivary, lacrimal, and other exocrine glands become infiltrated with CD4+ T cells and with some B cells.

- Antigen specific T cells
  - produce inflammatory cytokines (eg, IL-2, interferon-γ)
  - stimulate inflammatory response
    - Cytokines (TNF, FasL, IL1, IL6)
    - Proteolytic enzymes (MMP3, MMP9)
    - Production of autoantibodies by B cells Damage to the secretory ducts
  - secondary gland dysfunction

Symptoms and signs of SS Glandular

- Keratoconjunctivitis sicca
- Xerostomia
  - dysphagia
  - Secondary infection
  - Tooth decay and loss
  - Sialithiasis
  - Taste disturbances
  - Speech disturbances





Oral candidosis

Symptoms and signs of SS Glandular

- Keratoconjunctivitis sicca
- Xerostomia
- Dryness of skin (sometimes alopecia)
- Dryness of mucosa (cough)
- Pancreatitis

Symptoms and signs of SS
Extraglandular

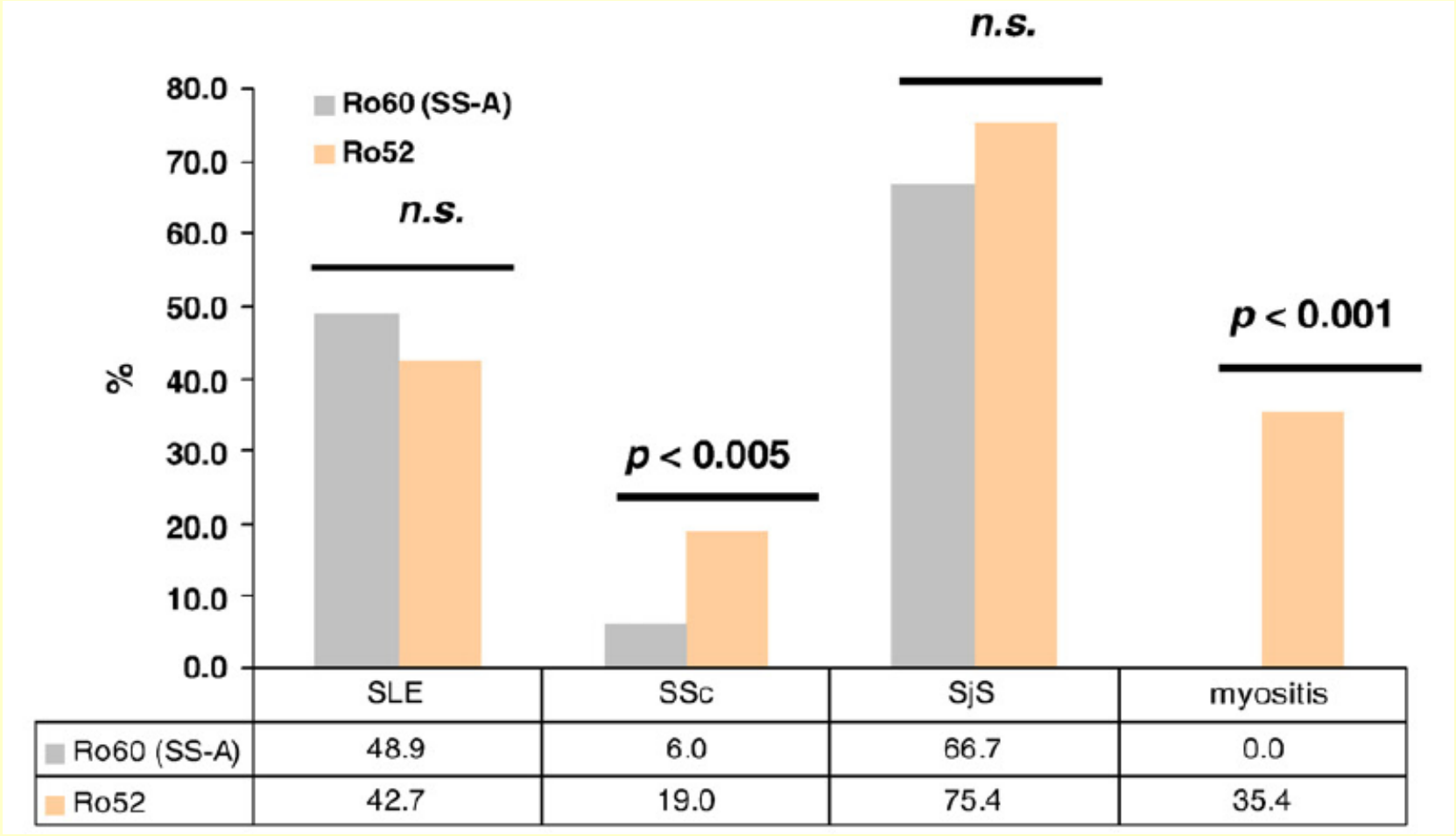
- Arthralgia (~50% of patients) artritis (~33% of patients)
- Generaliozed lymphadenopathy
- Raynaud syndrome
- Inflammation of tissues and organs
  - lungs
  - kidneys
  - vaskulitis (peripheral neuropathy)
- Lymphomy (NHL 40x more often)

Classification of SS

- **Primary SS**
- **Secondary SS**
  - vzniká na podkladě autoimunitních onemocnění pojivových tkání
  - asi 30% pacientů (RA, SLE, sklerodermie, polymyositida)

Biomarkers - autoantibodies

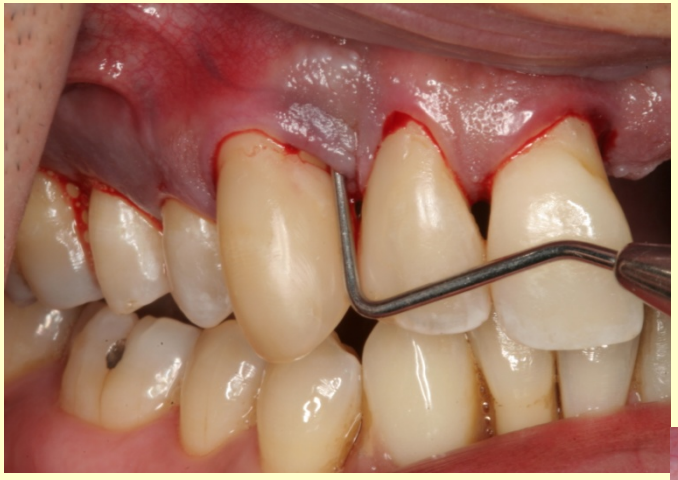
Low sensitivity and specificity

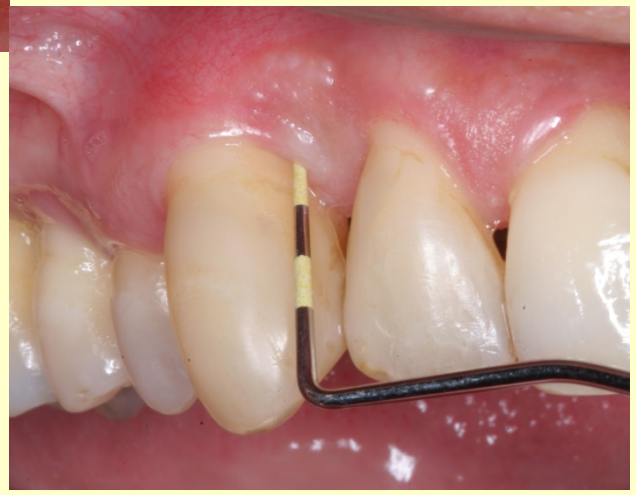


	SLE	SSc	SjS	myositis
Ro60 (SS-A)	48.9	6.0	66.7	0.0
Ro52	42.7	19.0	75.4	35.4

Protilatky anti-Ro60 jsou přítomné v seru pacientů 3-4 roky před rozvojem SLE

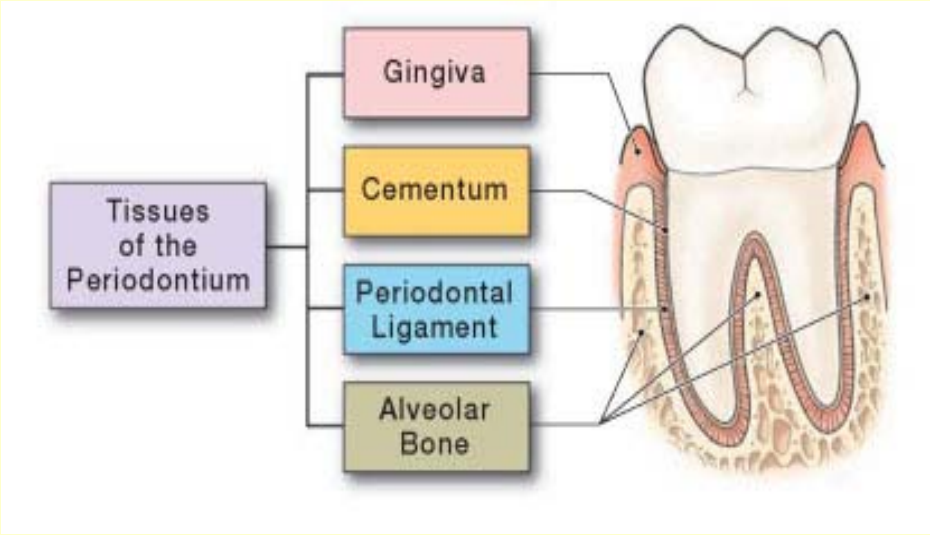
Patophysiology of Periodontal diseases





Periodontium

- Consists of the tissues that support the teeth
  - Gingiva
  - Cementum
  - Periodontal ligament
  - Alveolar bone



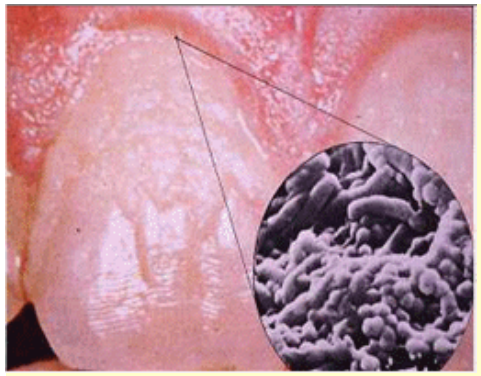
- Functional biologic system
  - Continuous reconstruction
  - Dependent on the presence of tooth

Periodontal diseases

- Diseases affecting gingivae and supporting structures of the teeth
- Classification
  - Gingivitis Acute X Chronic
    - Reversible inflammation
    - **Chronic marginal gingivitis** (CMG) is the most common
      - inflammatory reaction to the presence of plaque
  - Periodontal disease
    - **Adult periodontitis** (chronic inflammatory periodontal disease)

Periodontal inflammation

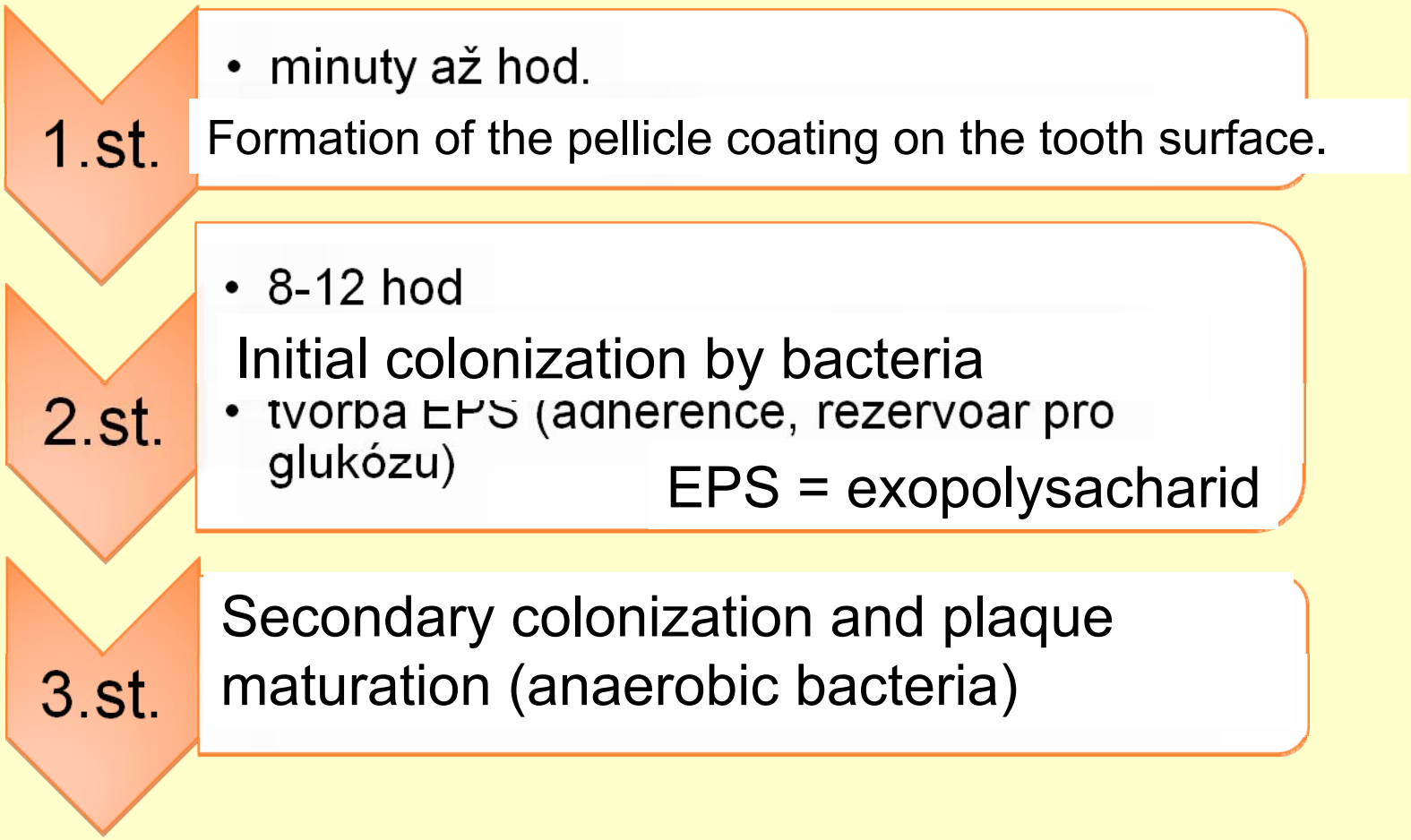
- Frequent disorder (~ 30% of the population between 35-40 is affected)
- Caused by insufficient oral hygiene and presence of dental plaque
- High risk groups:
  - Pregnant females
  - diabetics
  - Immunedeficient individuals (inherited, HIV infection, oncology patients, medication)



Dental plaque - composition

- Dental pellicle
  - protein film on the surface enamel (saliva glycoproteins to prevent continuous deposition of salivary calcium phosphate)
- Mikroorganisms
  - bacteria, mycoplasma species, yeasts, protozoa and viruses.
- Host cells
  - epithelial cells, macrophages, and leukocytes
- The intercellular matrix (20% to 30% of the plaque mass)
  - Organic and inorganic materials derived from saliva, gingival, crevicular fluid, and bacterial products.

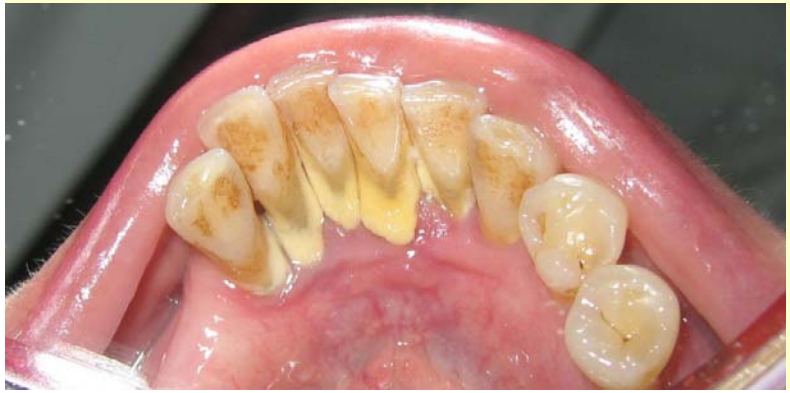
Plaque formation

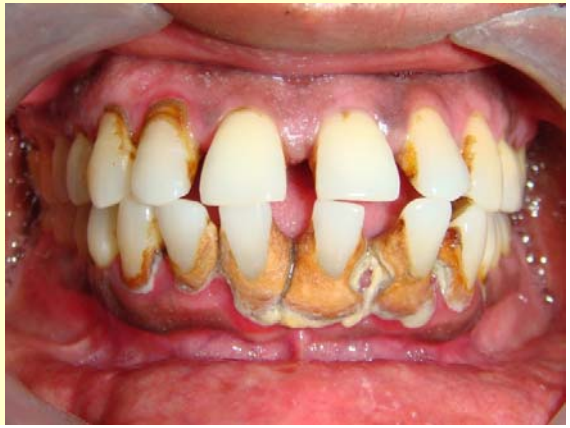


Pelikula (získaná kutikula)
tenká (0,5 až 1 μm) vrstvička vytvářející se na očištěném povrchu zubů během několika minut až hodin. Tvoří ji glykoproteiny adsorbované ze slin.

Dental Calculus (Tartar)

- Hard deposit that forms by mineralization of dental plaque
- Is covered by a layer of unmineralized plaque

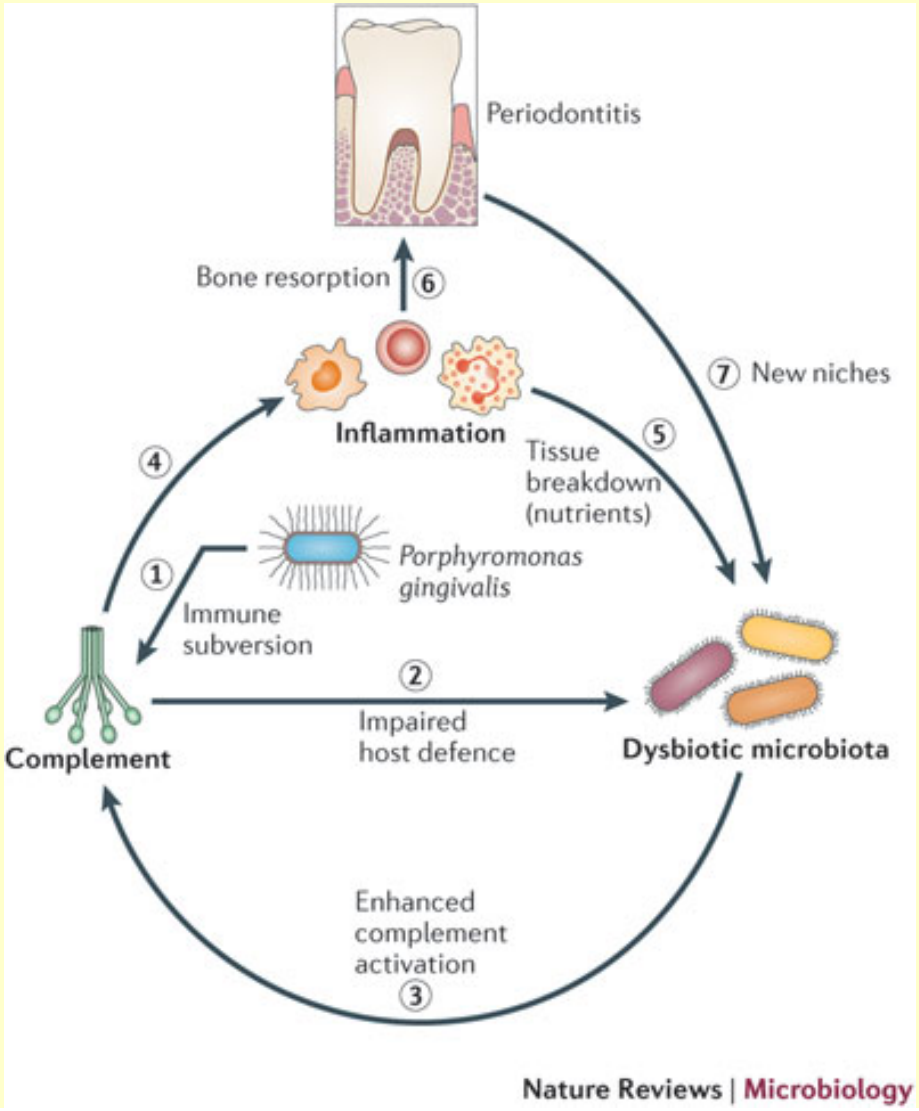




Etiology of periodontal disease

- **Causative bacteria**
  - Porphyromonas gingivalis
    - adult periodontitis
  - Actinobacillus actinomycetemcomitans (Aa)
    - localized juvenile periodontitis
  - Prevonela intermedia –
    - acute necrotizing ulcerative gingivitis
  - Capnocytophaga
    - periodontal disease in immunedeficient host
- **Host factors**
  - HLA association
  - > 50% of the periodontal disease is attributable to genetic factors

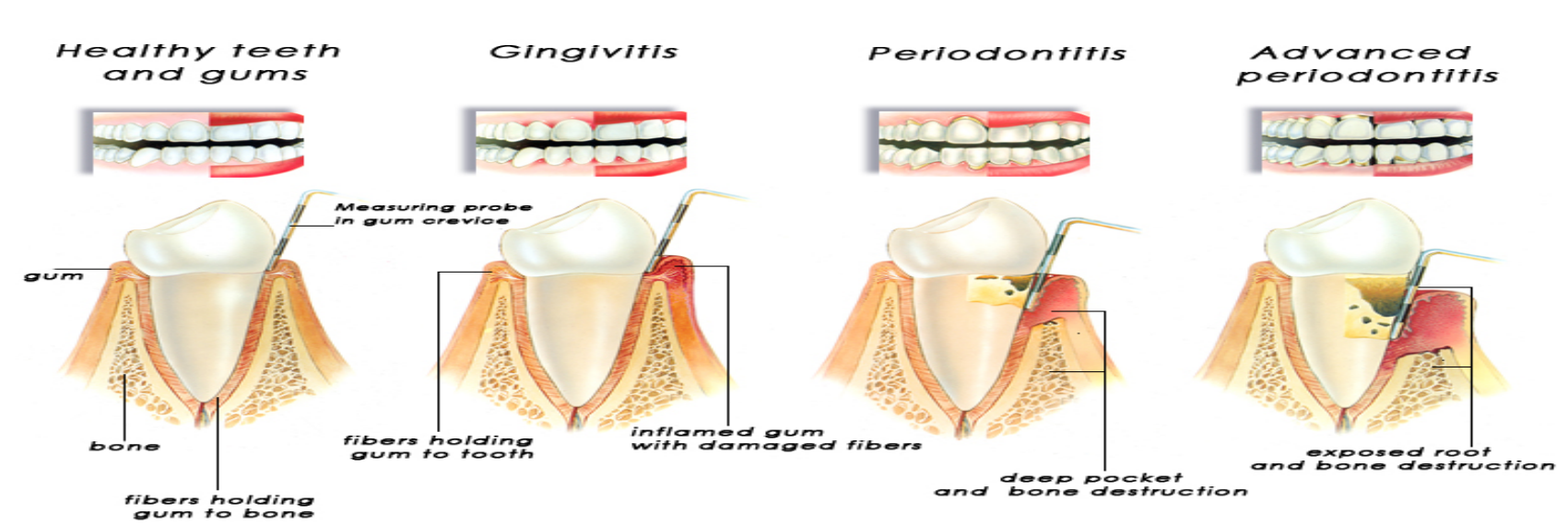
Porphyromonas gingivalis



- subverts complement and impairs host defence
- overgrowth of oral commensal bacteria - dysbiosis
- complement-dependent inflammation
- inflammatory bone resorption provides the dysbiotic microbiota with new niches for colonization
- vicious cycle

Periodontitis development

I. Initial lesion
II. Early lesion
III. Established lesion
IV. Advanced lesion

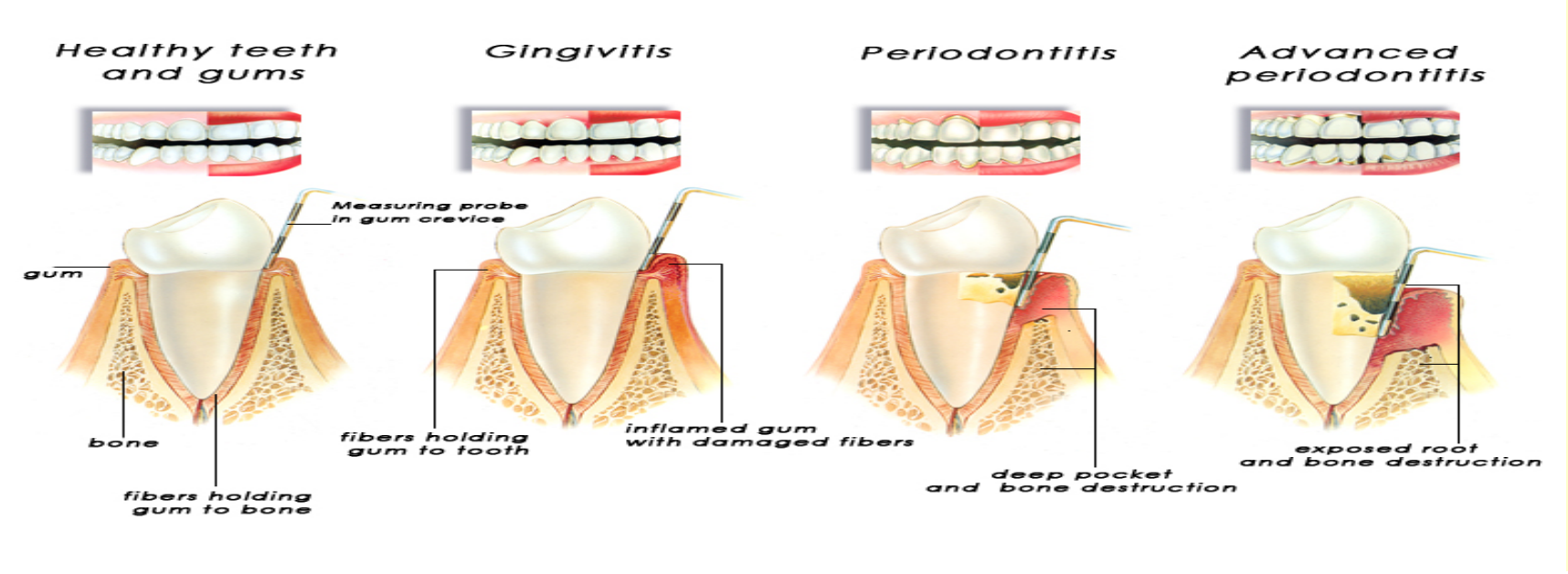


Periodontitis– Initial Lesion

- Gingivitis – localized inflammation to gingival sulcus
- PMN leucocyte infiltration
- Develop within 2-4 days of plaque accumulation
- Caused by activation of complement
  - alternative pathway (plaque components)
  - classical pathway (antibodies)

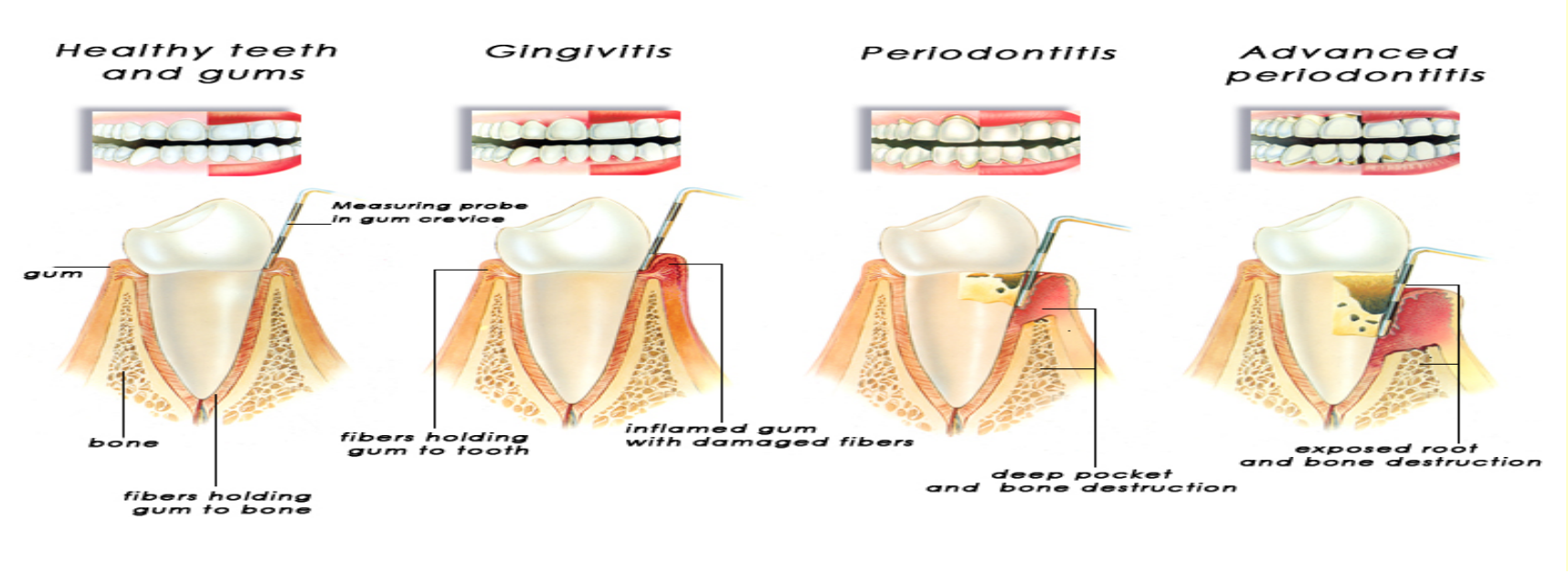
Periodontitis– Early Lesion

- Replacement of PMN infiltration by lymphocytes (T cells > B cells ~ 75%)
- About 2 weeks from plaque formation



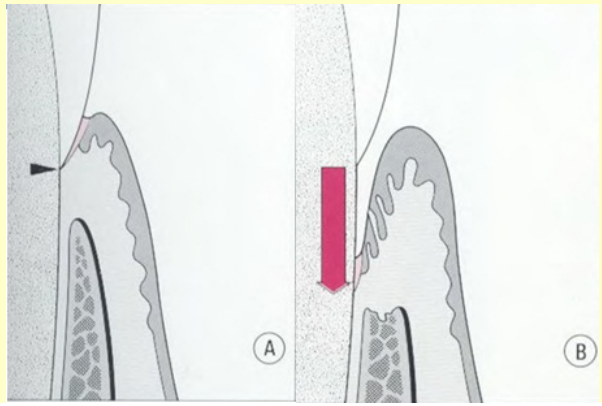
Periodontitis– Established lesion

- 2 -3 weeks after plaque accumulation
- Plasma cell infiltration (most IgG secretion)
- Loss of collagen within epithelium
- Deepening of gingival sulcus = pocket formation



Periodontitis– Advanced Lesion

- Infiltration with lymphocutes, plasma cells and macrophages
- Destructive state
- Porphyromonas gingivalis
- Pocket formation and ulceration of the pocket epithelium
- destruction of the collagenous periodontal ligament
- significant resorption of bone



Pathophysiology of oral mucosa

Mouth Ulcers

Recurrent Aphthous Stomatitis

Chronic Ulcerative Stomatitis

Recurrent Aphthous Stomatitis

- Affect up to 25% of population
- Cause??
  - Familial
  - Trauma, stress, tobacco deficiency/use
  - **deficiency: folic acid, vit. B12, Fe**
  - Menstrual cycle
  - Drugs (NSAID)
  - **Intestinal diseases (CD**, UC)
  - HIV infection (depends on the severity of immunodeficiency)

Pathogenesis

- Affects non-keratinized or slightly keratinized parts of oral mucosaizované
- Immune reaction cause damage to oral mucosa epithelial cells

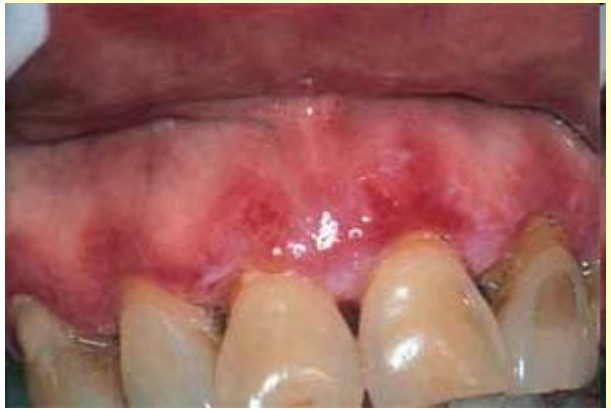
- Forms:
  - minor (~80%)
  - major (ulcerace > 1 cm)
  - herpetiformis (small aphtous lesions in clusters)

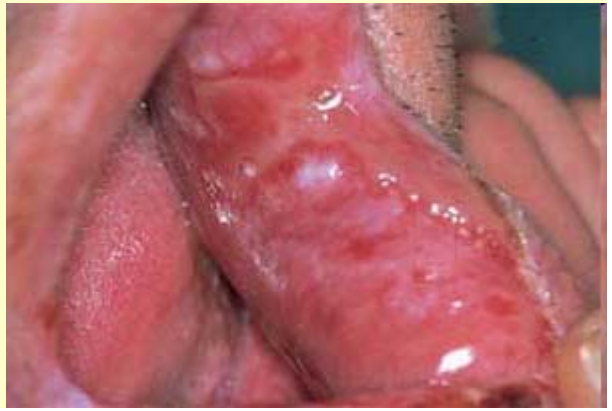
Diagnosis

- No standard dg. Test
  - Hematologic evaluation (CBC, Iron, Folic Acid, etc.)
  - Immune system and infectious disease evaluation

Chronic Ulcerative Stomatitis (CUS)

- Known from 1989
- Affects older women





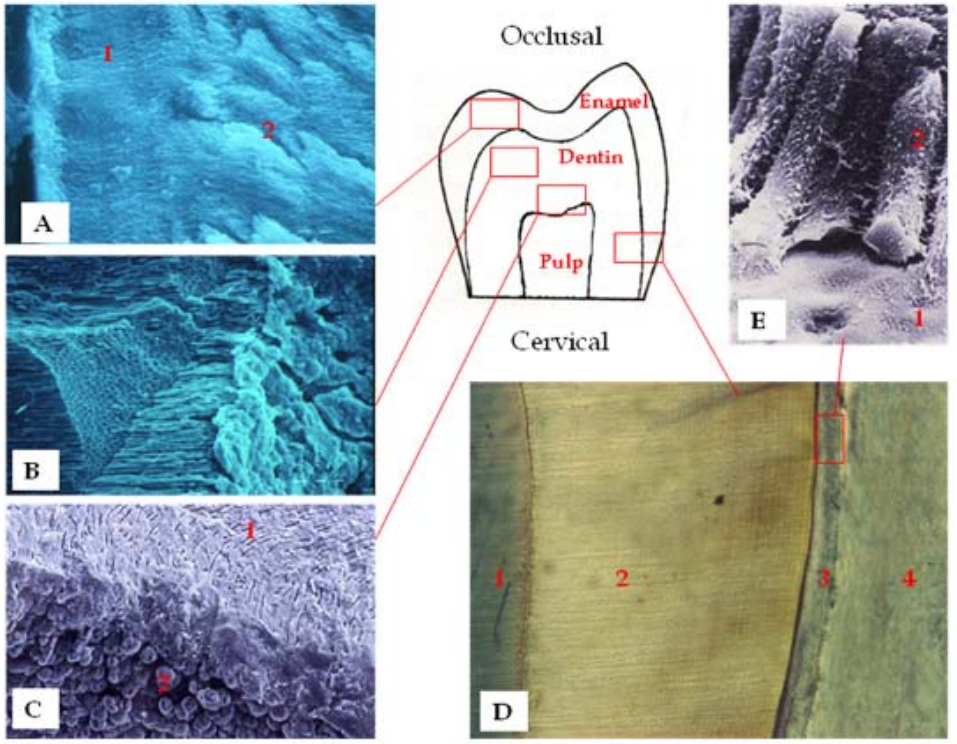
Chronic Ulcerative Stomatitis

- Antinuclear antibodies to squamous epithelia (Squamous epithelia-specific anti-nuclear Ab, SES-ANA)
  - Antibodies to keratinocyte protein KET (related to p53)
    - thymus, epithelial cells

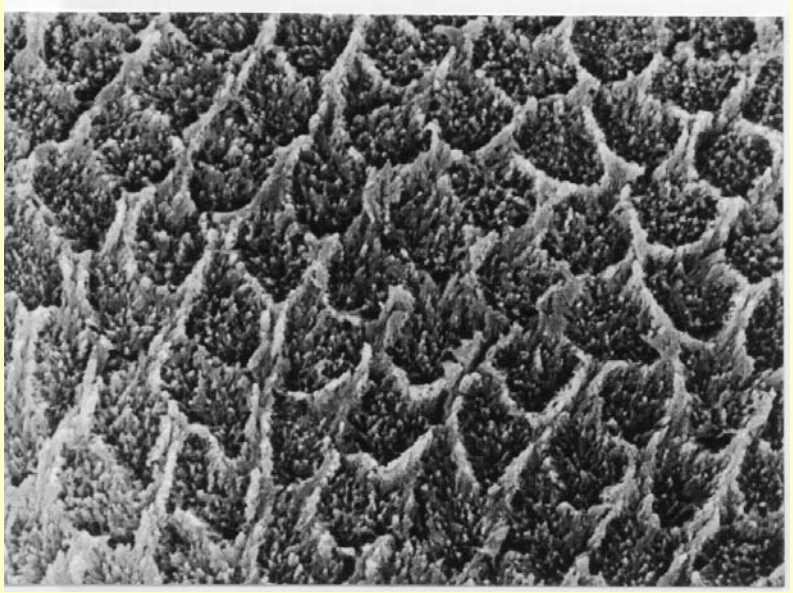
Pathophysiology of tooth diseases

Tooth developmental defects (enamel, dentine)

Dental caries (tooth decay)



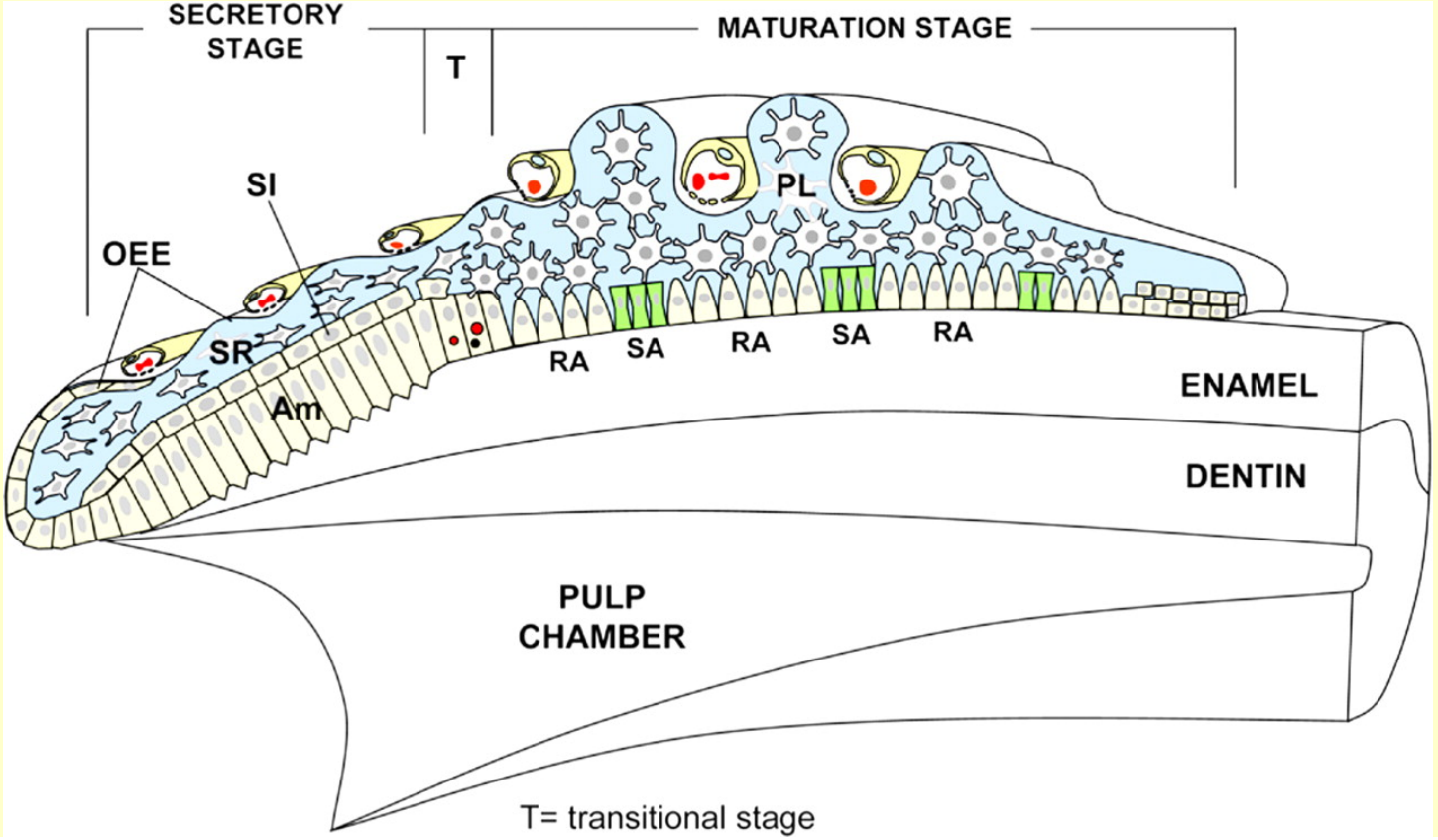
Developmental defects of tooth enamel



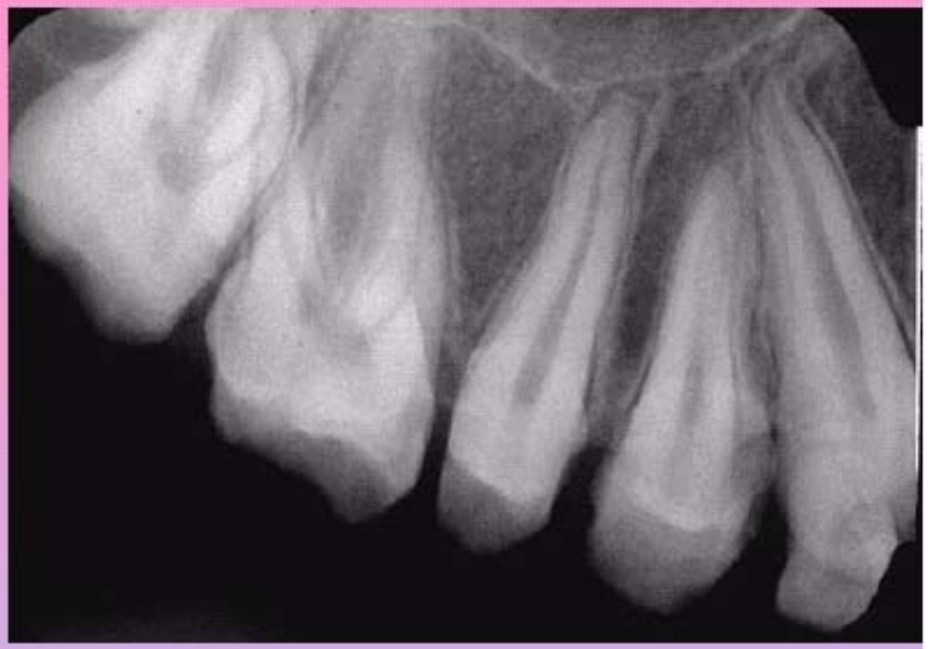
- 92- 96% of enamel consists of minerals
  - hydroxyapatite, a phosphate and calcium salt
- water and organic material

Amelogenesis

- Development proceed via a series of distinct stages
-



Amelogenisis Imperfecta



From the radiograph one can note that all of the teeth have the defect of having little or no enamel

Is a disfiguring inherited condition.

Occurs in 1 in 1000 -14,000.

hypoplastic (thin enamel)

hypocalcified (mineralisation defect)

hypomaturated

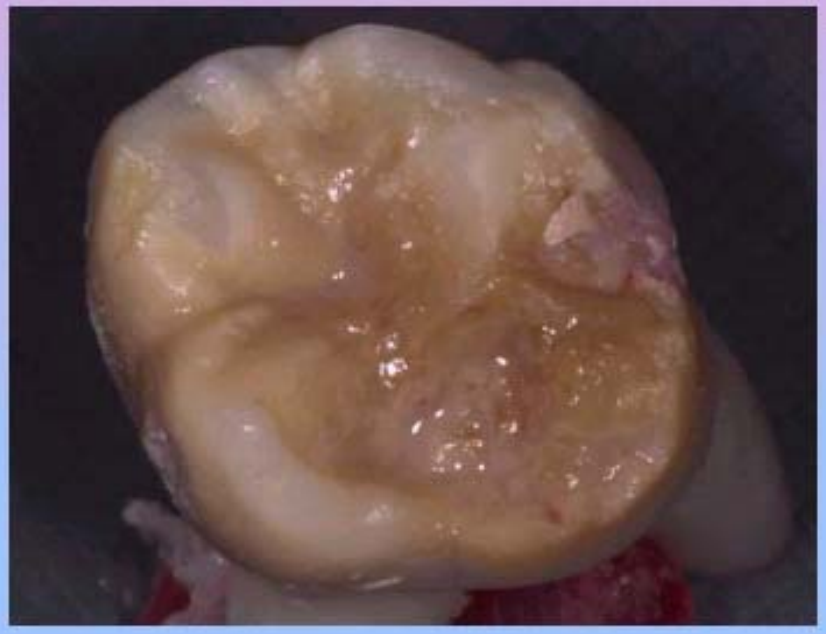
X-linked

14 sub types listed. Phenotypes include thin, smooth ,creamy or yellowed appearance, pits, localised. Hypocalcified are prone to caries and fracturing once exposed.

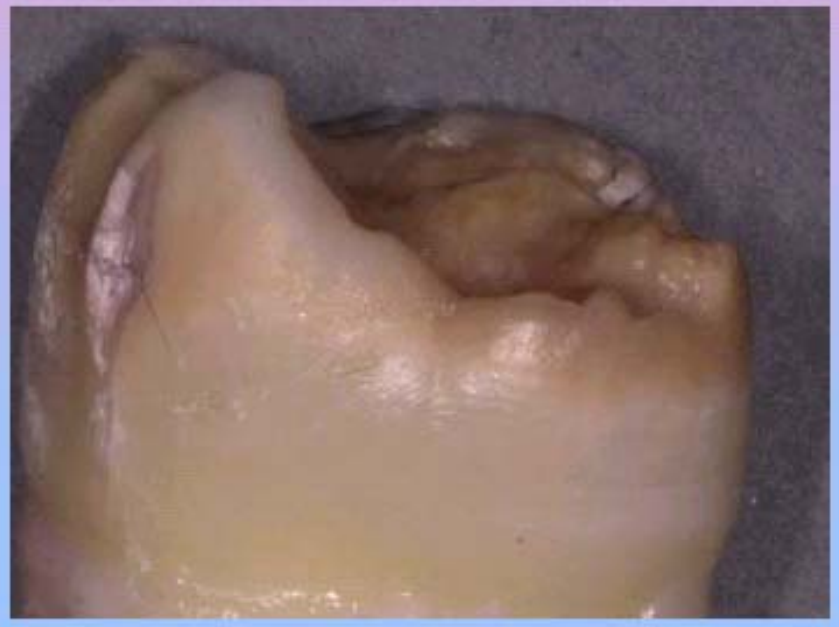
Normal enamel 83 –90 % by volume

AI hypocalcified enamel 53-50 %

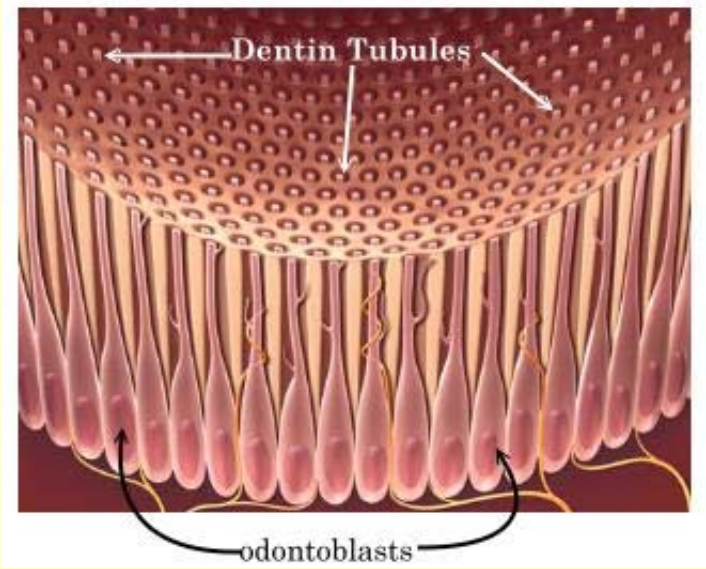
Hypocalcified enamel

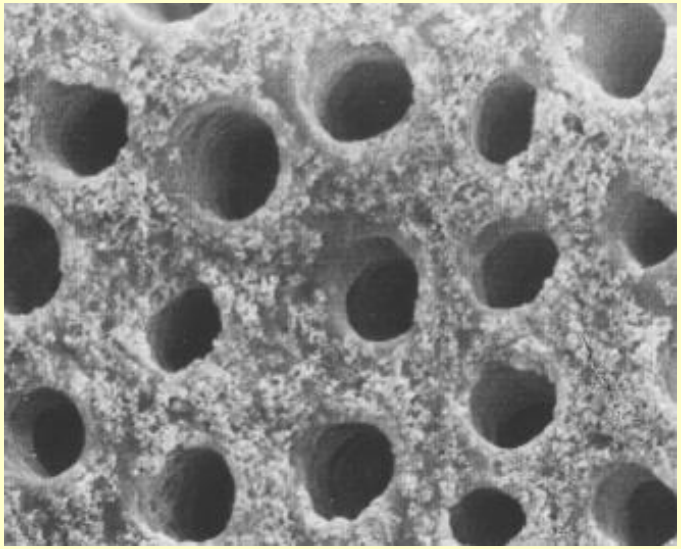


Hypoplastic enamel



Developmental defects of tooth dentine



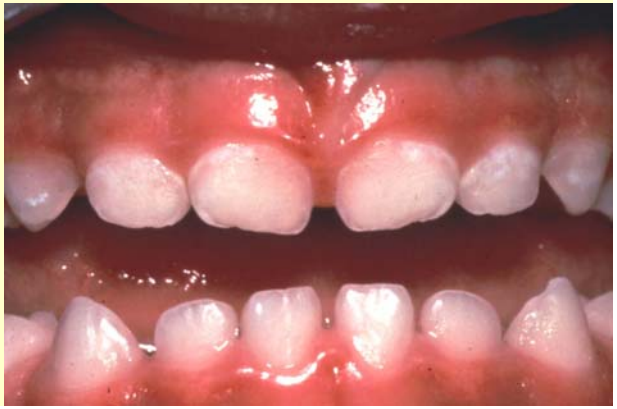


Dentine composition

- Calcified tissue
  - 70% mineral hydroxylapatite
  - 20% organic material
  - 10% water
- Covered by enamel on the crown and cementum on the root
- Dentinogenesis
  - initiated by the odontoblasts of the pulp
  - begins prior to the formation of enamel

Dentinogenesis imperfecta

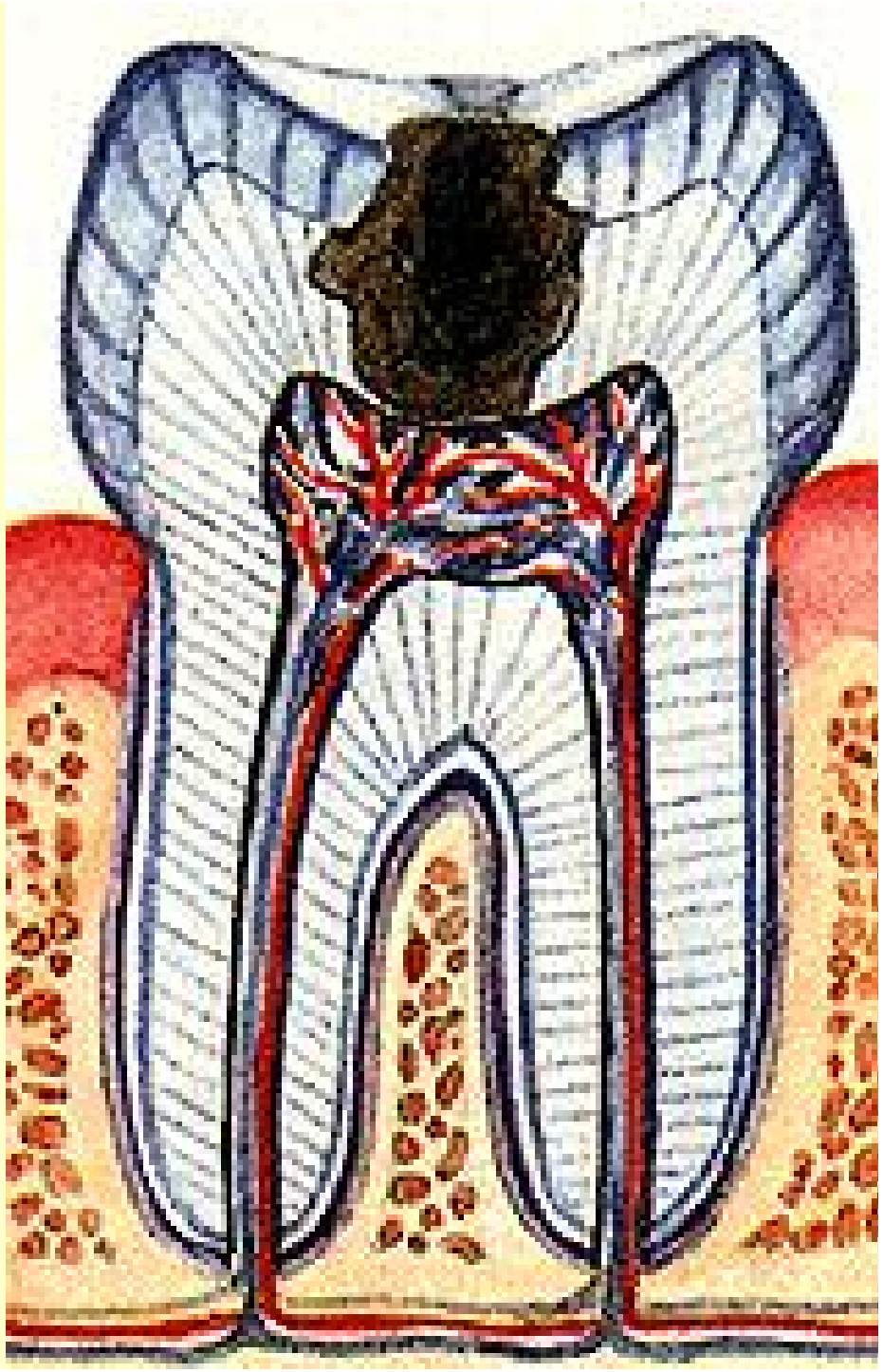
- estimated 1 in 6,000 to 8,000 people
- Teeth
  - discolored
    - blue-gray or yellow-brown (most often)
  - Translucent
  - weaker than normal
    - prone to rapid wear, breakage, and loss
  - Obliterated pulpal chamber



Three types of dentinogenesis imperfecta

- Type I occurs in people who have osteogenesis imperfecta
  - condition in which bones are brittle and easily broken.
  - caused by mutations in one of several genes (most often the *COL1A1* or *COL1A2* genes)
- Type II and type III usually occur in people without other inherited disorders
  - Mutations in the dentin sialophosphoprotein (*DSPP)* gene code for 3 proteins
    - Dentine sialo-, **phospho–,** glyco-protein
    - More than 20 mutations

Dental Caries



Dental Caries

- Prevalence of caries in developed countries remains at greater than 95% of the population.
- Localized destruction of the tooth by bacterial action
  - Cariogenic bacteria – production of acid
  - Carbohydrate in the diet –
    - metabolized by the bacteria
      - to produce acid
      - to produce of extracellular polysacharides (biofilm that helps bacteria colonization on the tooth surface)

The first isolation of cariogenic bacteria

Clark, 1924

****

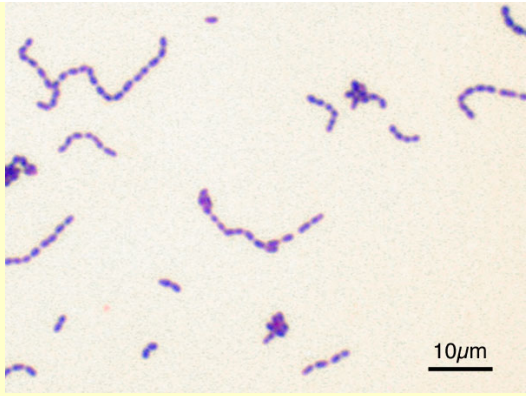
Isolation of cariogenic bacteria from caries lesions

Discovery of Mutans streptococci

Caries development

- Causative bacteria
  - **Streptococci species**
    - ***S. mutans****, S. sorbitus*
  - Lactobacilli species
    - L. acidophilus, L. oris, L. salivarius
  - Actinomyces species
    - A. viscosus, A. naeslundi
- Affects enamel and dentine
  - Demineralization by dissolution of the hydroxyapatit crystals by acids
  - Loss of organic components

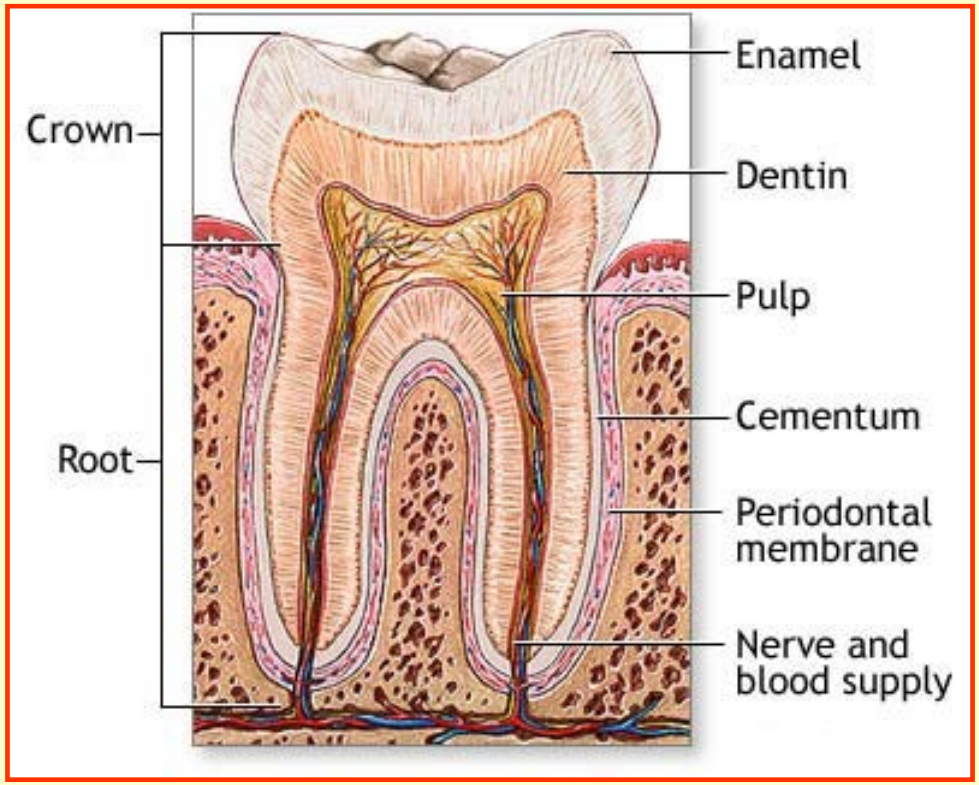
S. mutans

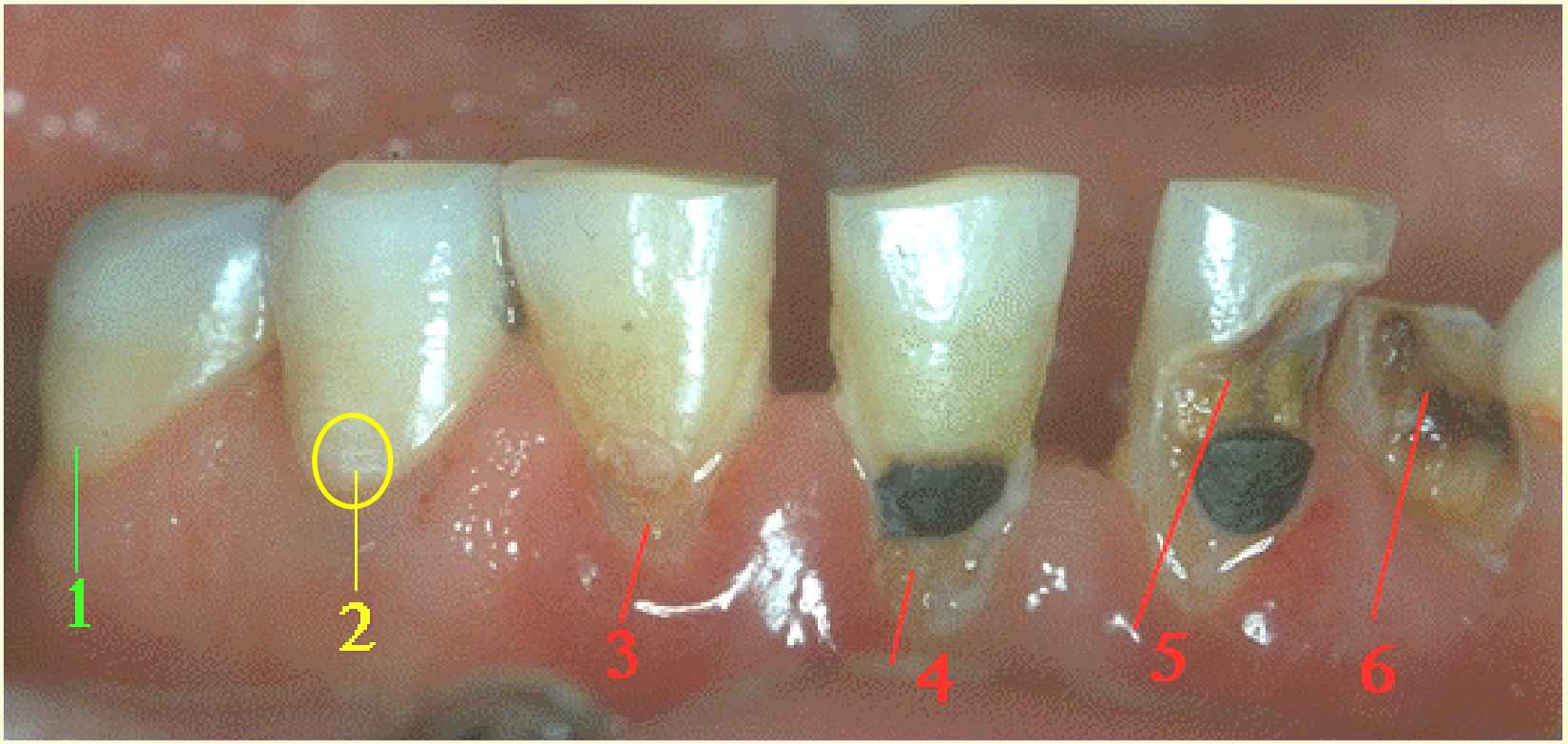


- Production of extracellular polysacharides from sucrose (insoluble in water)
- Highly acidogenic
- Number of S. mutans bacteria significantly higher in patients with caries (almost all subjects)
- Some lesions can develop in the absence of *S. mutans (*particularly in fissures)
- Occasionally large numbers of *S. mutans* can be found in plaque in the absence of caries

Dental Caries

Enamel Caries **Dentin Caries** **Cementum Caries (Root caries)**



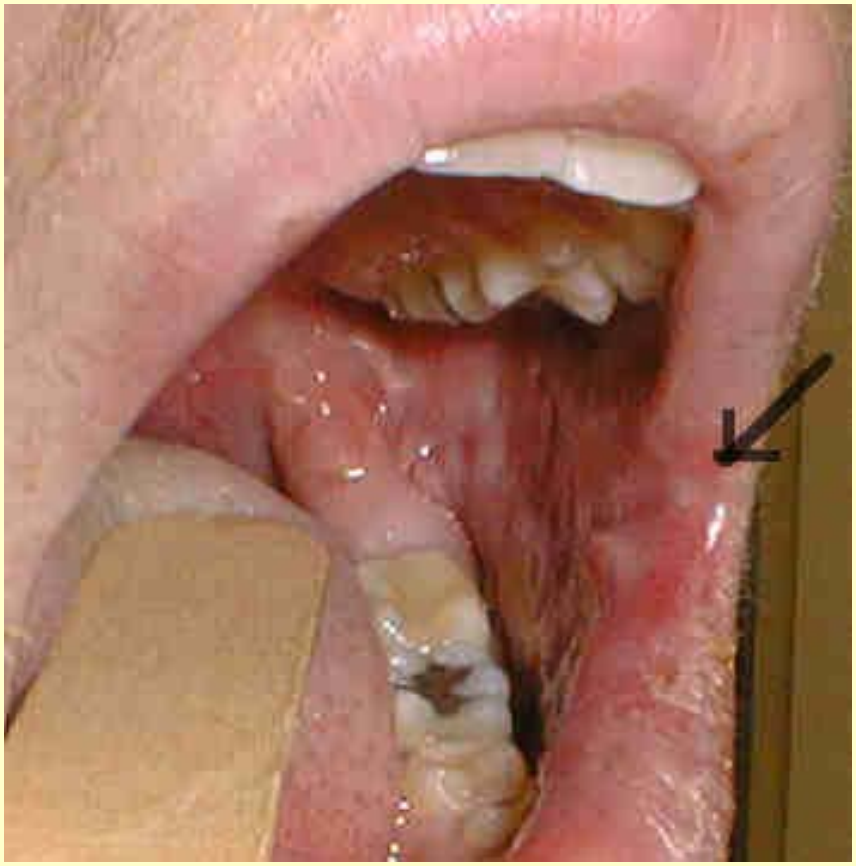


1. The first signs of demineralization.
2. A tooth surface without caries.
3. The enamel surface has broken down.
4. A filling has been made but the demineralization has not been stopped.
5. The demineralization proceeds and undermines the tooth.
6. The tooth has fractured.

Manifestation of systemic diseases in oral cavity

- Cardiovascular system diseases
  - Cyanosis – mucosa and lips
- Liver diseases
  - Jaundice (icterus)
- Protein calorie malnutrition – gingivitis, atrophy of tongue papillae, ulcers
- Vitamine deficiecy
- Inflammarory diseases (e.g. Crohn disease, Sjogren sy)
  - aphtouse stomatitis, mucosal edemas, ulcers, xerostomia

Manifestation of Crohn's Disease in Oral Cavity



Oral ulcerations, like in these pictures, were present in

95% of the patients with Crohn's disease

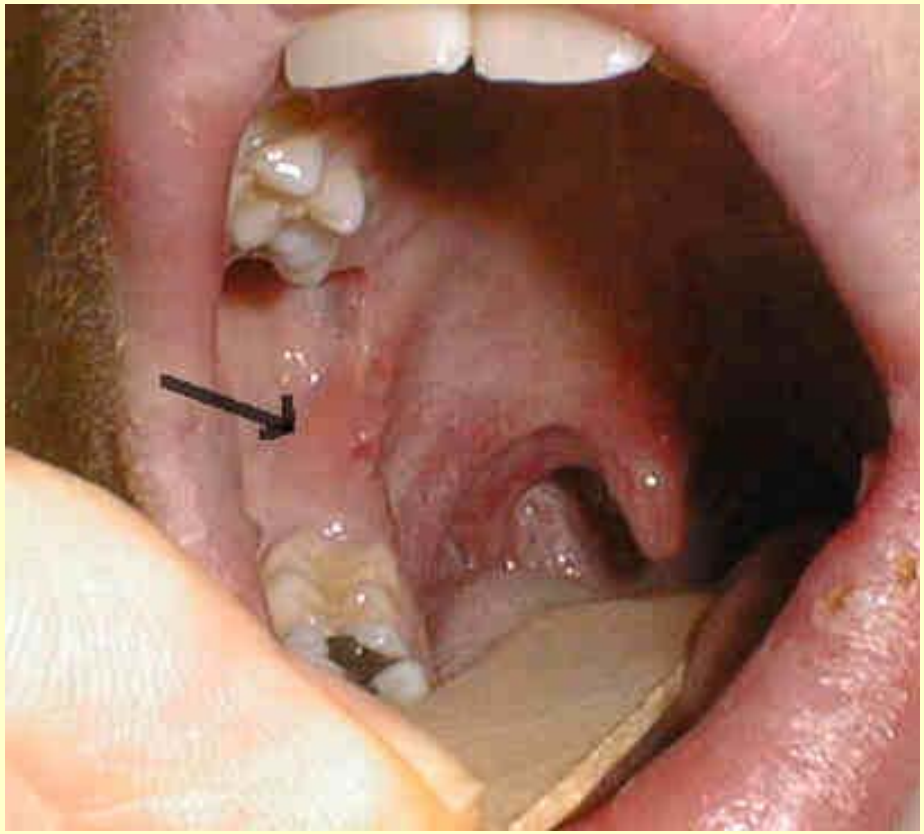
2% of the patients with ulcerous colitis

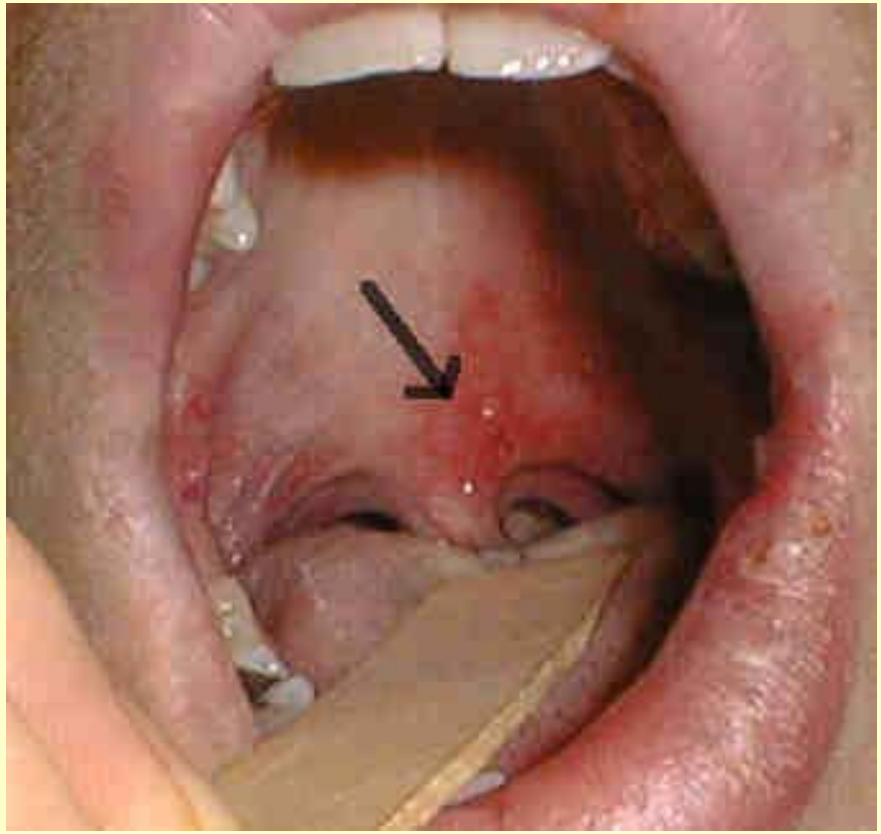
1% of the normal subjects

Cause: IBD or nutrition defect

pain and eating difficulties

Manifestation of Crohn's Disease in Oral Cavity

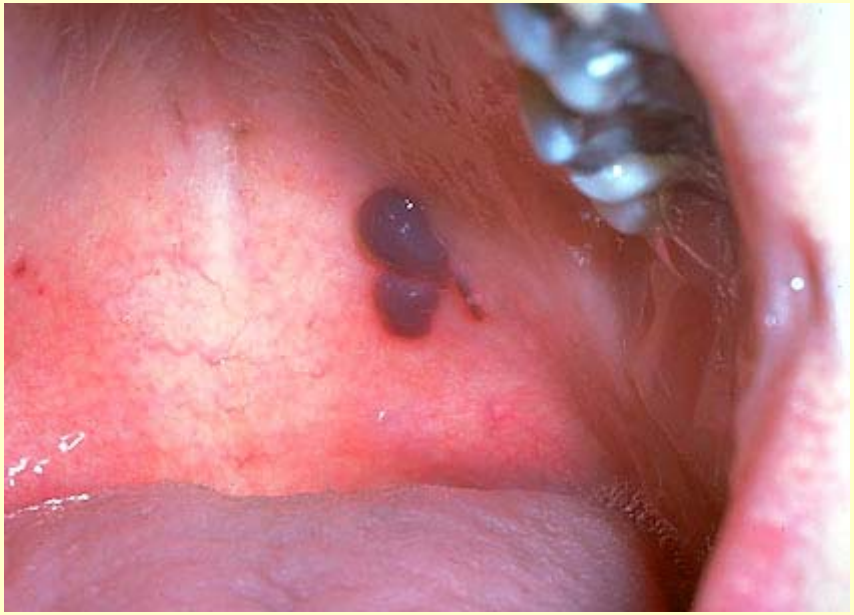




Manifestation of systemic diseases in oral cavity

- Cardiovascular system diseases
  - Cyanosis – mucosa and lips
- Liver diseases
  - Jaundice (icterus)
- Protein calorie malnutrition – gingivitis, atrophy of tongue papillae, ulcers
- Vitamine deficiecy
- Inflammarory diseases (e.g. Crohn disease, Sjogren sy)
  - aphtouse stomatitis, mucosal edemas, ulcers, xerostomia
- Hematologic diseases
  - pale mucosa (anemia)
  - gum bleeding, ulcers, gingiva infiltration with leukemia cells

A 24 year-old female in good health and who had just finished eating lunch when this "popped up“



This raised lesion of the soft palate may be:

a. traumatic hematoma

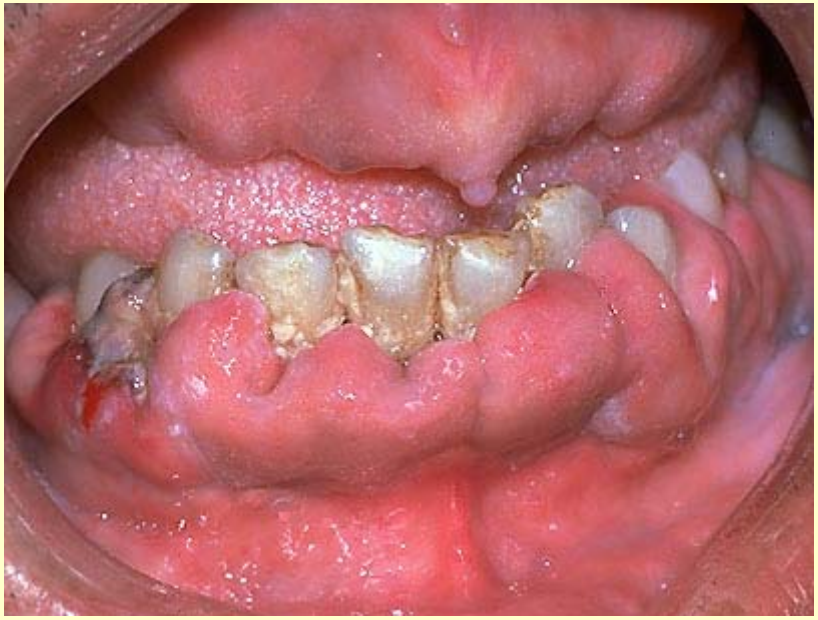
b. systemic problem

c. melanoma

d. hemangioma

A 40 year-old male:

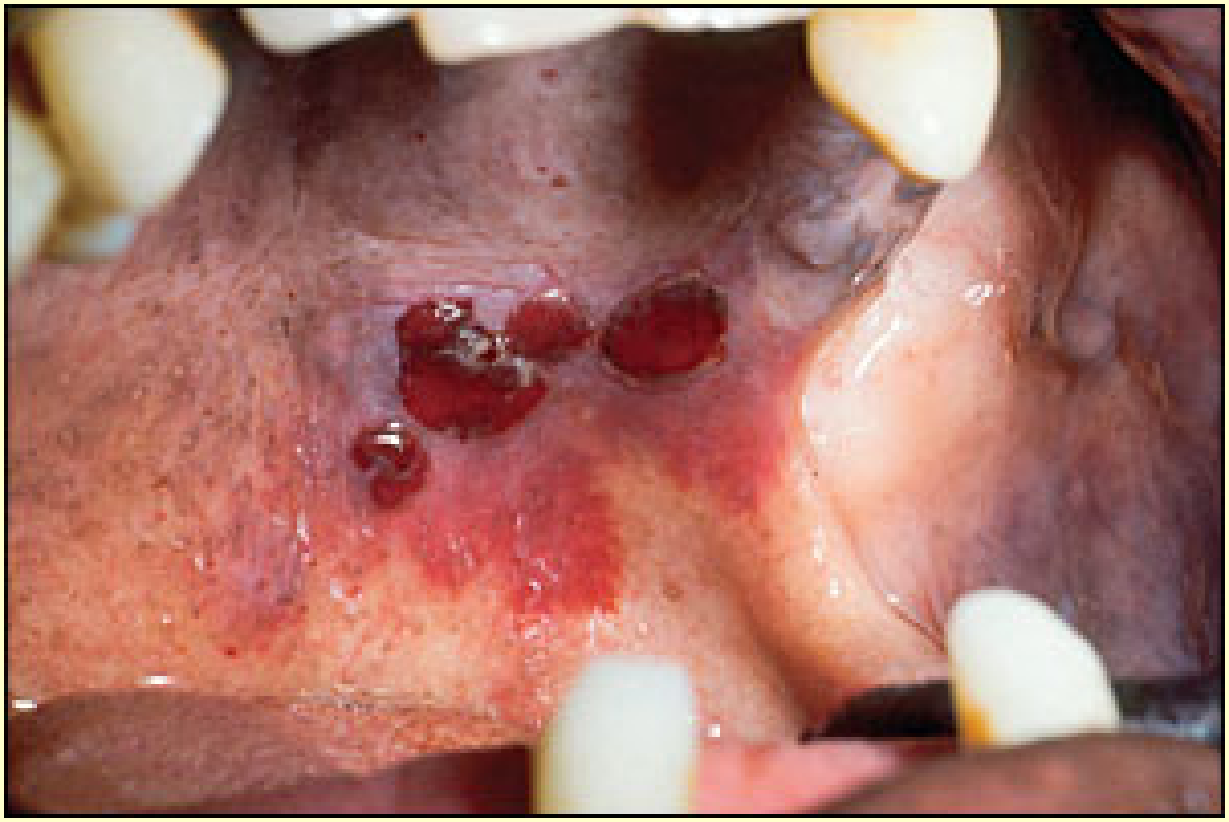
- who just recently had his **upper teeth removed**
- did not have mandibular gingivae in this condition
- he has **spontaneous bleeding** and feels badly
- he has an **abnormally high white blood count**



The history and clinical features suggest:

a. squamouse cell carcinoma
b. hormonal hyperplasia
c. hyperplasia due to leukemia
d. localized gingival hyperplasia due to calculus

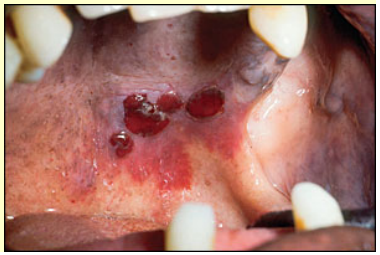
Idiopathic purpura and hemorrhagic bullae on the palatal mucosa



What is the diagnosis?

Thrombocytopenia

- manifestation usually when < 50 × 10^3 Plt / μL
- may be detected initially because of oral lesion development
- Minor trauma to the oral mucosa during routine function (such as chewing or swallowing) may produce various types of hemorrhagic lesions
  - petechiae
  - purpura
  - ecchymosis
  - hemorrhagic bullae
  - hematoma formation
- Gingival bleeding may result from minor trauma or occur spontaneously.



Dysphagia

Dysphagia

- Difficulty with swallowing
  - problems with the transit of food or liquid from the mouth to the hypopharynx or through the esophagus.

Consequences:

  - Compromised nutrition
  - Aspiration
  - Reduced quality of life

Normal transport of an ingested bolus

- depends on:
  - the consistency and size of the bolus
  - the caliber of the lumen
  - the integrity of peristaltic contraction
  - deglutitive inhibition of both the UES and the LES

Additional terminology of swallowing dysfunction

- ***Aphagia***
  - complete esophageal obstruction (acute)
- ***Odynophagia***
  - painful swallowing (e.g. mucosal ulceration within the oropharynx or esophagus)
- ***Globus pharyngeus***
  - foreign body sensation localized in the neck that does not interfere with swallowing and sometimes is relieved by swallowing.
- ***Phagophobia***
  - fear of swallowing and *refusal to swallow* may be psychogenic or related to anticipatory anxiety about food bolus obstruction, odynophagia, or aspiration

Classification of dysphagia

- By location
  - Oral
  - Pharyngeal
  - Esophageal

Classification of dysphagia

- By circumstances in which it occurs
  - *Structural dysphagia*
    - oversized bolus
    - narrow lumen
  - *Propulsive* (*motor) dysphagia*
    - abnormalities of peristalsis
    - impaired sphincter relaxation after swallowing
  - Combined
    - e.g. scleroderma
      - presents with absent peristalsis as well as a weakened LES that predisposes patients to peptic stricture formation

Oral and Pharyngeal (Oropharyngeal) Dysphagia

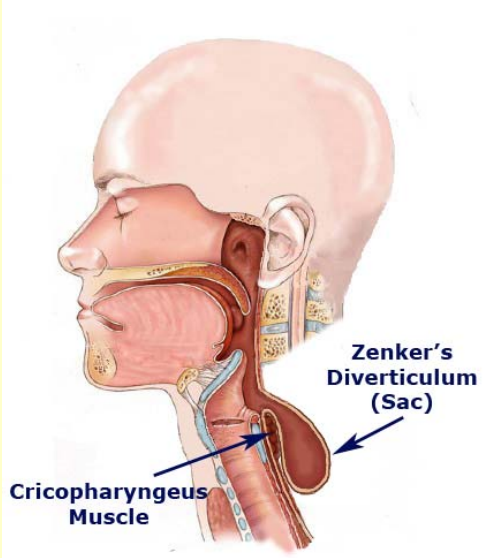
- Oral-phase dysphagia
- Pharyngeal-phase dysphagia
- Cause
  - **Neurologic** (cerebrovascular accidents, Parkinson's disease, and amyotrophic lateral sclerosis)
  - Muscular
  - **Structural** (Zenker's diverticulum, cricopharyngeal bar, and neoplasia)
  - **Iatrogenic** (surgery and radiation)
  - Infectious
  - Metabolic causes

Oral-phase dysphagia

- Poor bolus formation and control
- Food has prolonged retention within the oral cavity and may seep out of the mouth
- Drooling and difficulty in initiating swallowing
- Premature spillage of food into the hypopharynx with resultant aspiration into the trachea or regurgitation into the nasal cavity

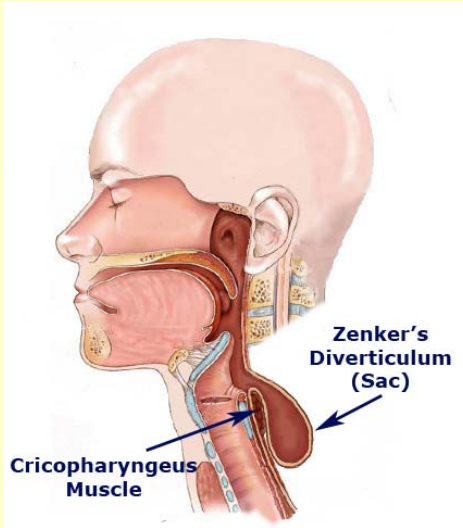
Pharyngeal-phase dysphagia

- Retention of food in the pharynx due to poor tongue or pharyngeal propulsion or obstruction at the UES
- **Zenker's diverticulum**
  - typically is encountered in elderly patients (estimated prevalence between 1:1000 and 1:10,000)
  - Manifestation:
    - Dysphagia
    - Regurgitation of particulate food debris
    - Aspiration
    - Halitosis



Pathogenesis of Zenker's diverticulum

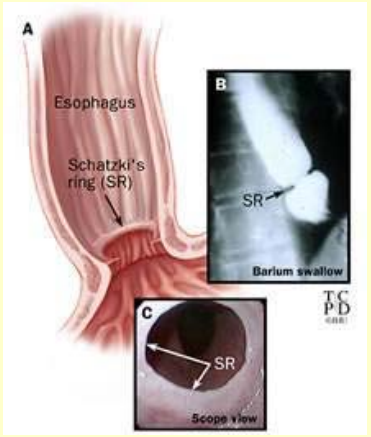
- Stenosis of the cricopharyngeus causes diminished opening of the UES
- Results in increased hypopharyngeal pressure during swallowing
- Development of a pulsion diverticulum immediately above the cricopharyngeus in a region of potential weakness (Killian's dehiscence)



Esophageal Dysphagia

- esophagus (18–26 cm x 2 cm x 3 cm) is anatomically divided into:
  - cervical esophagus (pharyngoesophageal junction to the suprasternal notch)
  - thoracic esophagus (to the diaphragmatic hiatus)
- Solid food dysphagia becomes common when the lumen is narrowed to <13 mm
  - can occur with larger diameters in the setting of poorly masticated food or motor dysfunction
- Circumferential lesions are more likely to cause dysphagia than are lesions that involve only a partial circumference of the esophageal wall

Common causes of esophageal dysphagia



- Structural causes
  - Schatzki's rings
  - Eosinophilic esophagitis
  - Peptic strictures
- Propulsive causes
  - abnormalities of peristalsis and/or deglutitive inhibition
  - Striated muscle diseases (usually involves both the oropharynx and the cervical esophagus)
  - Smooth muscle diseases (involve the thoracic esophagus and the LES - absent peristalsis)
    - absence of swallow-induced contraction
    - presence of nonperistaltic, disordered contractions.

- Dysphagia also occurs in the setting of gastroesophageal reflux disease without a stricture, perhaps on the basis of altered esophageal sensation, distensibility, or motor function.

Pathophysiology of esophageal diseases

Structural disorders

Mobility disorders

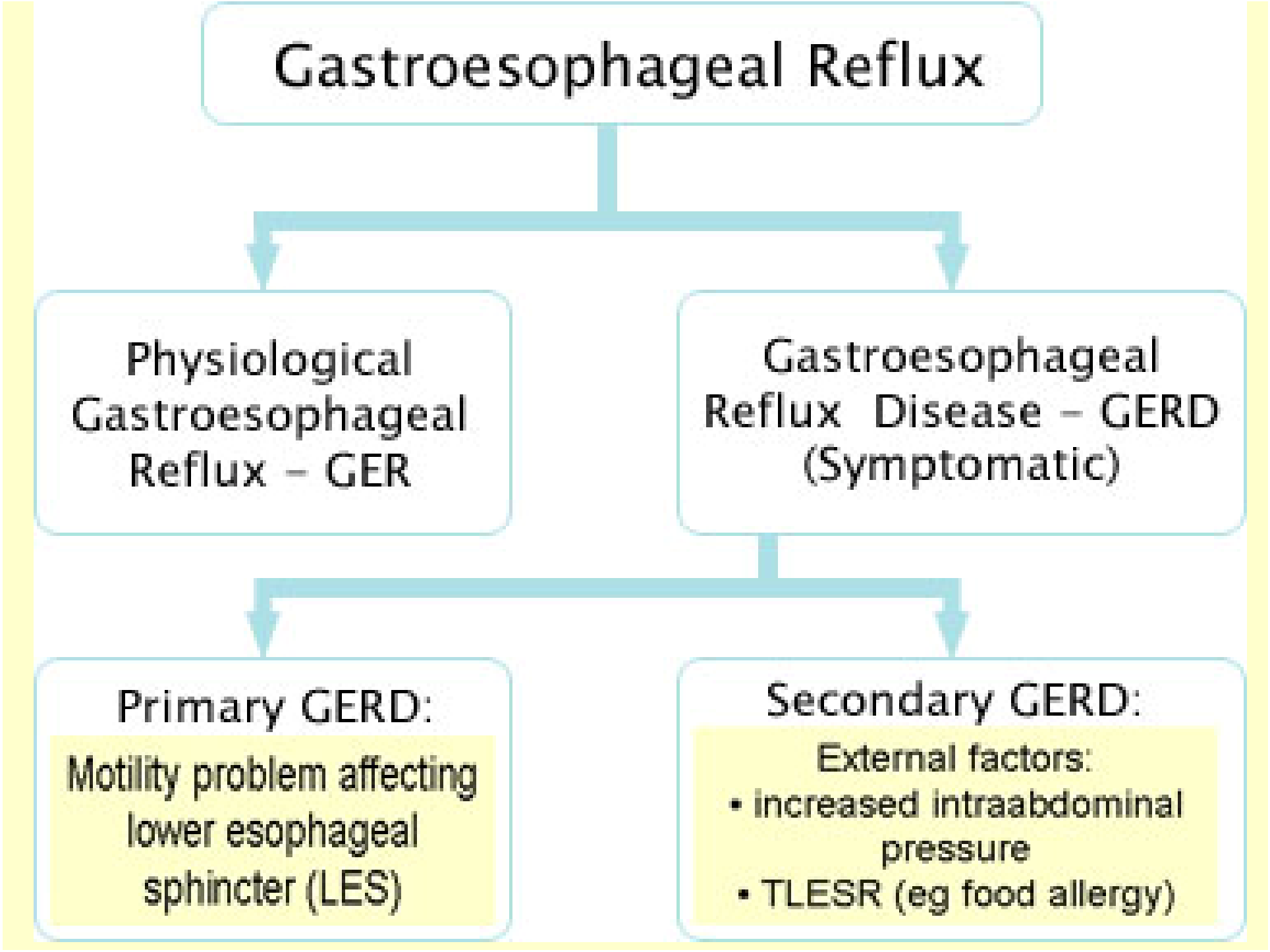
Structural disorders of esophagus

- Inflammation
  - acute (GER, bacteria toxins)
  - chronic (GER - stenosis - scarring, achalasia, tumors)
- Oesophageal ulcers – GER, ulcer disease, gastrinoma

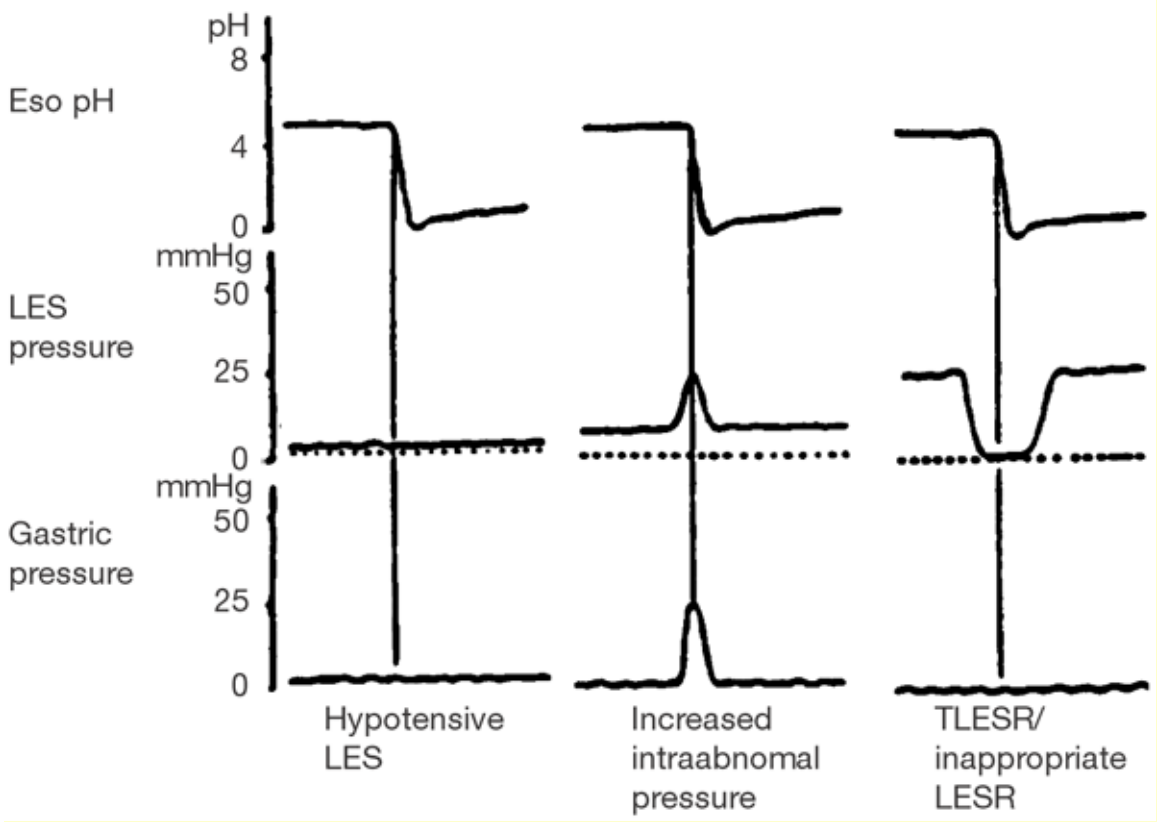
- Hiatal hernia
- Rings and webs
- Diverticula
  - may content meal, consequently infection, risk of perforation
- Varices
  - pathogenesis:
    - hypertension in v. portae (cirrhosis, trombus in v. portae
    - possibility of severe bleeding (!!!)
- Tumors
  - benign
  - malignant – squamous cell carcinoma, adenocarcinoma

Motility disorders of esophagus

- **Gastroesophageal reflux disease (GERD)**
- Achalasia
- Difuse esophageal spasm
- Hypertensive esophageal peristaltic contractions (nutcracker esophagus)
- Hypertensive and hypercontracting LES


Gastroesophageal Reflux
Physiological Gastroesophageal Reflux – GER
Gastroesophageal Reflux Disease – GERD (Symptomatic)
Primary GERD:
Motility problem affecting lower esophageal sphincter (LES)
Secondary GERD:
External factors:
• increased intraabdominal pressure
• TLESR (eg food allergy)

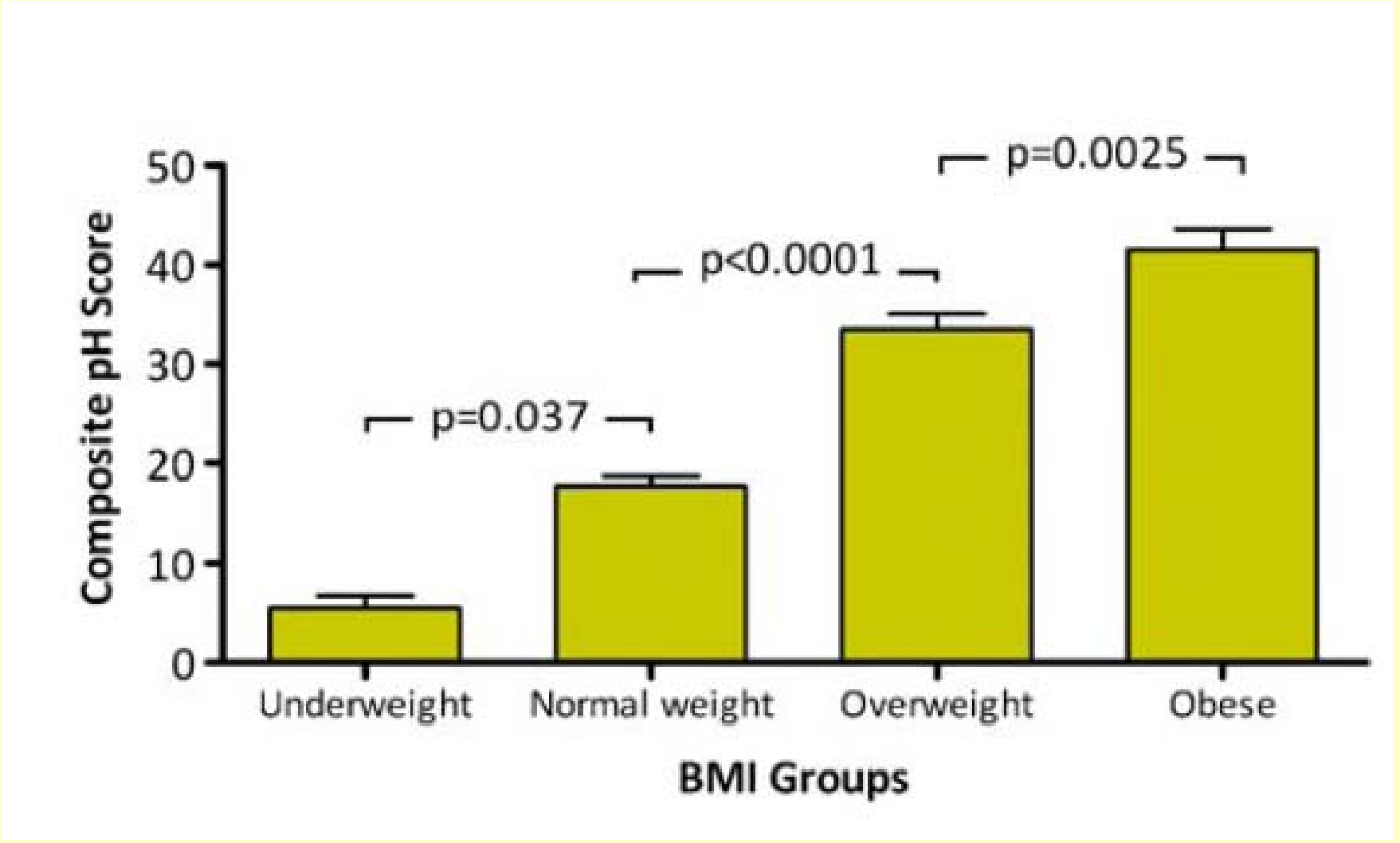
Mechanisms of LES incompetence in gastroesophageal reflux



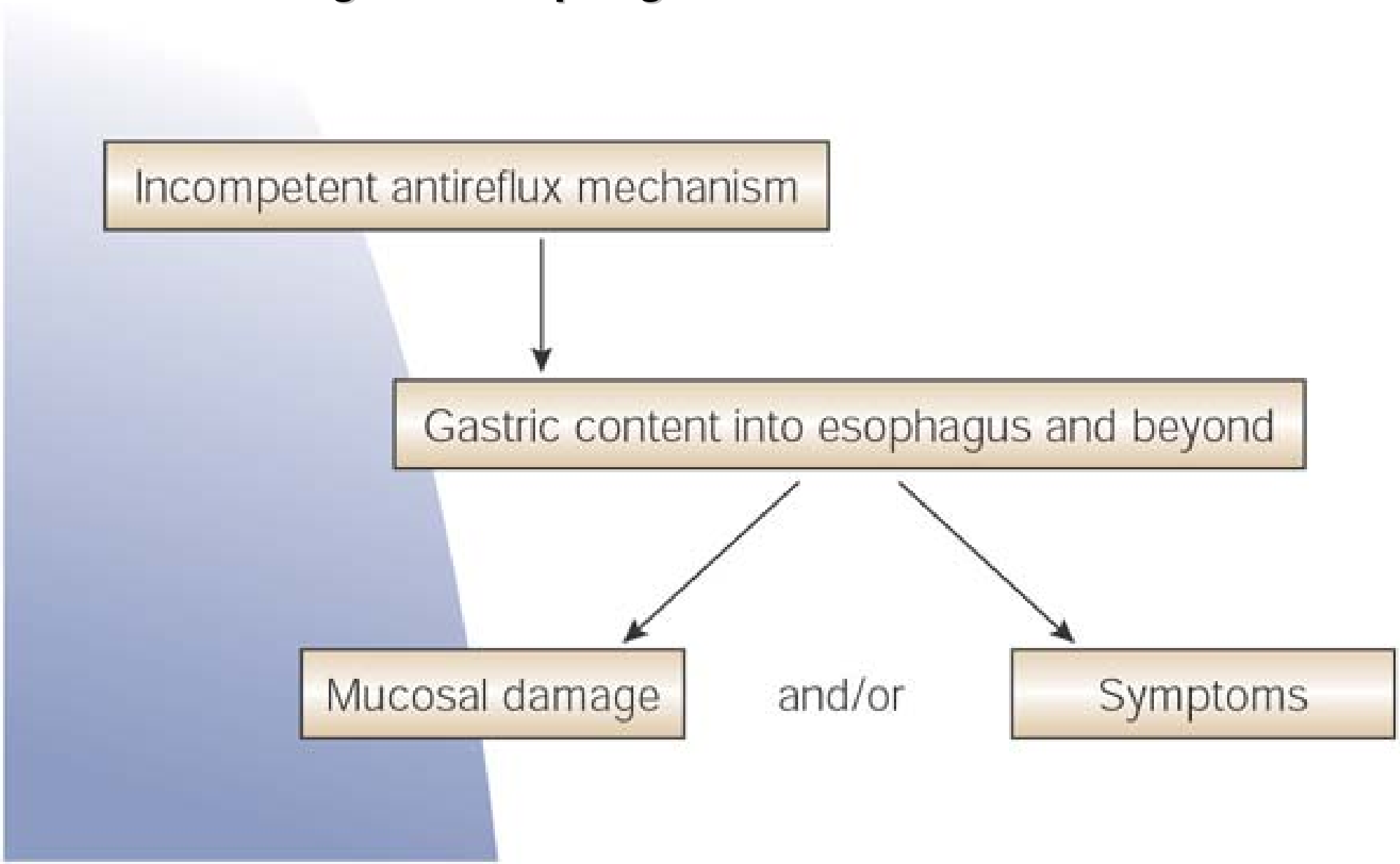
- Hypotensive LES
- Increased intragastric pressure (e.g. obesity, pregnancy).
- LES may exhibit frequent reflex transient LES relaxation (TLESR) vagovagal inhibitory reflex

Dodds WJ et al. N. Engl J Med. 1982;307(25):1547–1552

Obesity and Gastroesophageal Reflux



A simple overview of the pathogenesis of gastroesophageal reflux disease.



GI Motility online (May 2006) | doi:10.1038/gimo21

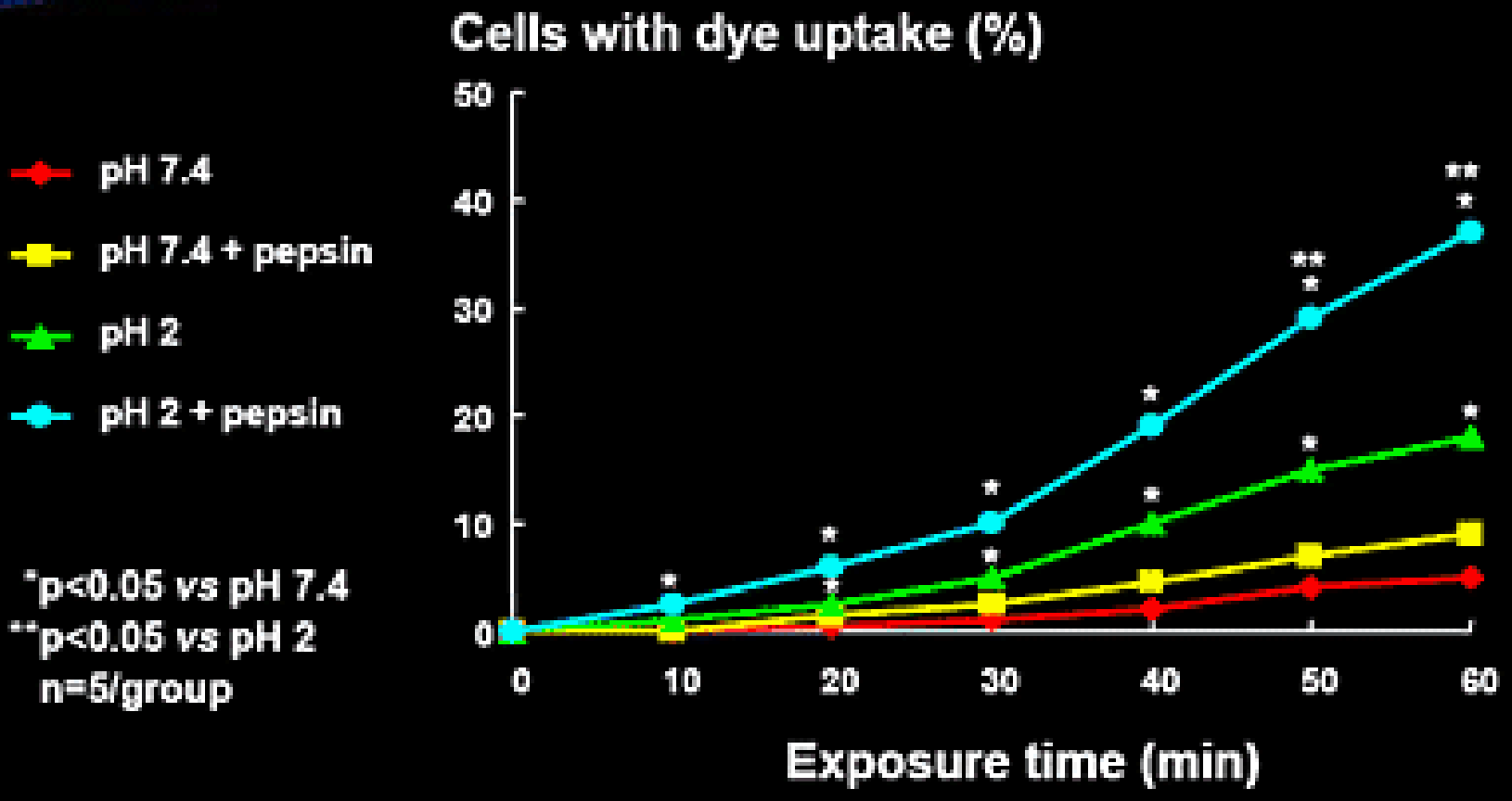
GERD

- Squamous mucosa of esophagus is more vulnerable to peptic digestion than columnar gastric epithelium

- Manifestation
  - Heartburn (pyrosis)
- Consequences
  - Inflammation of esophageal mucosa
  - Barrett's esophagus
  - Esophageal adenocarcinoma

- 7% of the population experiences heartburn daily and 44% at least once a month

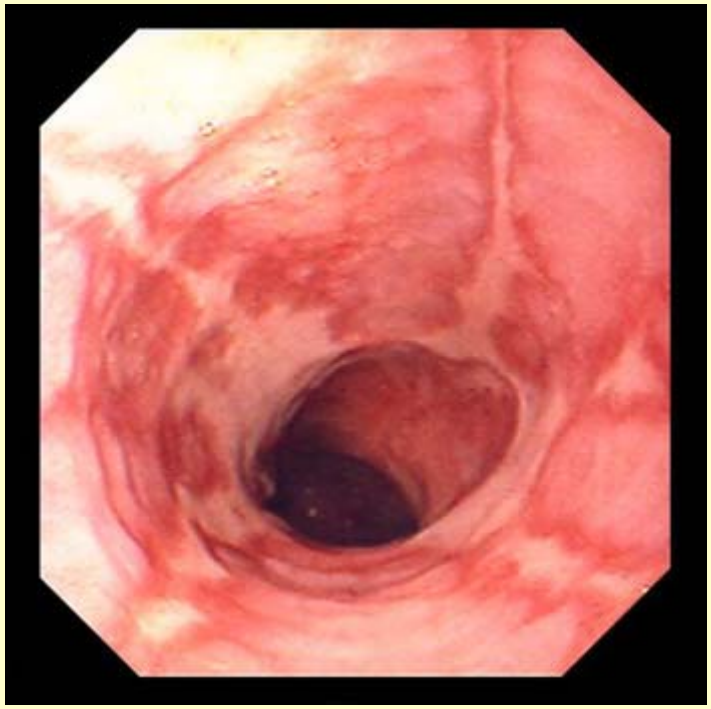
Esophageal epithelial injury: Acidified pepsin vs acidity alone



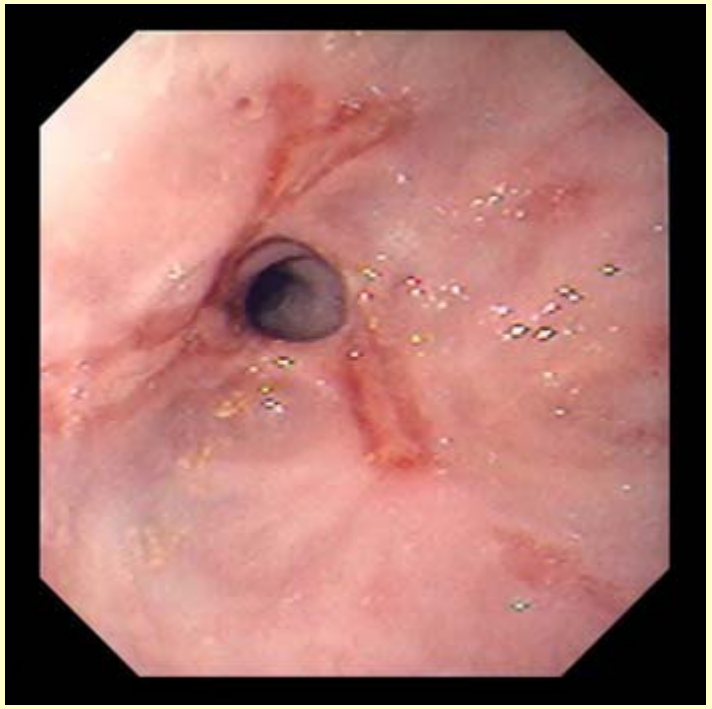
Tobey *et al, Am J Gastroenterol* 2001; 96: 3062

Complications of Gastroesophageal Reflux Disease (GERD)

Reflux esophagitis

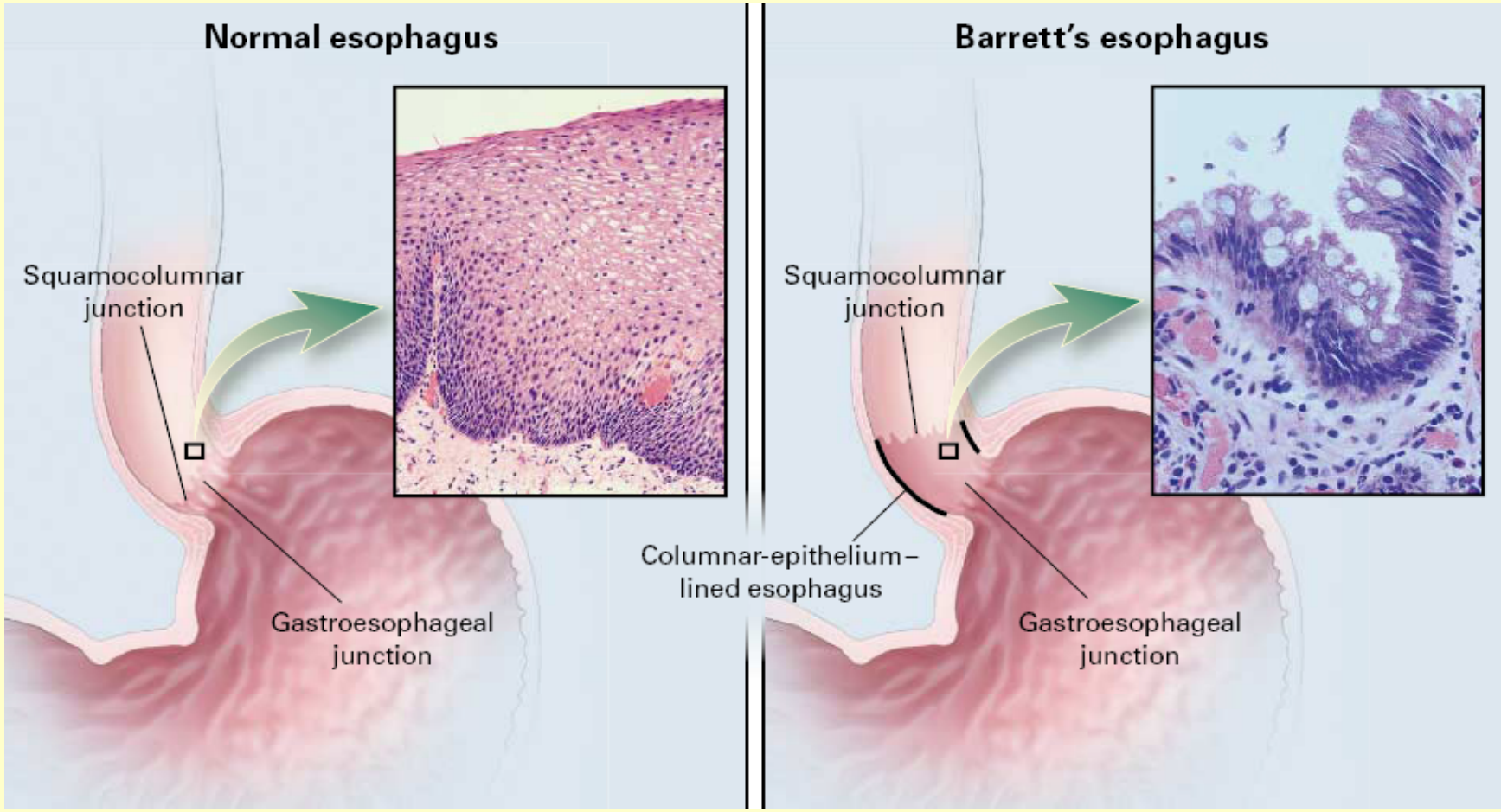


Peptic esofageal stricture



Reflux esophagitis
Barrett's Esophagus

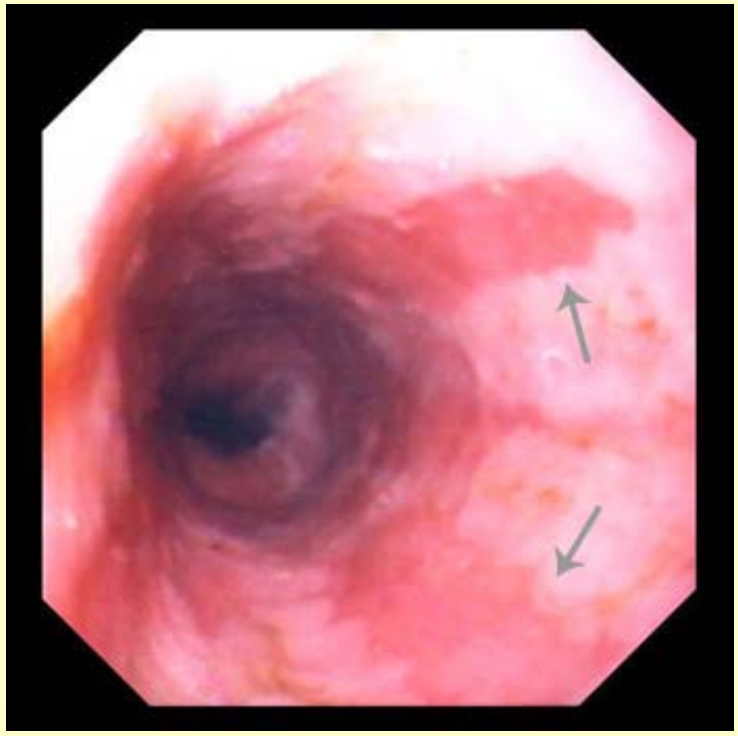
The squamocolumnar junction is proximal to the gastroesophageal junction

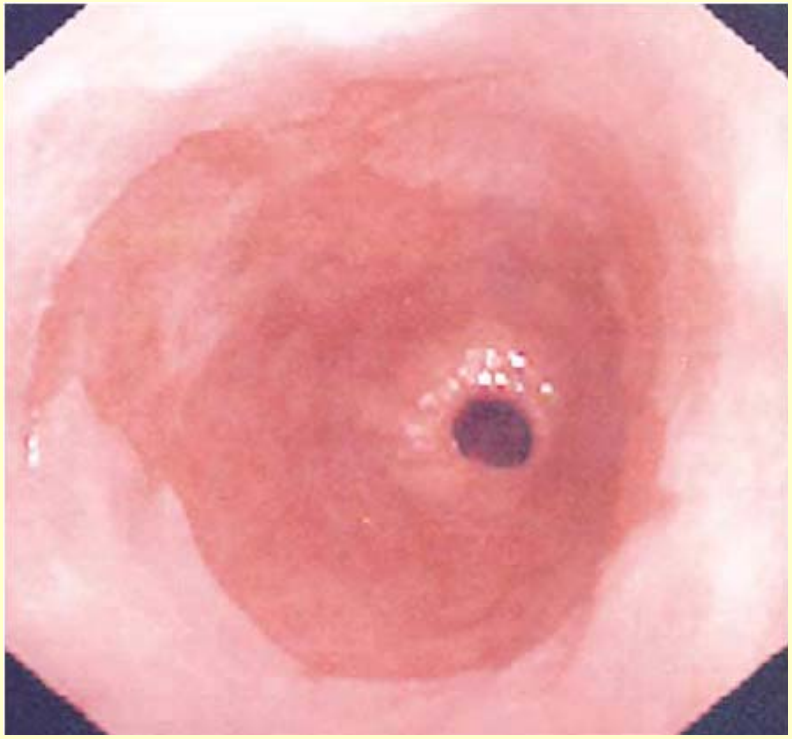


Esophagus: squamous epithelium; Stomach: columnar epithelium

Complications of Gastroesophageal Reflux Disease (GERD)

Barrett's esophagus



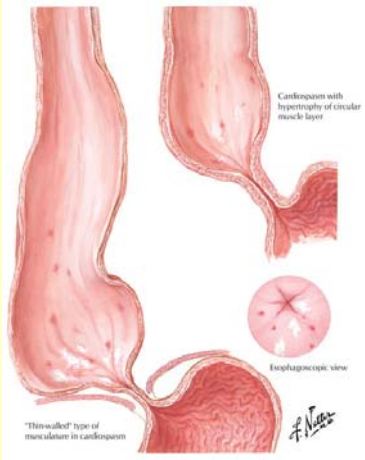


Presence of columnar epithelia in the lower esophagus, replacing the normal squamous cell epithelium = **METAPLASIA**

Achalasia

inhibitory neurons, which contain nitric oxide (NO) and vasoactive intestinal peptide (VIP) are slowly destroyed as part of the inflammatory reaction

- Motor disorder
- Involving the lower two thirds (smooth muscle segment) of the esophagus
- Caused by degeneration of intramural myenteric plexus neurons resulting in:
  - Absent peristalsis
  - Failure of deglutitive LES relaxation
- Symptoms
  - dysphagia, chest pain, and regurgitation



To remember

- Xerostomia (causes, consequences)
- Dysphagia (causes)
- Systemic diseases may manifest in oral mucosa (
- Gastroesophageal reflux disease (causes, pathogenesis)

END