Salivary gland pathology non-neoplastic diseases
- salivary glands - classified according to prevailing type of secretory cells:
  - **serous** glands, **mucous** glands and **mixed seromucous**
  - salivary gland tissue consists of- **acinar** cells of serous and mucous type- **myoepithelial** cells- **epithelial** cells of salivary ducts, mesenchymal cells of the connective tissue (adipose and fibrous, nerves, blood vessels), and inflammatory cells
  - according to the anatomic location - salivary glands include paired major glands (parotid, submandibular, sublingual) and minor glands of upper aerodigestive tract
• **1.- major glands** include **parotid**- the largest gland, enclosed by capsule, located anterior to the ear, composed of serous acini, secretory ducts
• -about 20 lymph nodes located in each parotid gland
• -**submandibular**-located in the submandibular triangle, seromucous gland
• -**sublingual** gland, the smallest of major glands, in the floor of mouth, prevailing mucous acini

• **2.- minor glands of the oral mucosa**
• -minor glands have mixed serous and mucous acini in varying proportions
• cellular components:
• -of particular interest- **myoepithelial cells (MEC)** - believed to have contractile properties that assist in secretion of saliva
• -microscopical examination shows that MECs are thin and spindle-shaped cells around acini and intercalated ducts situated between basement membrane and epithelial ductal cells
• -they display features of both smooth muscle cells and epithelium
Saliva

- Saliva is composed of water 99%,
- but also electrolytes, (natrium, potassim, calcium, chloride ions, magnesium, fluorine, iodine, phosphateshydrogencarbonates
- Mucus – mucopolysacharides, glycoproteins
- Antiseptic substances- (thiocyanate, hydrogen peroxide, and secretory immunoglobulin A)
- Enzymes
  - α-amylase - breaking down starch into simpler sugars
  - lysozymes – damage bacteria
  - lipase- Salivary lipase plays a large role in fat digestion in newborn infants as their pancreatic lipase still needs some time to develop
  - Others (phosphatases, lactoperoxidases)
- Opiorphin – a newly researched pain-killing substance found in human saliva
- Epidermal growth factor or EGF
- pH – neutral (pH = 7 - 8) – buffering system
Daily salivary output

• There is much debate about the amount of saliva that is produced in a healthy person per day; estimates range from 0.75 to 1.5 liters per day while it is generally accepted that during sleep the amount drops to almost zero.

• In humans, the submandibular gland contributes around 70–75% of secretion, while the parotid gland secretes about 20–25% and small amounts are secreted from the other salivary glands. During night – production is reduced to nearly zero.

• In elderly people – physiological reduction of salivation

• Pathological reduction: dehydration, stress, drugs (antihistamines and antidepressants, spasmylics, diuretics).
Saliva

Mechanical oral clearance
Food digestion
Antibacterial properties
Enamel remineralization (calcium + phosphate minerals)
Mediate selective adhesions and bacterial colonization
Buffering system (activated glands content more bicarbonates
Protective function (dental and soft tissue of the oral cavity)
Source of DNA (cancer dg...)
Funcional disorders

- The production of saliva is stimulated both by the sympathetic nervous system and the parasympathetic nervous system.
- The saliva stimulated by sympathetic innervation is thicker, and saliva stimulated parasympathetically is more watery.
- Sympathetic stimulation of saliva is to facilitate respiration, whereas parasympathetic stimulation is to facilitate digestion.
- Increased production - sialorea (ptyalismus) – foreign bodies, (new dentures), ulcerations of the oral cavity, stress, tumors,
- Decreased production - xerostomia
Developmental disorders

- Very rare
- Aplazia (one or more lobes, or the entire gland)
- Accessory or ectopic gland (in lymph node)
- Congenital polycystic degeneration of parotid gland—girls, fluctuating enlargement
- Anomalies of ducts (congenital atresia, ectasia may be associated with bronchiektasias)
Inflammation

• Etiology
  – Bacterial
  – Viral
  – Autoimmune

• Acute bacterial sialoadenitis
• Chronic interstitial sialoadenitis
• Epidemic parotitis (Mumps)
• Cytomegaloviral sialoadenitis
• Autoimmune sialoadenitis
Acute bacterial sialadenitis

• Mostly as ascending infection
• Less frequently hematogenically (sepsis, scarlet fever) lymphogenically
• Risk factors: decreased salivation, (dehydration, post-operative diuretics...), cachexia, sialolithiasis Poor oral hygiene
• Staphylococcus aureus, Streptococcus viridans, Streptococcus pneumoniae
• Catarrhal, catarrhaly purulent, absceding
• Complication: fistulation, flegmone, tromboflebitis of facial venes
Acute bacterial sialadenitida

Clinical features

• Painful swelling
• Reddened skin
• Edema of the cheek, periorbital region and neck
• fever
• malaise
• raised ESR, CRP, leucocytosis
• purulent exudate from duct punctum
Viral sialadenitis

- Sialotropic viruses
- Hematogenic spread in viremia
  - Clinically manifested glandular inflammation
  - Persistent infection $\rightarrow$ reactivation
  - Only in saliva (polio, lyssa, influenza, ...)


Epidemic parotitis, mumps

- RNA paramyxovirus, mostly in the childhood contagious disease through contact with respiratory secretions, such as saliva from an infected person (droplets aerosol). Mumps can also be spread by sharing food and drinks.

Mumps is contagious from approximately 6 days before the onset of symptoms until about 9 days after symptoms start.

The incubation period (time until symptoms begin) can be from 14–25 days, but is more typically 16–18 days.

Symptoms last 7-14 days.

Clinically:
- (30-40% cases - inapparently!)
  - headache
  - uni- / bi-lateral enlargement of parotis, also submandibular and, sublingual gl.
**Parotitis epidemica**

- Infection of other organ systems
- Mumps viral infections in adolescent and adult males carry an up to 30% risk that the testes may become infected (orchitis or epididymitis), which can be quite painful; about half of these infections result in testicular atrophy and in rare cases sterility can follow.
- Spontaneous abortion in about 27% of cases during the first trimester of pregnancy.
- Mild forms of meningitis in up to 10% of cases (40% of cases occur without parotid swelling)
- Oophoritis (inflammation of ovaries) in about 5% of adolescent and adult females, but fertility is rarely affected.
- Pancreatitis in about 4% of cases, manifesting as abdominal pain and vomiting
- Encephalitis (very rare, and fatal in about 1% of the cases when it occurs) Profound (91 dB or more) but rare sensorineural hearing loss uni- or bilateral. Acute unilateral deafness occurs in about 0.005% of cases.
- After the illness, lifelong immunity to mumps generally occurs; reinfection is possible but tends to be mild and atypical.
Mumps
Cytomegaloviral sialadenitis

• kids
  – Transplacental transmission
  – per partum by cervical secret
• Adults
  – immunosupression
  – generalized infection
  – Infected saliva, transplantation, dialysis
  – + CMV hepatitis, myocarditis, polyradiculoneuritis
• Mi: intranuclear or cytoplasmatic inclusions in ductal epithelium
Chronic sialadenitis

- From previous acute infl.
- Primarily chronic infl.
- Risks:
  - Sialolithiasis
  - Trauma
  - Thicken food
  - Scarring
  - Tumor
- chronic recurrent sialadenitis
- chronic sclerosing sialadenitis
- obstructive sialadenitis
chronic recurrent sialadenitis

Clinical features:
• unilateral/bilateral
• mild pain / swelling
• common after meals
• duct orifice is reddened and flow decreases
• may or may not have visible/palpable stone.
• Parotid gland
  – Recurrent painful swellings
• Submandibular gland
  – Usually secondary to sialolithiasis or stricture
• microscopy
  – Lymphocytic infiltration+ fibrosis + acinic atrophy
• attac (7-10 days) + remission (month ); trigger ???
• If there are attacks more than approximately 3 times per year or severe attacks, surgical excision of the affected gland should be considered
Chronic sclerosing sialadenitis

- Küttner’s „tumor“ (1896)
- Middle, old age,
- gl. submandibularis
- Clinically (dif. dg. Malignant tu)
  - bilateral x unilateral; focal x diffuse
  - tough, non-painful
- microscopy
  - fibrosis, lymphoplasmocytic inflammation, vasculitis
- Belongs to „IgG4-related diseases“ !!!
- Therapy: corticoids, extirpation
Chronic sclerosing sialadenitis
Chronic obstructive sialadenitis

• Duct obstruction
  – sialolithiasis
  – tumors
  – Trauma
  – Small salivary glands– denture pressure, smoking
HIV and salivary glands

- Children (20%), very typical for HIV!
- May be very early manifestation
- Unknown pathogenesis
- Clinically
  - Parotid enlargement (in 60% bilateral), xerostomy
- Microscopy
  - Follicular hyperplasia of intraglandular LN
  - Lymphocytic inflammation (CD8+)
  - Multiple lymphoepithelial cyst
- dif. dg.: Sjögren’s syndrome
Pneumoparotitis

- Air being forced through Stensen’s duct, resulting in pneumoparotitis. This may occur as a transient or recurrent phenomenon. Recurrent parotid insufflation is not entirely benign and may predispose to sialectasias, recurrent parotitis, and even subcutaneous emphysema.

- Glass-blowers, trumpeters, kids
Pneumoparotitis
Postactinic sialadenitis

• As a complication of irradiation of head and neck malignant tumor
• Serous gland are more sensitive than mucinous
• predisposing to ascending bacterial sialadenitis
• Small glands – xerostomy $\rightarrow$ decay $\rightarrow$ osteomyelitis
• Th: symptomatic, artificial saliva
Specific sialadenitis

• sarcoidosis
• tuberculosis
  – Very rare
  – Lymphogenically from oral cavity and oropharynx
Sjögren’s syndrome

- It is named after Swedish ophthalmologist Henrik Samuel Conrad Sjögren (1899-1986)

- = sicca syndrom, keratoconjunctivitis sicca

- Autoimmune disease
  - Ab x cytoplasmic antigens of ductal epithelium

- Middle aged female (F : M=10 : 1)

- Clinically: xerostomia ± xerophtamia (dry eye)+ nasal gland

- Sometimes all exocrine glands
  - decreased sweting pruritus, xeroderma (dry skin);
  - gastritis with achlorhydia, pankreatitis,
  - chronic bronchitis, interstitial pneumonia;
  - vaskuliti (petechie), Raynaud’s phenomenon;
  - artritida
Sjögren’s syndrome

• Primary (in its own right)
• Secondary
  – rheumatoid arthritis, systemic lupus erythematosus, scleroderma, primary biliary cirrhosis
• microscopy
  – Lymphoplasmodnocellular inflammation (CD4) around dilated ducts (MALT-like) → basal cell proliferation → lymphoepithelial islet
  – Acinic atrophy → xerostomia (50% pts.)

• Risc of MALToma, large cell lymphoma!!!
• Irreversible damage!!!
Sjögren’s syndrome

• Clinically:
  – Difficulties with swallowing, eating, speaking,
  – Dry, reddish, thin mucosa, lobulated tongue
  – Frequent infection - Candida
  – Dental plaque, decay
  – Acute absceding parotitis
Sjögren’s syndrome
Sjögren’s syndrome angular stomatitis
The typical picture of a patient with long-standing xerostomia due to SS. The lack of appreciation of the likelihood of rapid cervical caries has led to multiple restorations.
Swelling of the palatal minor salivary glands in Sjogren’s syndrome – a much less common finding than that of parotid swelling.
Parotid swelling in Sjogren’s syndrome.
A keratoconjunctivitis resulting from the reduced tear secretion in Sjogren’s syndrome.
Lymphoepitelial sialadenitis

- known by a variety of names, including Mikulicz disease, benign lymphoepithelial lesion, and myoepithelial sialadenitis (MESA) could be a form of primary Sjogren’s syndrome.

- often bilateral and in parotis

- Mikulicz syndrome = enlargement
  - + lymphoma, leukemia, ...

- Middle aged females

- parotis – 80-90% unilateral,

- Clinically:
  - Non - painful, 0 systemic sy (no sicca sy)
Differential diagnosis of xerostomia

• organic
  – Sjögren’s syndrome
  – irradiation
  – HIV infection
  – sarcoidosis
  – amyloidosis

• functional
  – Dehydratation
  – Psychological (depression)
  – Drugs
  – Diabetes mellitus
Sialolithiasis

• Middle aged male (M : F ... 2 : 1)
• submandibularis (85%) → parotis (6-10%)
  – Course of Wharton´s duct
  – Property of saliva
• Intraductal close to orrifice (50%) → intraductal → intraparenchymatous
• Etiology
  – Inflammation, desquamation of epitelial cells, Ca ions + nidus
• Clinically
  – Saliváry colic x asymptomatic
Sialadenosis (sialosis)

- It is also referred to as *sialosis* or "*nutritional mumps*"
- Sialadenosis is a non-neoplastic, noninflammatory enlargement of the salivary gland
- the parotid gland, often bilateral
- It results from acinar cell hypertrophy

- wide range of etiologies:
  - endocrine abnormalities like diabetes mellitus, thyroid gland disease, adrenal gland disease
  - nutritional deficiencies,
  - alcoholism,
  - cirrhosis,
  - pregnancy
  - bilimia
  - certain drugs, especially antihypertensives, β-sympatomimetics.
Cysts

• retention
  – Elderly men
  – Desquamation of epithelial cells, trauma, inflammation
• Mucocele – mucinous glands (lip, buccal mucosa,
  • Ranula – mouth floor –subliqual gland

• traumatic cysts / pseudocysts
Cyst

Dysotogenetic cysty

*branchial cleft cysts (lymphoepithelial cyst)*

– Embryonal epithelial inclusions in LN or a result from a failure of obliteration of the branchial cleft, which in fish develop into gills
– Unilateral, solitary
– Most branchial cleft cysts are asymptomatic, but they may become infected
– The cyst wall will be composed of either squamous or columnar cells with lymphoid infiltrate, often with prominent germinal centers. The cyst may contain granular and keratinaceous cellular debris. Cholesterol crystals may be found in the fluid extracted from a branchial cyst.
Necrotizing sialometaplasia

- unknown etiology - spontaneous x microtraumata
- Middle aged males, smokers
- Lobular infarction (ischemic necrosis) with or without extravasation of mucus.
- 2. Pseudoepitheliomatous hyperplasia at the periphery of the ulcer.
- 3. Squamous metaplasia of ducts and acini.
- 4. Inflammation secondary to extravasated mucous.
- 5. Preservation of lobular architecture.
- 12
- Because of the metaplasia, it is frequently misdiagnosed as squamous cell carcinoma
- Spontaneous healing within 1-2 month
Adenomatous hyperplasia

• Rare
• Not painful
• Clinically mimics tumour
• Microscopy:
  – Normal gland, no inflammation