Kazan (Volga region) Federal University
Institute of Fundamental Medicine and Biology
Department of Morphology and General Pathology

Pathophysiology of the oral cavity

Lecturer
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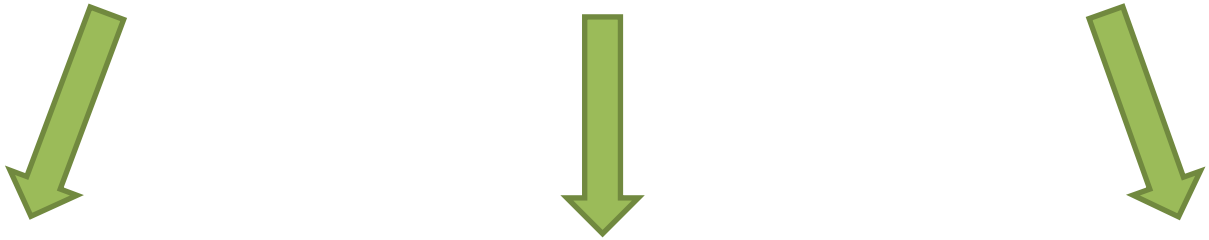
PATHOLOGY OF ORAL CAVITY



ORAL MUCOSA

SALIVARY GLANDS

HARD TISSUES (TEETH+JAWS)

I. Pathology of oral mucosa

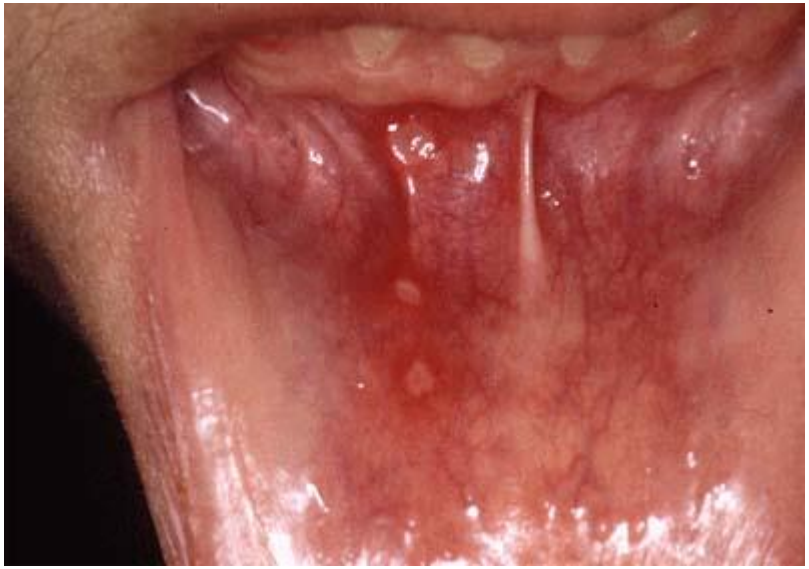
Overview of oral mucosa diseases

- Idiopathic recurrent aphthous ulcers affect 15%–20% of the population; severe cases can be debilitating
- Oral ulcers may also be associated with Crohn disease and other gastrointestinal disorders or due to herpes simplex, other viral infections, vasculitis, or other autoimmune disorders
- Candidiasis of the oral cavity is common and painful. Predisposing factors include immunosuppression, hyposalivation, and use of steroids or antibiotics
- Hair leukoplakia is due to Epstein–Barr viral infection and may be the presenting sign of HIV/AIDS

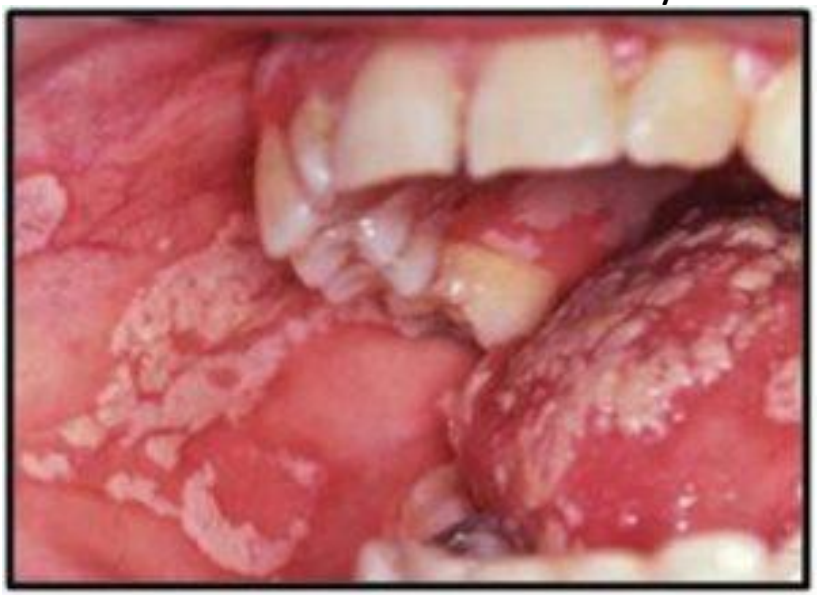
Overview of oral mucosa diseases

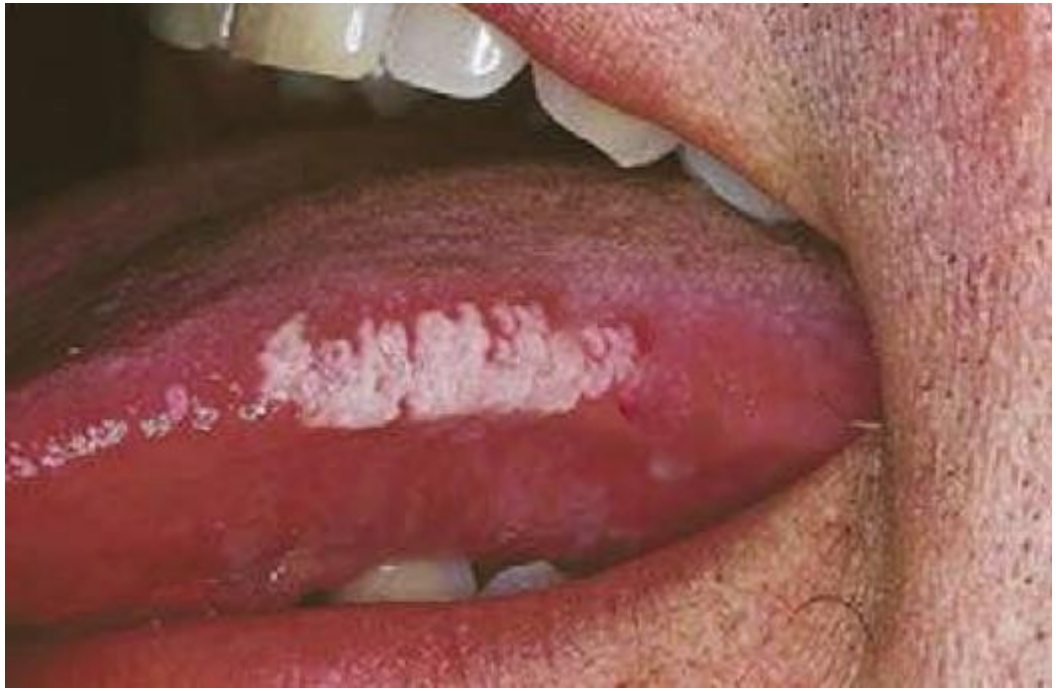
- Oral lichen planus (LP) and lichenoid reactions affect 1%–2% of the population and are the most common cause of desquamative gingivitis; LP probably reflects a hypersensitivity response to endogenous or exogenous antigens
- Leukoplakia is a premalignant condition associated with smoking and/or alcohol ingestion that must be distinguished from LP and benign frictional keratoses
- Bullous diseases that affect the mouth include pemphigus, pemphigoid, and lupus erythematous
- Intraoral pigmented lesions include nevi, postinflammatory hyperpigmentation, drug reactions, tattoos, and rarely melanoma.

Aphthous ulcers

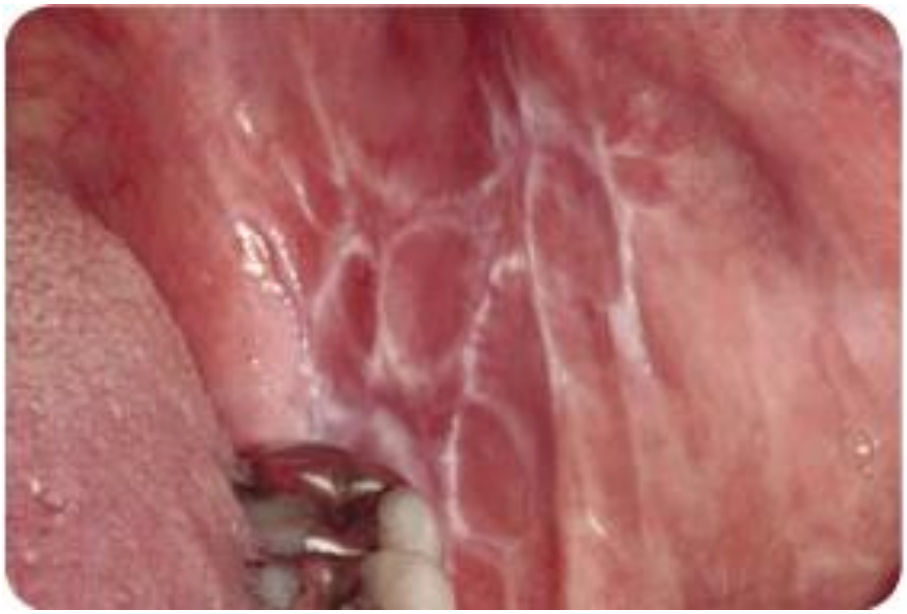


Candidiasis of the oral cavity



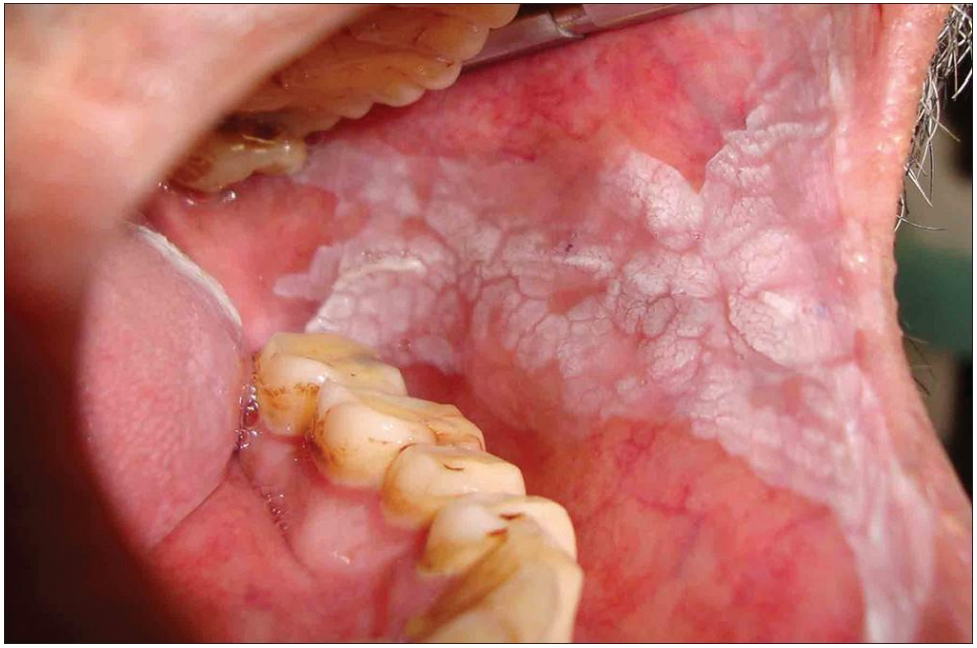


Hair leukoplakia

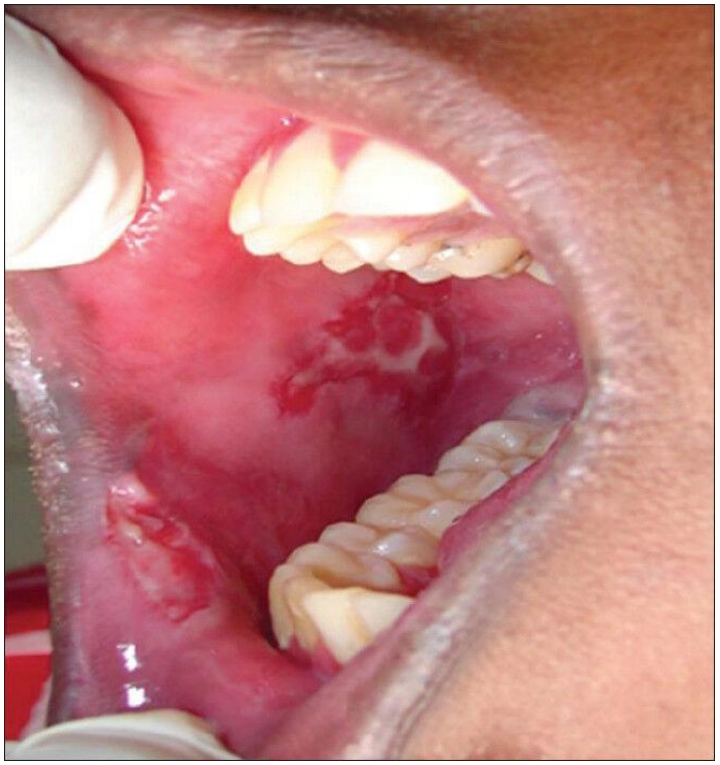


Oral lichen planus

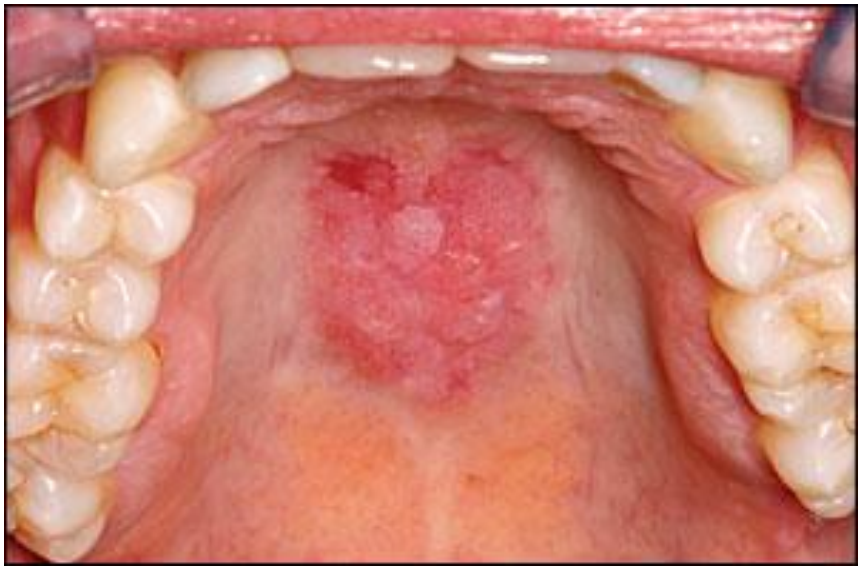
Leukoplakia



Bullous diseases

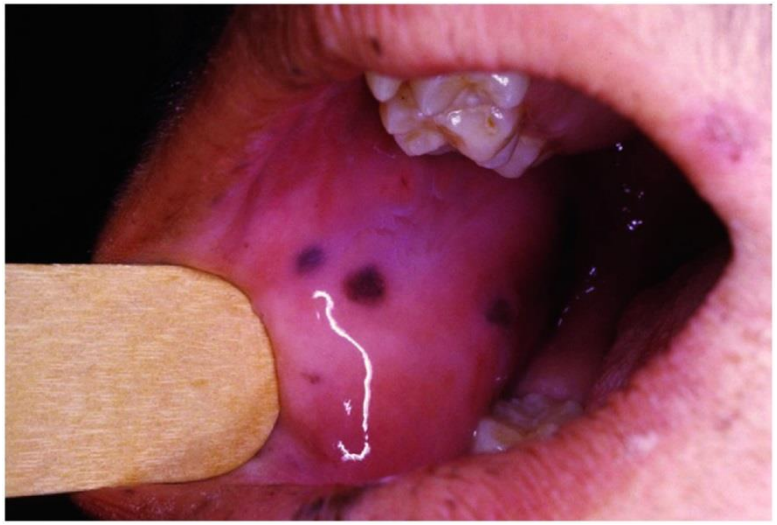


pemphigus

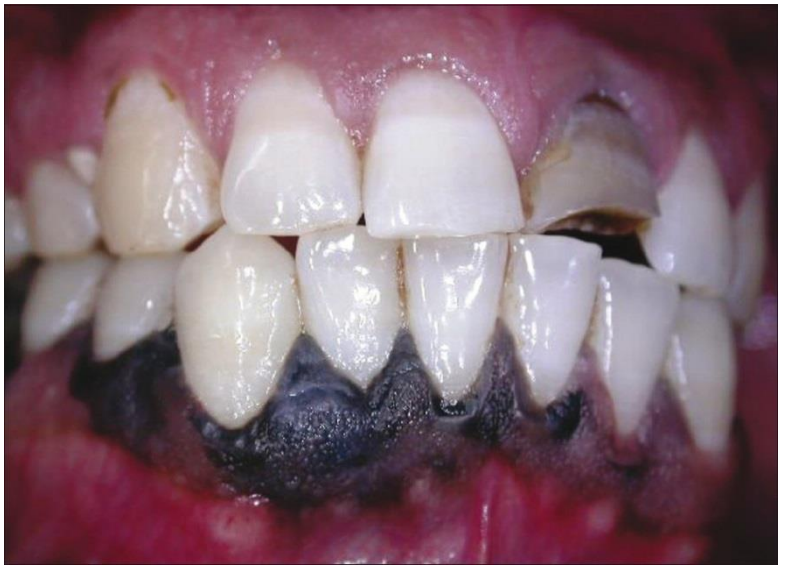


lupus erythematous

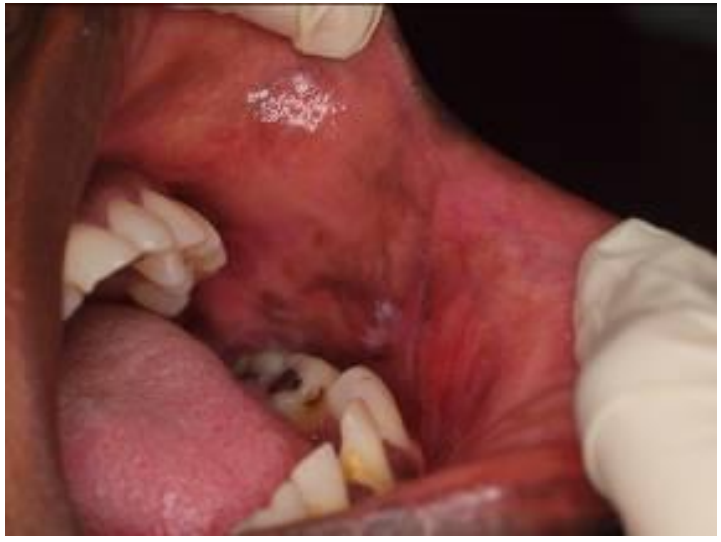
Intraoral pigmented lesions



nevus



melanoma

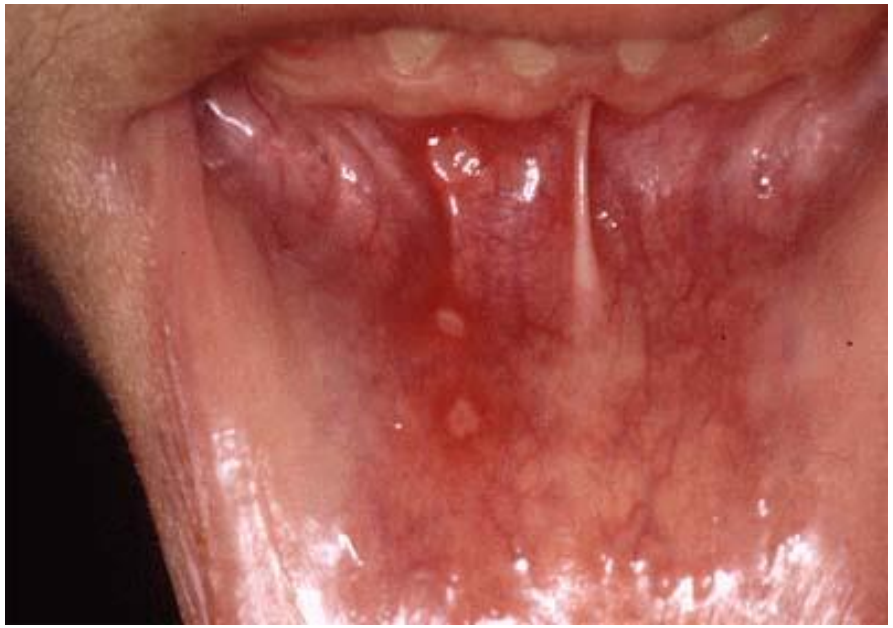


postinflammatory pigmentation in lichen planus

Oral inflammatory lesions

- Aphthous ulcers (Canker sores)
- Herpes Simplex Virus Infections
- Oral Candidiasis (Thrush)

Aphthous Ulcers (Canker Sores)



- Common superficial mucosal ulcerations
- Up to 40% of the population.
- First 2 decades of life
- Extremely painful
- Cause : unknown
- More prevalent within some families
- May be associated with celiac disease, inflammatory bowel disease (IBD) and Behcet disease.
- Resolve spontaneously in 7 to 10 days but can recur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Herpes Simplex Virus Infections

Etiology :

– Herpes simplex virus (HSV) type I,

– HSV type II (herpes genitalis)

• Clinical features and pathogenesis:

– Primary infection in children 2-4 y.o

– Usually asymptomatic, dormant virus in the nerve ganglia

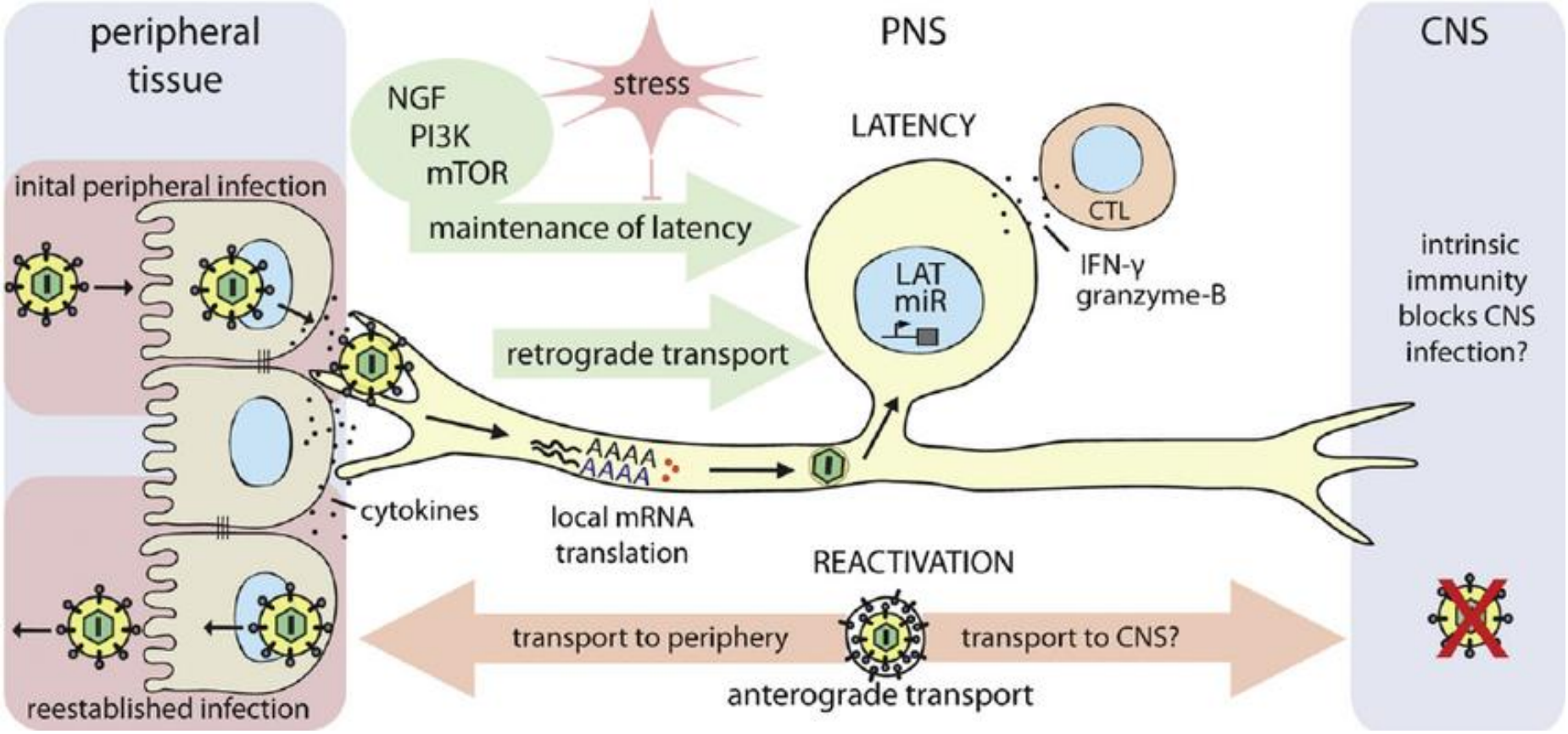
& can be reactivated.

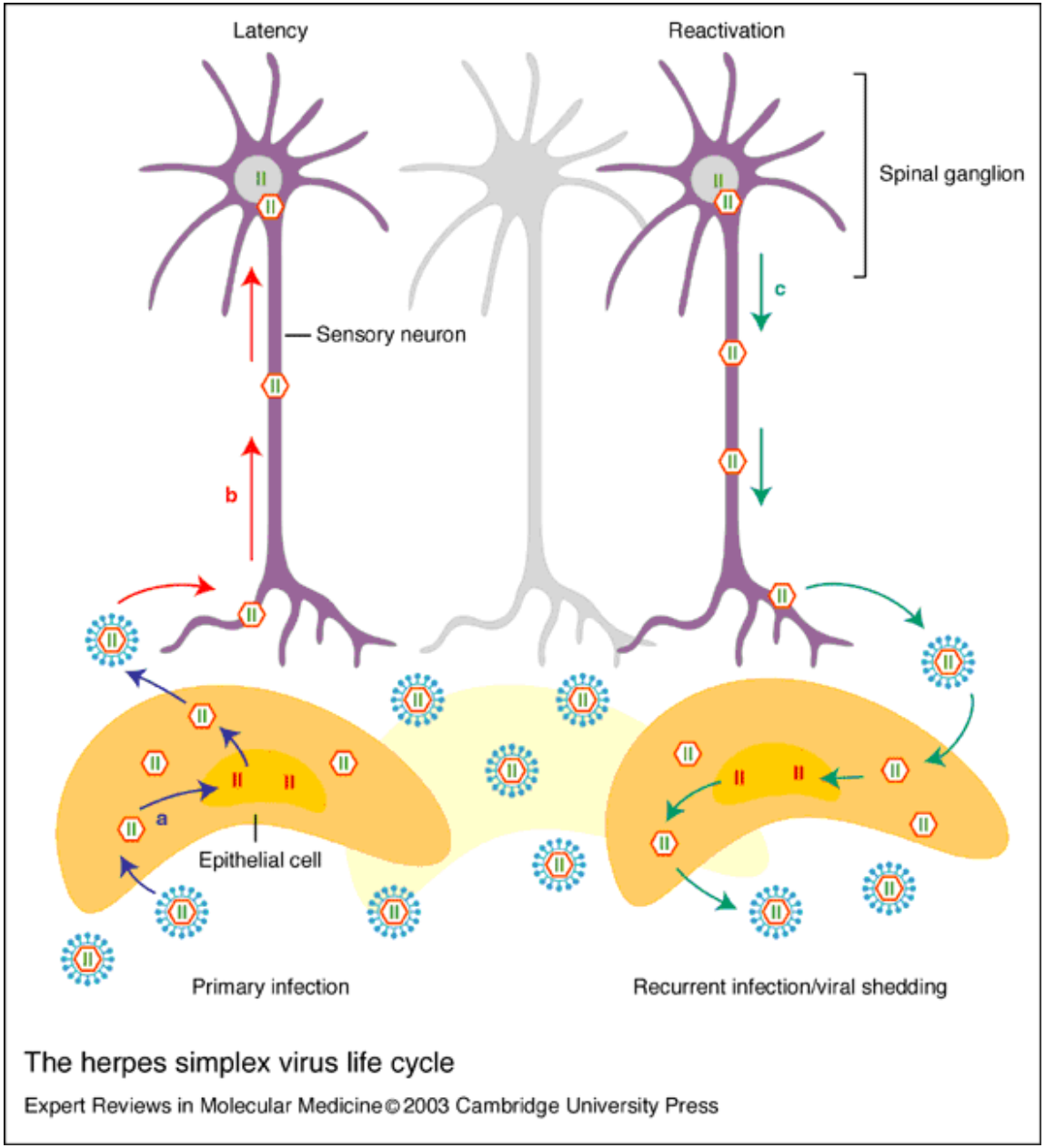
– Some manifests as acute herpetic gingivostomatitis – generalised vesicles and ulcerations

– Causes of reactivation: trauma, allergies, UV light exposure, URTI, pregnancy, menstruation, immunosuppression, exposure to extreme temperature

– Self healing, resolved within 7-10 days.

– antiviral agents are available.


peripheral tissue
PNS
CNS
NGF
PI3K
mTOR
stress
LATENCY
CTL
inital peripheral infection
maintenance of latency
LAT miR
IFN-γ
granzyme-B
intrinsic immunity blocks CNS infection?
retrograde transport
AAAA
AAAA
cytokines
local mRNA translation
REACTIVATION
transport to periphery
transport to CNS?
anterograde transport
reestablished infection



The herpes simplex virus life cycle

Oral Candidiasis

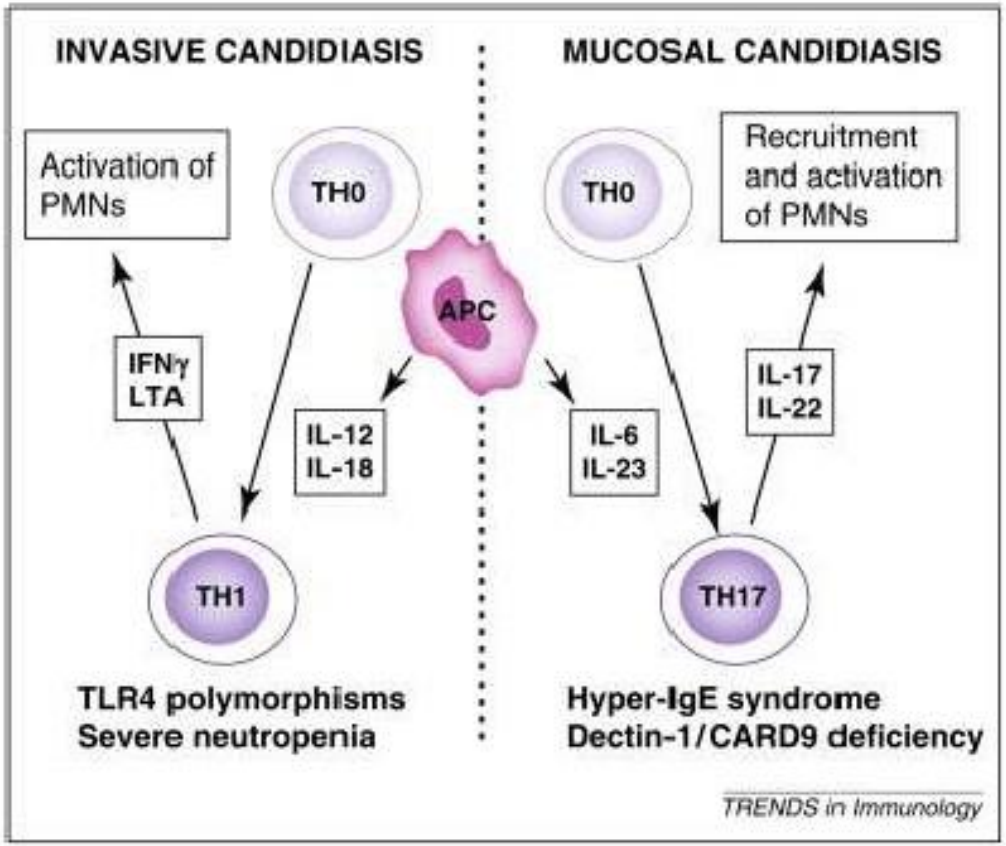
Most common fungal infection of the oral cavity

- *C. albicans* - Normal oral flora
- Became disease when impaired protective mechanisms.
- Common in DM, anemia on antibiotics or glucorticoid therapy,immunodeficiency.

Etiology of oral candidiasis

Local factors	Systemic factors
• Impaired local defense mechanisms	• Impaired systemic defense mechanisms
• Decreased saliva production	• Primary or secondary immunodeficiency
• Smoking	• Immunosuppressive medications
• Atrophic oral mucosa	• Endocrine disorders- Diabetes
• Mucosal diseases (Oral lichen planus)	• Malnutrition
• Topical medications – corticoids	• Malignancies
• Decreased blood supply (radiotherapy)	• Congenital conditions
• Poor oral hygiene	• Broad spectrum antibiotic therapy
• Dental prostheses	
• Altered or immature oral flora	

Mechanism of *Candida albicans* activation



Candida albicans induces a T helper 1 (T_H1) and T_H17 cell-mediated immune response that is essential to clear the fungi.

Summary: Oral inflammatory lesions

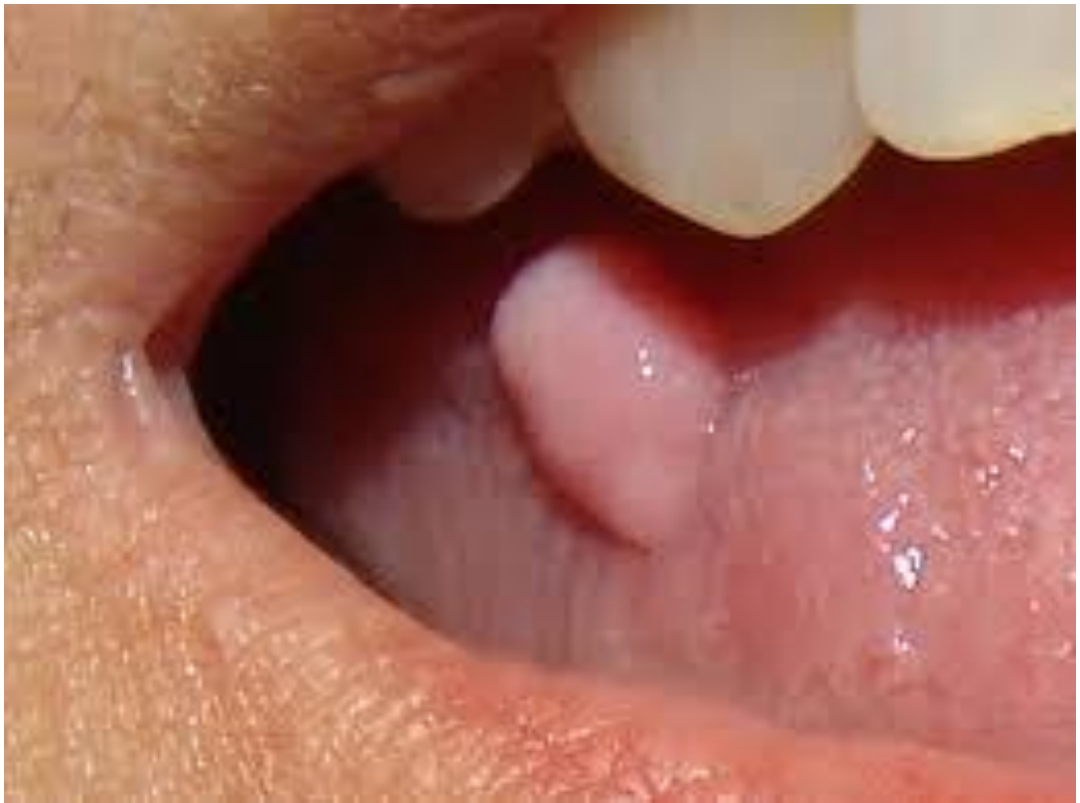
Aphthous ulcers are painful superficial ulcers of unknown etiology that may be associated with systemic diseases.

Herpes simplex virus causes self-limited infection that presents with vesicles (cold sores, fever blisters) that rupture and heal, without scarring, and often leave latent virus in nerve ganglia. Reativation can occur.

Oral candidiasis may occur when the oral microbiota is altered. Invasive disease may occur in immunosuppressed individuals.

Proliferative lesions

- Fibromas
- Pyogenic granulomas



Fibromas

Submucosal nodular fibrous tissue masses

- Chronic irritation causes reactive connective tissue hyperplasia

Site : buccal mucosa along the bite line

Tx :

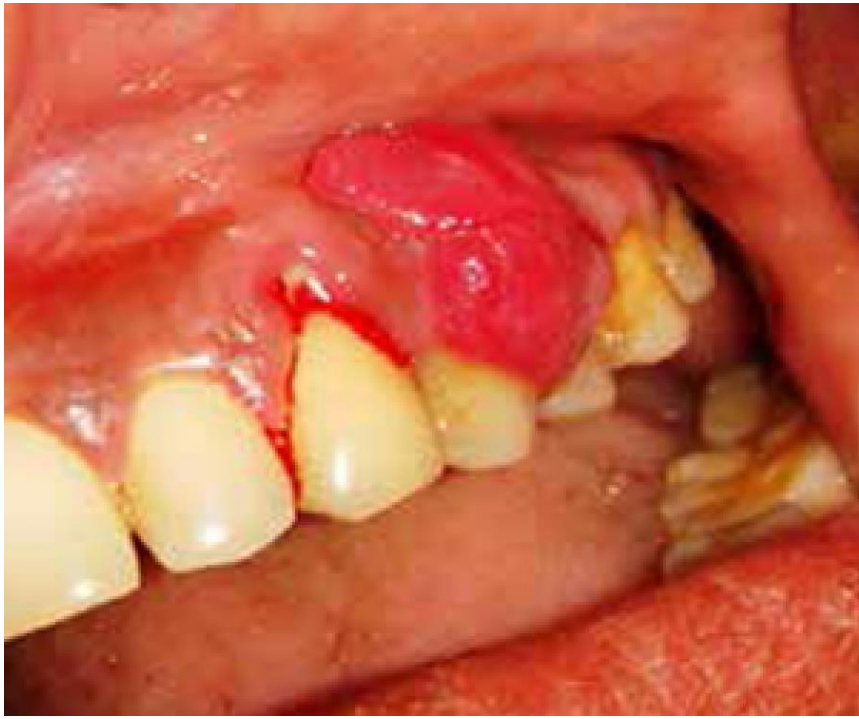
– complete surgical excision

– Removal of the source of irritation

Pyogenic granuloma

Pedunculated mass,

- Location : gingiva of children, young adults and pregnant women
- Richly vascular, ulcerated, red to purple colour
- Growth can be rapid – simulate malignant neoplasm
- HPE : dense proliferation of immature vessels.
- Can regress, mature into dense fibrous masses or develop into a peripheral ossifiying fibroma
- Tx : complete surgical excision



Exfoliative cheilitis

Exfoliative cheilitis is a rare reactive condition presenting as continuous peeling of the lips

- affect both sexes equally and mainly affects young adults less than 30 years of age

Some patients diagnosed with exfoliative cheilitis actually have a localised form of psoriasis.

- can be made worse by:

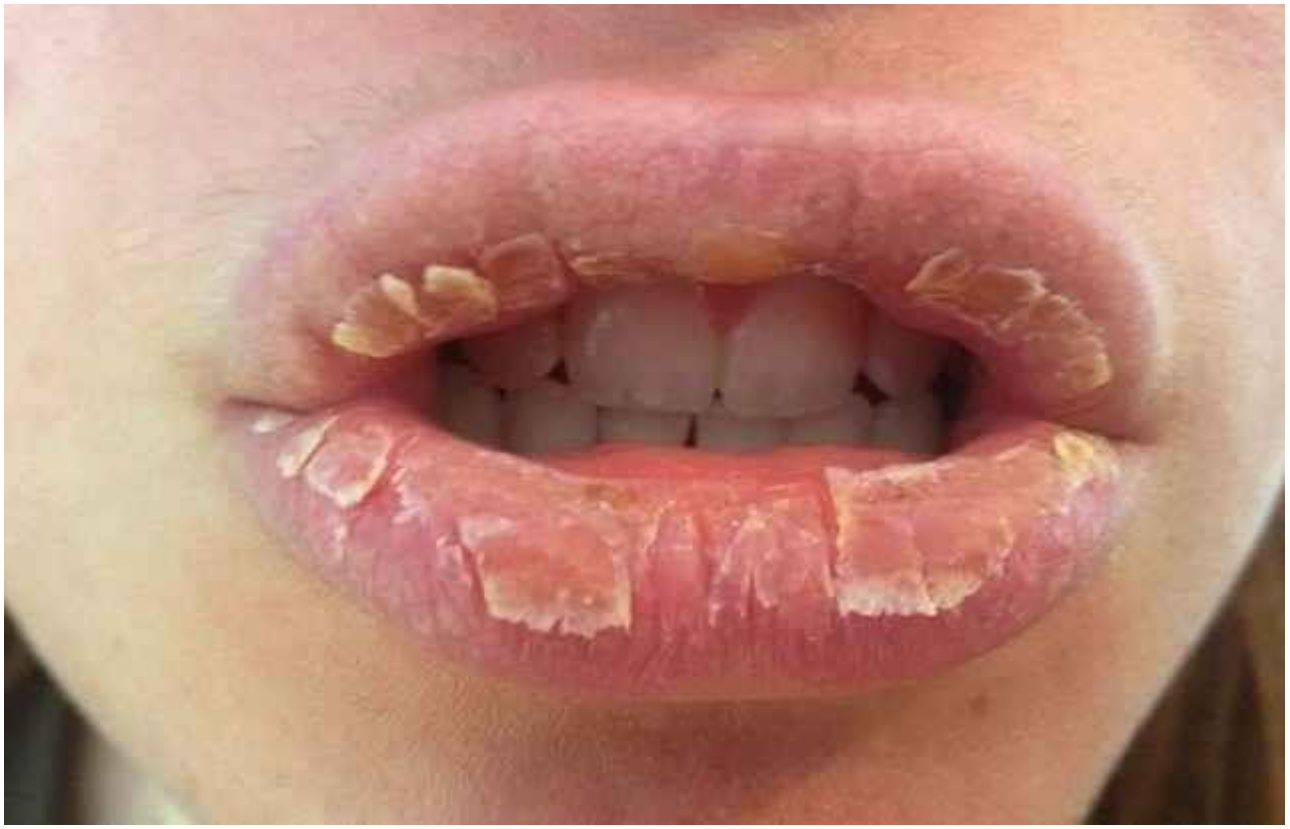
Mouth breathing

a) Lip licking
b) Lip sucking
c) Lip picking
d) Lip biting
e) Bacterial (Staphylococcus aureus) or yeast infection (Candida albicans)

Poor oral hygiene has also been reported in association with exfoliative cheilitis and considered to be a possible predisposing trigger. One form of the condition is associated with HIV infection.

Whatever the cause, excessive keratin formation results in the abnormal peeling.

Exfoliative cheilitis



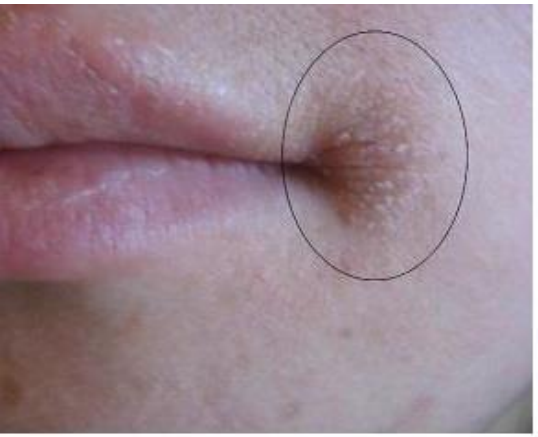
Angular cheilitis (angular stomatitis)

Polyetiological inflammatory condition localized on one or both corners of the lips characterized with redness, swelling, and irritated skin that breakdown and crust. Main role in pathogenesis belongs to **immunosuppression.**

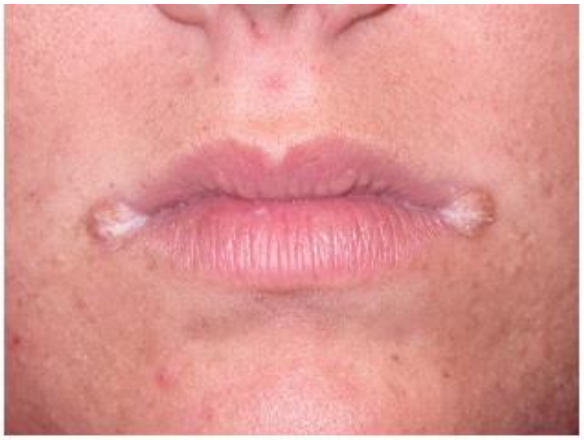
Etiology

- Bacterial infection
- Candida infection
- Polymycrobial infection or mixed bacterial/fungal infection
- Angular herpes simplex
- Vitamin B2 (riboflavin) deficiency
- Vitamin B5, B12, B3 or folic acid deficiency
- Iron and Zinc deficiencies
- Hormonal imbalances
- Bad weather conditions
- Irritation of the skin caused by makeup cosmetics, lipsticks or balms, mouthwashes, toothpastes, etc.
- Contact dermatitis or other allergy
- Alcoholism
- Celiac disease
- Dehydration and not drinking enough water
- Mouth breathing that creates a continuous air flow around the mouth leading to dry lips
- Poor Habits like licking or biting the lips
- Smoking cigarettes
- Systemic disorders
- Drugs

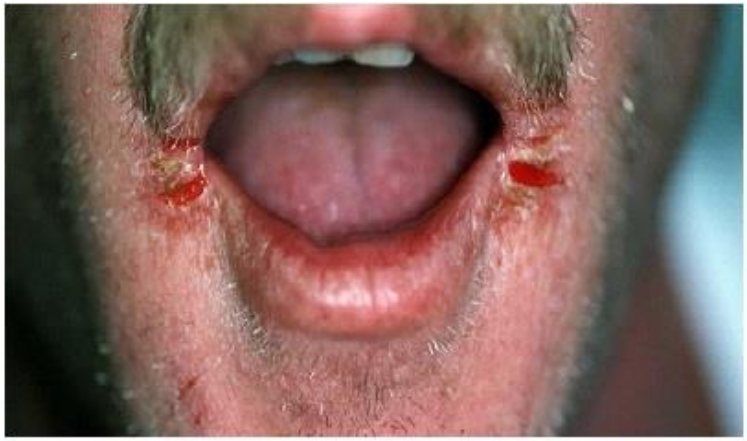
Angular cheilitis



Minor Angualar Cheilitis



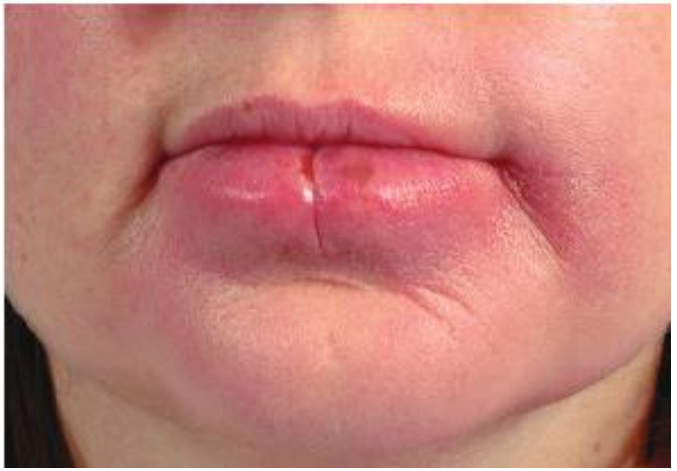
Mild Angular Cheilitis



Severe Angular Cheilitis

Chronic (median) lip fissure

- A hereditary predisposition for weakness in the first branchial arch fusion seems to exist.
- In some persons, more often in males than in females, this weakness eventually leads to development of a median lip fissure.
- The fissure becomes symptomatic when it is infected



Stevens-Johnson syndrome

- Stevens-Johnson syndrome is a type IV (subtype C) hypersensitivity reaction that typically involves the skin and the mucous membrane

Classification

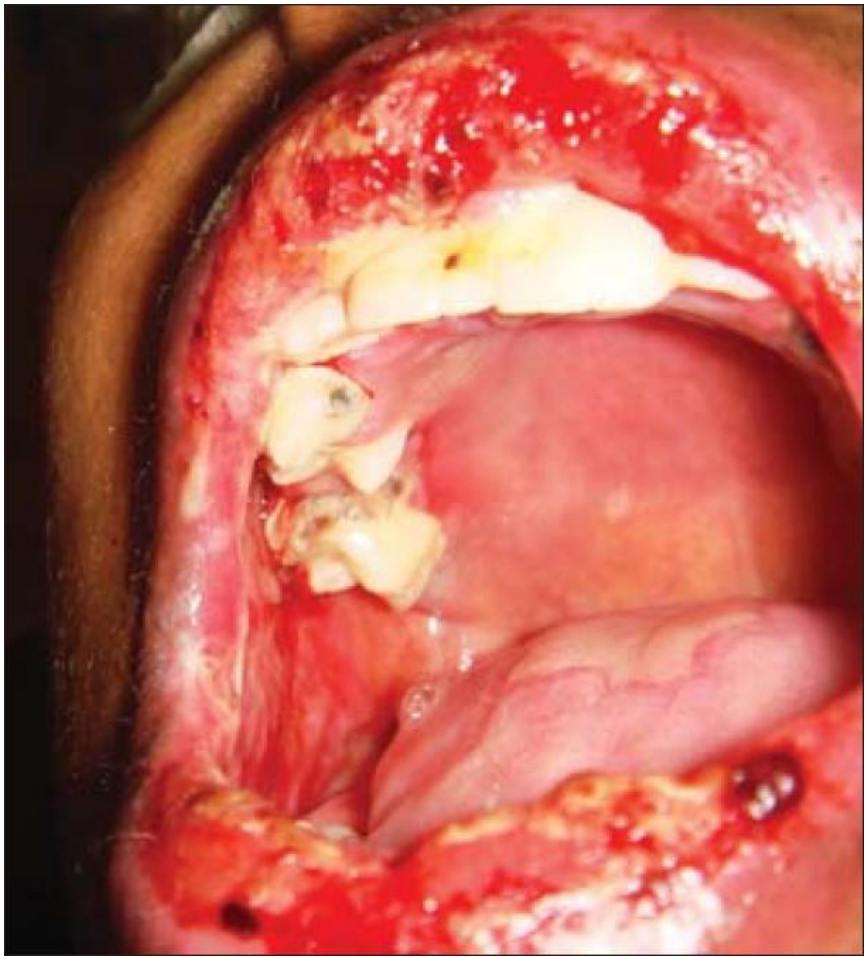
- Stevens-Johnson syndrome: A minor form of toxic epidermal necrolysis, with less than 10% body surface area (BSA) detachment
- Overlapping Stevens-Johnson syndrome/toxic epidermal necrolysis: Detachment of 10-30% of the BSA
- Toxic epidermal necrolysis: Detachment of more than 30% of the BSA

Stevens-Johnson syndrome

Typical prodromal symptoms of Stevens-Johnson syndrome are as follows:

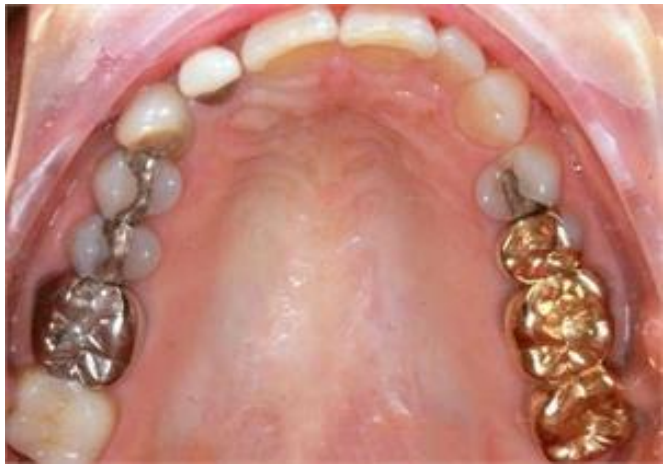
- Cough productive of a thick, purulent sputum
- Headache
- Malaise
- Arthralgia
- Patients may complain of a burning rash that begins symmetrically on the face and the upper part of the torso.

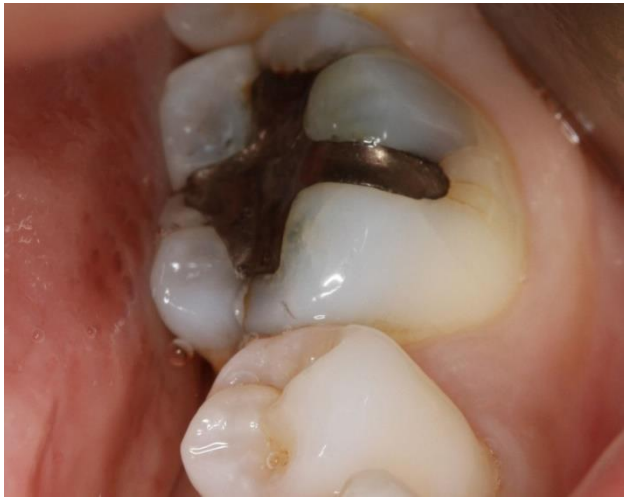
Stevens-Johnson syndrome



Oral galvanism

Galvanism is a condition in which soft tissue maybe caused by a potential difference created by dissimilar metals in the oral cavity, with saliva serving as the electrolyte. Galvanic currents can be measured – indicating metal ion release.





Oral galvanism: symptoms

- metallic or a salty taste
- burning mouth,
- tingling,
- rashes,
- tooth sensitivity
- pain.

However, the effect of electrogalvanism is not limited to the oral cavity, it also has systemic implications such as

- chronic fatigue
- loss of memory,
- headaches,
- sleep disturbances
- irritability

Oral galvanism types

- The classic example of dental galvanism is that of a silver amalgam placed in opposition or adjacent to a tooth restored with gold. These dissimilar metals in conjunction with saliva and body fluids constitute an electric cell. When brought into contact, the circuit is shorted, the flow of electrical current passes through the pulp, and the patient experiences pain.
- A second potential pathway for these currents may occur between teeth in the same arch but not in contact with one another.
- The third and most widely recognized form of electrolytic action as the source of a patient's pain and discomfort is the rather classic one of dissimilar metals coming into contact when the mandibular and maxillary teeth occlude.
- A fourth type of galvanic situation occurs when two adjacent teeth are restored with dissimilar metals. The current flows from metal to metal through the dentine, bone and tissue fluids of both teeth.

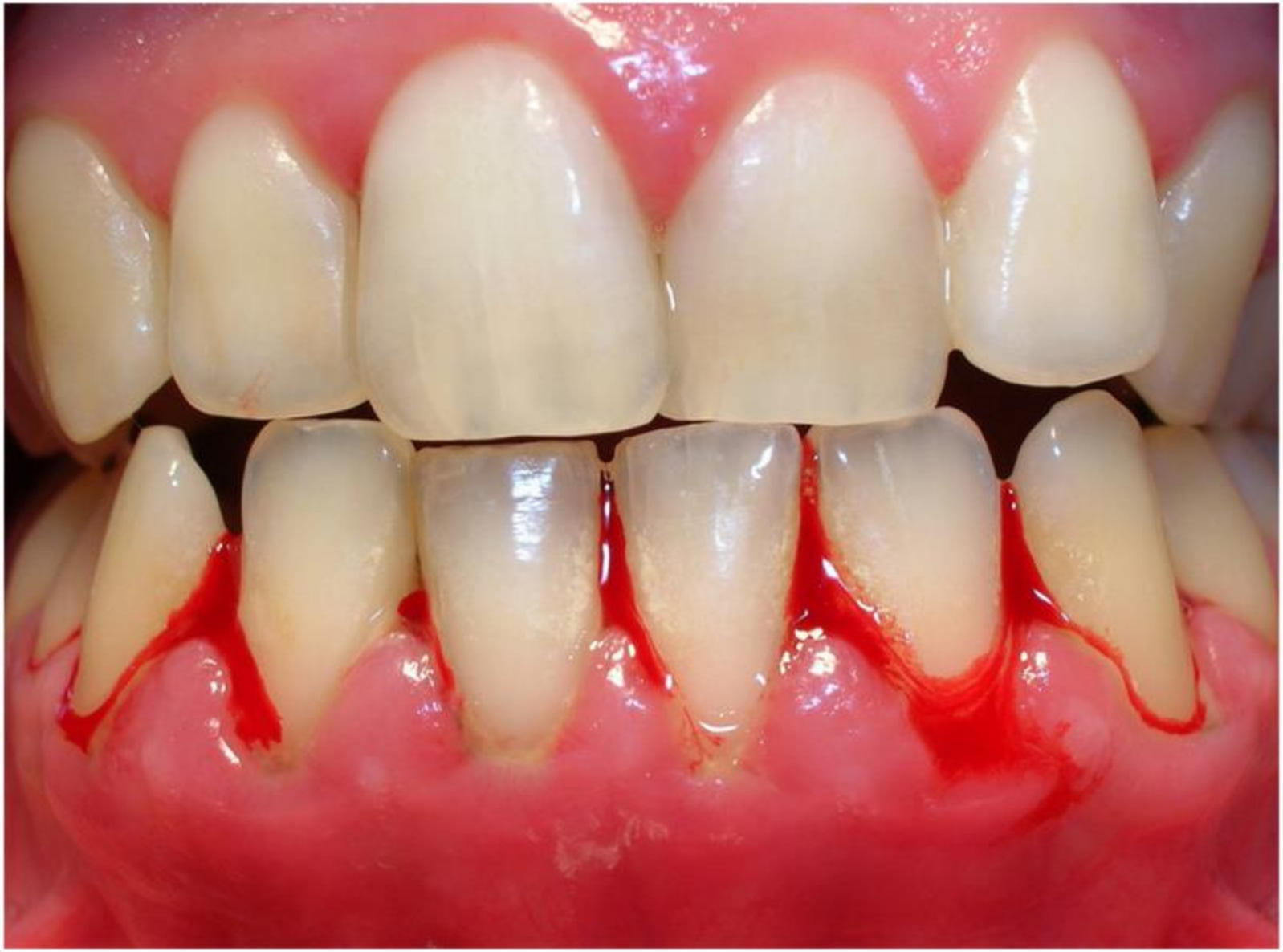
Gingivitis – only oral mucosa
Periodontitis = Oral mucosa + hard tissues

Gingivitis

Gingiva : squamous mucosa in between the teeth and around them.

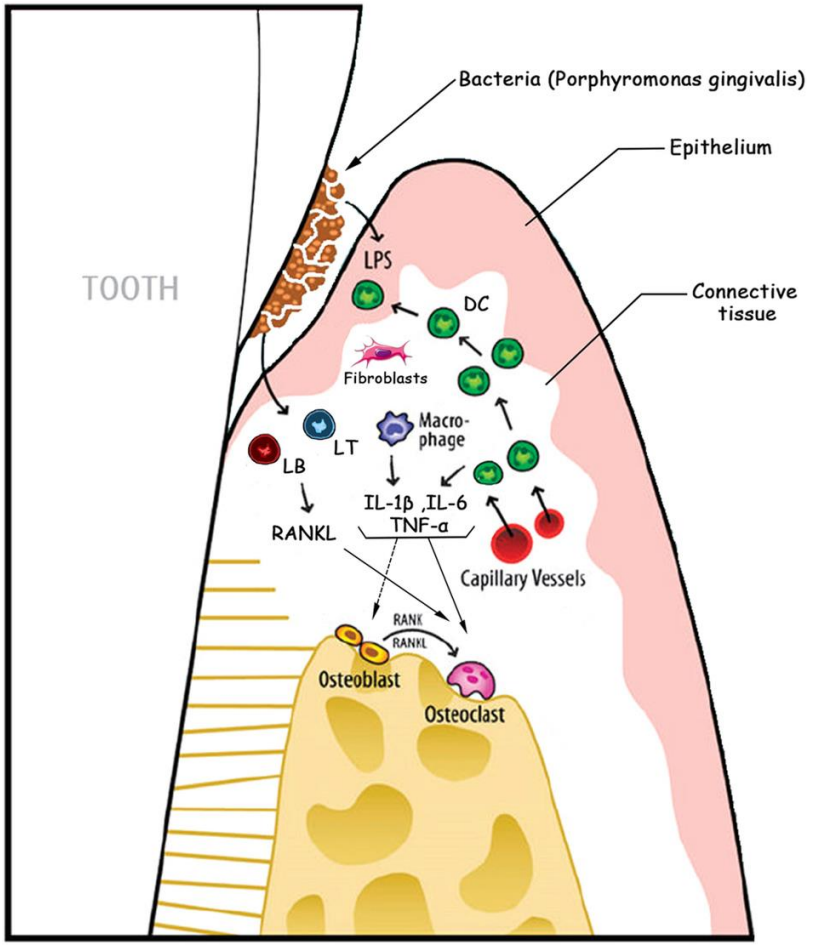
- Gingivitis : inflammation of the mucosa and associated soft tissues.
- Due to lack of proper oral hygiene→accumulation of dental plaque and calculus
- Dental plaque is a sticky, colourless biofilm that builds in between and on the surface of the teeth,
- Components of dental plaque:

– oral bacteria,
– proteins from oral saliva
– desquamated epithelial cells

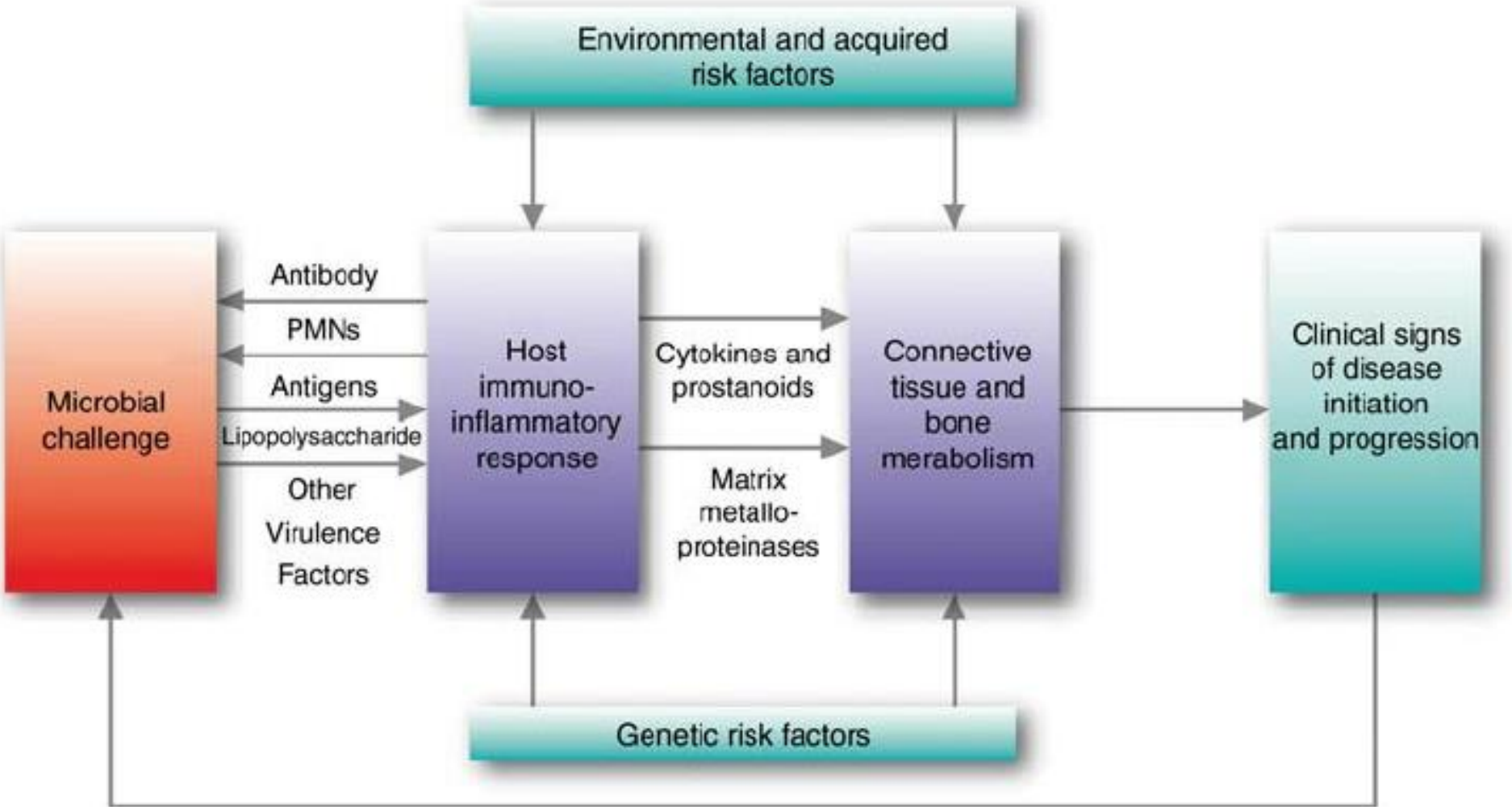


Periodontitis

Inflammatory process affecting the supporting structures of the teeth : periodontal ligaments, alveolar bone and cementum
May cause complete destruction of periodontal ligament and alveolar bone →loss of attachment → loosening and loss of teeth.



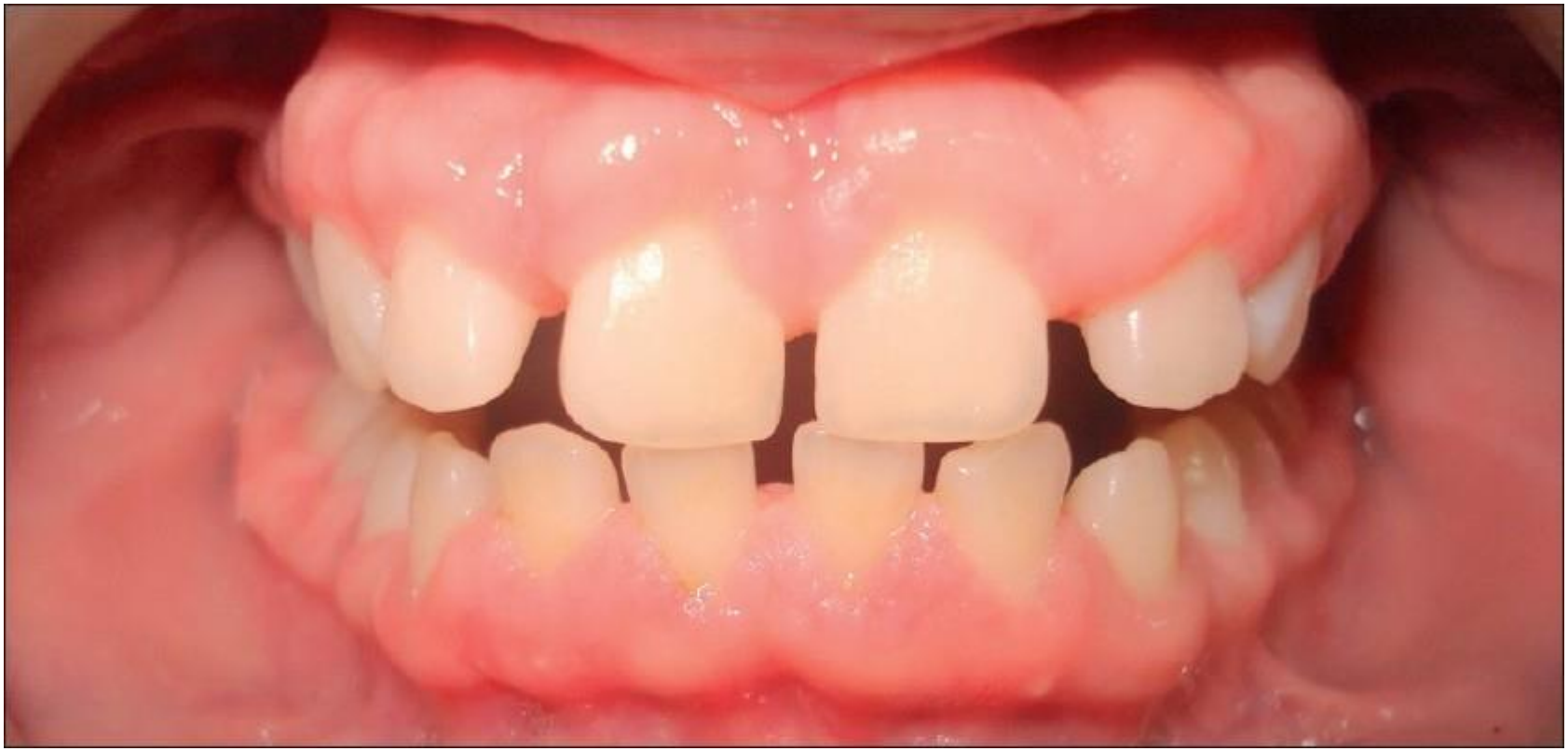
Model of pathogenesis of periodontits



Periodontitis

- Can be associated with several systemic diseases : AIDS, leukemia, Crohn's disease, diabetes mellitus, Down Syndrome, sarcoidosis and syndrome associated with polymorphonuclear defects (Chediak-Higashi syndrome, agranulocytosis and cyclic neutropenia)
- Can also be etiologic factor for systemic diseases : infective endocarditis, pulmonary and brain abscess and adverse pregnancy outcome.

Gingival fibromatosis



II. Pathology of salivary glands

Saliva

Introduction

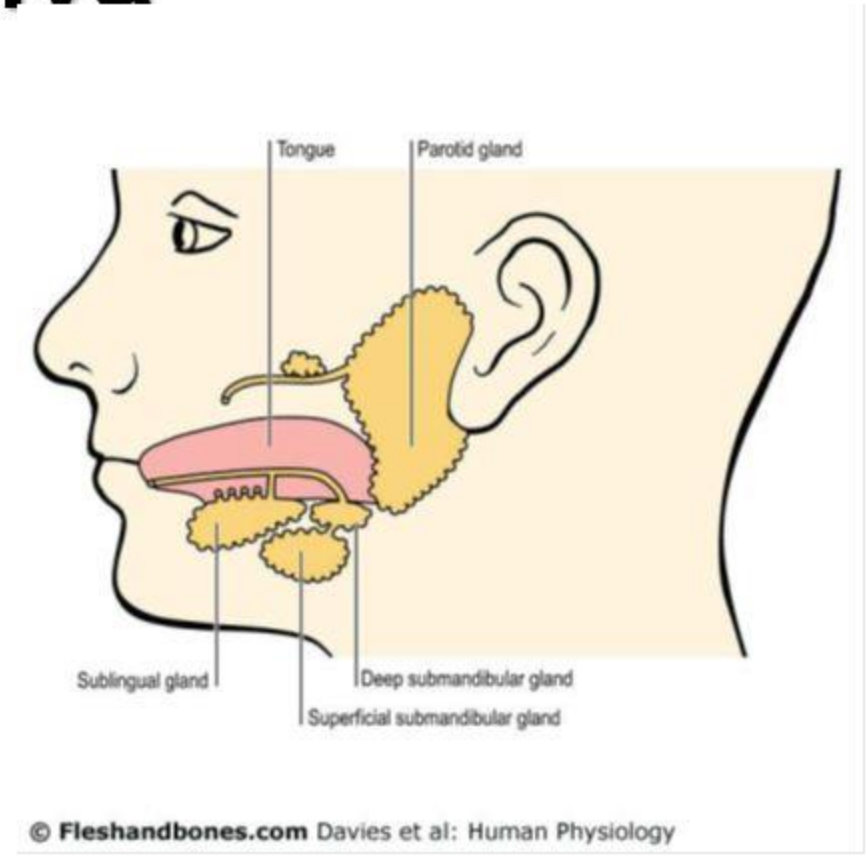
The Major Salivary Glands:

***Parotid-produces serous secretion containing alpha amylase enzyme (ptyalin)**

***Submandibular-produces serous and mucous secretion**

***Sublingual-similar to submandibular secretion**

***The Minor Salivary Glands-buccal glands secret only mucus**



Salivary Flow:

*1-1.5 L/day

Major flow in unstimulated state comes from **Submandibular

Major flow in stimulated state comes from **Parotid

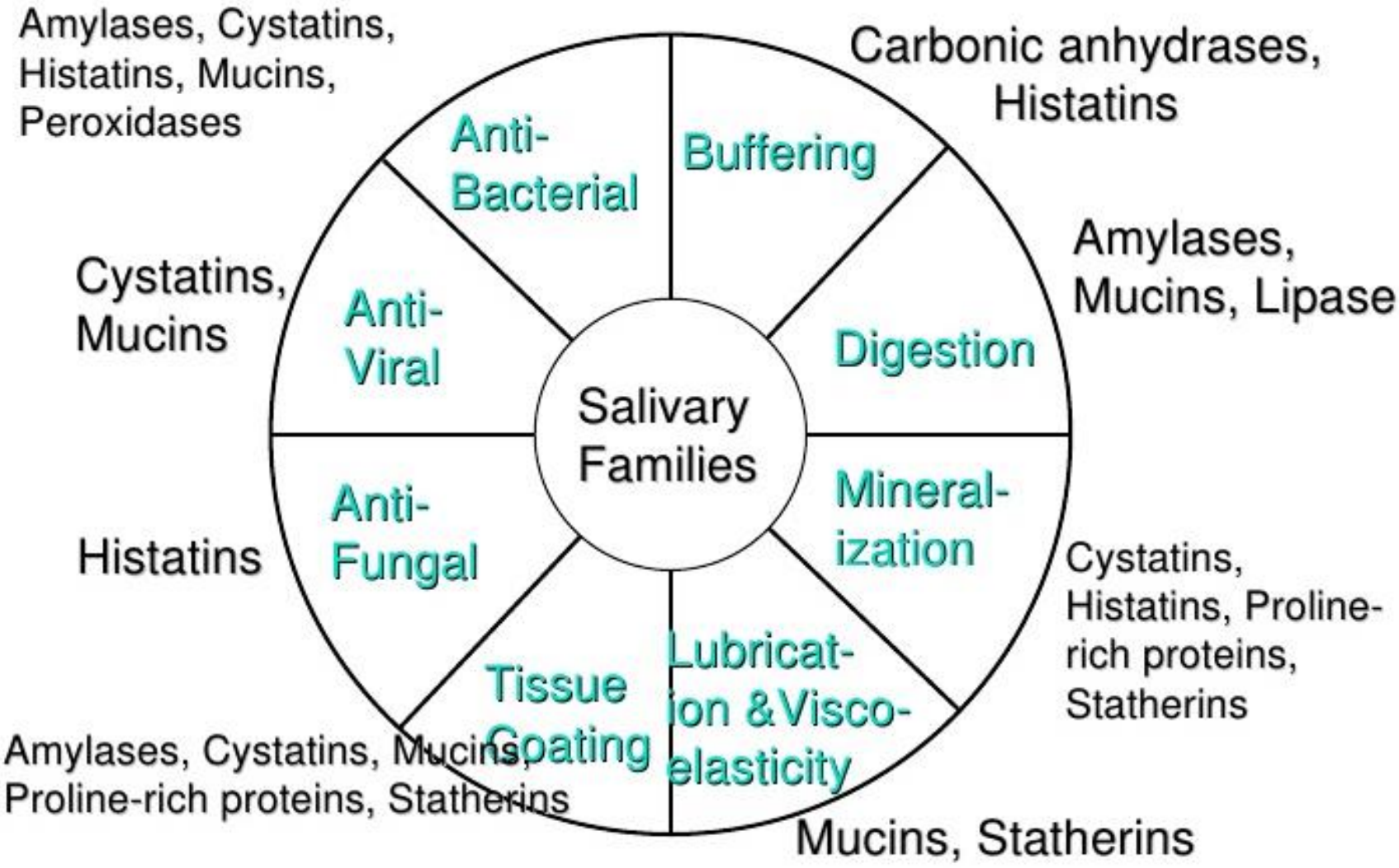
Salivary α-amylase (ptyalin) is produced predominantly by the parotid glands, and mucin is produced mainly by the sublingual and submandibular salivary glands

Saliva

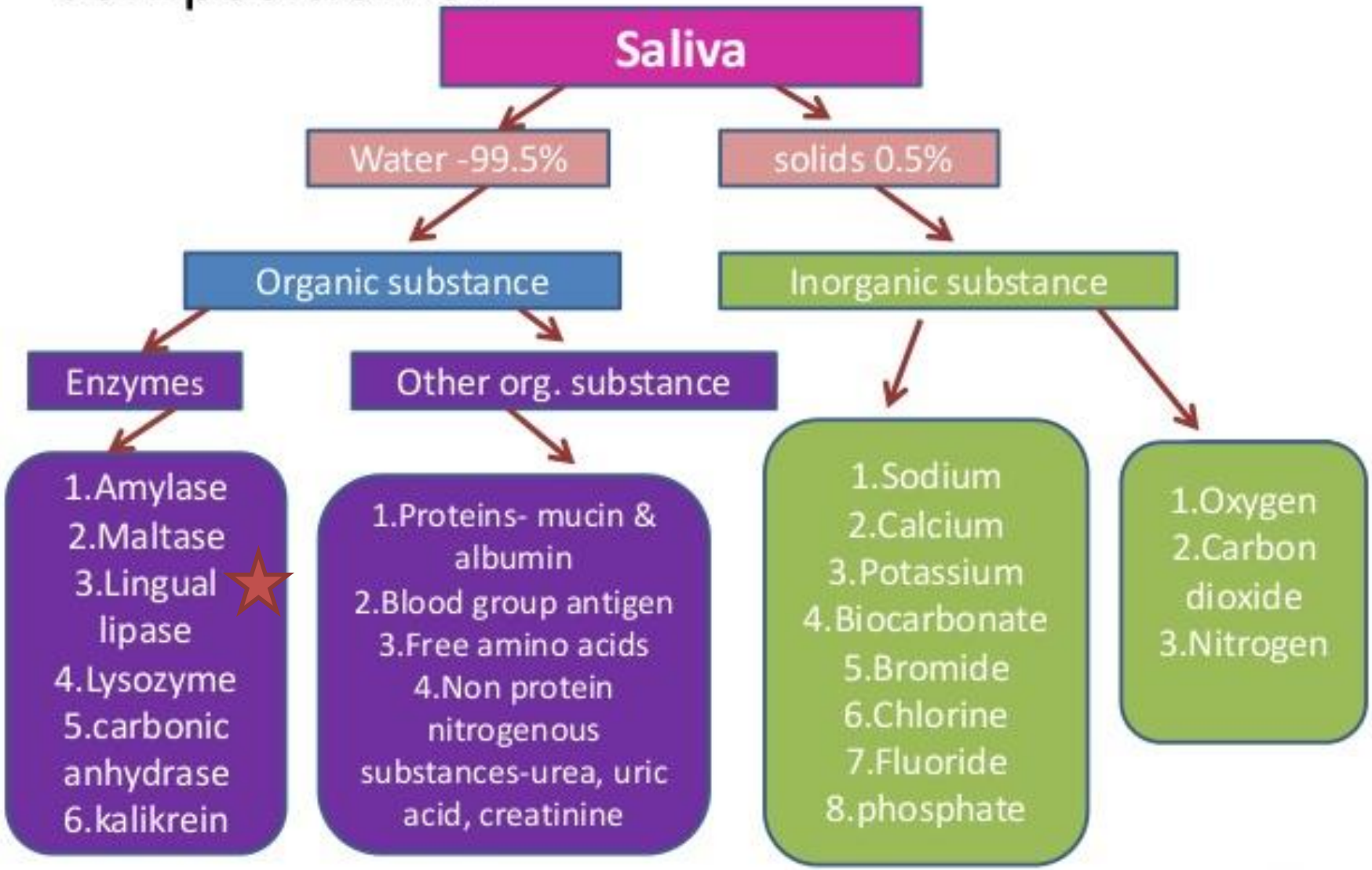
Function	Description
Lubricant	Coats and protects the mucosa against mechanical, thermal, and chemical irritation
Cleanses the teeth	Clears food from the oral cavity and oral mucosa
Ion reservoir	Facilitates remineralization of the teeth
Buffer	Neutralizes plaque pH after eating
Antimicrobial	Secretory immunoglobulins, enzymes, and other salivary proteins help regulate the oral flora
Pellicle formation	A protective layer of salivary protein that forms over enamel acts as a diffusion barrier
Digestion	Salivary amylase initiates the digestion of starch
Facilitates taste	Saliva is a solvent and therefore allows the interaction of foodstuff with taste buds
Water balance	Dehydration causes a reduction in salivary flow rate with an associated oral dryness; this should stimulate a need to increase fluid intake

Sleep
40 ml saliva will be produced over 7 hours
Awake
300 ml of unstimulated saliva over 16 hours
200 ml of stimulated saliva during meals—over 54 minutes

Functions of saliva



Composition of



Classification of salivary glands diseases

Congenital

- Aplasia
- Atresia
- Ectopic salivary gland tissue

Acquired

- Vascular
- Infective
- Traumatic
- Autoimmune
- Inflammatory
- Neurological
- Neoplastic
- Diverticulum
- Unknown (sialolithiasis, sialoadenosis)

CONGENITAL PATHOLOGY OF SALIVARY GLANDS

Aplasia

- Aplasia of any one or group of salivary glands may be, unilaterally or bilaterally.
- The congenital absence of major salivary glands is an **extremely rare** disorder.
- It becomes manifest with the development of **xerostomia** and its sequelae.

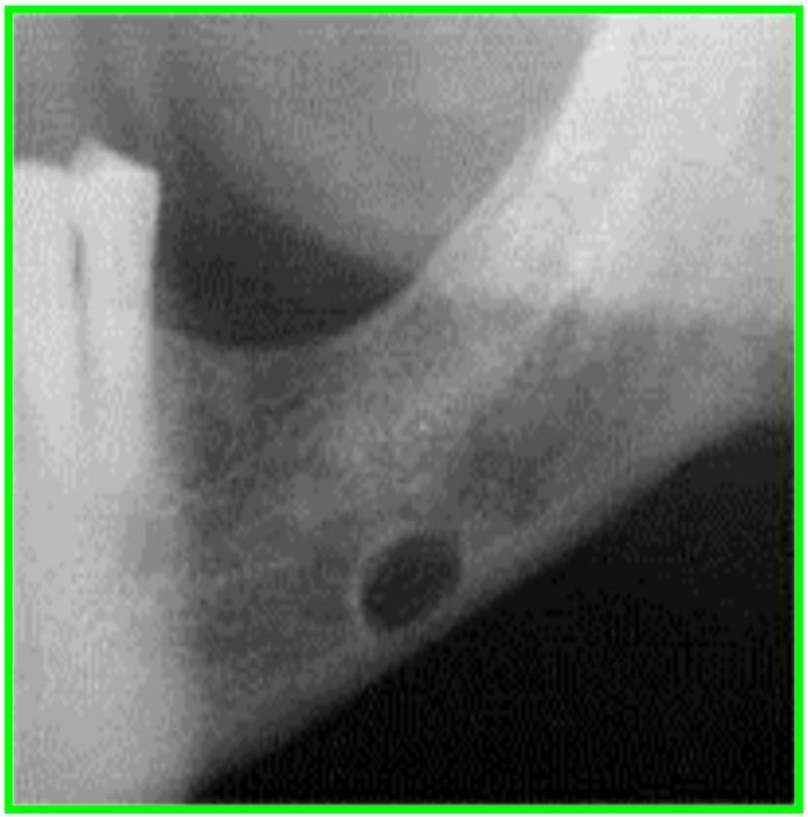
Atresia

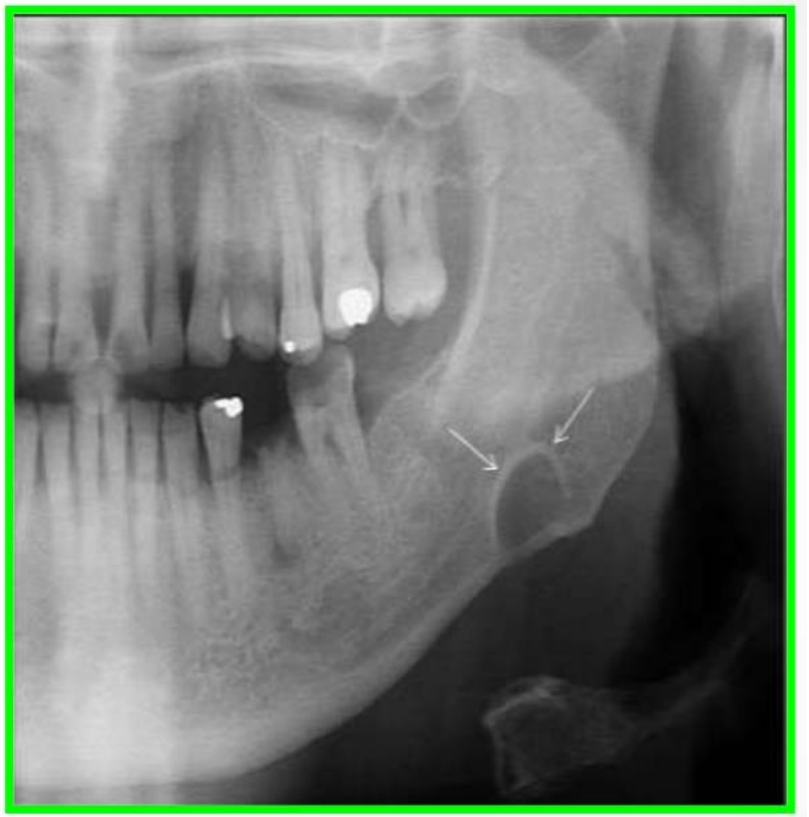
- Uncommon congenital ***absence*** or ***closure*** of a duct or tubular structure (failure of canalization or orifice formation)
- It leads to **distention** of the gland followed by atrophy.
- It may affect the submandibular duct and a ***cyst*** (***Retention cyst***) may develop as a consequence.

Stafne defect ("Latent or Static Bone Cyst", Stafne Bone Cyst)

- **Developmental disorder**
- **Ectopic** salivary gland tissue inside the mandible;
  - Overextension of an accessory lateral lobe of the **submandibular gland** during development of the mandible causing anatomic indentation of the posterior lingual mandible.
  - Very rarely the sublingual salivary glands in the anterior area of the mandible.

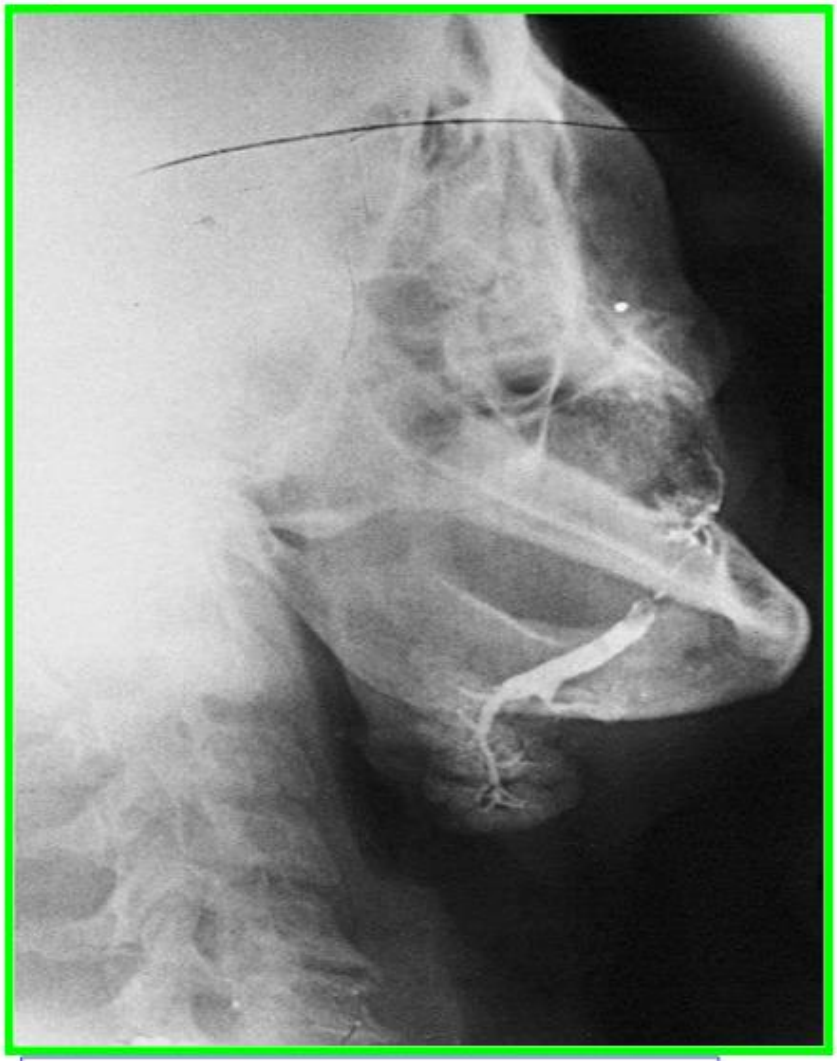
Clinical Features of Latent Bone Cyst





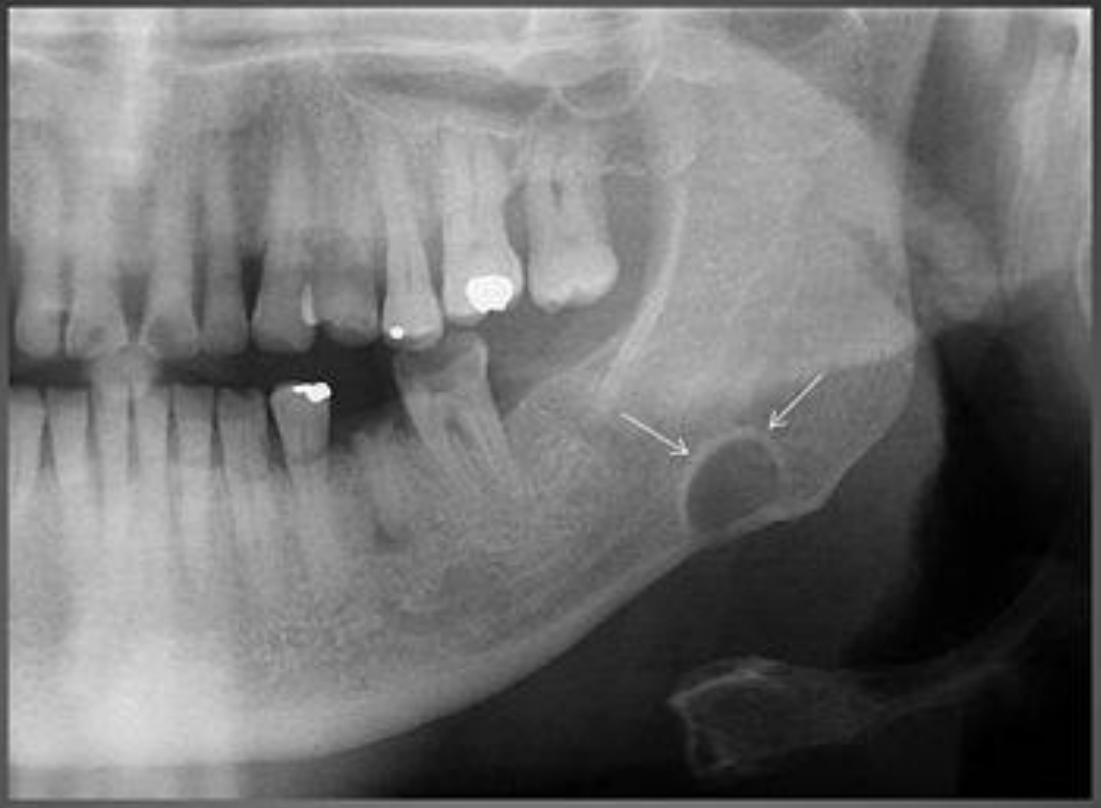
- **Asymptomatic**, **well-circumscribed cystic lesion** within the bone, usually **below the inferior alveolar canal**. Occasionally bilateral

Sialography of Latent Bone Cyst



Sialogram

injection of radiopaque material in the orifice of the salivary gland duct.



Stafne Bone Cavity

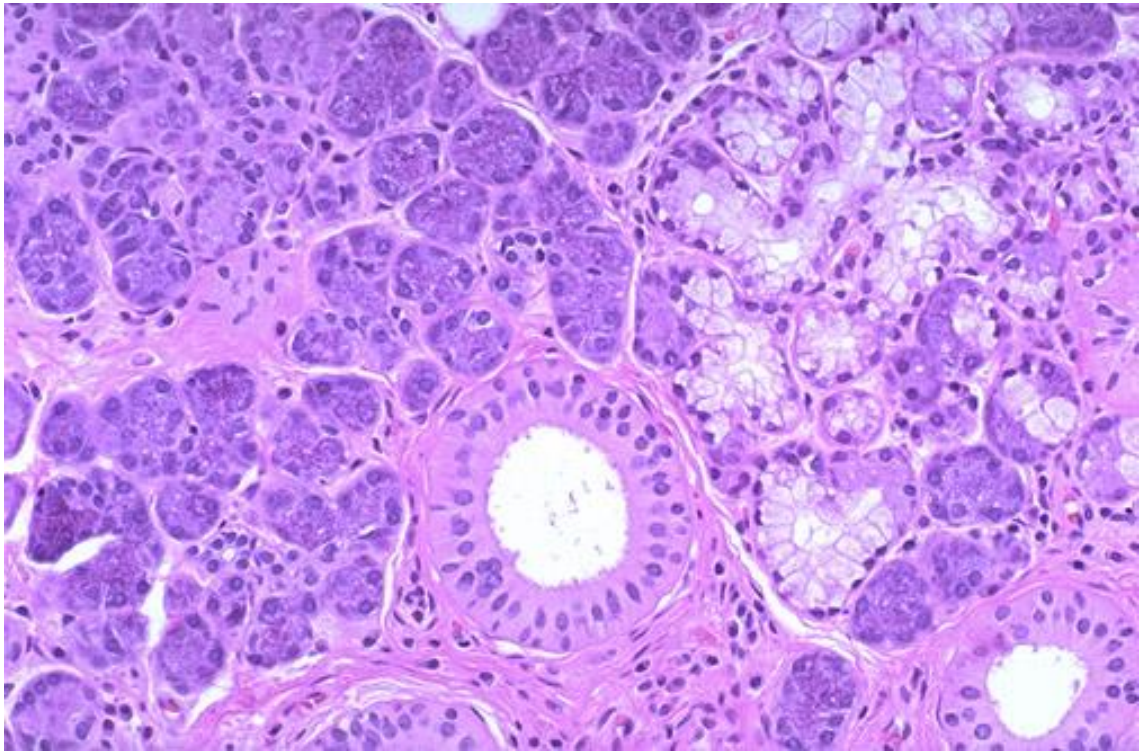
Non-odontogenic 'cyst' (not a true cyst)

Corticated defect in the posterior mandible, below the ID canal

May contain part of the submandibular gland

Biopsy

Reveals **normal salivary gland tissue**



ACQUIRED PATHOLOGY OF SALIVARY GLANDS

Infective

Bacterial

- Ascending sialadenitis
- Recurrent parotitis of childhood

Viral

- Mumps
- HIV parotitis

Inflammatory

Obstructive sialadenitis

Sjögren's syndrome

Sarcoidosis

Sialosis

Neoplasms

Pleomorphic salivary adenoma

Adenolymphoma

Mucoepidermoid carcinoma

Acinic cell carcinoma

Adenoid cystic carcinoma, etc.

Drug-associated

Alcohol

Iodine compounds

Thiouracil

Sulfonamides

Phenothiazines

Chlorhexidine

Endocrine

Acromegaly

Diabetes

Metabolic

Alcoholic cirrhosis

Malnutrition

Others

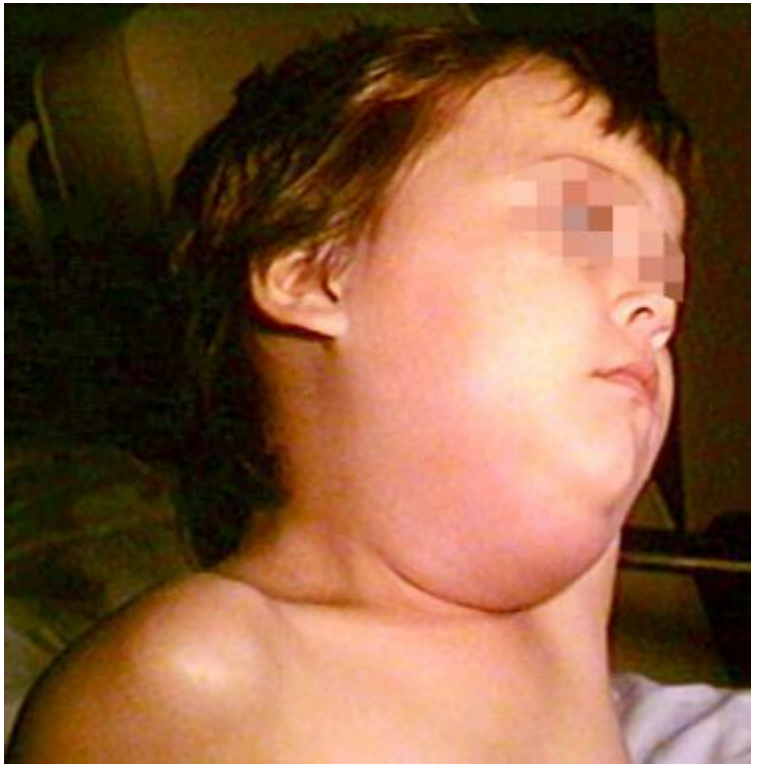
Sarcoidosis

Necrotizing sialometaplasia

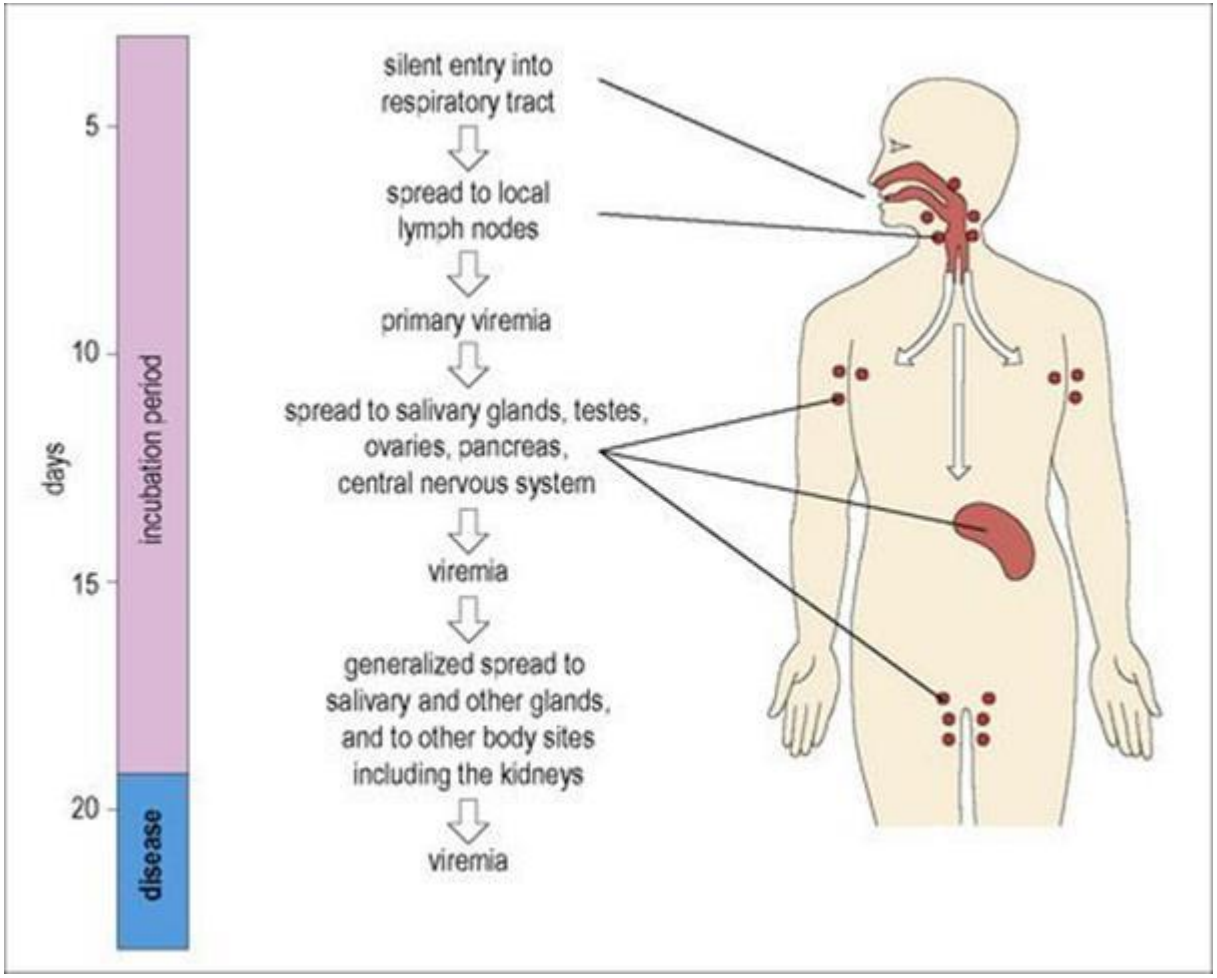
Epidemic parotitis (mumps)

Mumps is an acute, self-limited, systemic viral illness characterized by the swelling of one or more of the salivary glands, typically the parotid glands. The illness is caused by the RNA virus, Rubulavirus.

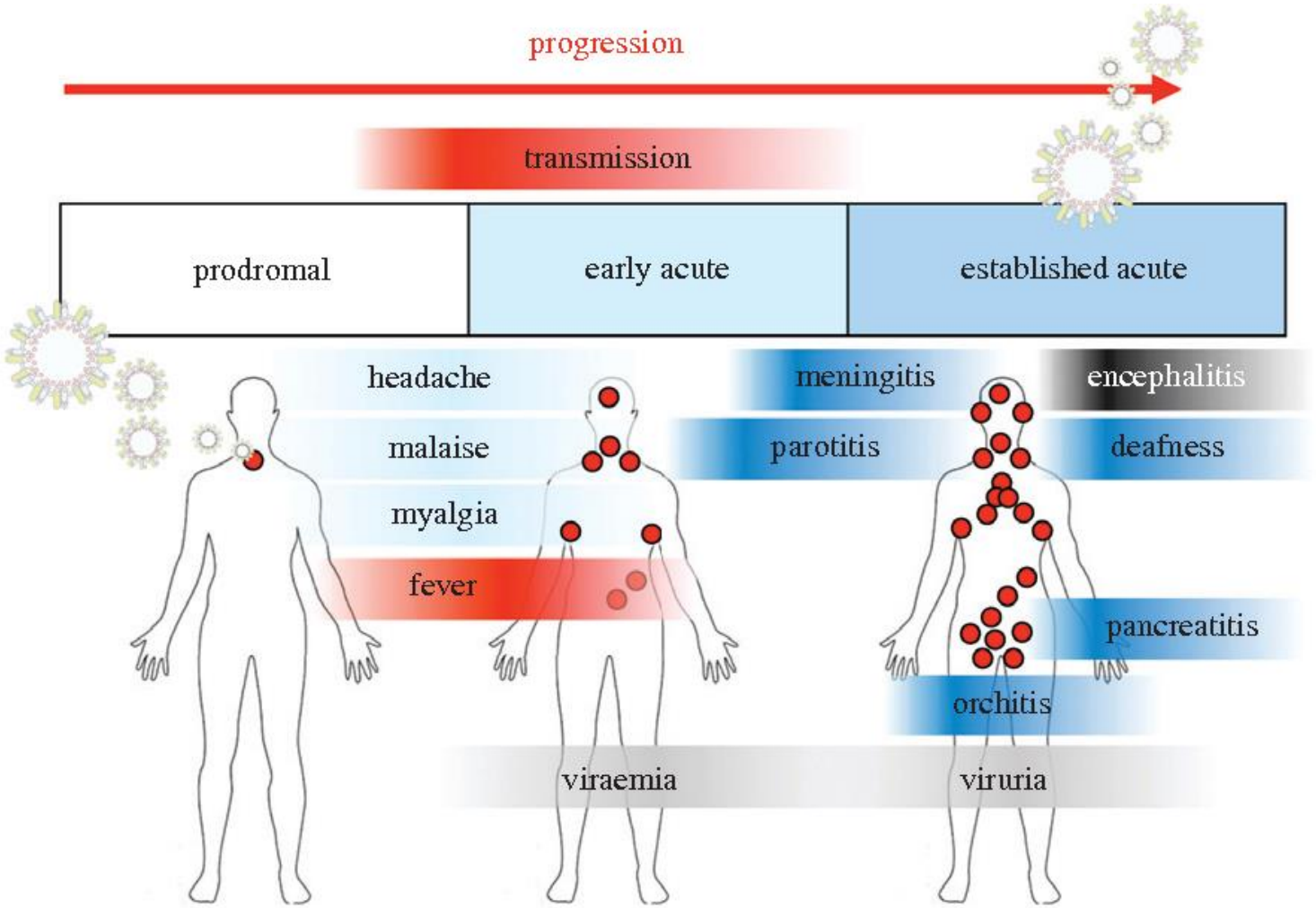
Lack of immunization, international travel, and immune deficiencies are all factors that increase risk of infection by the *Paramyxovirus* mumps virus.
Parotitis also takes place in patients with HIV.



Pathogenesis of mumps



Course of the mumps



Xerostomia

Dry mouth due to decrease production of saliva

- Causes : autoimmune syndrome (Sjogren Syndrome), radiation therapy, tx with anticholinergic, antidepressant/ antipsychotic, diuretic, antihypertensive, sedative, muscle relaxant, antihistamine
- Pathology : dry oral mucosa, atrophy of tongue papillae, fissure, ulcer, enlarge salivary glands
- Complications : dental caries, candidiasis, difficulty in swallowing and speaking.

Xerostomia

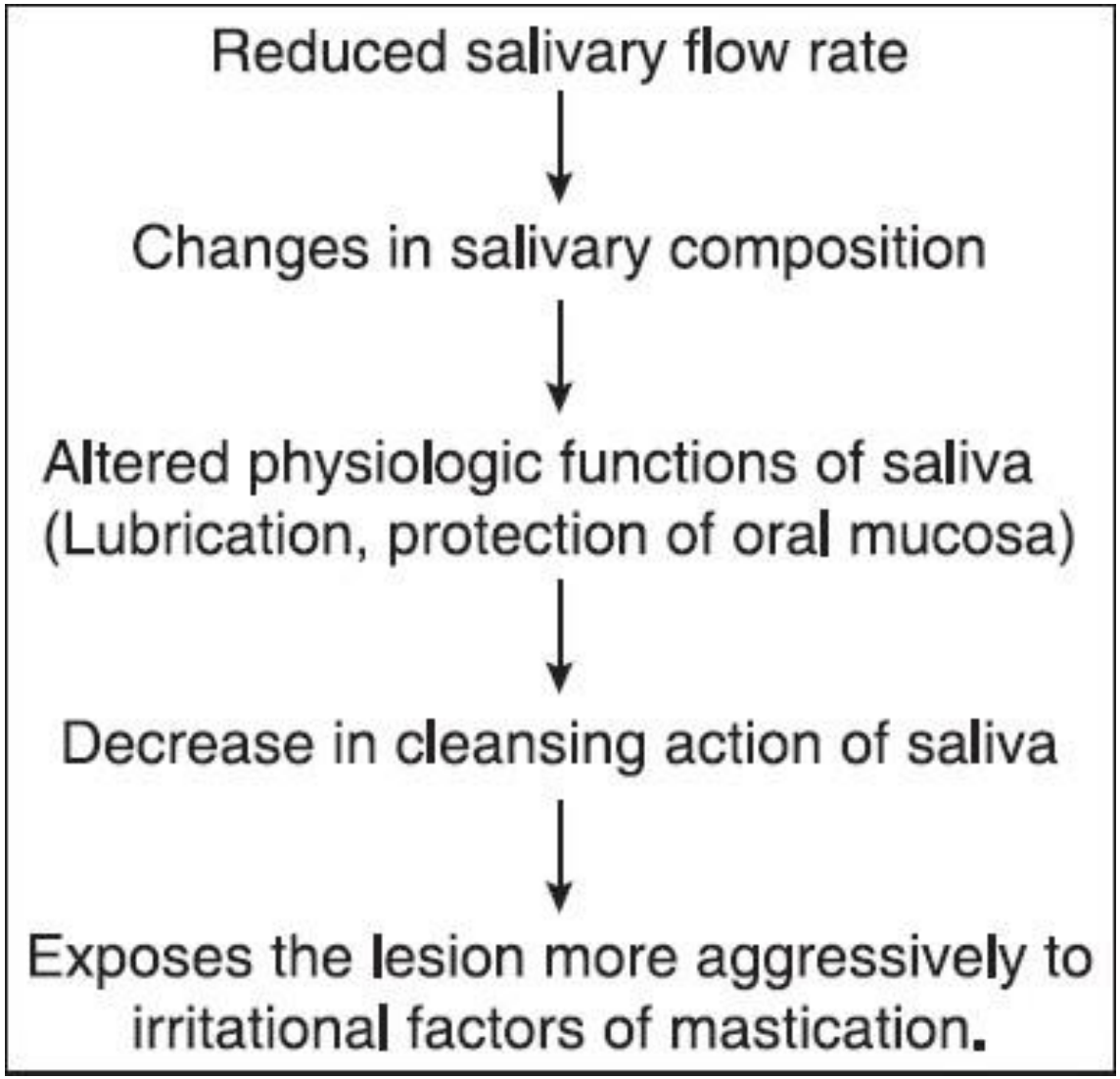
- Up to 80% of patients receiving radiotherapy may experience xerostomia
- Xerostomia may occur
  - Within a few days following treatment and for a period of several months; yet, be reversible
  - Months or years after treatment, when the condition is progressive, irreversible, and negatively impacts a patient's quality of life

Xerostomia

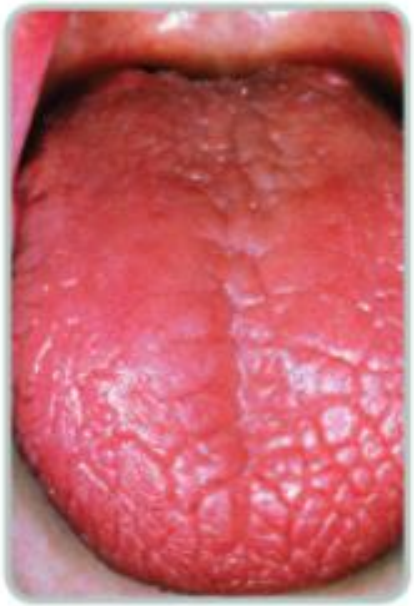
Primary or Direct causes	Secondary or indirect causes
Sjogrens syndrome	Radiation therapy
Type 1 and 2 diabeties mellitus	Chemotherapy
Gestational diabeties	Drugs
Thyroid disease	Rheumatoid disorders
Adrenal conditions	Scleroderma
Renal and hepatic diseases	Mixed connective tissue diseases
Hepatitis C viral infection	Systemic erythematus lupus
HIV	Graft versus host disease
	Anorexia and bulimia
	Alcohol
	Smoking tobacco

Category	Names of the drugs
Antihistamines	Diphenhydramine, chlorpheniramine
Decongestants	Pseudoephedrine
Antidepressants	Amitryptiline
Antipsychotics	Haloperidol, phenothiazine derivatives
Antihypertensive	Reserpine, methyldopa, chlorothiazide, furosemide, metoprolol, calcium channel blockers
Anticholinergics	Atropine, scopolamine

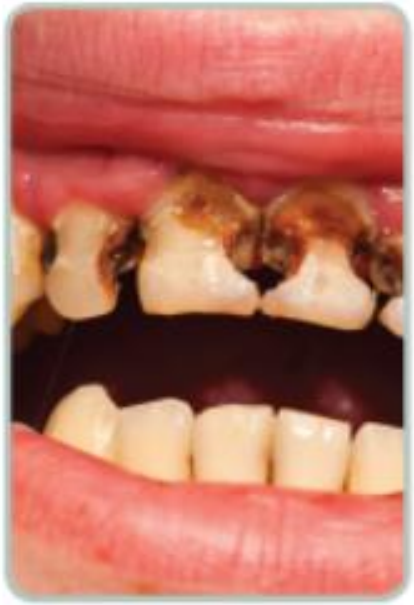
Xerostomia: pathogenesis



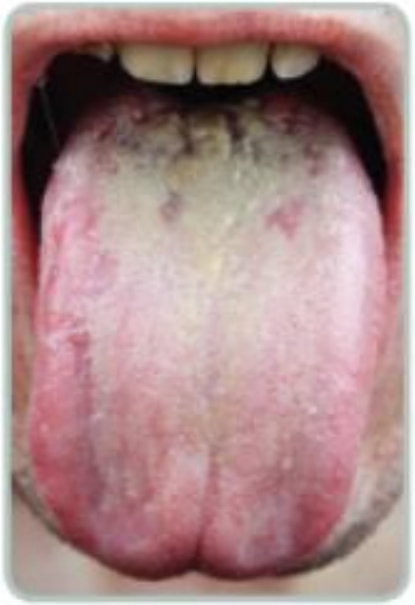
Xerostomia can lead to many devastating and life-altering symptoms[4,5]



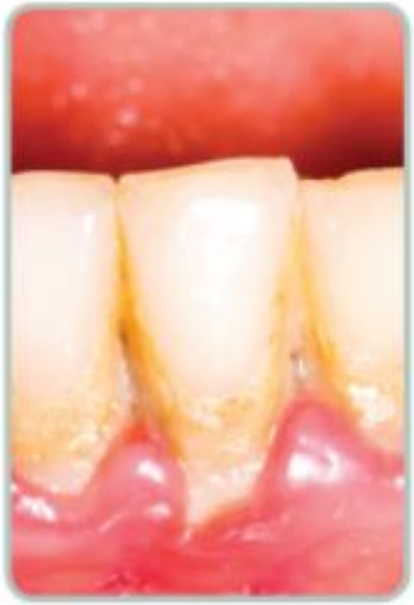
Patients may experience cracked, dry lips and tongue.[4,5]



Patients may develop dental caries (decay cavities) at the cervical margin or neck of the teeth and abnormal buccal mucosa.[4,5]



Patients may experience oral infections such as candidiasis (thrush).[4,5]



Patients may produce less saliva, which may lead to cavities, gingivitis and bleeding, and halitosis.[4,5]

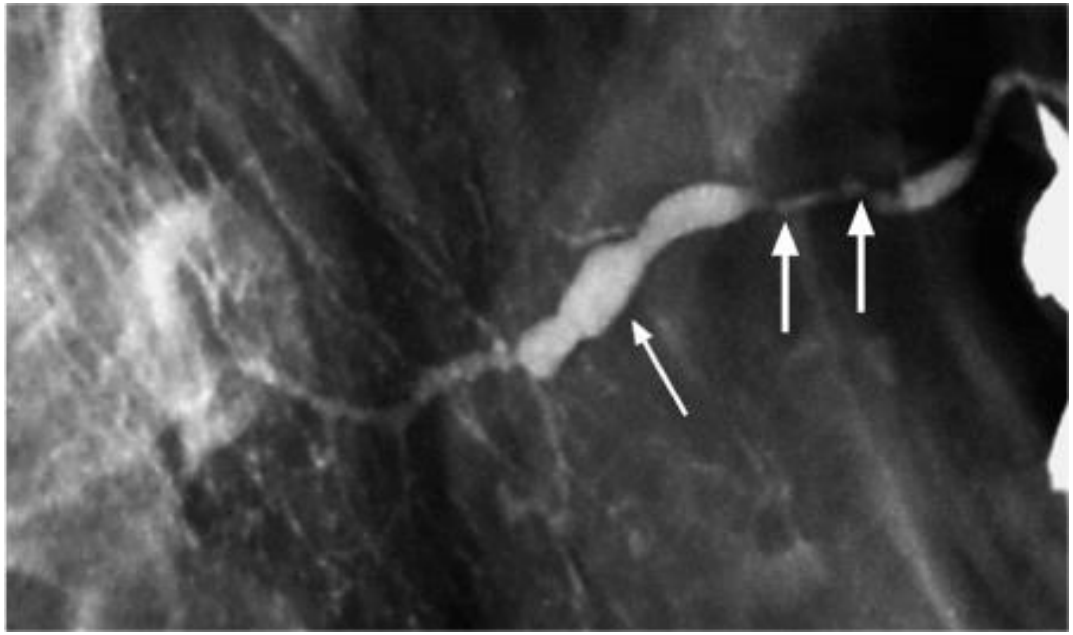
Sialaadenitis

Inflammation of salivary glands caused by:

1) Infections
2) Immune-mediated mechanisms
3) Occlusion of ducts

Signs and symptoms:

- tender, painful lump in the cheek or under the chin
- fever, chill and general weakness



Chronic sialoadenitis of the parotid gland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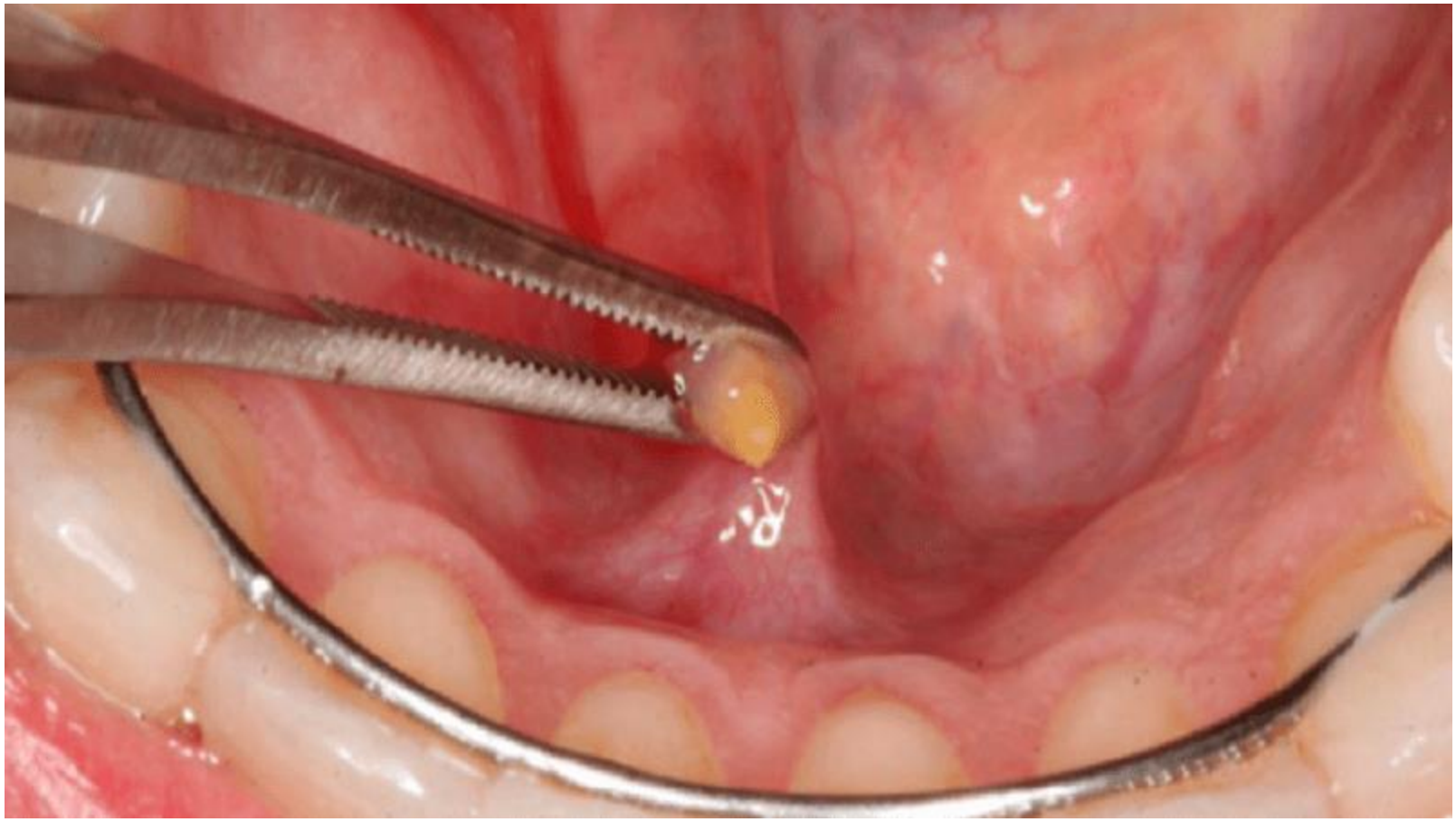
Sialolithiasis

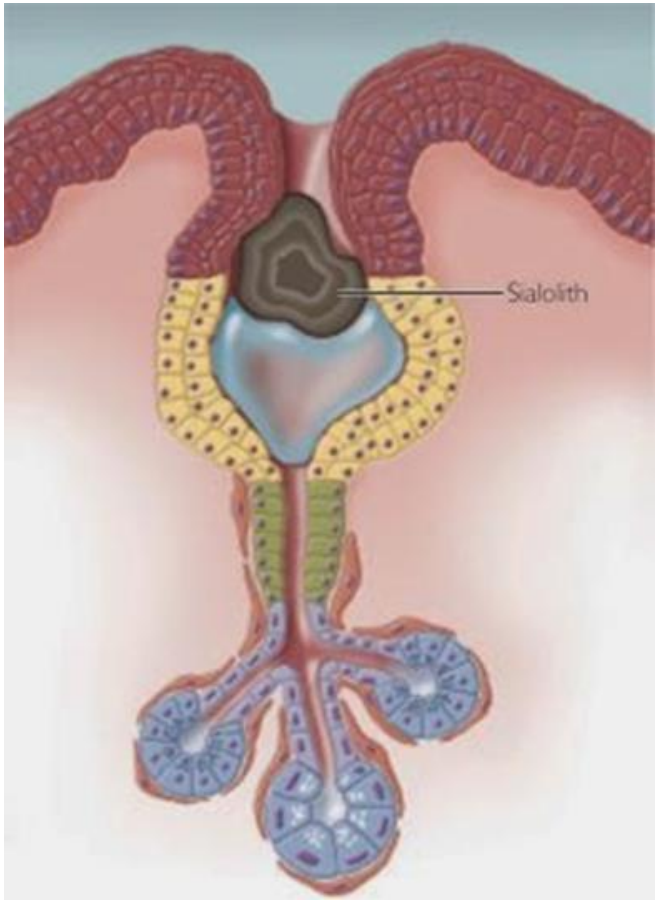
Sialolithiasis or salivary stone or salivary calculi are a condition in which a mass of crystallized minerals are formed in the salivary ducts

- Most common – submandibular gland
- Usually more than one stone is formed in the duct
- The size of the stone may range from a few mm to more than 2 cm and appears as round or oval rough or smooth solid masses.
- The color of the stone is usually yellowish or yellowish white.
- As the saliva is rich in calcium, stones are typically made up of hydroxyapatite and calcium phosphate

Sialolithiasis



Sialolithiasis



Causes of stone formation

Dehydration can cause high viscosity and decreasing of water proportion in the saliva, which makes the calcium and phosphates present in the saliva to form a stone. This stone obstructs the salivary duct and its gland.

Yet there are some other factors that afford to this condition are as follows:

- Salivary stagnation
- Reduced food intake
- Calcium salt precipitation
- Epithelial injury near the salivary duct may create unwanted salivary stone
- Less salivary secretion
- Constant use of medications for anti-psychotic, anti-hypertensives and anti-histamine drugs which really affect the manufacture of saliva of the mouth.
- Frequent use of diuretics and anticholinergics.
- In some diseases like Sjorgen's syndrome, lupus, and autoimmune disease attacks the salivary glands by the body's own immune system.

Risk factors

- Radiation therapy of the mouth
- Trauma
- Smoking
- Gout
- Hyperparathyrodism
- Chronic periodontal disease

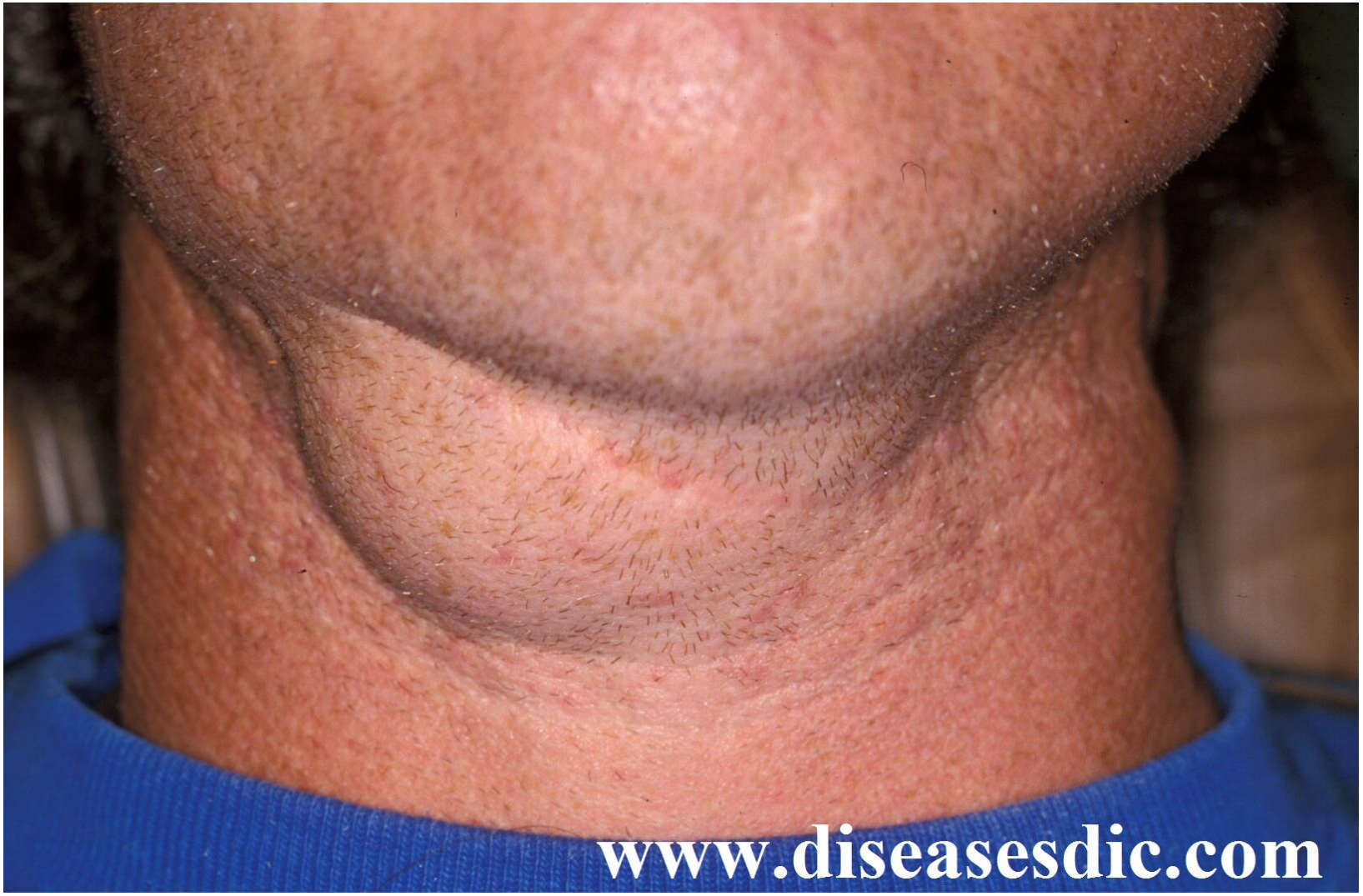
Mechanism of sialolith formation

The definite mechanism of sialolithiasis is still unknown. It is believed that at the beginning a **small and soft nidus** is formed within the salivary gland and its ducts due to being large, long, and having slow salivary flow.

- Nidus is composed of protein, bacteria, mucin, and desquamated epithelial cells.
- Once if the nidus forms, it allows crystallization of minerals similar to concentric lamellae due to the precipitation of calcium salts.
- Later the size of salolithiasis increases with time as layer by layer of calcium salts deposition.
- A very small salivary stones is expelled from the duct along with the salivary secretions, but the larger stones are continues to grow until the duct is fully closed

Clinical manifestations

- Facial swelling
- Swelling and pain around the jaw and ear
- Painful lump under the tongue
- Swelling of affected glands occurs while eating a food
- Difficult in opening mouth
- Dry mouth
- Bacterial infection occurs when the mouth glands are filled with stagnant saliva
- Fever and chillness may associate with gland infections
- Redness around the infected gland
- Foul taste in the mouth


www.diseasesdic.com

Complications of sialolithiasis

- Eating food is tedious work
- Ulceration, fistula, and sinus tract in the affected area may develop a chronic form of sialolithiasis
- Lobular fibrosis and necrosis of gland acini can occur which results in loss of salivary secretion in the glands.
- Acute suppurative sialoadenitis and duct narrowing (stricture)
- Untreated sialolith for long term lead to painful infections, scarring, and forms abscess in the salivary gland.

Sialoadenosis (sialosis)

Uncommon, benign, non-inflammatory, non-neoplastic enlargement of a salivary gland, usually the parotid gland but occasionally affects the submandibular glands and rarely, the minor salivary glands.

This enlargement is bilateral, symmetrical and painless (it is often painless but not invariably so).

In general, the enlargement is asymptomatic and the cause is *idiopathic*.

In this disorder, both *parotid glands* may be diffusely enlarged with only modest symptoms. Patients are aged 30 - 69 years at onset and the sexes are equally involved. The glands are soft and non-tender.

Sialoadenosis (sialosis)
Suspectible causes

- Nutritional disorders
- Endocrine diseases
- Drugs
- Autonomic neuropathy
- Changes in salivary aquaporin water channels

Sialoadenosis (sialosis)

- **Nutritional Disorders**

Any disorder that affects the digestion of food or its absorption over a prolonged period, can result in *sialosis* (pancreatitis, malnutrition)

- **Endocrine diseases**

Diabetes Mellitus (reported prevalence of *sialosis* in diabetes ranging from 10% to 80%)
Pregnancy
Acromegaly

Sialoadenosis (sialosis)

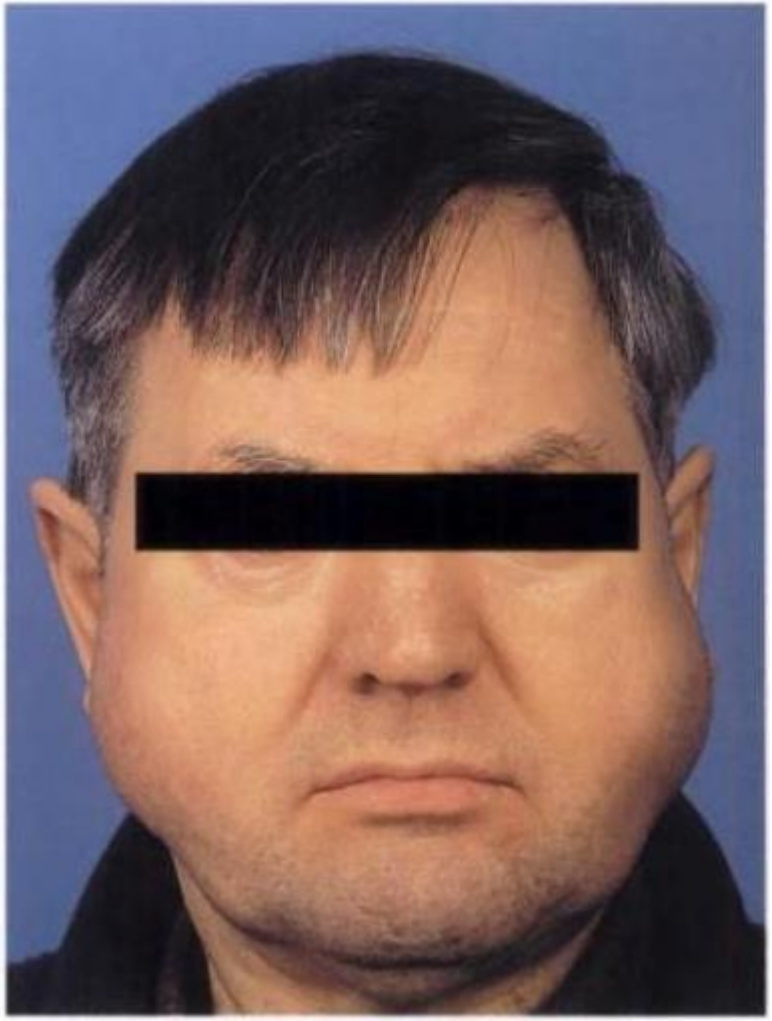
- Drugs
  - *Antihypertensive drugs*
  - *Alcohol abuse ± liver cirrhosis + hepatic steatosis* and *alcoholic hepatitis*
  - *Sympathomimetics* such as *isoprenaline*
  - *Phenylbutazone*
  - *Anti-thyroids* & *phenothiazines*
- Autonomic neuropathy

sympathetic nerve dysfunction

-> increase in *zymogen storage* in the cell

-> acinar cells enlargement

Sialoadenosis (sialosis)



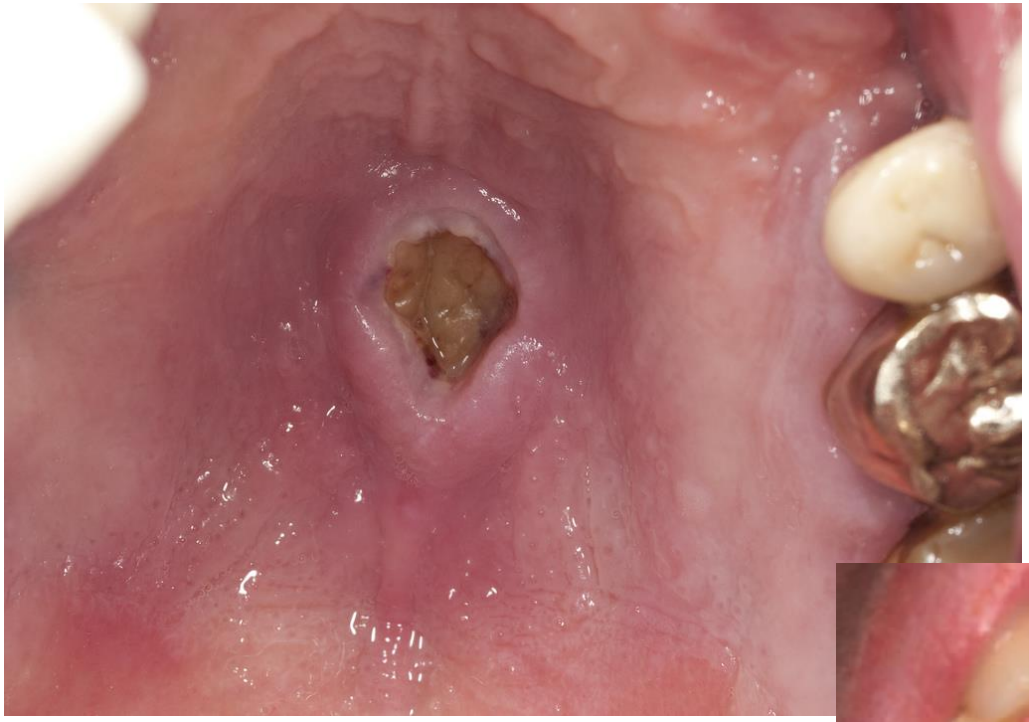
Necrotizing sialometaplasia

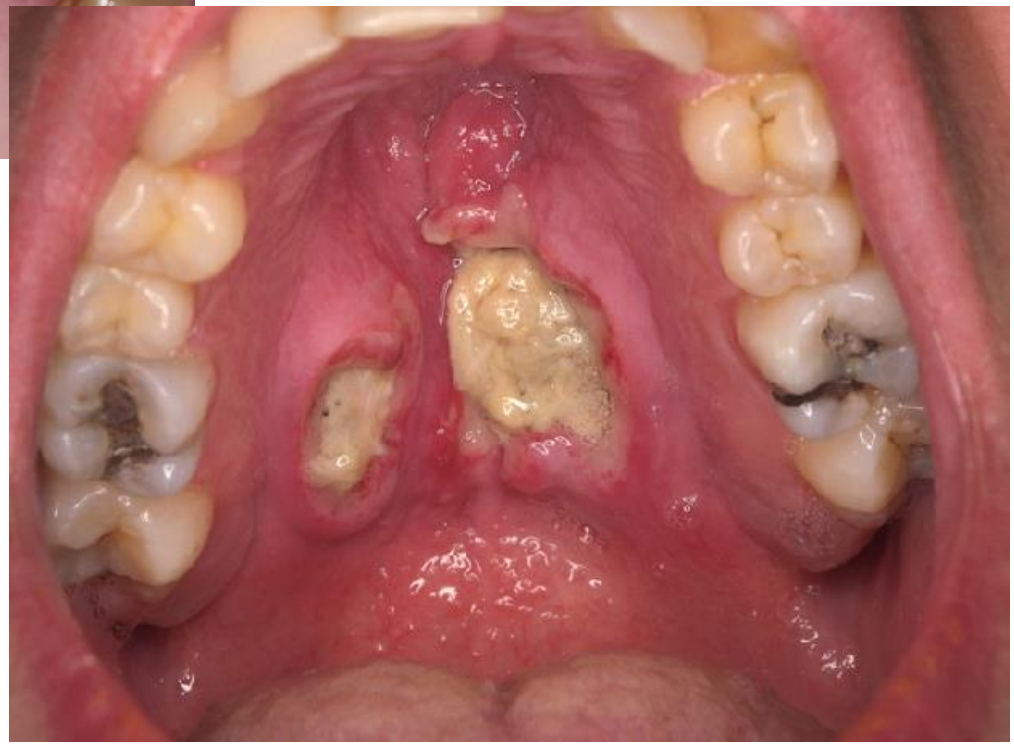
is a nonneoplastic inflammatory condition of the salivary glands

- Necrotizing sialometaplasia was first reported to involve the minor salivary glands of the oral cavity, particularly those of the palate.
- Seventy-five percent of all cases occur on the posterior palate.
- In addition, necrotizing sialometaplasia is recognized in the parotid and submandibular salivary glands, minor mucous glands in the lung, nasal cavity, larynx, trachea, nasopharynx, and maxillary sinus.

Necrotizing sialometaplasia: etiology

- In most cases of necrotizing sialometaplasia, the etiology is believed to be related to vascular ischemia.
- In an experimental study in a rat model, local anesthetic injections induced necrotizing sialometaplasia.
- Tobacco use is suggested as a possible etiologic risk factor for necrotizing sialometaplasia.

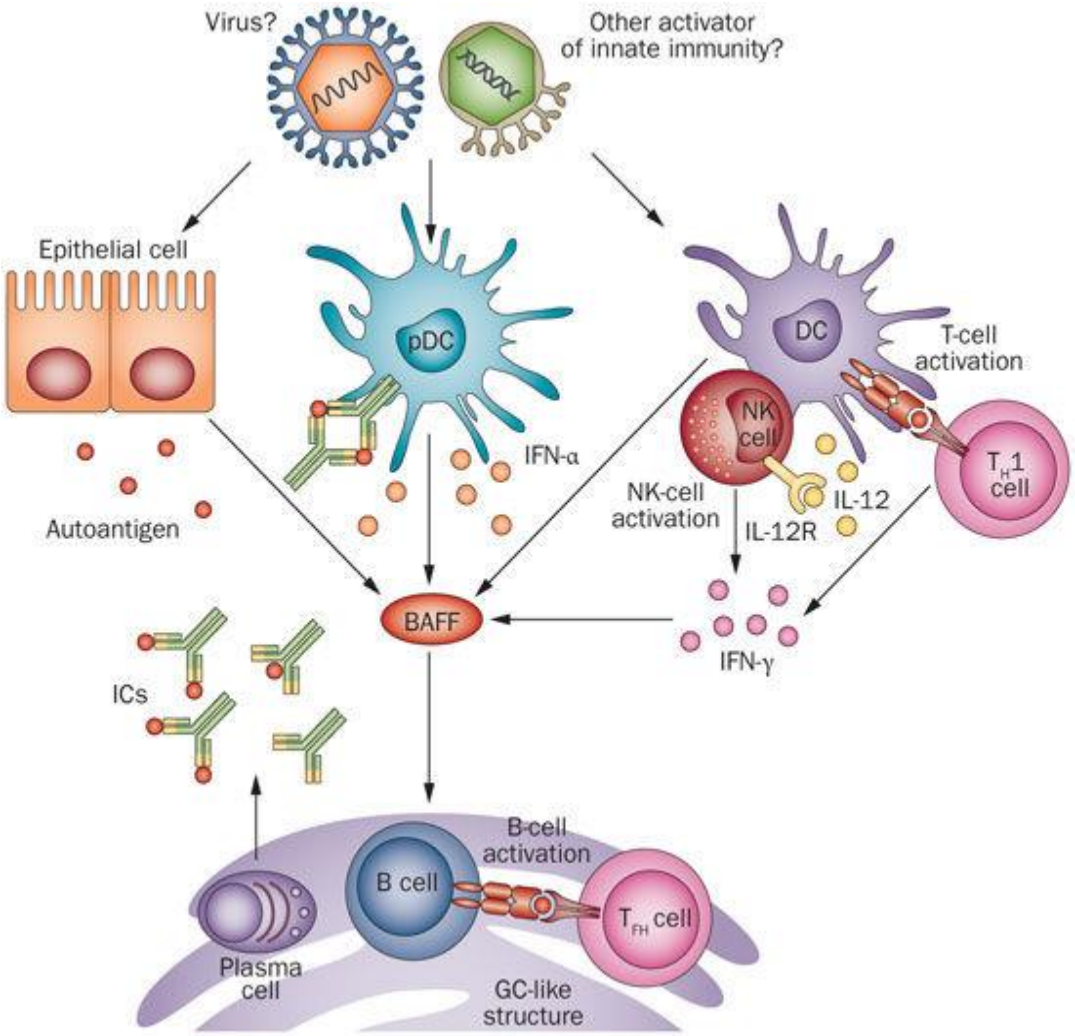


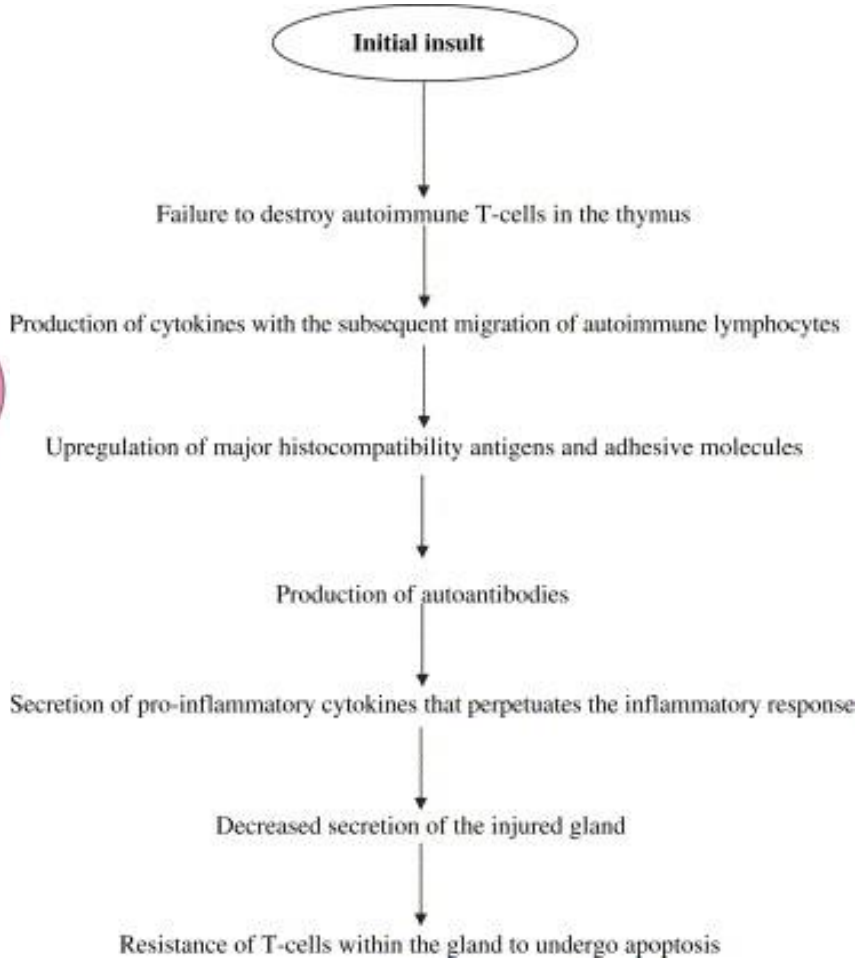


Sjogren's syndrome

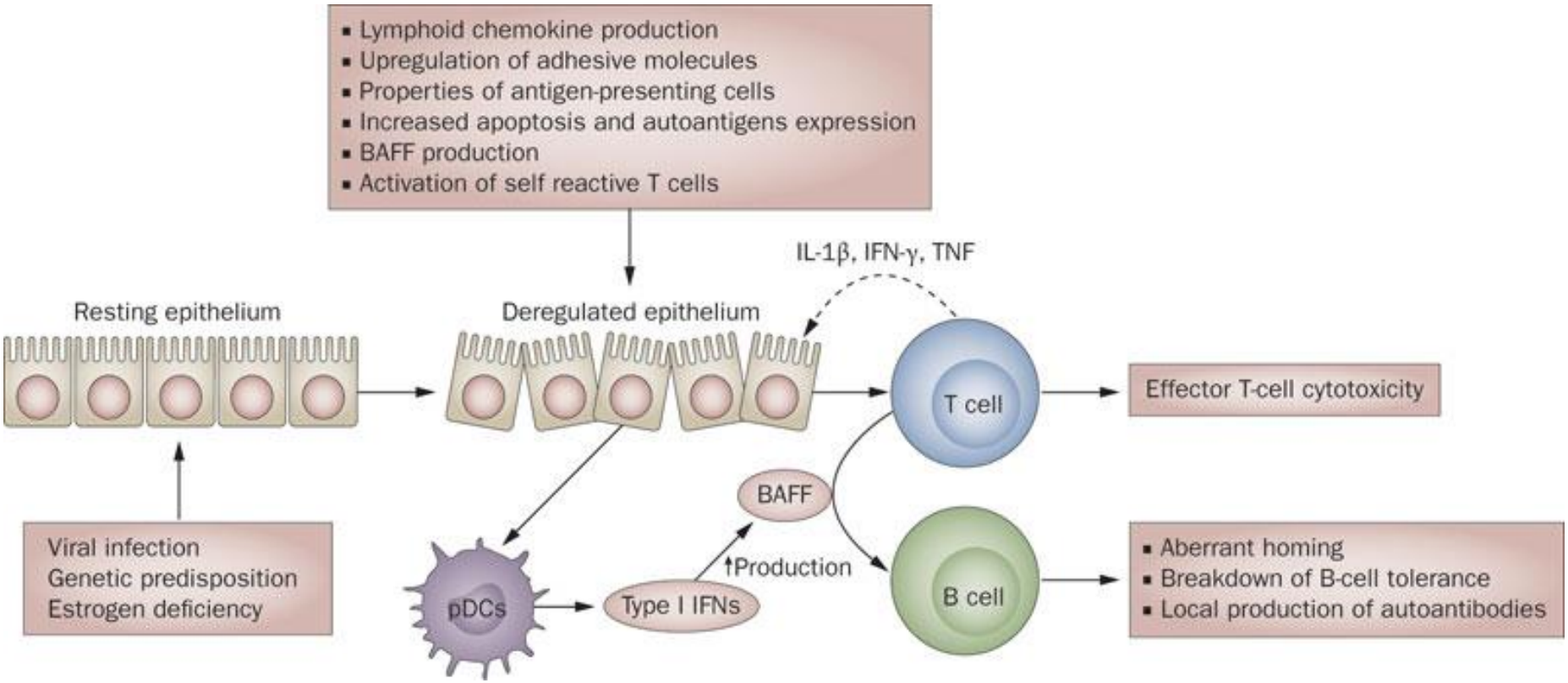
- is an autoimmune systemic chronic inflammatory disorder characterized by lymphocytic infiltrates in exocrine organs. The disorder most often affects women, and the median age of onset is around 50 to 60 years

Sjogren's syndrome: pathogenesis

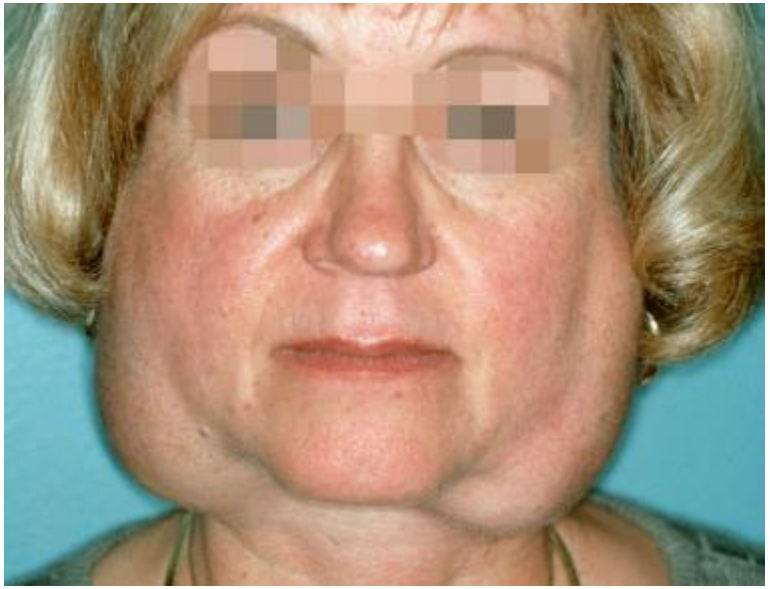




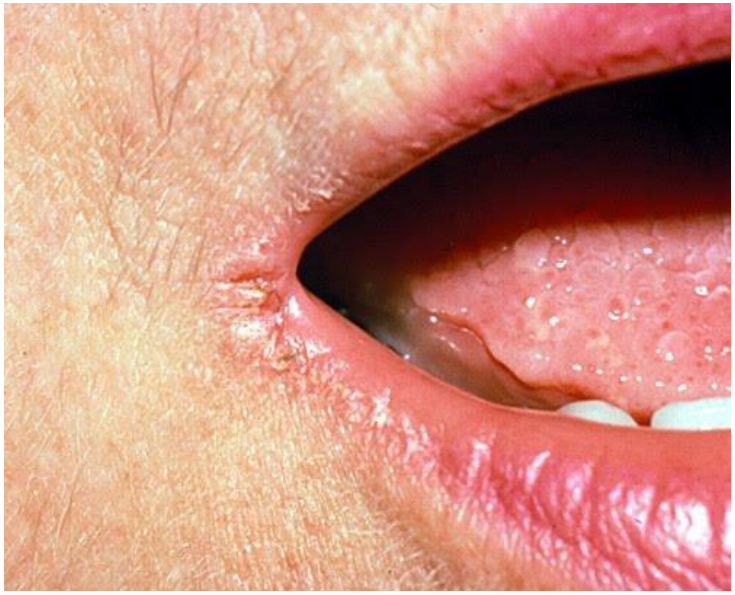
Sjogren's syndrome: pathogenesis



Sjogren's syndrome



Marked bilateral parotid gland enlargement



Angular cheilitis

Sialorrhea (drooling, ptyalism)

Increased salivation

The term drooling commonly refers to anterior drooling and should be distinguished from posterior drooling, in which saliva spills over the tongue through the faucial isthmus

Drooling is common in normally developed babies but subsides between the ages 15 to 36 months with establishment of salivary continence. It is considered abnormal after age 4

Pathogenetic background:
↑ cholinergic stimulation
↓ cholinesterase

Sialorrhea

- result of hypersecretion **(primary sialorrhea)** of the salivary glands
- more commonly due to impaired neuromuscular control with dysfunctional voluntary oral motor activity that leads to an overflow of saliva from the mouth **(secondary sialorrhea)**

Sialorrhea: etiology

- During sleep (Sometimes while sleeping, saliva does not build up at the back of the throat and does not trigger the normal swallow reflex, leading to the condition)
- Cerebral palsy
- Stroke
- Amyotrophic lateral sclerosis
- Tumors of the upper aerodigestive tract
- Parkinson's disease
- Rabies
- Mercury poisoning
- Venom of snakes and insects

Associates with fever or trouble swallowing

- Retropharyngeal abscess
- Peritonsillar abscess
- Tonsillitis
- Mononucleosis
- Strep throat

Pathology of hard tissues

Teeth

Tooth pathology

CONGENITAL

- Size of teeth
- Shape and form of teeth
- Number of teeth
- Structure of teeth
- Growth of teeth

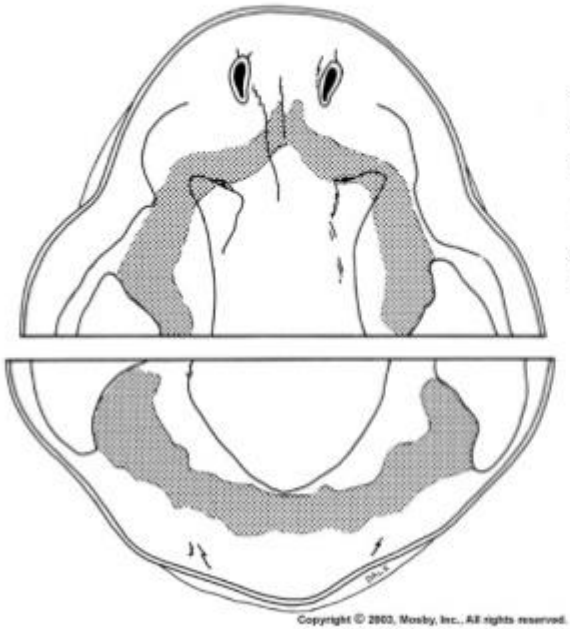
ACQUIRED

Dental caries
Dental abscess

Congenital tooth pathology

Initiation of Tooth Development

The initiation of tooth development begins at 37 days of development with formation of a continuous horseshoe-band of thickened epithelium in the location of upper and lower jaws – **Primary Epithelial Band**

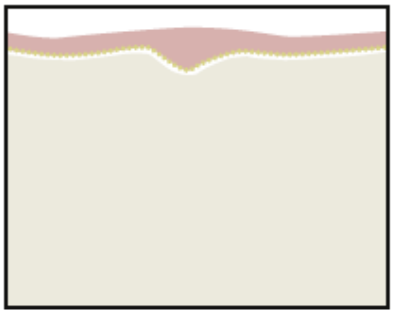
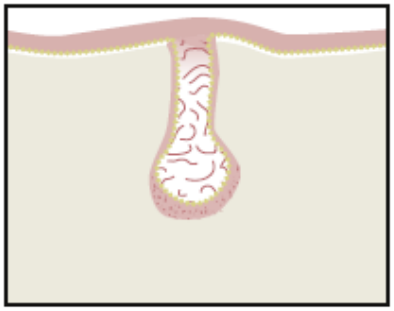
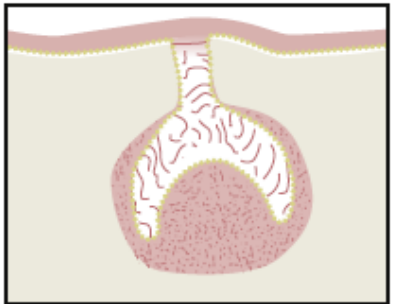


Each band of epithelium will give rise to 2 sub divisions:

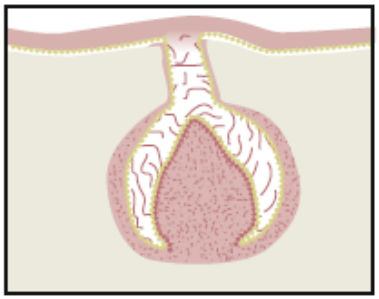
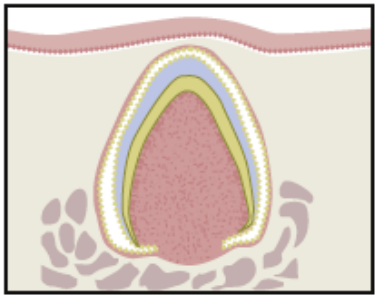
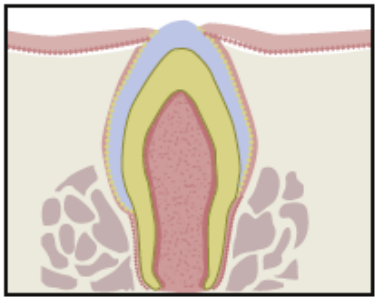
1. Dental lamina and
2. Vestibular lamina

Figure from Ten Cate's Oral Histology, Ed., Antonio Nanci, 6th edition

Stages of tooth development

STAGE AND TIME SPAN*	MICROSCOPIC STRUCTURE	MAIN PROCESSES	HISTOLOGIC FEATURES
Initiation stage at sixth to seventh week		Induction	Ectoderm lining stomodeum gives rise to oral epithelium and then to dental lamina; adjacent to deeper ectomesenchyme, which is derived from the neural crest cells. Both tissue types are separated by a basement membrane.
Bud stage at eighth week		Proliferation	Growth of dental lamina into bud shape that penetrates growing ectomesenchyme.
Cap stage at ninth to tenth week		Proliferation, differentiation, morphogenesis	Formation of tooth germ as enamel organ forms into cap shape that surrounds inside mass of dental papilla, with an outside mass of dental sac, both from the ectomesenchyme.

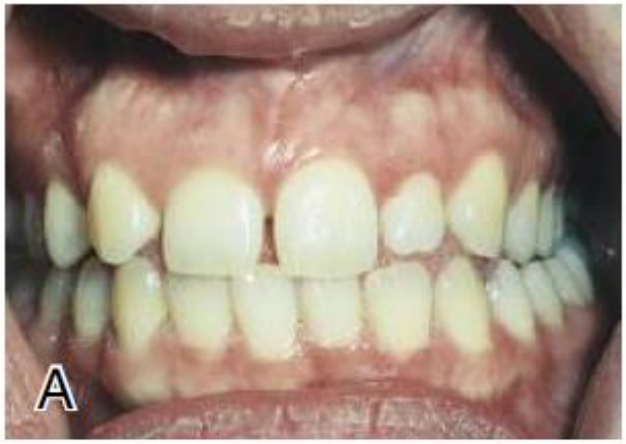
Stages of tooth development

Bell stage at eleventh to twelfth week		Proliferation, differentiation, morphogenesis	Differentiation of enamel organ into bell shape with four cell types and dental papilla into two cell types.
Apposition stage at various times		Induction, proliferation	Dental tissue types secreted in successive layers as matrix.
Maturation stage at various times		Maturation	Dental tissue types fully mineralize to mature form.

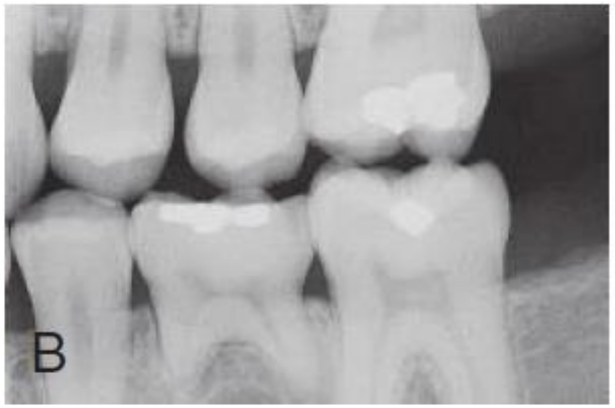
Common Dental Developmental Disturbances with Involved Developmental Stage

Initiation stage

Disturbance: Anodontia, partial or complete
Description: Absence of permanent or primary teeth that commonly include permanent third molar, maxillary lateral incisor **(A),** and second premolar **(B)** with partial anodontia
Etiologic factors: Hereditary, endocrine dysfunction, systemic disease, excess radiation exposure that prevent tooth germ(s) formation
Clinical ramifications: Disruption of occlusion and esthetic complications that are treated by prosthetic replacement with partial or full dentures, bridges, and/or implants



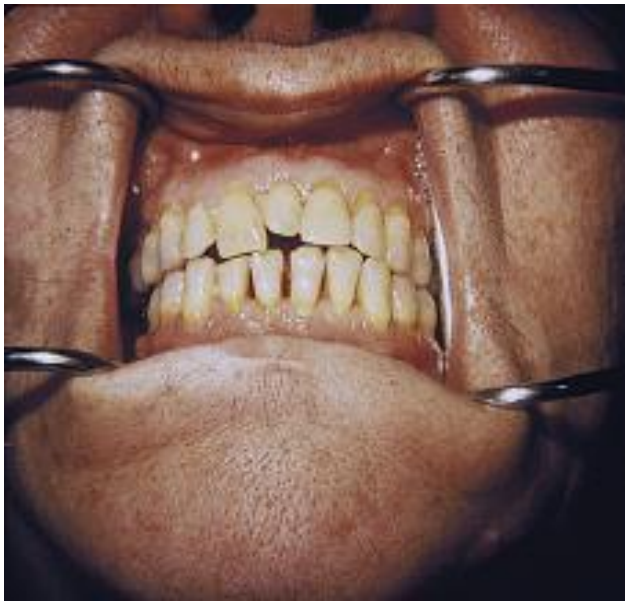
Absent permanent maxillary lateral incisor



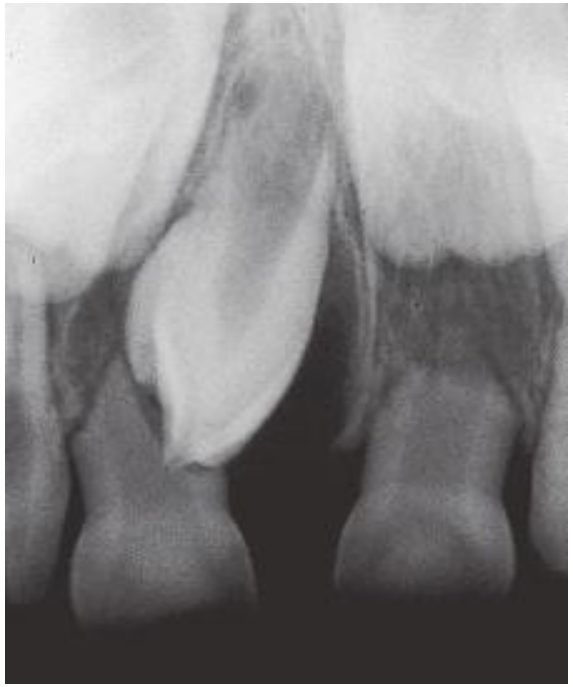
Absent permanent mandibular second premolar

Initiation stage

Disturbance: Supernumerary tooth or teeth
Description: Development of one or more extra teeth that are commonly found between the permanent
maxillary central incisors (mesiodens—**C, D**), distal to third molars (distomolar), and premolar region (perimolar)
Etiologic factors: Hereditary with extra tooth germ(s) formation from persisting dental lamina cluster(s)
Clinical ramifications: Crowding, failure of eruption, and disruption of occlusion that are treated by
surgical removal if needed and/or orthodontic therapy



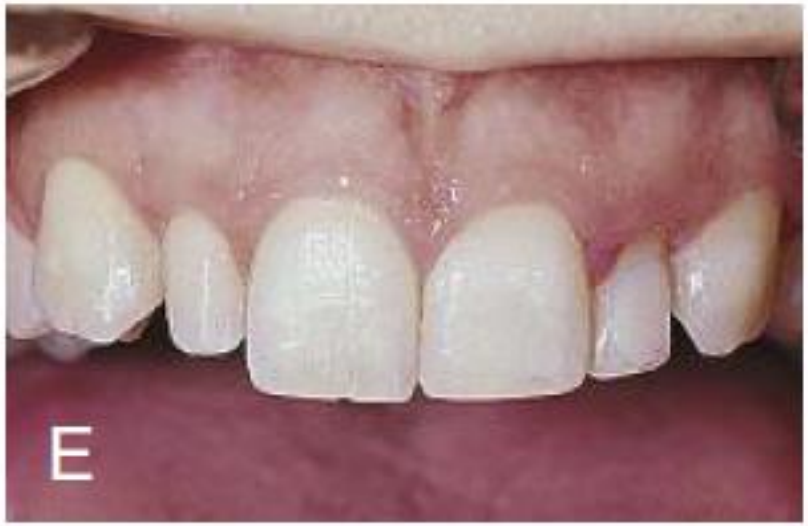
C



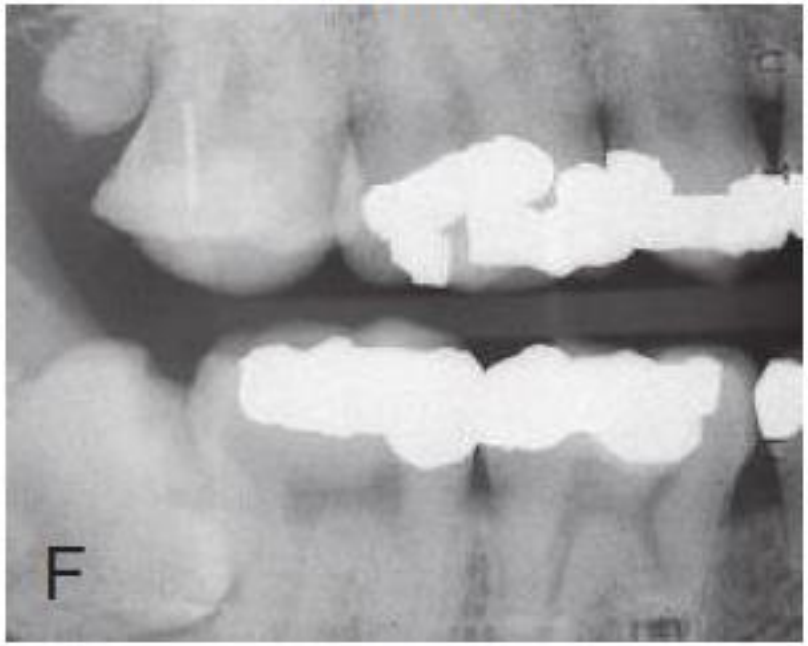
D

Bud stage

- **Disturbance:** Microdontia or macrodontia, partial or complete
- **Description:** Abnormally small or large teeth that commonly affects permanent maxillary lateral incisor **(E)**
- and third molar with partial microdontia **(F)**
- **Etiologic factors:** Hereditary with partial; endocrine dysfunction with complete
- **Clinical ramifications:** Esthetic and spacing complications that are treated with full restorative crown on microdontic tooth (lateral incisor) and/or possibly extraction (third molar)



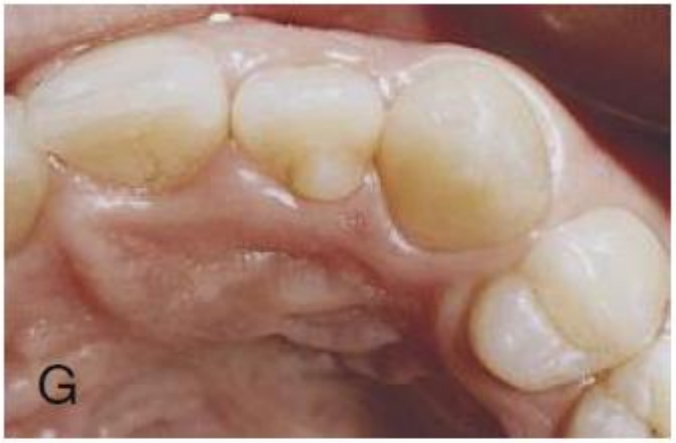
Peg lateral

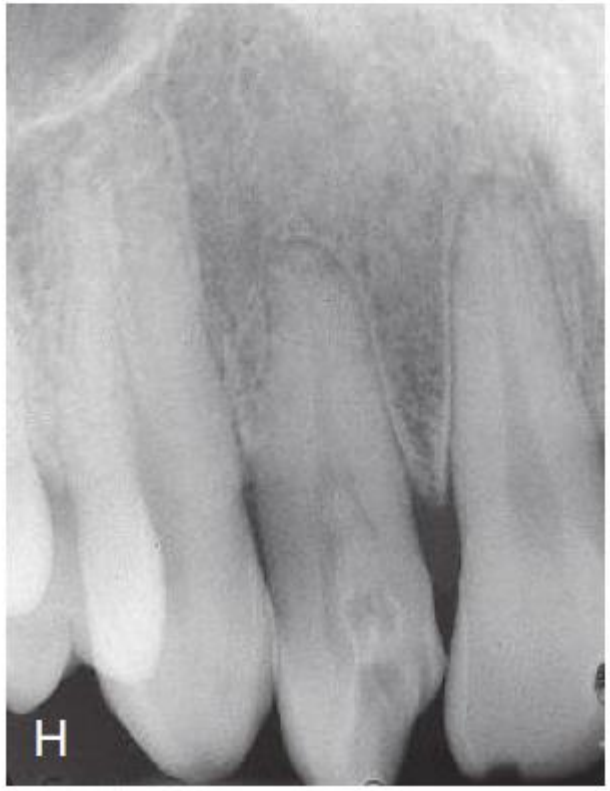


Peg molar

Cap Stage

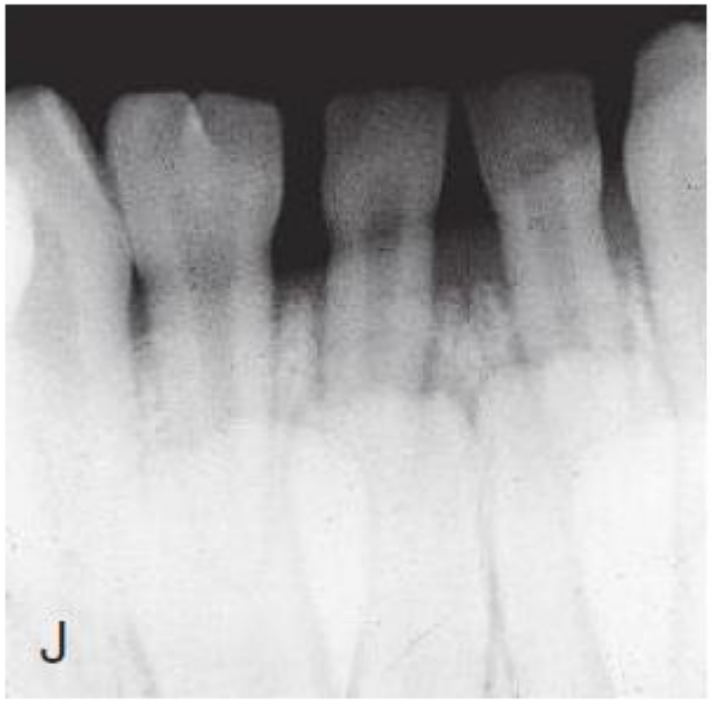
- **Disturbance:** Dens in dente **(G, H)**
- **Description:** Enamel organ invaginates into the dental papilla that commonly affects the permanent maxillary
- lateral incisor
- **Etiologic factors:** Hereditary
- **Clinical ramifications:** Deep lingual pit that may need endodontic therapy





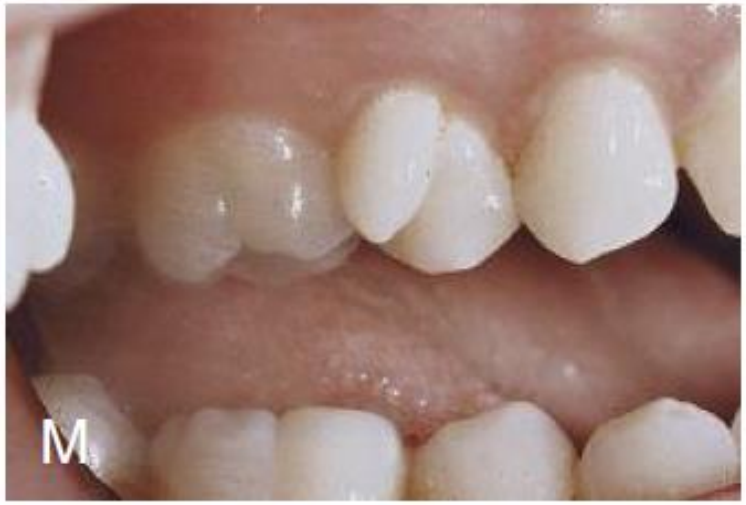
Cap Stage

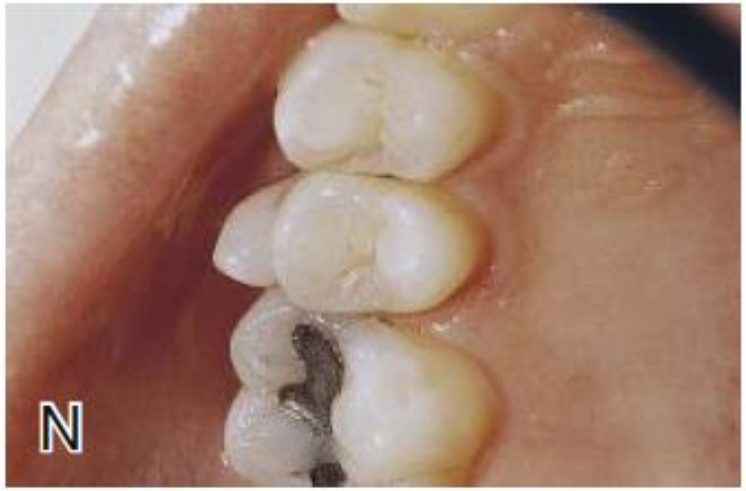
- **Disturbance:** Gemination **(I, J)**
- **Description:** Tooth germ tries to divide and develops large single-rooted tooth with one pulp cavity and
- “twinning” commonly in crown of anteriors with correct number in the permanent or primary dentition
- **Etiologic factors:** Hereditary
- **Clinical ramifications:** Esthetic and spacing complications that can be treated by orthodontic therapy



Cap Stage

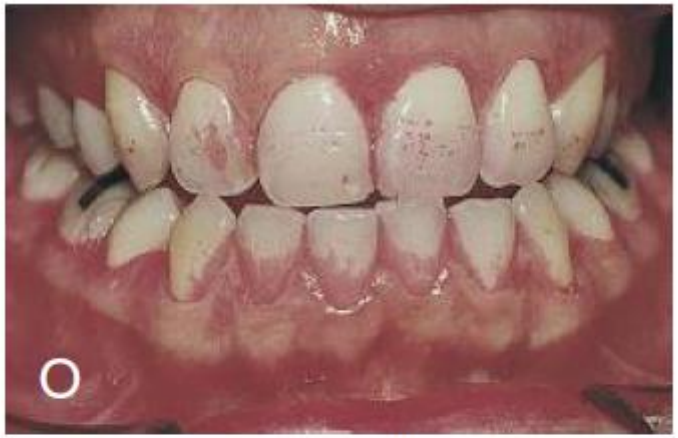
- **Disturbance:** Tubercle **(M, N)**
- **Description:** Small, rounded enamel extensions forming extra cusps that is commonly found on permanent
- posteriors occlusal surface or anteriors lingual surface
- **Etiologic factors:** Trauma, pressure, or metabolic disease that affects enamel organ
- **Clinical ramifications:** Occlusal complications



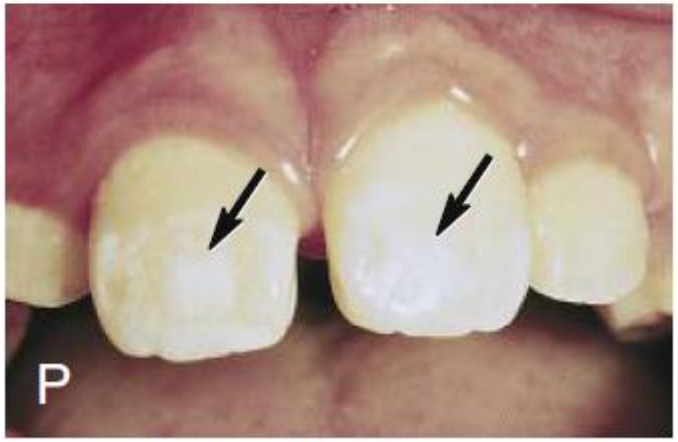


Apposition and Maturation Stage

- **Disturbance:** Enamel dysplasia
- **Description:** Faulty enamel development from interference involving ameloblasts that results in enamel
- pitting (enamel hypoplasia, **O**) and/or intrinsic color changes (enamel hypocalcification, **P**) with possible
- changes in enamel thickness
- **Etiologic factors:** Local or systemic from traumatic birth, systemic infections, nutritional deficiencies, or
- dental fluorosis
- **Clinical ramifications:** Esthetic and function complications



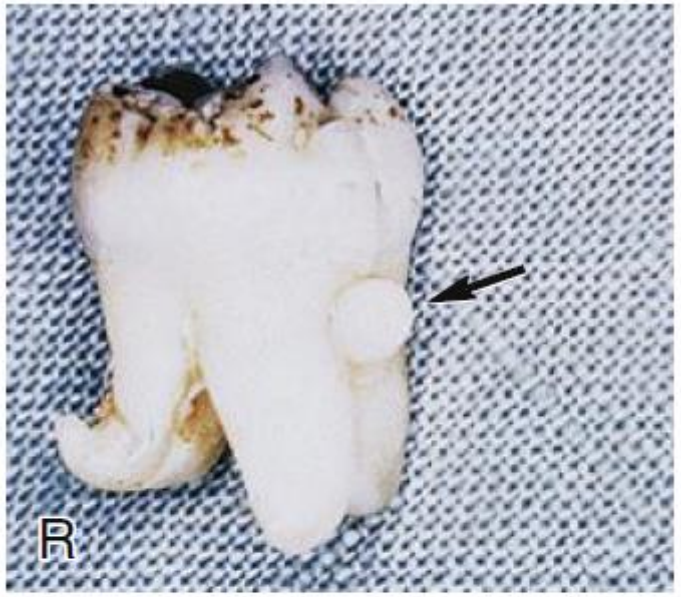
Enamel hypoplasia (with disclosing solution)

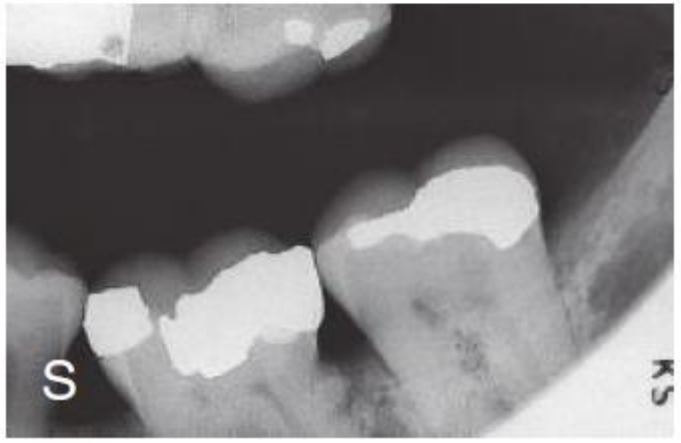


Enamel hypocalcification *(arrows)*

Apposition and Maturation Stage

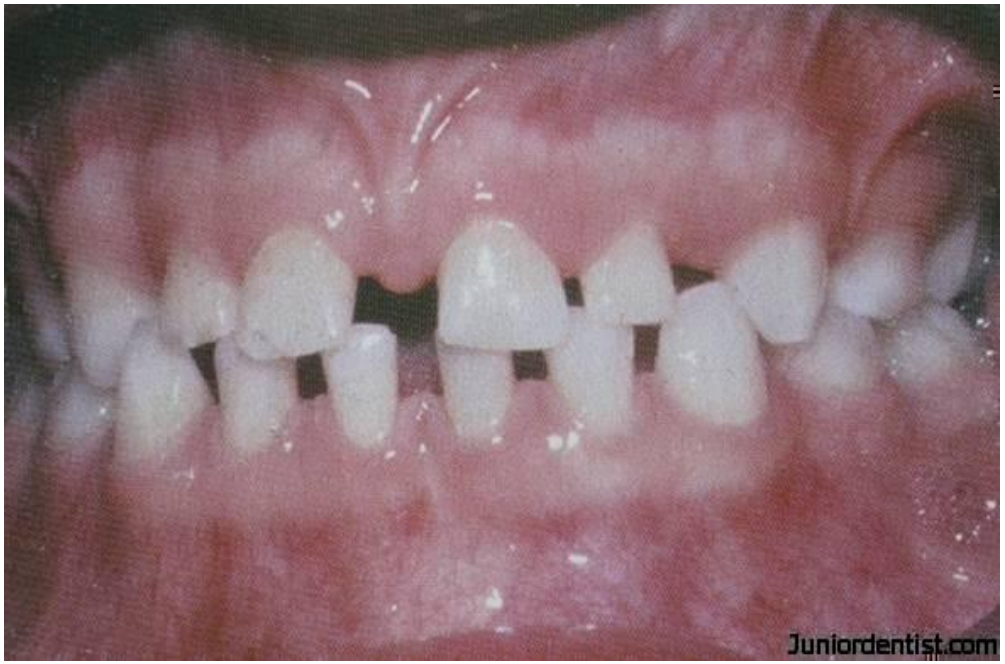
- **Disturbance:** Enamel pearl **(R, S)**
- **Description:** Enamel sphere on root *(arrow)*
- **Etiologic factors:** Displacement of ameloblasts to root surface
- **Clinical ramifications:** Confused as calculus deposit on root and may prevent effective homecare

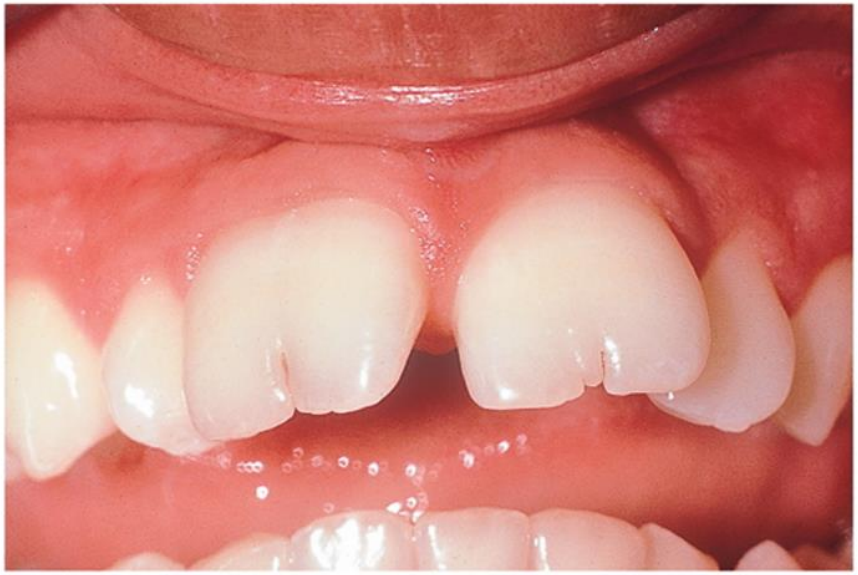




- Size of teeth

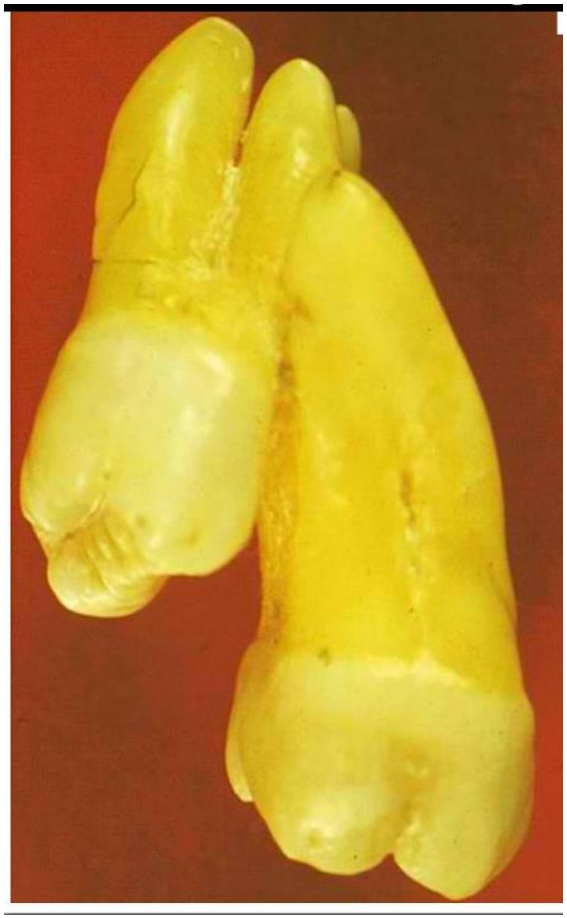
- Microdontia
- Macrodontia

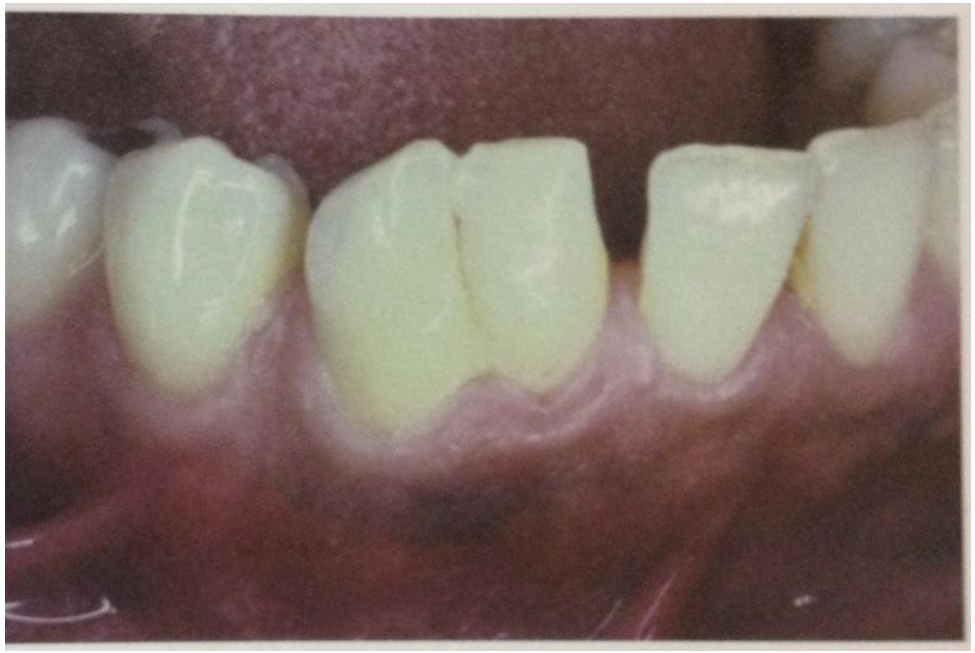




○ Shape and form of teeth

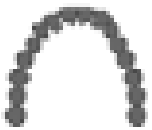
- Crown
- Root





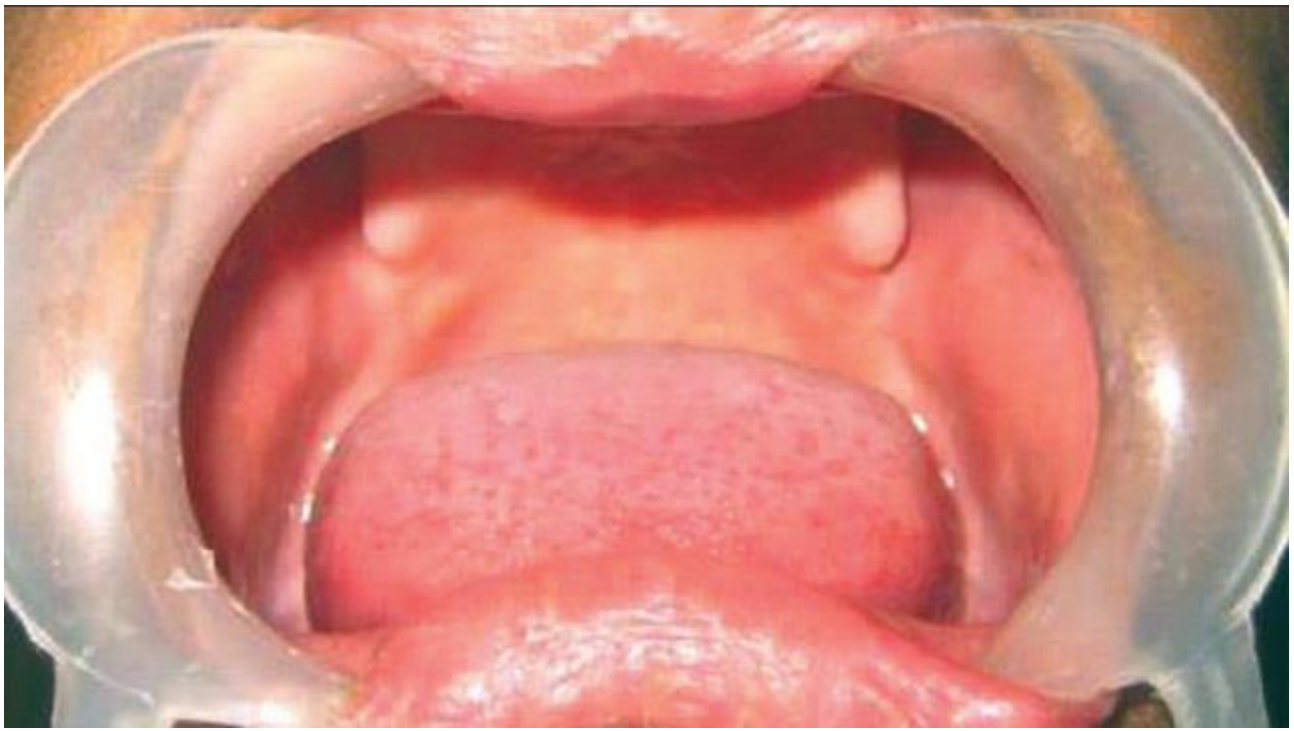
- Number of teeth

Congenital teeth pathology

Hypodontia	Oligodontia	Anodontia
		
Tooth loss except third molars	More than 6 teeth missing	All teeth missing
2-10(15)%	0.1-1%	Extremely rare
Msx1, Pax9	Msx1, Pax9, Axin2	

- Number of teeth

Anodontia



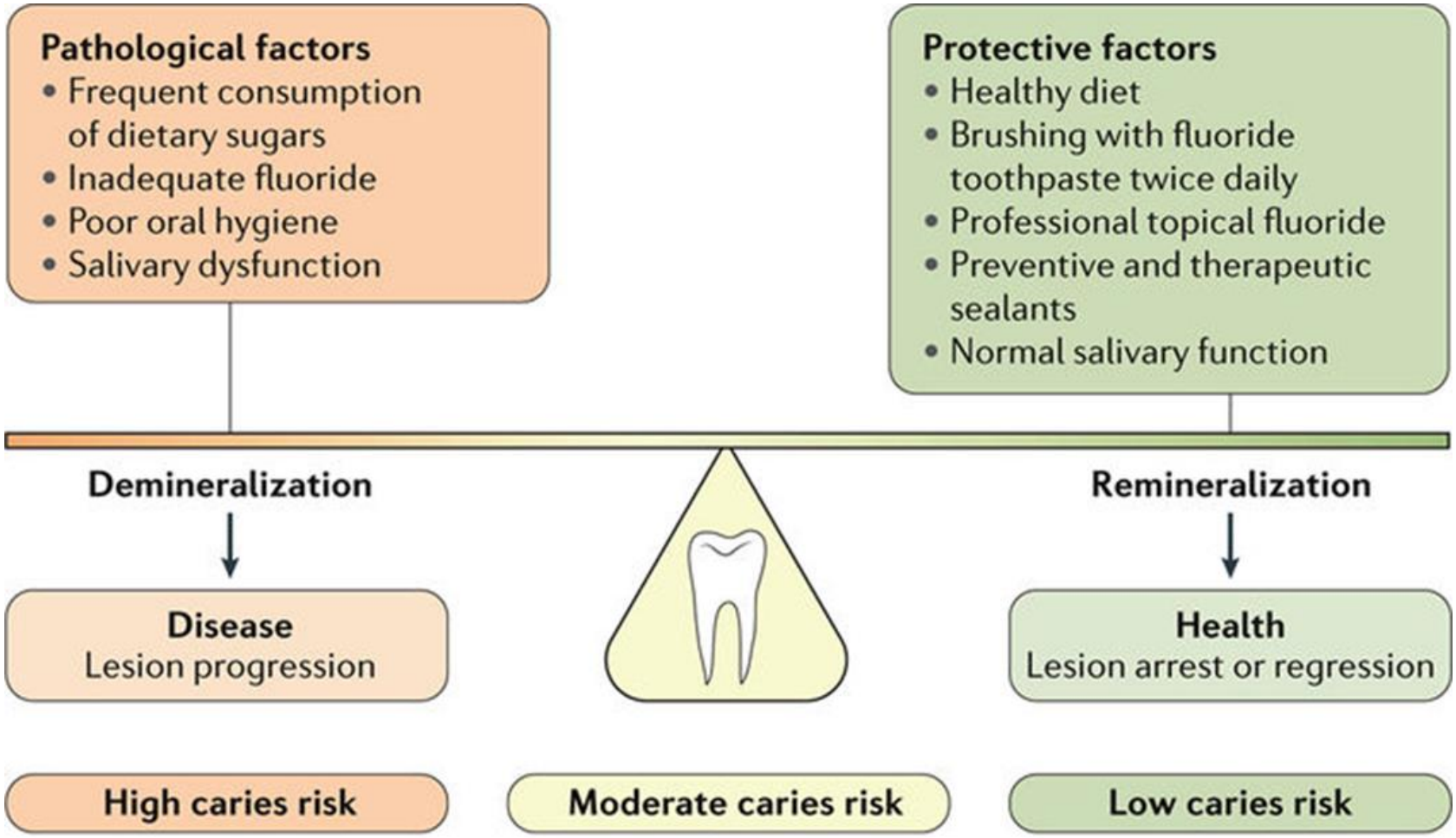
Dental caries

Dental caries is an irreversible microbial disease of the calcified tissues of the teeth, characterized by demineralisation of inorganic portion and destruction of organic substance of the tooth, which often leads to cavitation

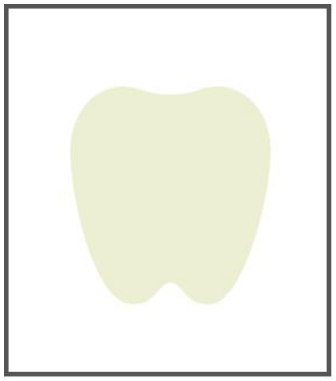
(Shafer's Textbook of Oral Pathology, 6th edition)

Most common cause of tooth loss before age 35

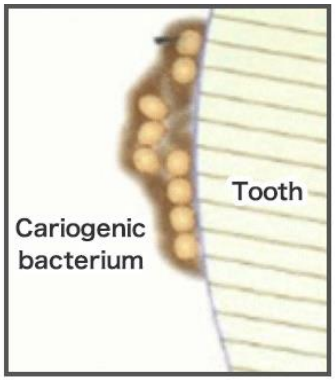
Pathogenesis : bacteria ferments sugar from carbohydrate →acid metabolic end products → mineral dissolution of tooth structure



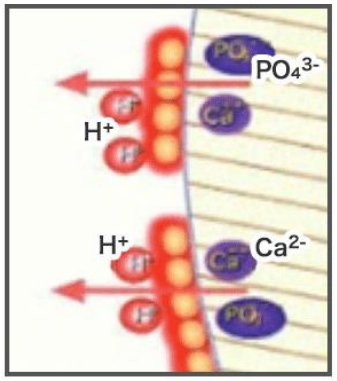
Nature Reviews | Disease Primers



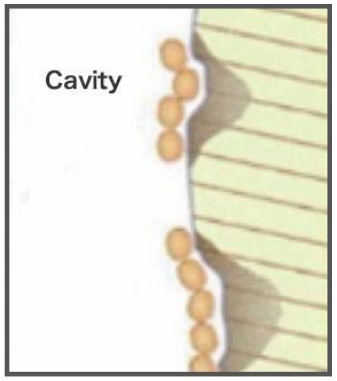
Cariogenic bacterium infection



Fixation to the tooth surface



Decalcification due to acid produced by cariogenic bacteria



Cavity formation

Role of carbohyrdates

Cariogenicity of Carbohydrates determined by:

- Sticky, solid Carbohydrate more cariogenic than liquid
- Mono or di- saccharides more cariogenic than polysaccharide
- Sucrose is more cariogenic than fructose
- While Xylitol, sorbitol and Sachharin are found to be non- cariogenic.

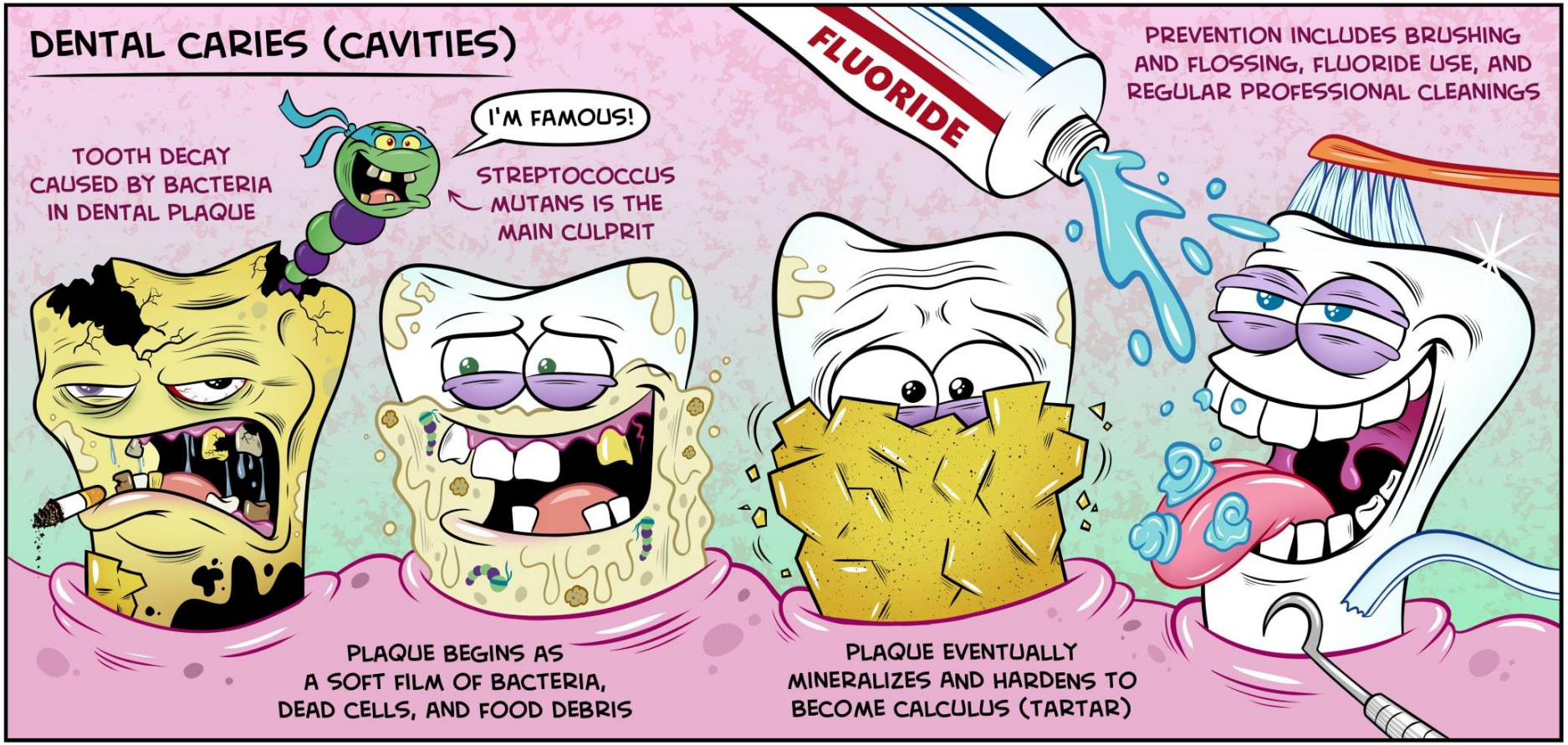
Role of microorganisms

Erdl, in 1843, first associated filamentous microorganisms to caries on a causative basis

- Oral organisms can demineralise tooth enamel in vitro and produce lesions similar to the naturally occurring dental caries; Miller, 1889
- Streptococcus mutans is invariably isolated from carious lesions in the teeth of British patients; Clark, 1924
- Certain bacteria with acidogenic potential can be isolated and identified from the carious lesions; Florestano, 1942

Role of microorganisms

- S. mutans : development of early carious lesions in enamel
- Lactobacilli : associated with dentinal caries
- Actinomyces : associated with root surface caries
- Vellionella: possibly anti-cariogenic



Virulence properties of *S. mutans*

- Adhesion, acidogenicity, and acid tolerance
- Each of these properties works coordinately to alter dental plaque ecology.
- The ecological changes are characterized by increased proportions of *S. mutans* and other species that are similar lacidogenic and aciduric.
- The selection for a cariogenic flora increases the magnitude of the drop in pH following the fermentation of available carbohydrate and increases the probability of enamel demineralization.

Virulence factors of *S. mutans*

- Production of acid
- Adhesins
  - Wall-associated protein A (WapA)
  - *S. mutans* LraI operon (SloC)
  - Glucan-binding proteins A and C
- Adherence mechanism

The metabolism of *S. mutans*

- Key to the pathogenesis of dental caries
  - The fermentation of these carbohydrates is the principal source of energy for *S. mutans*

    Genome sequence shows that *S. mutans* can metabolize a wider variety of carbohydrates than any other G(+) microorganism
  - The glycolytic pathway leads to the production of pyruvate,

    to lactic acid (by LDH activity), formate, ethanol and acetate
  - The acidic environments are responsible for the damage of tooth structure
  - Acid tolerant – based on a membrane-bound, acid stable, proton-translocating ATPase

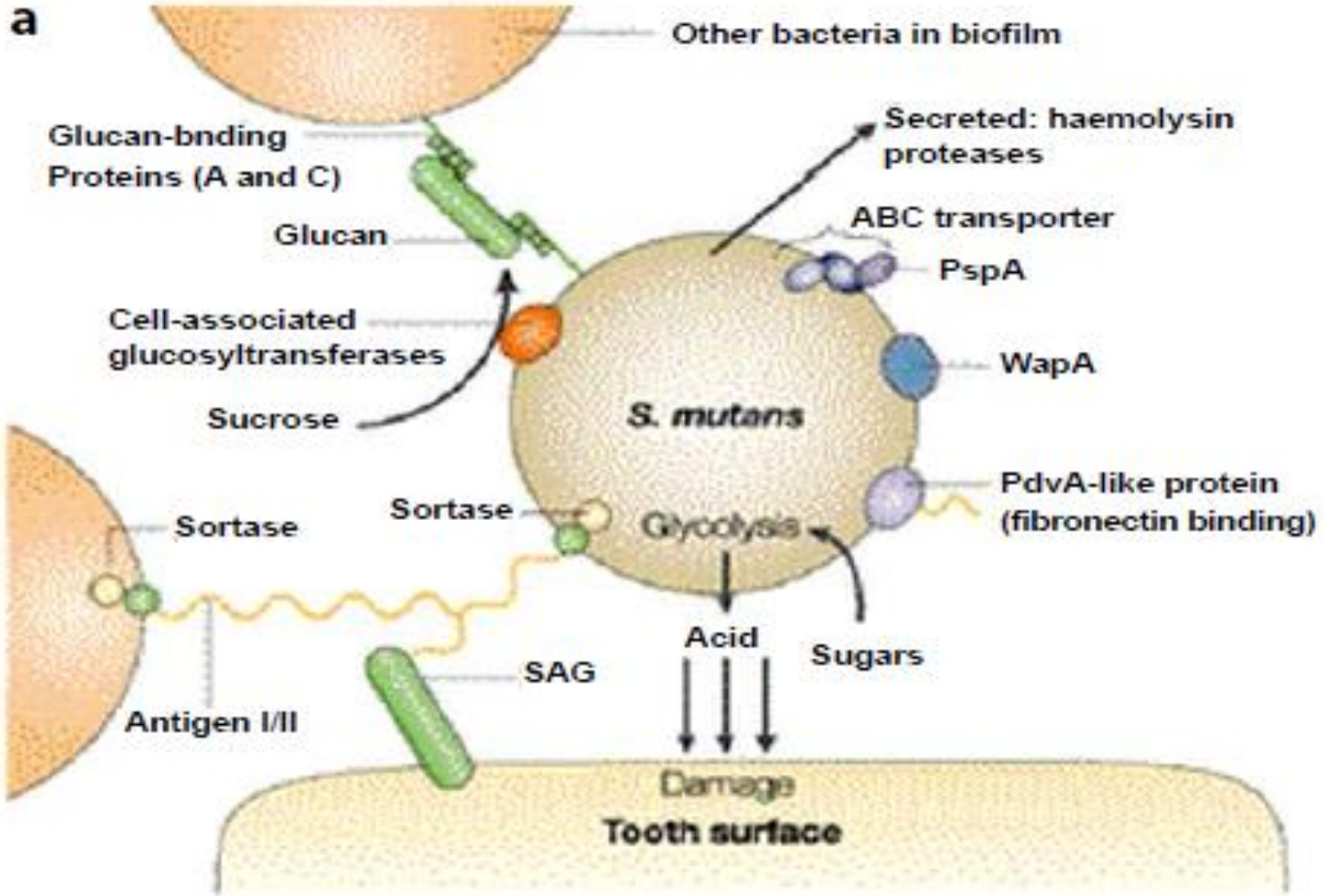
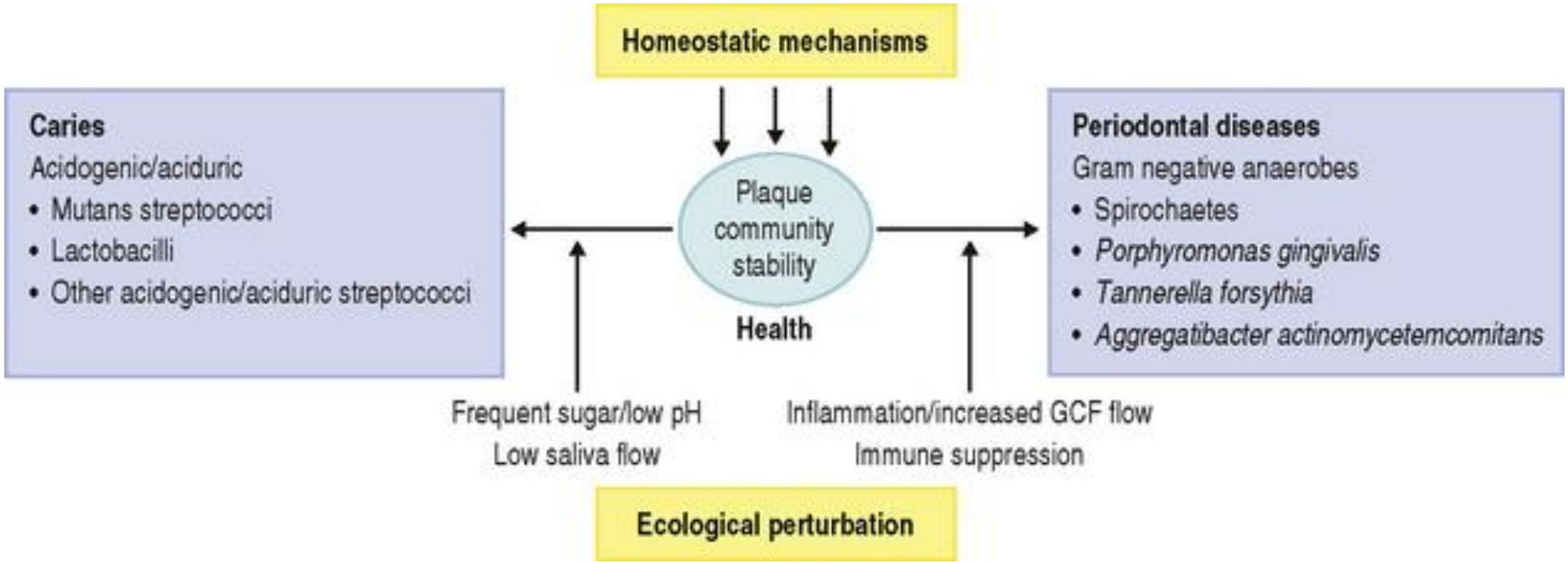


Figure 3: Adhesion [76].

Lactobacilli

- Gram-positive bacteria which are commonly isolated from the oral cavity.
- Cariogenic, highly acidogenic organisms, however, has low affinity for tooth surfaces.
- Associated more with carious dentine and the advancing front of caries lesions rather than with the initiation of the disease.
- Usually lactobacilli comprise less than 1% of the total cultivable microflora. However, their proportions and prevalence may increase at advanced caries lesions both of the enamel and of the root surface.


Homeostatic mechanisms
Caries
Acidogenic/aciduric
• Mutans streptococci
• Lactobacilli
• Other acidogenic/aciduric streptococci
Plaque community stability
Health
Periodontal diseases
Gram negative anaerobes
• Spirochaetes
• Porphyromonas gingivalis
• Tannerella forsythia
• Aggregatibacter actinomycetemcomitans
Frequent sugar/low pH
Low saliva flow
Inflammation/increased GCF flow
Immune suppression
Ecological perturbation

Pathology of hard tissues

Jaws