

SALIVARY GLANDS

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- ▶ *Definition*
- ▶ *Classification Of Salivary Glands*
- ▶ *Anatomy of salivary glands*
- ▶ *Development of salivary glands*
- ▶ *Structure Of Salivary Glands*
- ▶ *Histology of major salivary glands*
- ▶ *Saliva*
- ▶ *Clinical considerations*

DEFINITION

- ▶ *These are compound tubuloacinar exocrine glands found in oral cavity that secrete complex fluid known as **saliva**.*

CLASSIFICATION OF SALIVARY GLANDS

- ▶ *Based on size*
- ▶ *Based on type of secretory cells*

Based on size:

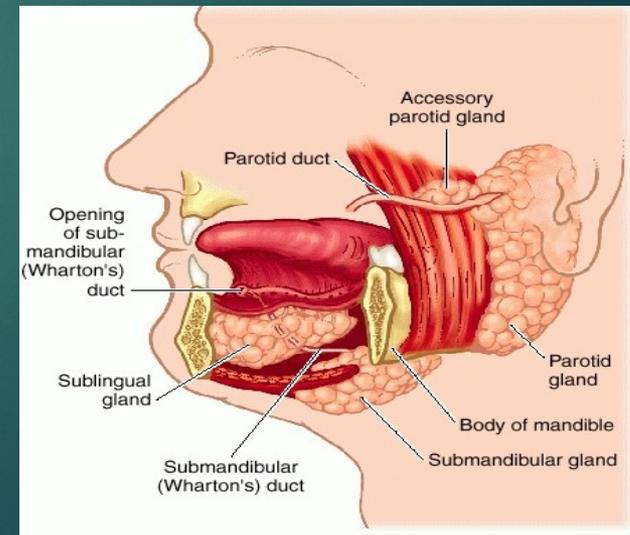
1. Major salivary glands

2. Minor salivary glands

1. Major salivary glands

▶ Collection of secretory cells aggregated into large bilaterally paired extra oral glands with extended duct system through which the gland secretions reach the mouth.

- Parotid
- Submandibular
- Sublingual



2. Minor salivary glands

▶ Collection of secretory cells scattered throughout the mucosa & submucosa of the oral cavity with short ducts opening directly onto mucosal surface.

- Serous glands of Von Ebner.
- Anterior lingual glands.
- Lingual, buccal, labial, palatal glands, glossopalatine and retromolar glands

2. Based on type of secretory cells

1. Serous : *Parotid*

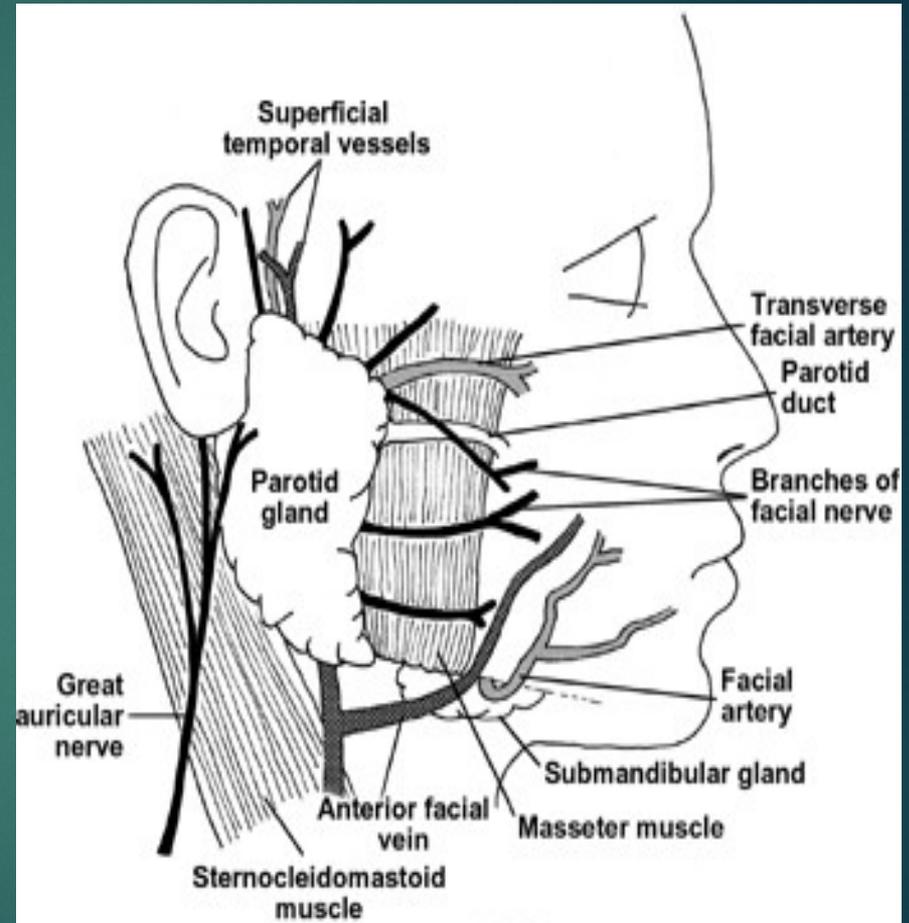
2. Mixed (seromucous):
Submandibular

3. Mucous: *Minor salivary glands.*

ANATOMY OF SALIVARY GLANDS

Parotid gland:

- ▶ *Largest* salivary gland
- ▶ *60 to 65%* of total saliva.
- ▶ *Pyramidal in shape.*
- ▶ *Weighs between 14 & 28g.*
- ▶ *Superficial portion of gland is located subcutaneously, in front of the external ear & deeper portion lies behind ramus of mandible.*
- ▶ *Associated with facial nerve.*

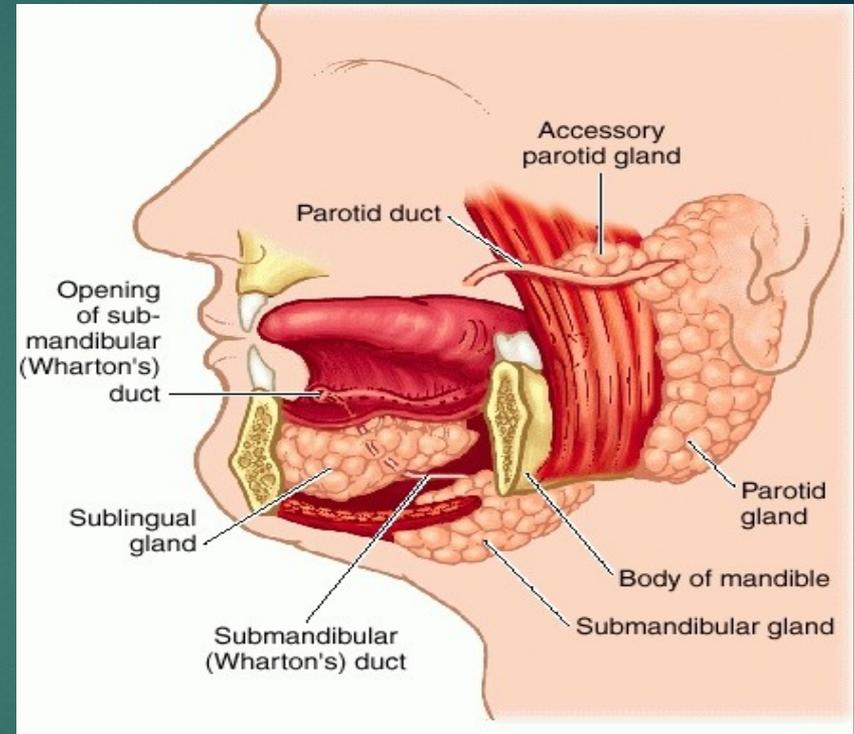


▶ Stenson's duct:

- runs forward across masseter muscle, turns inwards at the anterior border of masseter & opens at a papilla in oral cavity just opposite second maxillary molar crown.

-5cmx3cm

-A small portion of parotid forms **accessory gland** associated with stenson's duct, just anterior to the superficial portion of gland



Nerve supply:

▶ Sensory supply-Greater auricular and auriculotemporal nerve

▶ Parasympathetic supply:

Glossopharyngeal nerve (Preganglionic fibers) synapse in the otic ganglion. Postganglionic fiber enter the gland through the auriculotemporal nerve.

▶ Sympathetic Supply:

Postganglionic fibers from plexus on external carotid artery or middle meningeal arteries.

▶ Vascular supply & Lymphatic drainage :

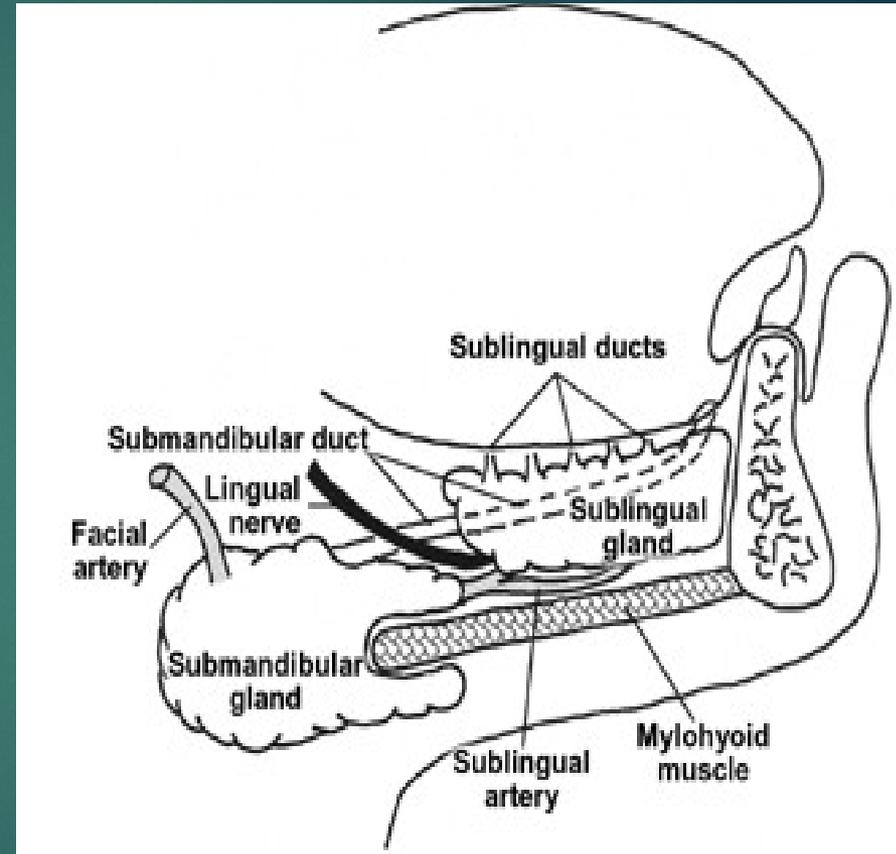
Arterial supply-External carotid artery

Venous drainage-External jugular vein

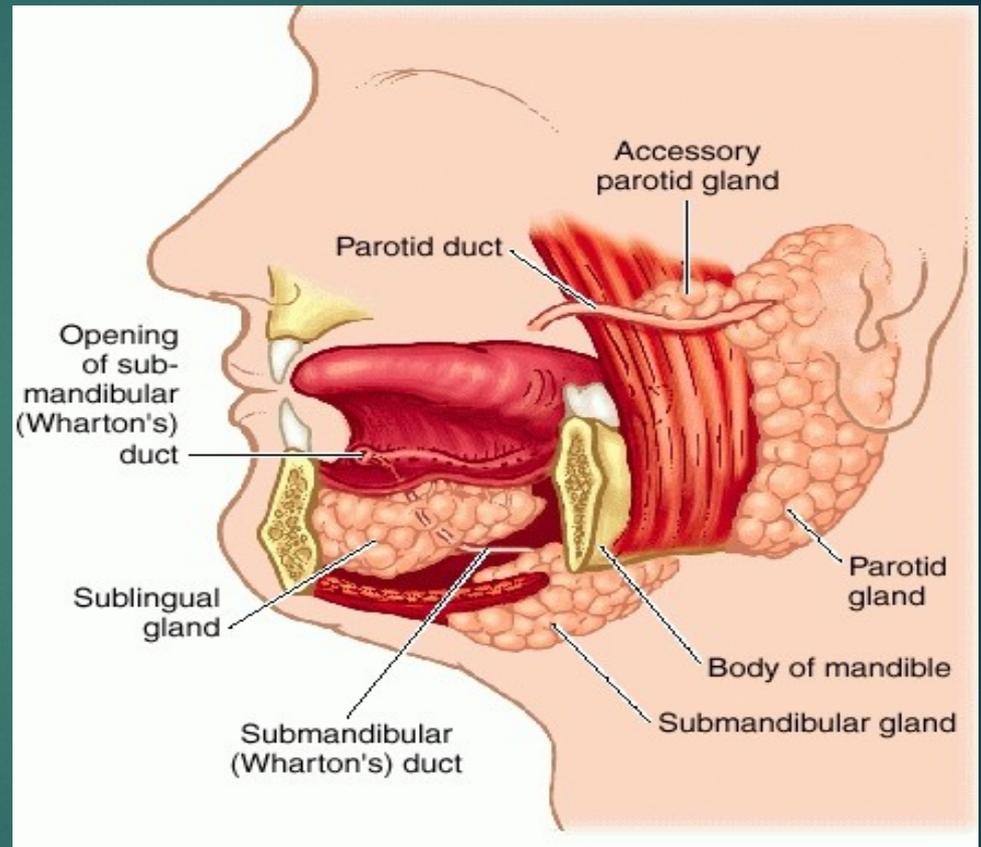
*Lymphatic drainage-Upper deep cervical
lymph nodes.*

Submandibular gland:

- ▶ 10 to 15 gm.
- ▶ 2 to 30% of total saliva.
- ▶ Located at Posterior portion of floor of mouth, medial aspect of mandible & wrapping around posterior border of mylohyoid.



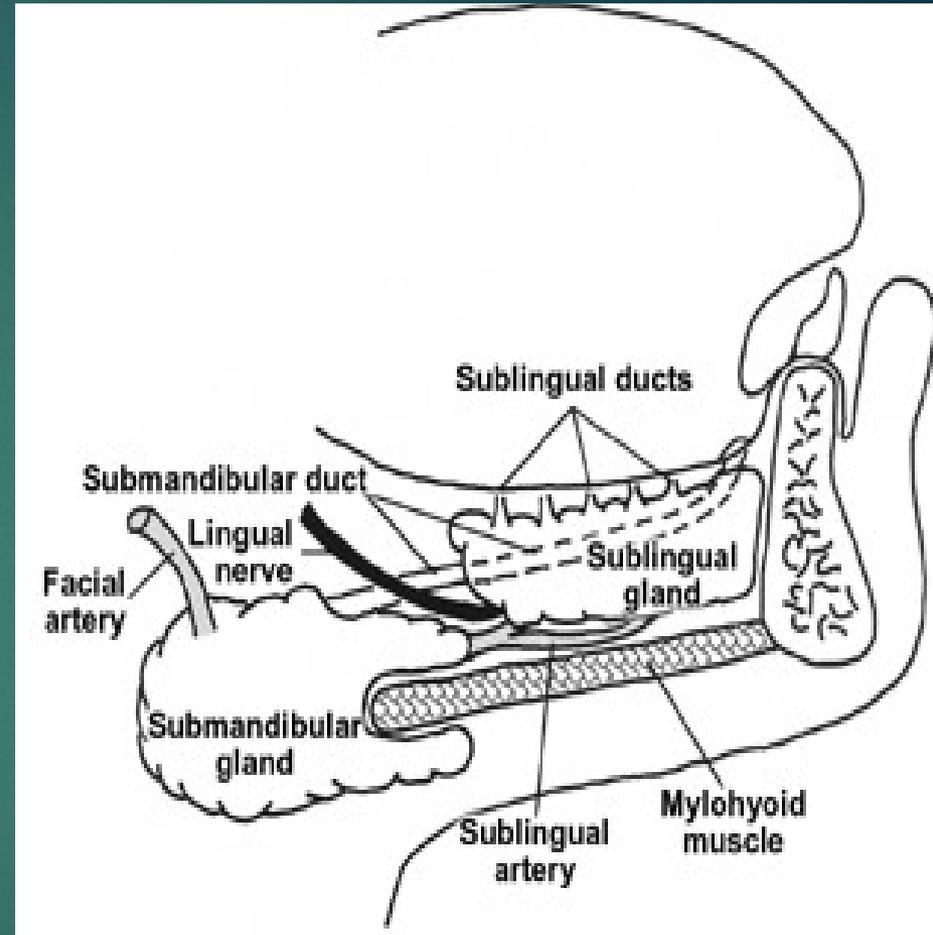
- **Wharton's duct** runs forward and opens into the mouth beneath the tongue, lateral to lingual frenum.



- ▶ Blood supply: Facial and lingual arteries.
- ▶ Lymphatic drainage: Submandibular lymph node & deep cervical lymph nodes.
- ▶ Nerve supply:
Parasympathetic supply: Facial nerve reaching gland through the lingual nerve & submandibular ganglion.
Sympathetic Supply:
Postganglionic fibers from plexus on facial artery

Sublingual gland:

- ▶ *Smallest* major salivary gland
- ▶ *2gm.*
- ▶ *2.5%* of total saliva.
- ▶ Located at anterior part of floor of the mouth, just between mucosa & mylohyoid muscle.
- ▶ Open into oral cavity through series of small ducts (*duct of Rivinus*) opening along sublingual fold and open through large duct- *Bartholin's duct*, that opens with submandibular duct at sublingual caruncle.



- ▶ Blood supply: Sublingual & submental arteries.
- ▶ Lymphatic drainage: Submental lymph nodes
- ▶ Nerve supply:

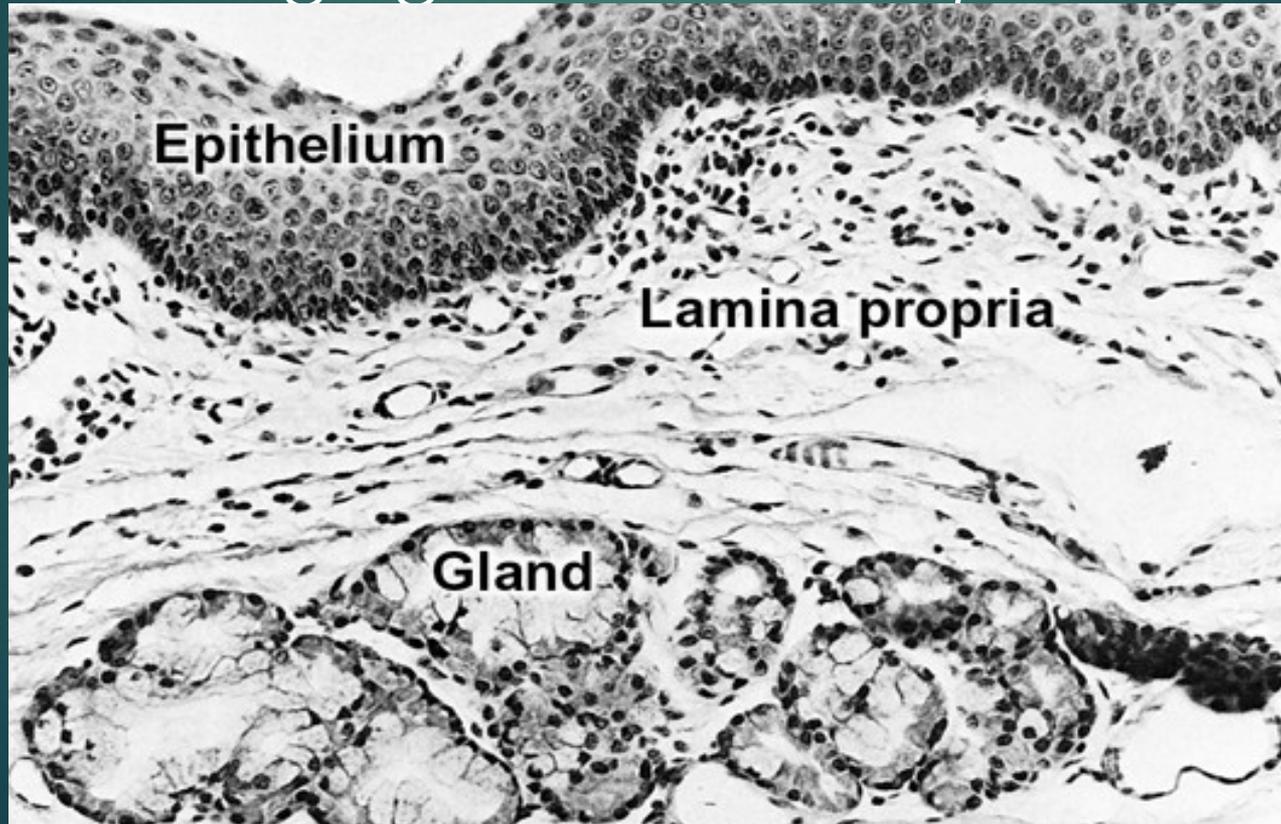
Parasympathetic supply: Facial nerve reaching gland through the lingual nerve & submandibular ganglion.

Sympathetic Supply:

-Postganglionic fibers from plexus on facial artery.

Minor Salivary gland:

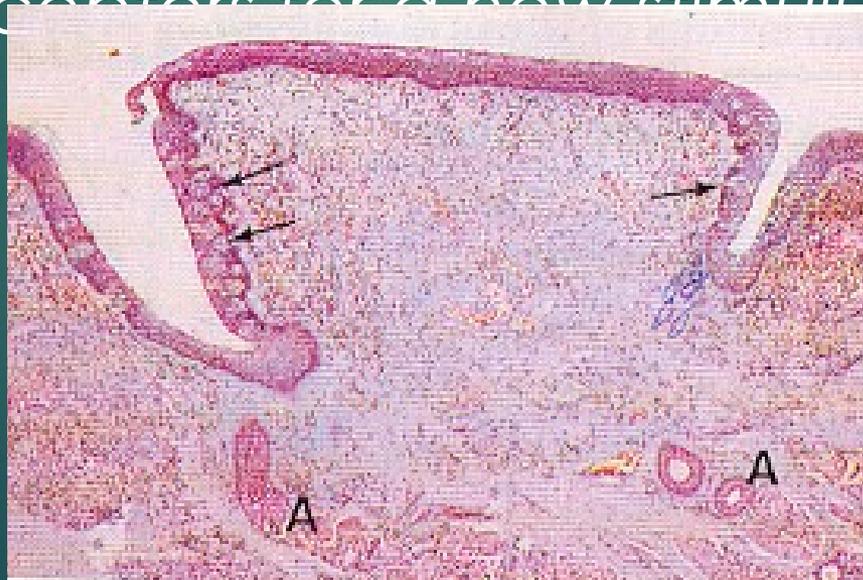
- ▶ No. between *600 and 1000*.
- ▶ Exist as aggregates of secretory tissue present in submucosa throughout most of the oral cavity.
- ▶ Not seen in gingiva & anterior part of hard plate.



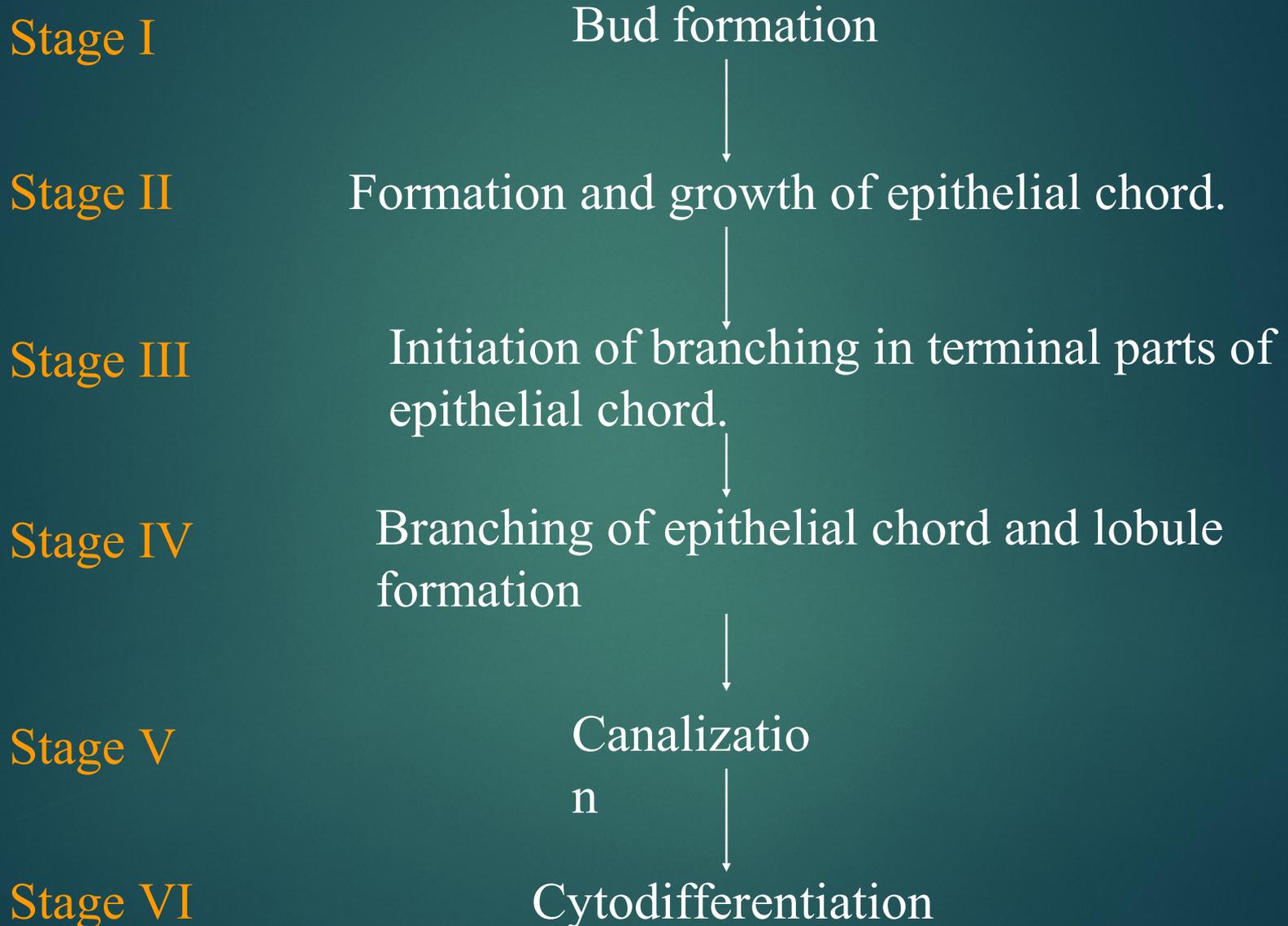
- ▶ *Rich in mucin, antibacterial proteins and secretory immunoglobulin.*
- ▶ *Continuous slow secreting glands, thus have a important role in protecting and moistening oral mucosa, especially when major salivary glands are mostly inactive.*

Von Ebners's Lingual serous gland

- ▶ Located in tongue and open into the troughs surrounding circumvallate papillae on the dorsum of tongue and at the foliate papillae on the side of tongue.
- ▶ Secrete digestive enzymes & proteins that are thought to play role in taste process
- ▶ Fluid of their secretion cleanse the trough & prepare the taste receptors for a new stimulus.



DEVELOPMENT OF SALIVARY GLANDS



Stage I (Bud formation) :

- ▶ *Develops as proliferation of oral epithelium into underlying ectomesenchyme (condensing around bud).*
- ▶ *A thin basal lamina separates the bud from underlying mesenchyme.*
- ▶ *Interaction of the epithelium with underlying condensing mesenchyme associated with salivary glands provide optimum environment for gland formation.*

Stage II (Formation and growth of epithelial chord):

- Proliferation of the epithelial bud into the underlying mesenchyme results in long epithelial cords.
- The mesenchyme (*MES*) around the developing glandular epithelium also proliferates.
- *Basal lamina is believed to play a role in influencing the morphogenesis & differentiation of the salivary glands.*



Stage III (Initiation of branching in terminal parts of epithelial chord):

- ▶ *Epithelial chord proliferates & its end branch into bulbs.*



Stage IV (Branching of epithelial chord and lobule formation):

- Terminal ends branch extensively forming numerous bulbs - **cleft formation**.
- ECM component deposition within clefts apparently serve to stabilise them.
- Connective tissue component below epithelial chord forms capsule & surrounds entire gland.

• Hypothesis:

-Epithelial Mesenchymal Interactions.

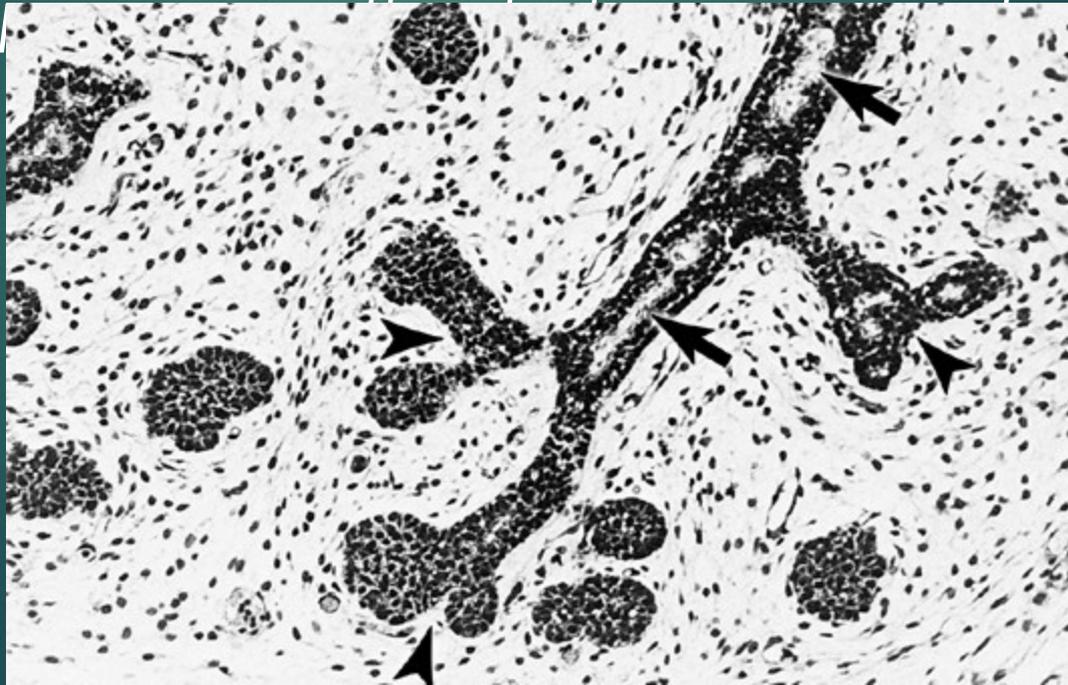
Fibroblast growth factor family & their receptors

Transforming growth factor- β

-Differential contraction of actin filament at the basal and apical ends of the epithelial cells

Stage V (Canalization):

- ▶ Lumen formation takes place at distal ends of chord, then in proximal and at last in central part.
- ▶ Lumen forms within the ducts before they develop within the terminal buds.
- ▶ *Apoptosis* of centrally located cells.
- ▶ *Different rates of proliferation* of outer and inner layers of epithelial chord.
- ▶ *Secretion of fluid* by ductal cells which increases the hydrostatic pressure within the duct.

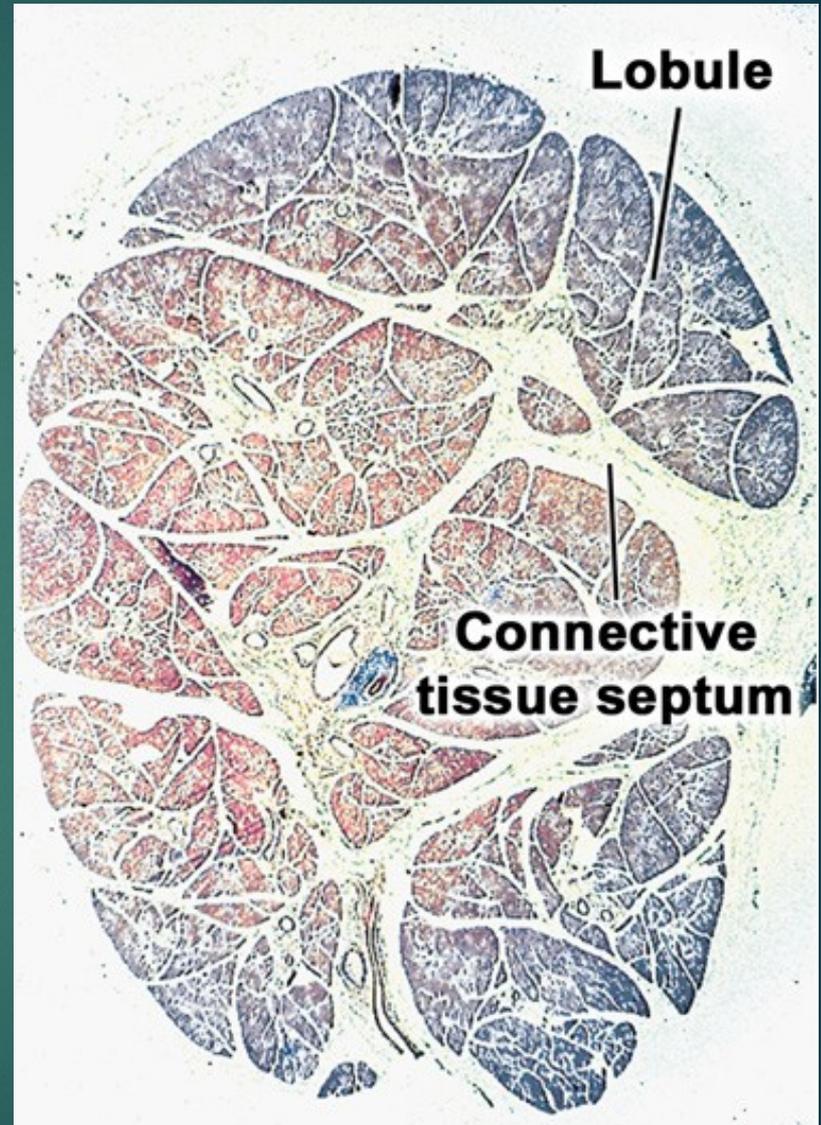


Stage VI (Cytodifferentiation):

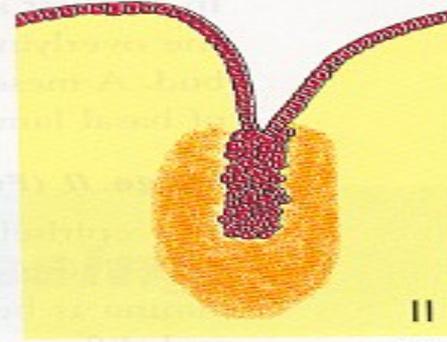
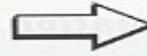
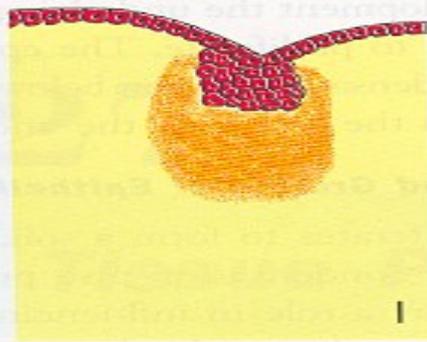
- ▶ *Following lumen formation in the terminal buds, epithelium consists of two layers of cells.*
- ▶ *Inner cells differentiate into mucous or serous cells depending upon type of specific gland.*
- ▶ *Some of the outer cells of epithelium differentiate into myoepithelial cells that are present around secretory end piece and intercalated ducts.*
- ▶ *Portion of epithelial bud close to the oral cavity forms main excretory duct, distal portion forms secretory end piece.*

▶ As epithelial parenchyma increase in size, connective tissue component around them diminishes and remains as a thin layer.

▶ Thicker partition of connective tissue (septa), continuous with the capsule and within which run nerves & blood vessels supplying gland,



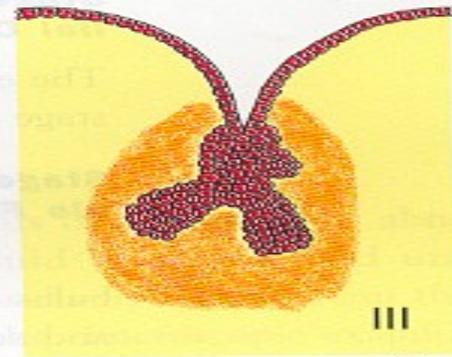
- ▶ Parotid: 4-6th week of I.U. life.
- ▶ Submandibular :6th week of I.U. life.
- ▶ Sublingual and minor salivary gland : 8th week of I.U.life.
- ▶ Maturity of secretory end piece: During last 2 months of gestation.
- ▶ Secretory component of Gland continues to grow postnatally while as ductal, connective tissue component and vascular component decreases- up to two years of age.



II

Stages in the development of Salivary glands

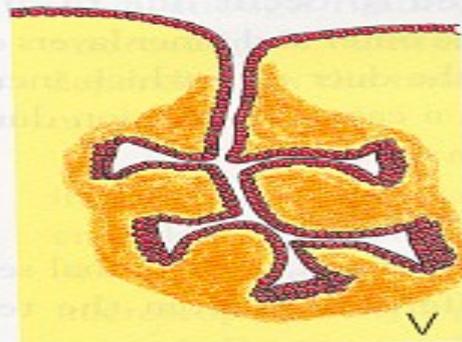
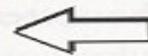
- I. Bud formation
- II. Cord formation
- III. Branching of cords
- IV. Lobule formation
- V. Canalization of cords
- VI. Cytodifferentiation



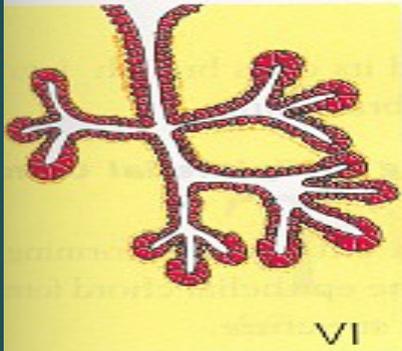
III



IV



V

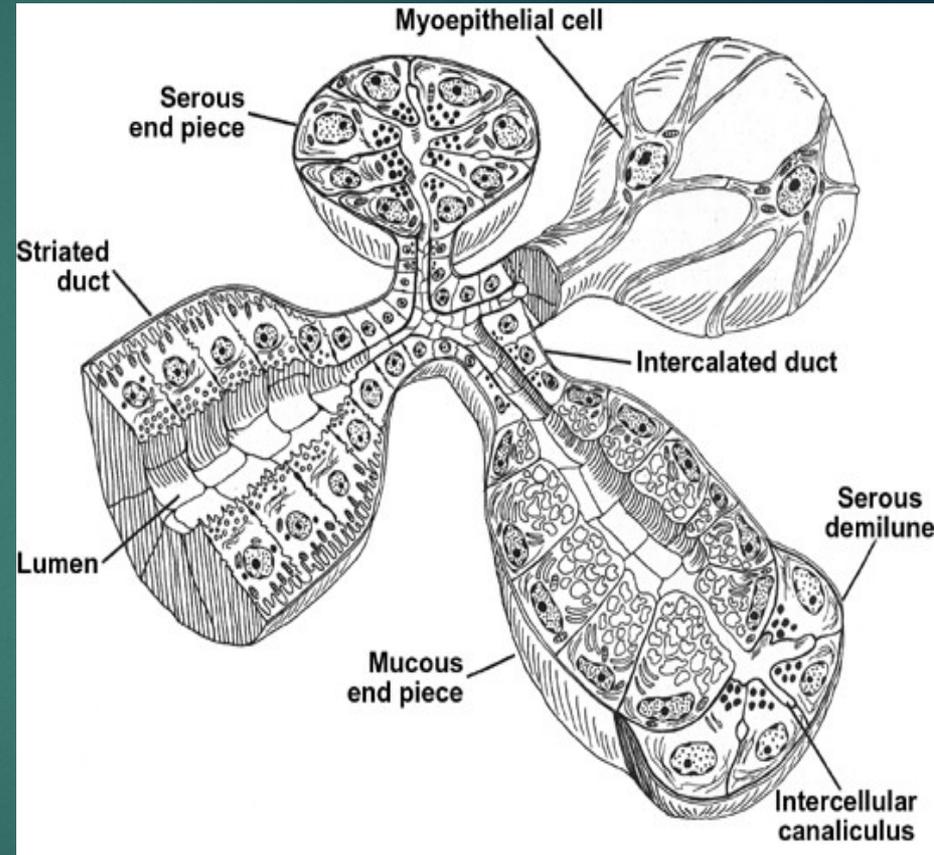


VI

DEVELOPMENT OF SALIVARY GLANDS

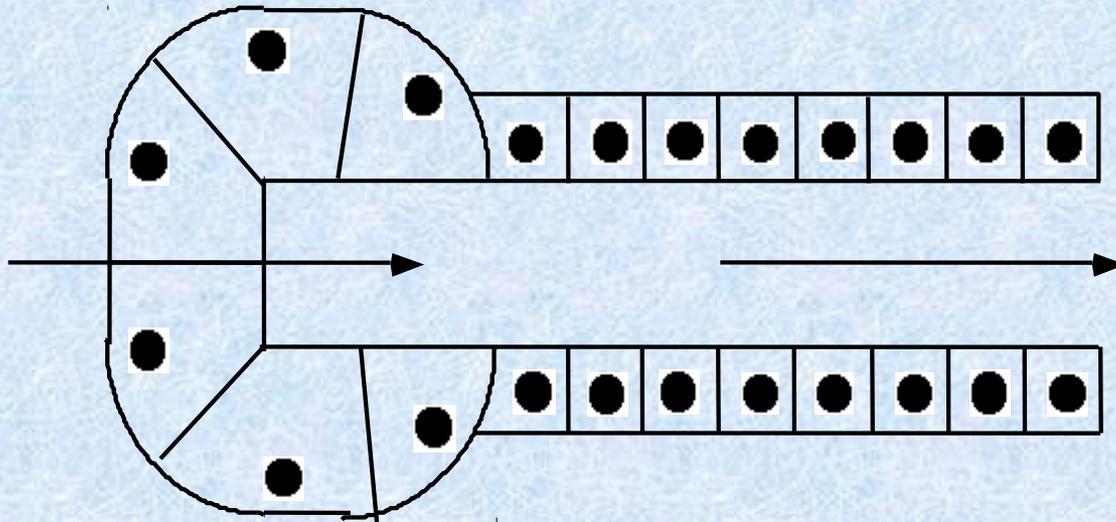
STRUCTURE OF SALIVARY GLANDS

- ▶ Comprises of
 - a series of secretory end piece or *acini*.
 - connected to the oral cavity by a *system of ducts*.



Secretory end piece or accini:

- Consists of secretory cells, which are arranged in a **roughly spherical configuration** around a central lumen or cavity.
- Show a great diversity in size, shape, and cell number.

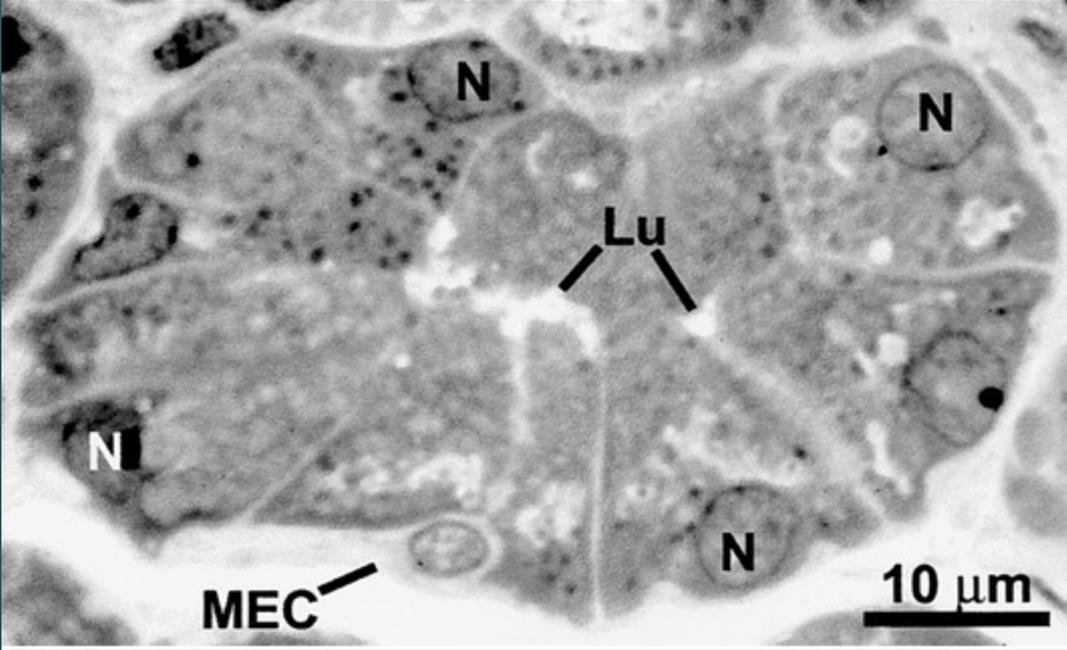


- 2 types of cells
 - Serous cells
 - Mucous cells

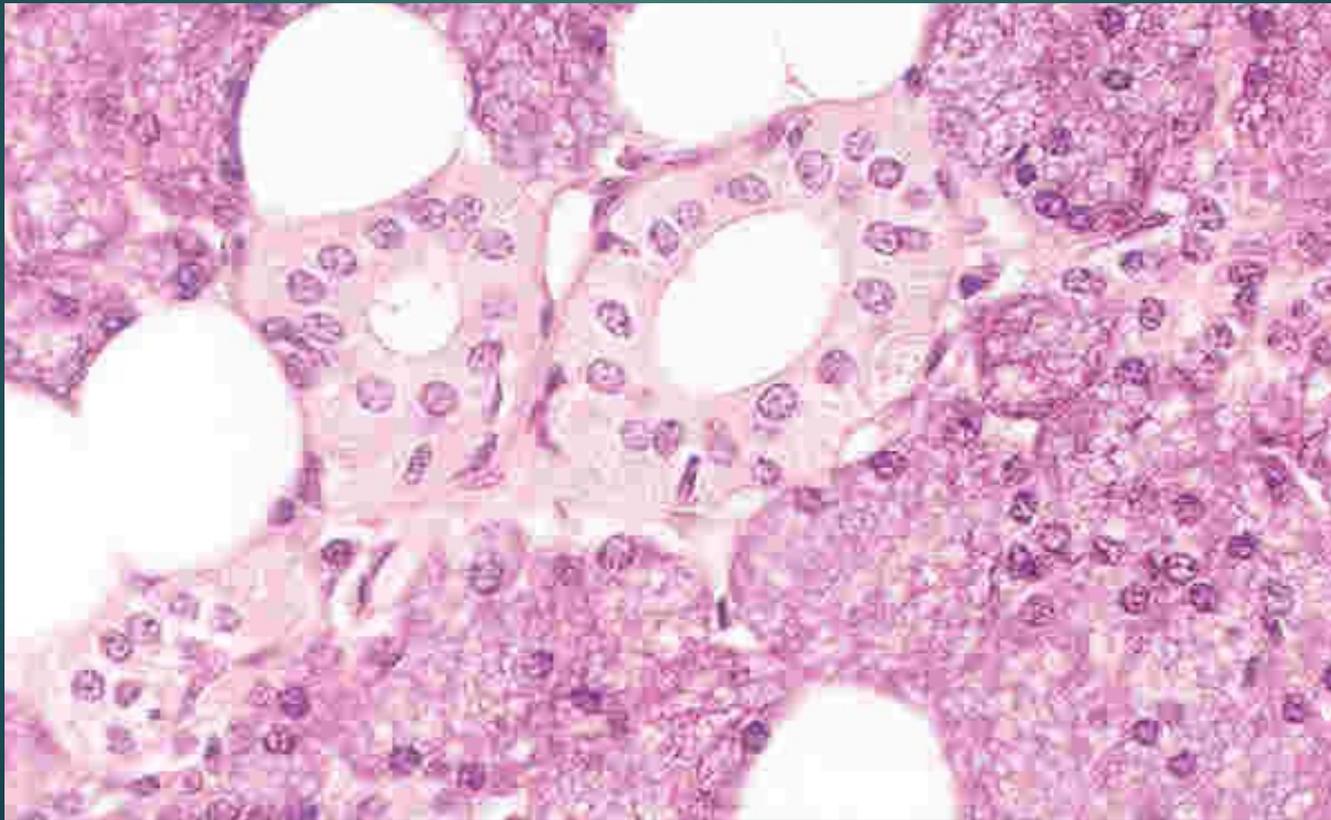
Serous Cells:

- ▶ *Parotid & submandibular gland.*
- ▶ *Serous cells are also present in demilune formations at the blind ends of mucous secretory tubules (submandibular and sublingual glands).*
- ▶ *Secretions of serous cells are proteinaceous -usually enzymatic, antimicrobial, calcium-binding.*

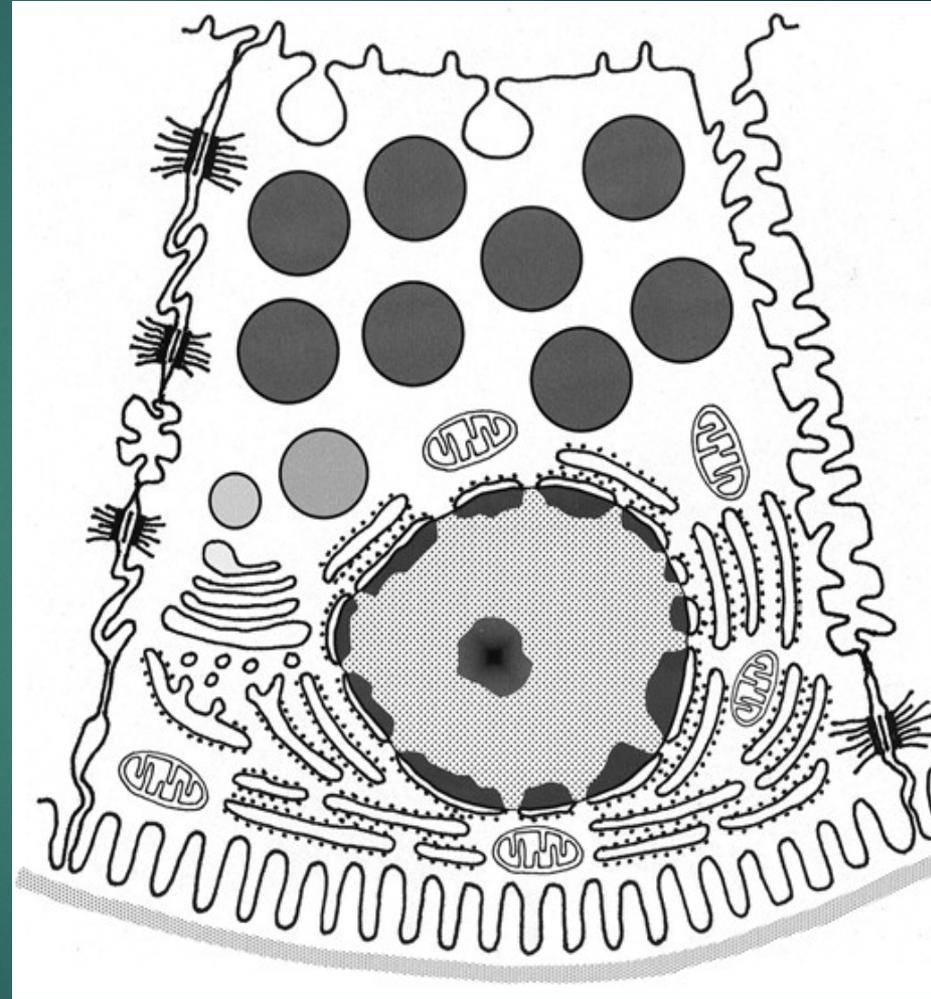
▶ Secretory end piece consisting of serous cells are typically spherical and consist of 8 to 12 cells surrounding a central lumen.



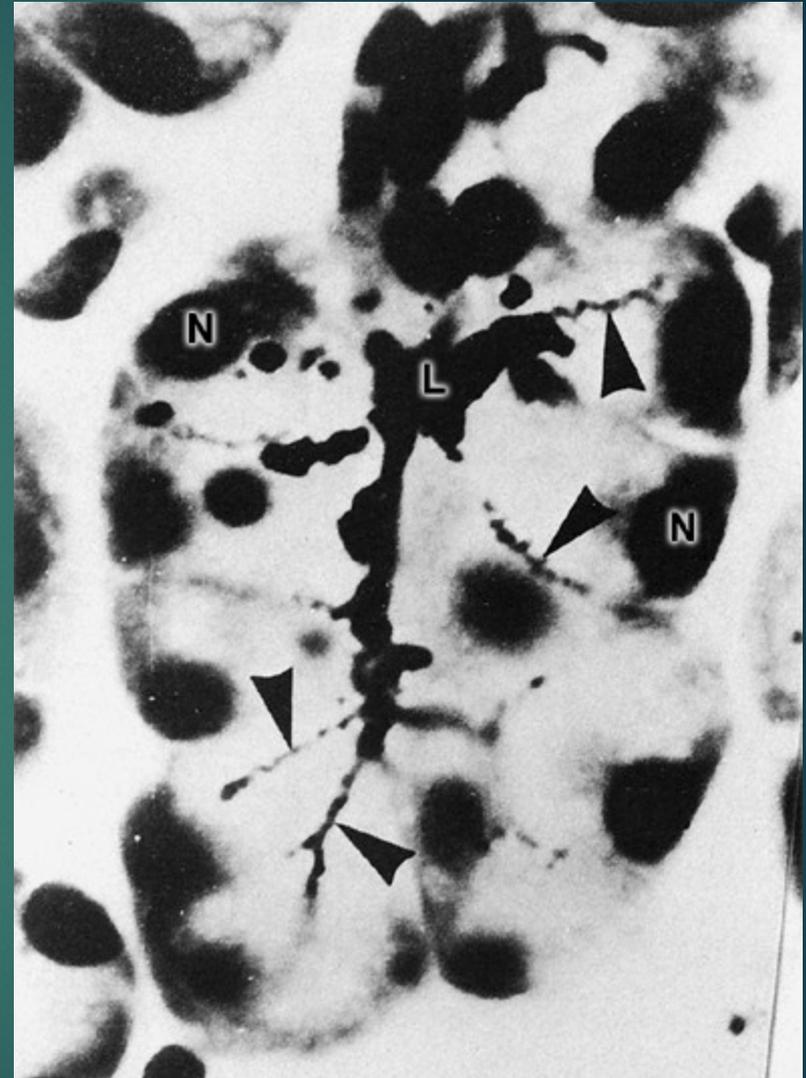
- ▶ *Pyramidal in shape, with broad base adjacent to connective tissue stroma & apex situated towards the central lumen.*
- ▶ *Nucleus is spherical & situated at the basal third of the cell. Sometimes binucleated.*



- ▶ Cytoplasm stains intensely with H and E.
- ▶ Apical cytoplasm is filled with secretory granules(macromolecular component of saliva).
- ▶ Basal cytoplasm contains RER, which converge towards the golgi complex located just apical or lateral to nucleus.
- ▶ Also contain cytoskeleton components,



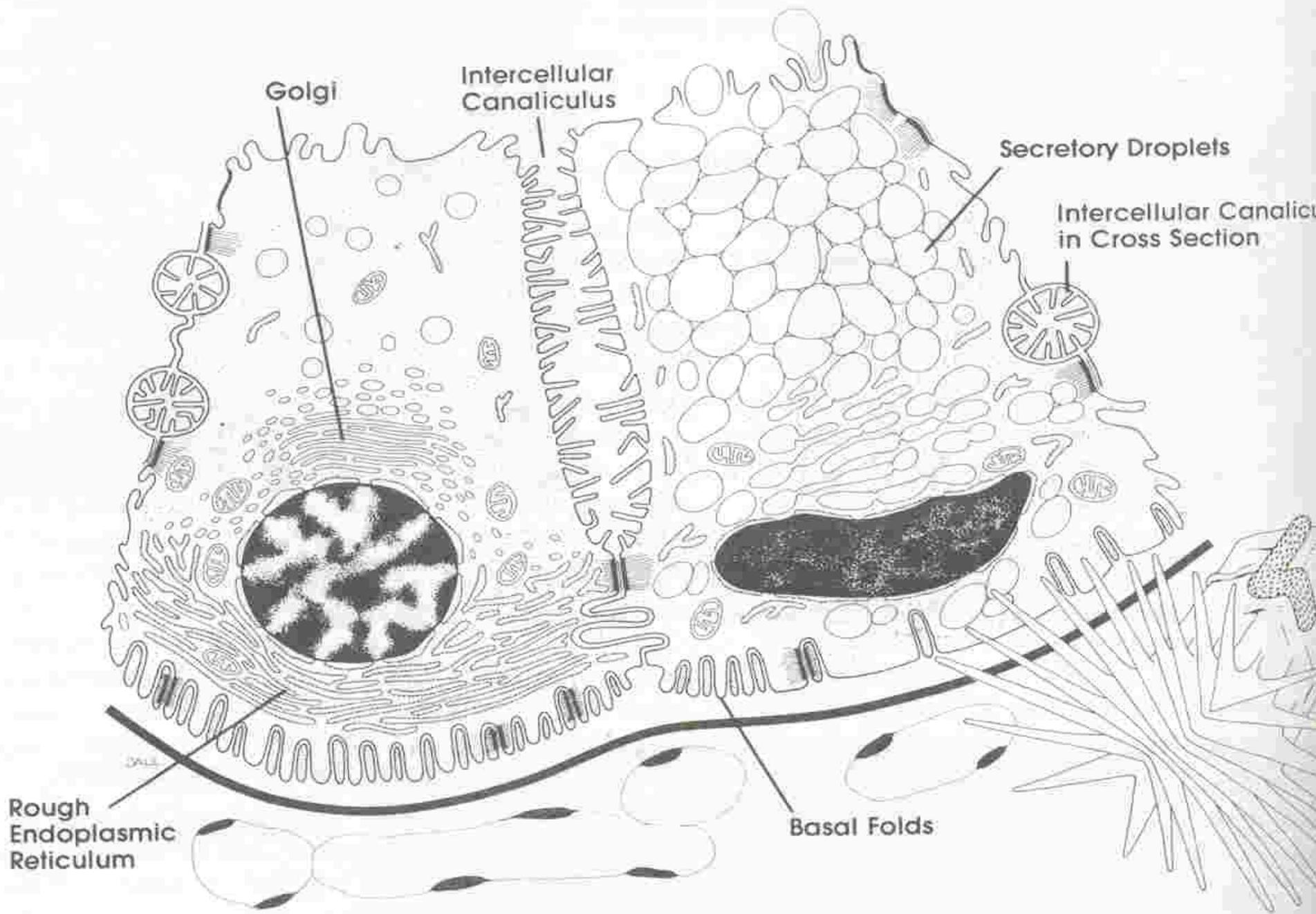
- The lumen of serous end piece has small extensions in the form of *intercellular canaliculi* (found between adjacent serous cells).



Lumen and intercellular canaliculi in a serous end piece

Plasma membrane exhibits several specializations:

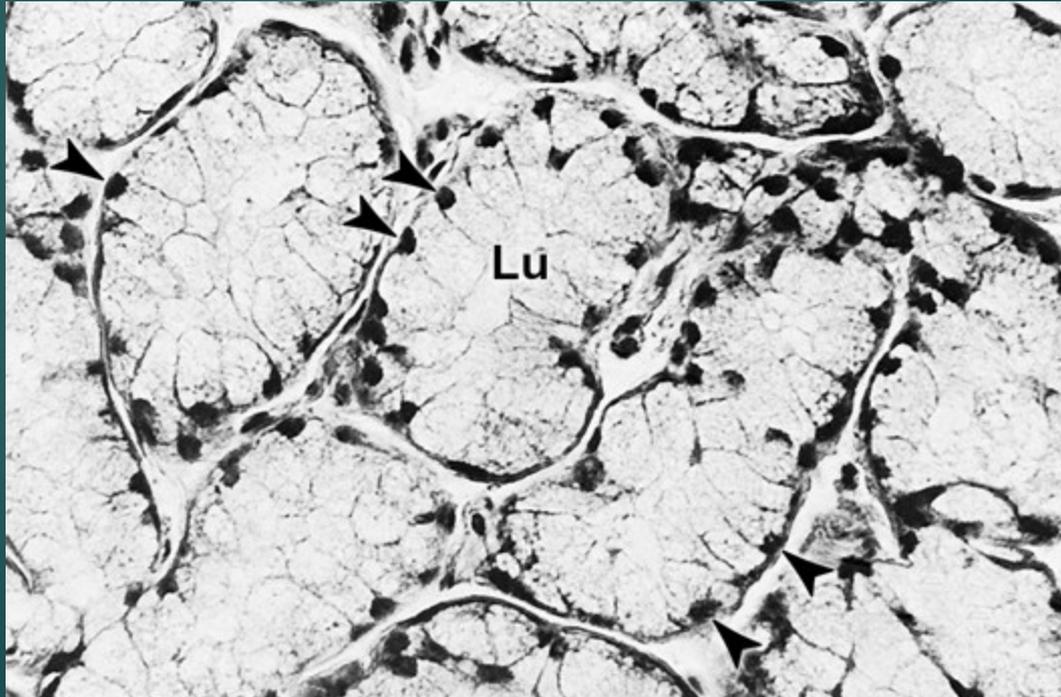
- ▶ *The surface of the seromucous cell lining both the central lumen & canaliculi possess a delicate **microvilli** that extend into luminal and canalicular spaces.*
- ▶ *Space between basement membrane and basal plasma membrane may be increased by **complex foldings** (0.5 microns) of the basal plasma membrane.*
- ▶ *Canaliculus terminates in the form of a classic junctional complex consisting of a tight junction (zona occludens), an adherent junction & a desmosome.*
- ▶ *Cells are supported by a basement membrane*



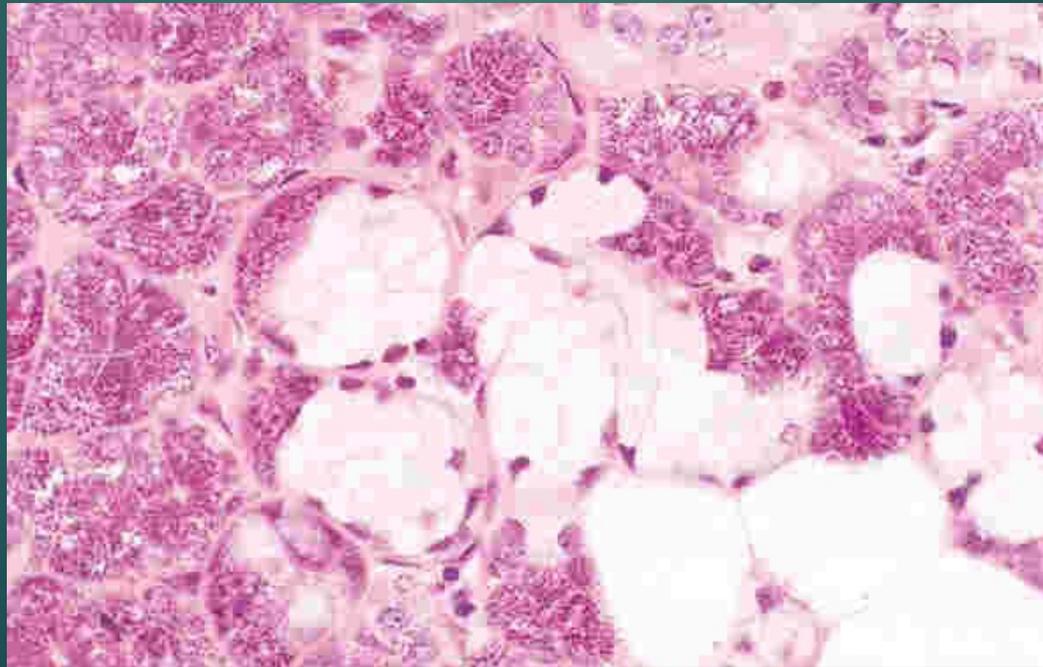
Mucous cells:

- ▶ *Predominant secretory cell type of the sublingual gland & most of minor salivary glands.*
- ▶ *Also occur in submandibular gland.*
- ▶ *Secretion consists of large amount of mucins -lubrication, effective barrier, aggregation of microorganisms.*

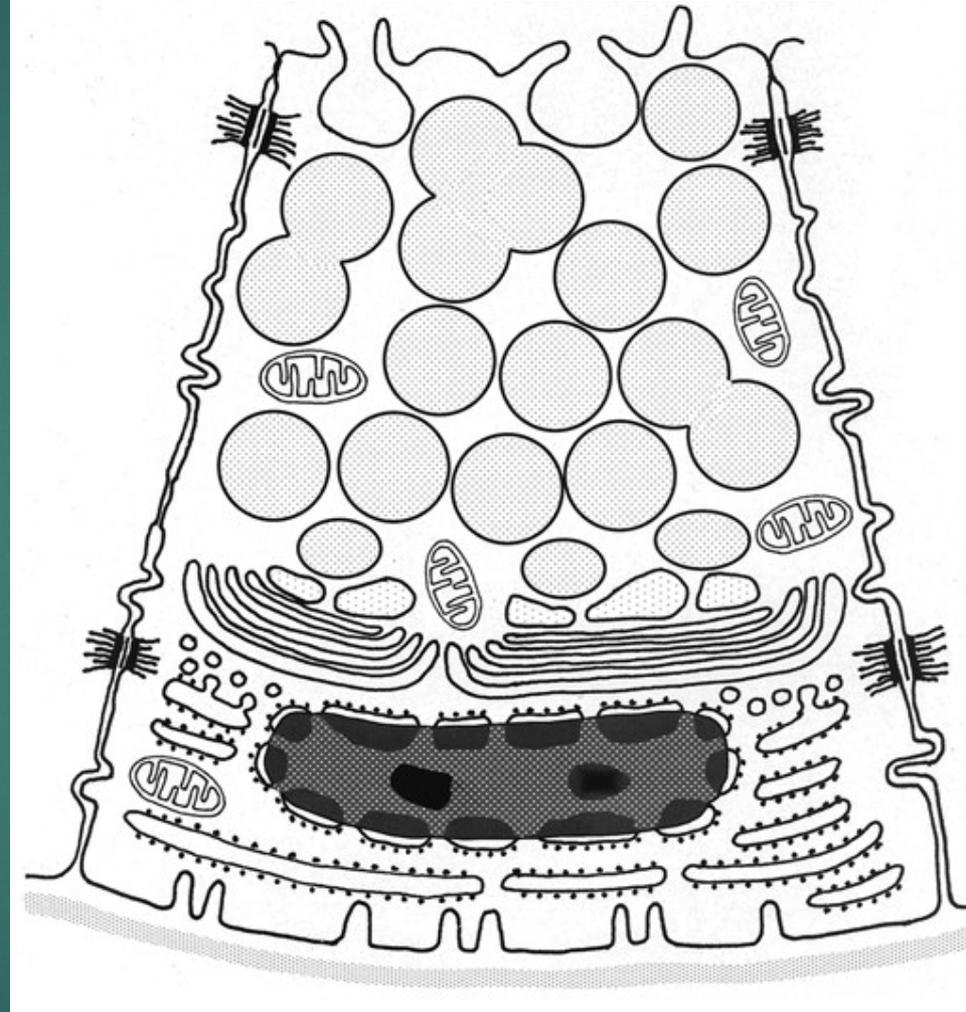
- ▶ *Secretory component of mucous cell accini consists of round or tubular configuration.*
- ▶ *Larger lumen.*
- ▶ *Larger than serous cells.*
- ▶ *Pyramidal in shape.*
- ▶ *Broader luminal surface.*



- ▶ *Flattened nucleus situated towards its base*
- ▶ *Apical cytoplasm is filled with mucous secretory droplets.*
- ▶ *Stain poorly in H & E.*
- ▶ *PAS or Alcian blue +ve*

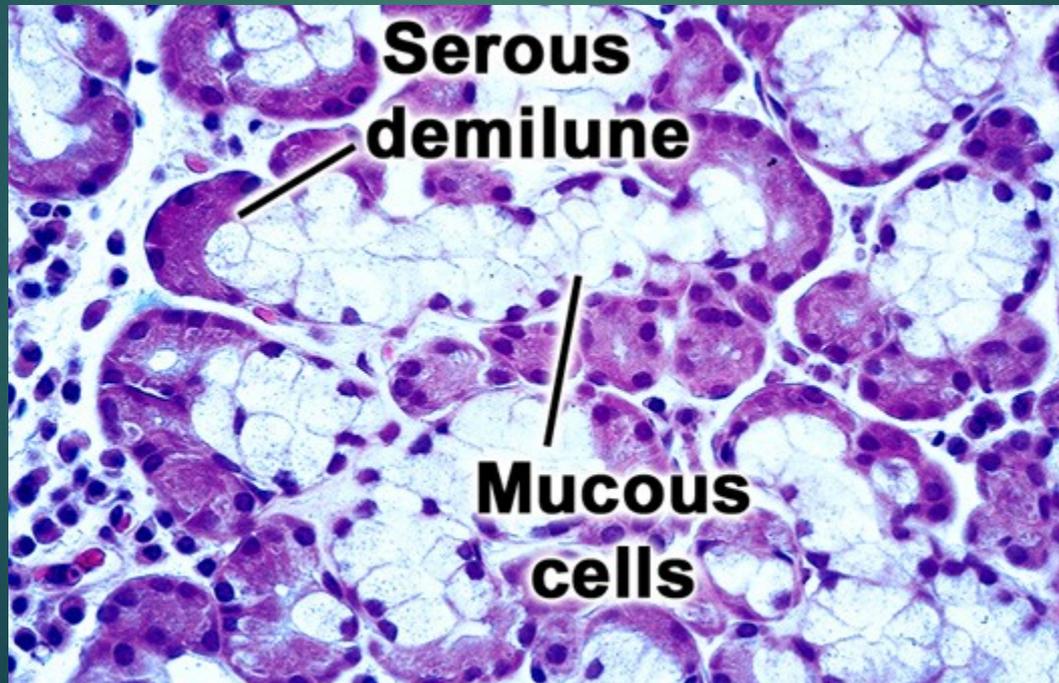


- ▶ Mucous droplets are larger and more irregular in shape - *Electron lucent droplets*
- ▶ More prominent Golgi complexes.
- ▶ Also contain cytoskeleton components, RER, mitochondria, lysosomes and peroxisomes but less prominent.
- ▶ Like serous cells, mucous cells are joined by intercellular junctions.
- ▶ Lack intercellular canaliculi.



Demilunes Of Gianuzzi

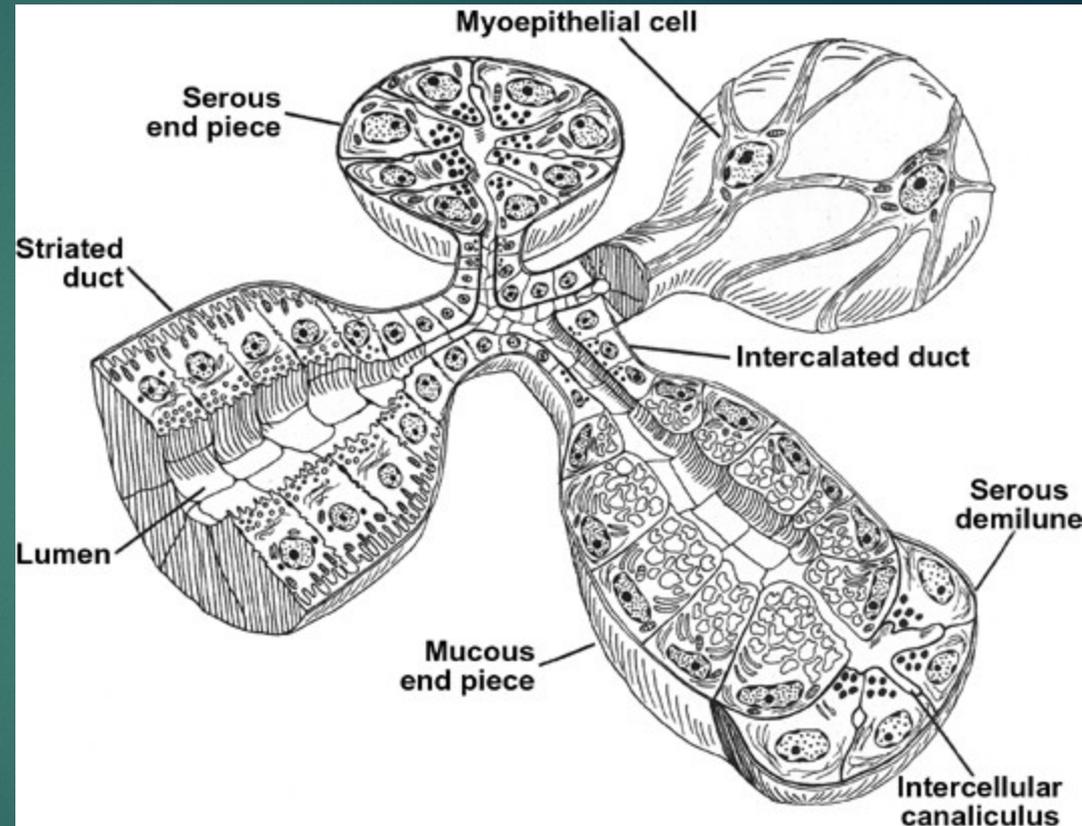
- ▶ Mucous cells accini may be capped at the blind end by crescents of several serous cells.
- ▶ Their secretion reach the lumen of the end piece through intercellular canaluculi between mucous cells at the end of the tubule.



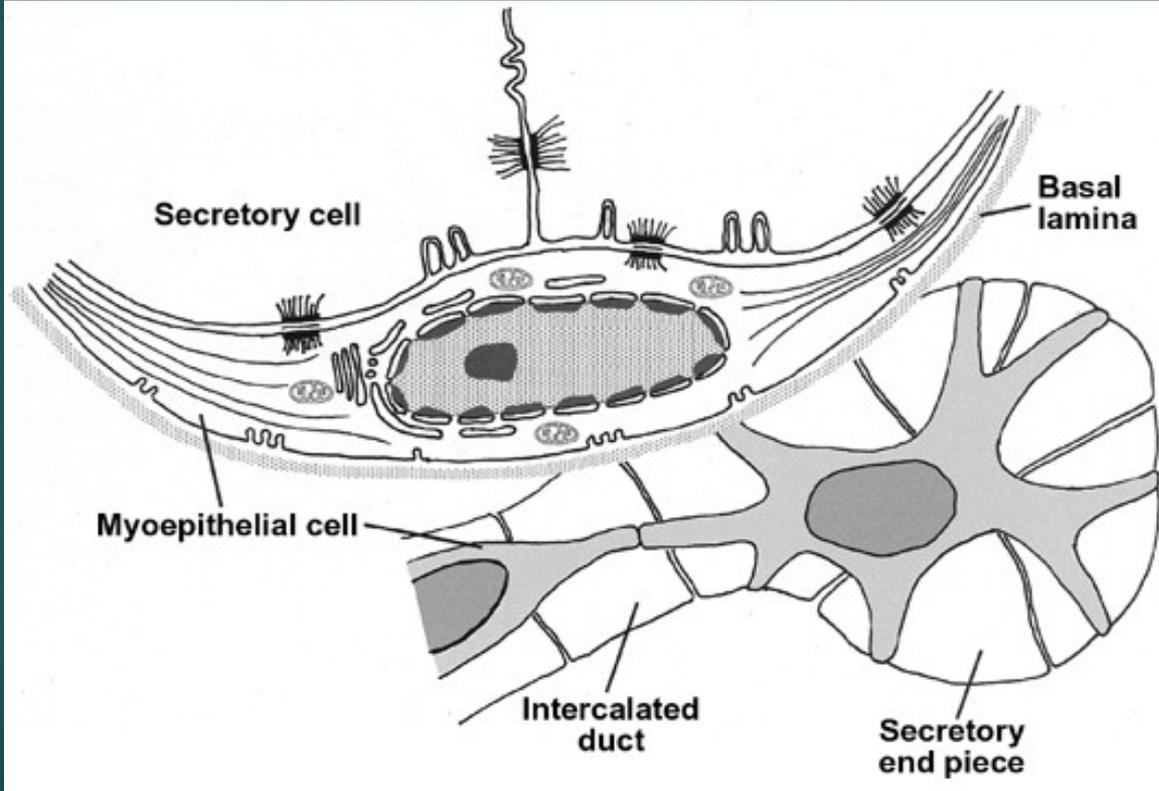
Myoepithelial Cells

(Basket cells):

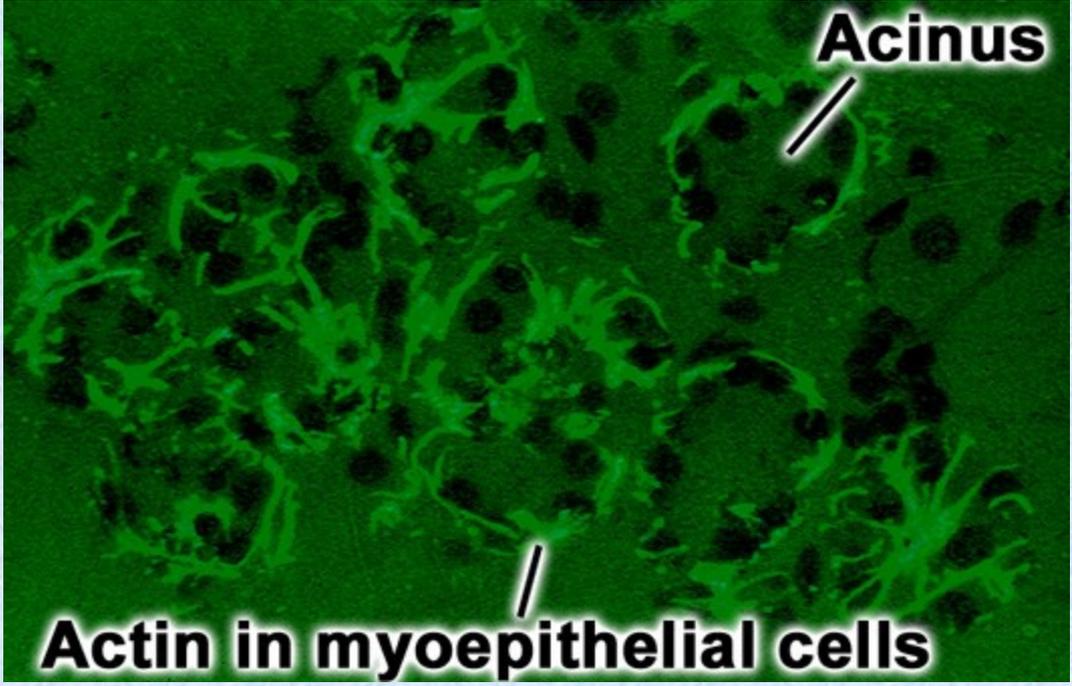
- ▶ Contractile cells located around the terminal secretory units and the first portion of the duct system, **intercalated duct**.
- ▶ Located between basal lamina and secretory or duct cells and are joined by desmosomes.
- ▶ Similar to smooth muscle cells but are derived from



- ▶ They are stellate or spider like, with a flattened nucleus surrounded by a small amount of perinuclear cytoplasm, & long branching process that embrace the secretory duct cells.



▶ *The processes are filled with filaments of actin and soluble myosin.*



Salivary gland immunostained to demonstrate actin in the contractile myoepithelial cells.

- ▶ Cell membrane has numerous caveolae - *initiation of contraction*.
- ▶ Cellular organelle are located in perinuclear cytoplasm.
- ▶ Only their nuclei is visible in ordinary H & E section.
- ▶ Myoepithelial cells related to intercalated ducts are more spindle shaped and have fewer processes.

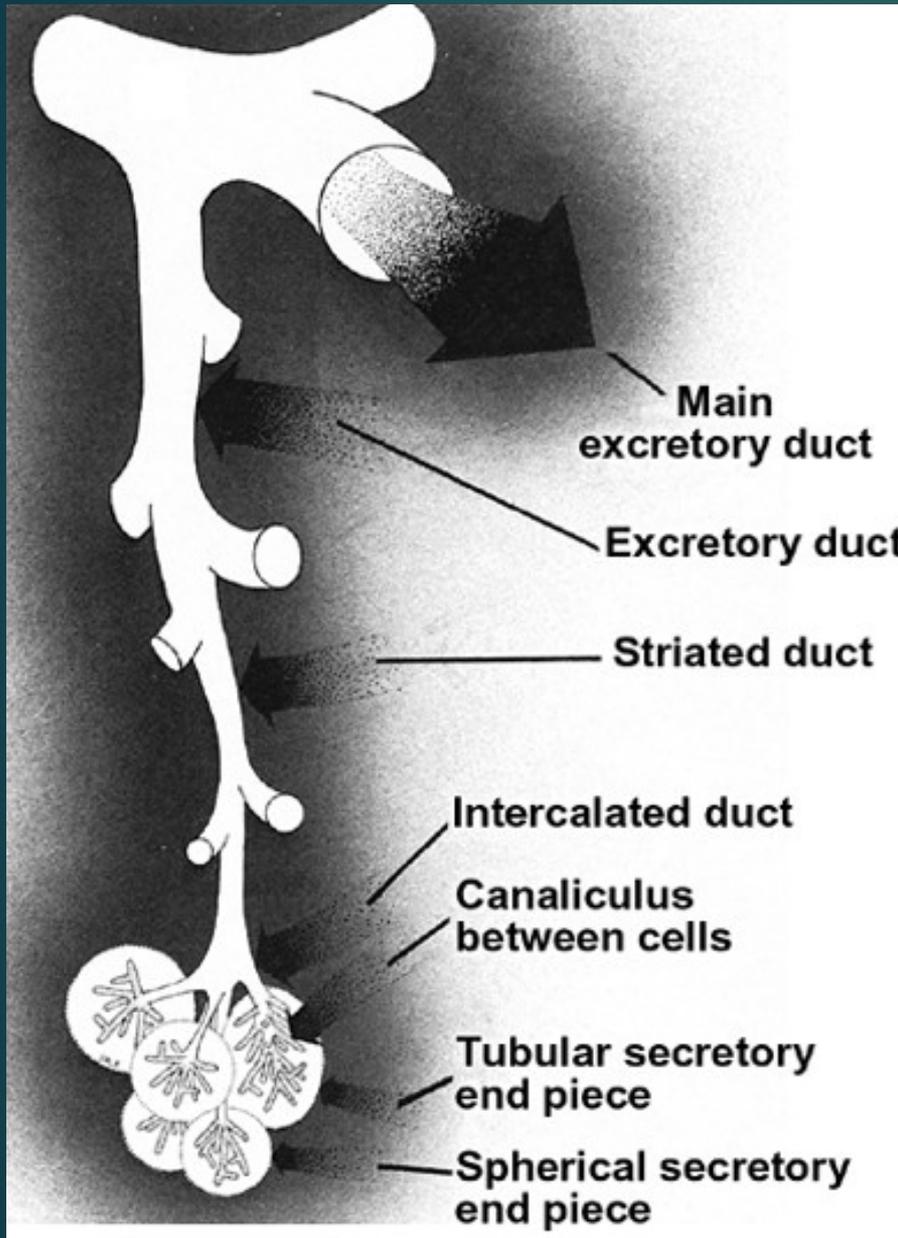
Functions:

- ▶ *Expulsion of saliva from secretory end piece to ductal system.*
- ▶ *Contraction of myoepithelial cells of intercalated ducts may shorten or widen the ducts , helping in maintaining their patency.*
- ▶ *Maintaining cell polarity and structural integrity of secretory end piece.*
- ▶ *Produce proteins that have **tumour suppressor activity**, such as proteinase inhibitors (e.g., tissue inhibitors of metalloproteinases) and antiangiogenesis factors and that cell may act as effective invasive barrier against epithelial neoplasms.*

DUCTS:

- ▶ 3 classes of ducts
 - *Intercalated*
 - *Striated*
 - *Terminal*

- ▶ *Terminal secretory units* opens into a small duct called the *intercalated duct*. These ducts join to form larger *striated ducts* which finally empty into a larger *excretory duct*.



Ductal system of a salivary gland:

Main excretory duct opens into the oral cavity. Excretory ducts are mostly located in the interlobular connective tissue.

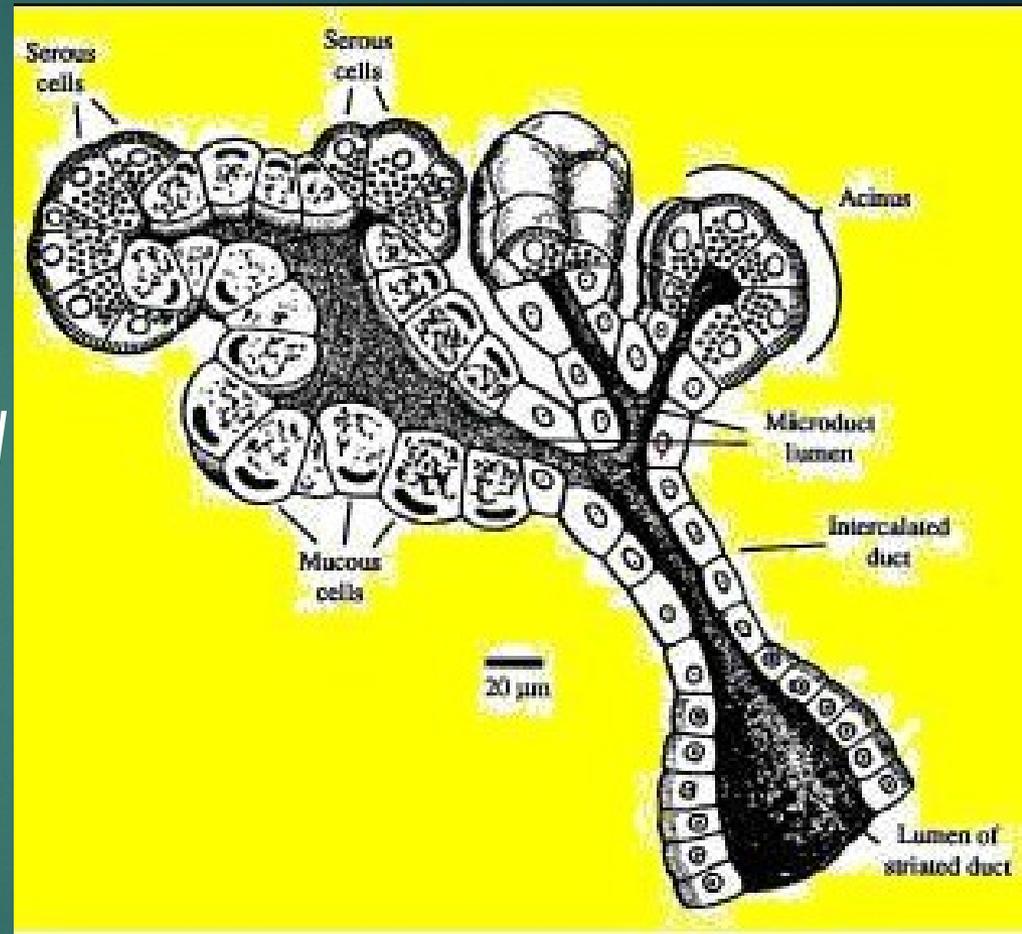
Striated ducts are the main intralobular ductal component.

Intercalated ducts vary in length and connect the secretory end pieces with the striated ducts.

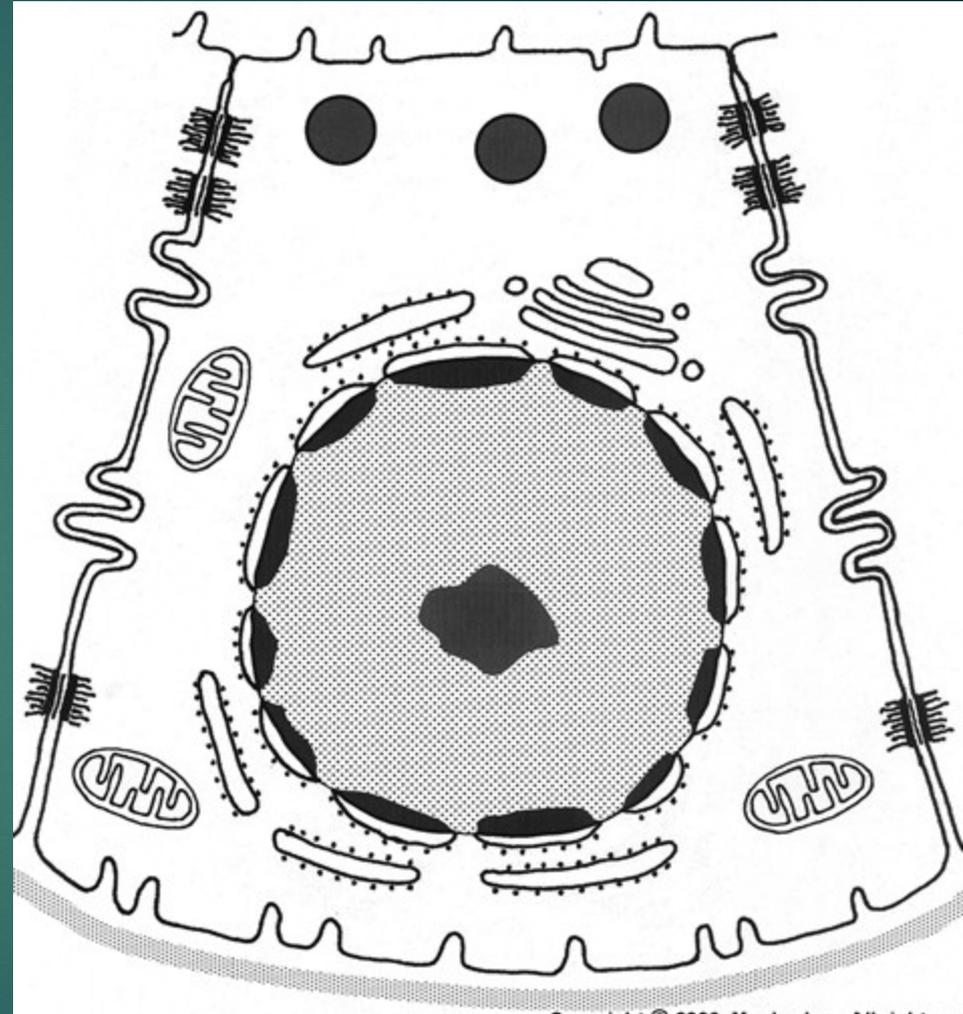
Intercellular canaliculi are extensions of the lumen of the end piece between adjacent secretory cells that serve to increase the luminal surface area available for secretion.

Intercalated Ducts:

- ▶ Small ducts into which secretory end piece empties.
- ▶ Lined by a single layer of low cuboidal cells and myoepithelial bodies and their processes.
- ▶ Overall diameter is less than secretory end piece but their lumen is larger than secretory end piece.



- Centrally placed nucleus
- Little cytoplasm – RER and Golgi apparatus.
- A few secretory granules may be found in the apical cytoplasm, especially cells located near end pieces.
- Few microvilli projecting into lumen.
- Joined to adjacent cells by apical junctional complexes and scattered desmosomes & gap junctions and have folded processes that interdigitate with similar processes of adjacent cells.



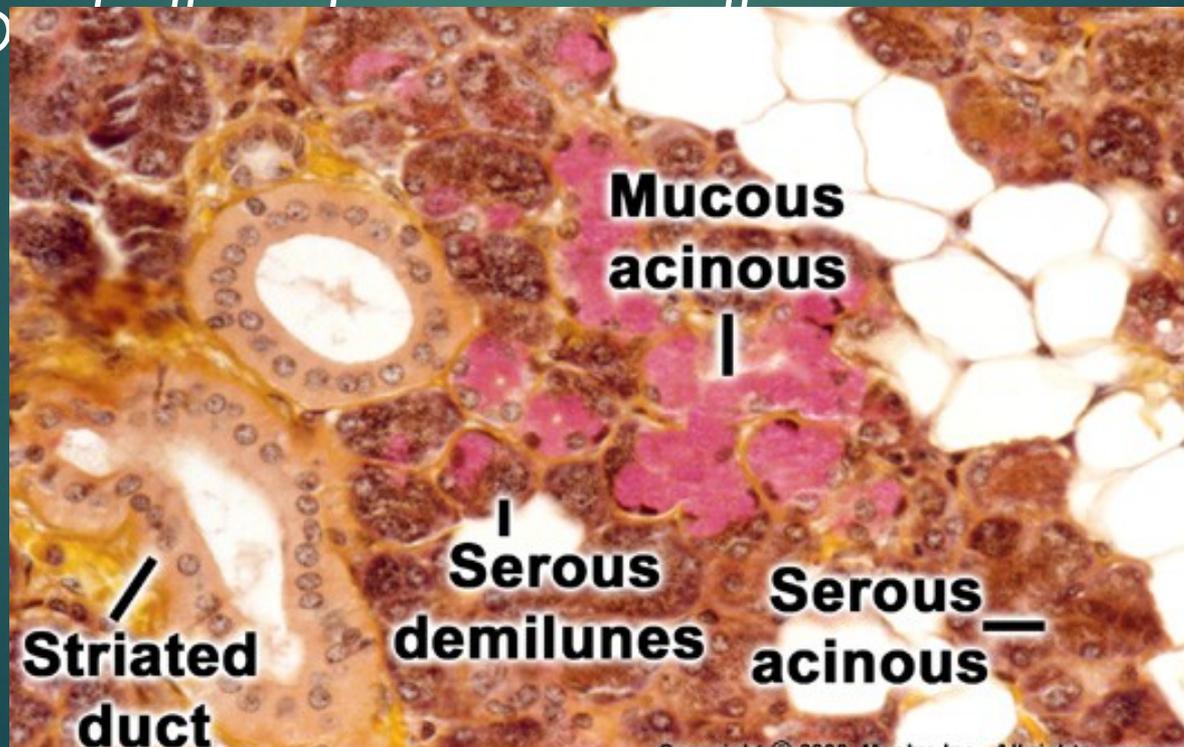
- ▶ *Long intercalated duct : Parotid*
- ▶ *Shorter : Submandibular*
- ▶ *Poorly developed in : sublingual*

Function:

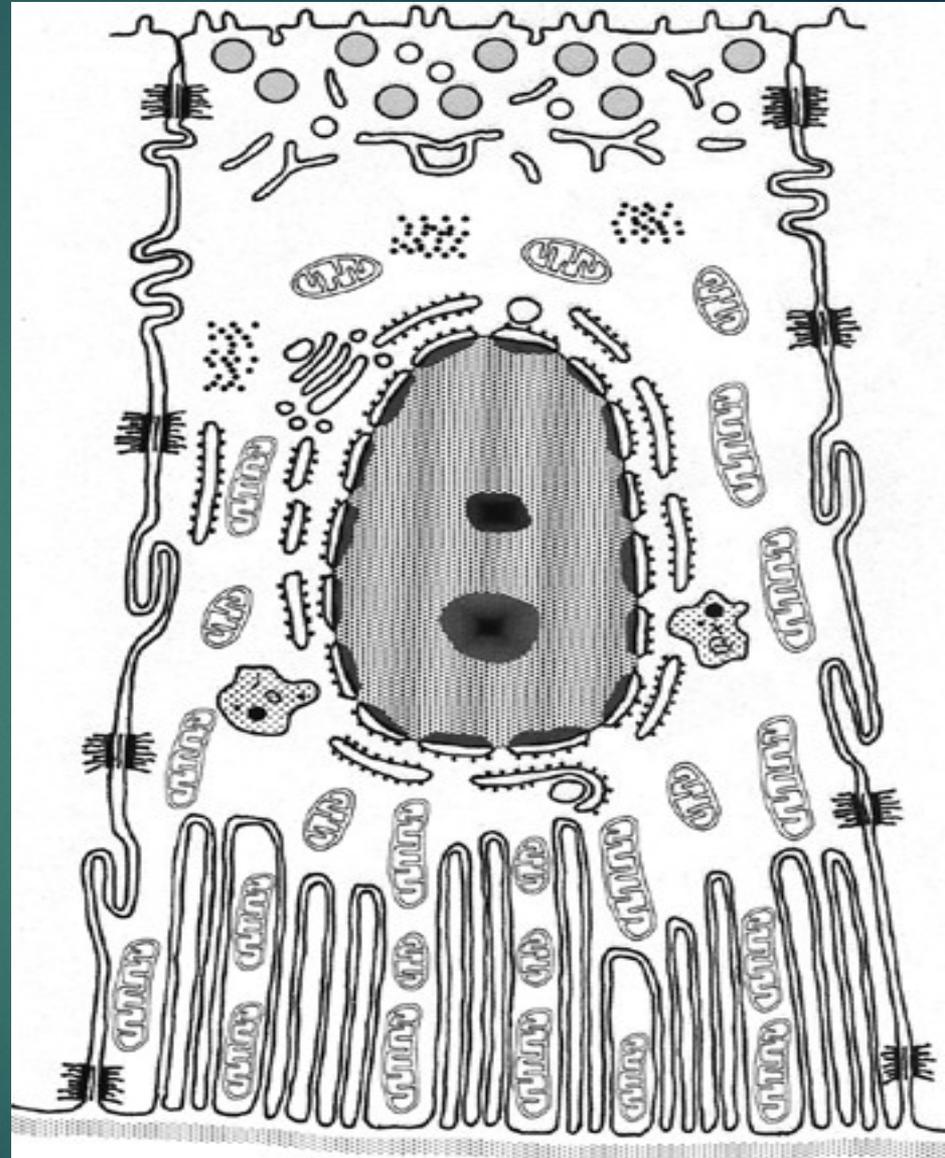
- Channel for salivary flow
- Contributes to the salivary secretion – lysozymes & lactoferrin.
- Reservoir of undifferentiated cells that may undergo proliferation & differentiation to replace damaged or dying cells in the end pieces and striated ducts.

Striated ducts:

- ▶ Larger duct into which the intercalated ducts empty.
- ▶ Main ductal component in intralobular portion of gland.
- ▶ Lined by simple cuboidal epithelium.



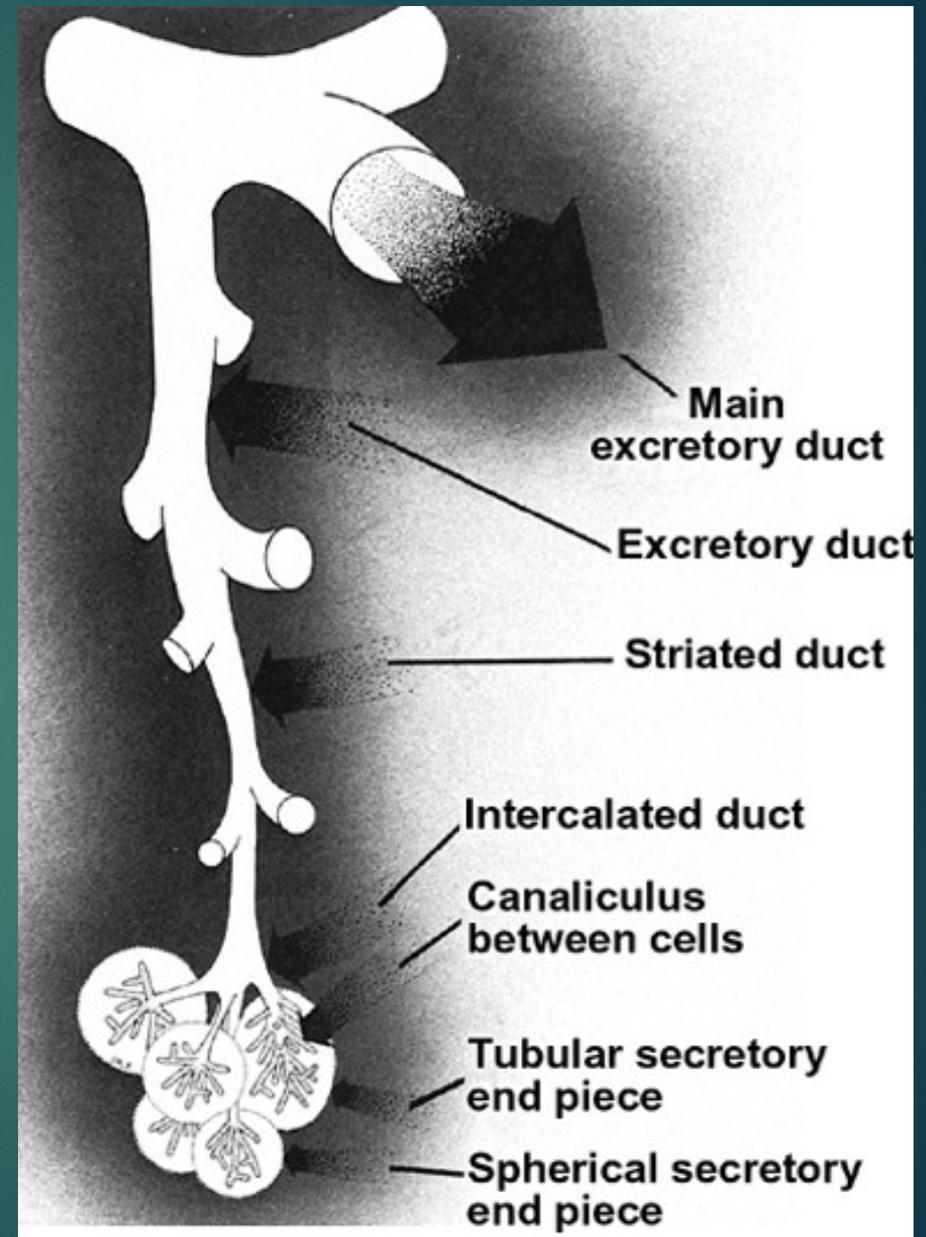
- ▶ Centrally placed spherical nucleus.
- ▶ Pale acidophilic cytoplasm
- ▶ **Basal striation** perpendicular to the base of the cells
-Mitochondria are lying in cytoplasmic partitions produced by infoldings of the basal plasma membrane.
- ▶ RER and Golgi apparatus and few secretory granules and deposits of glycogen in



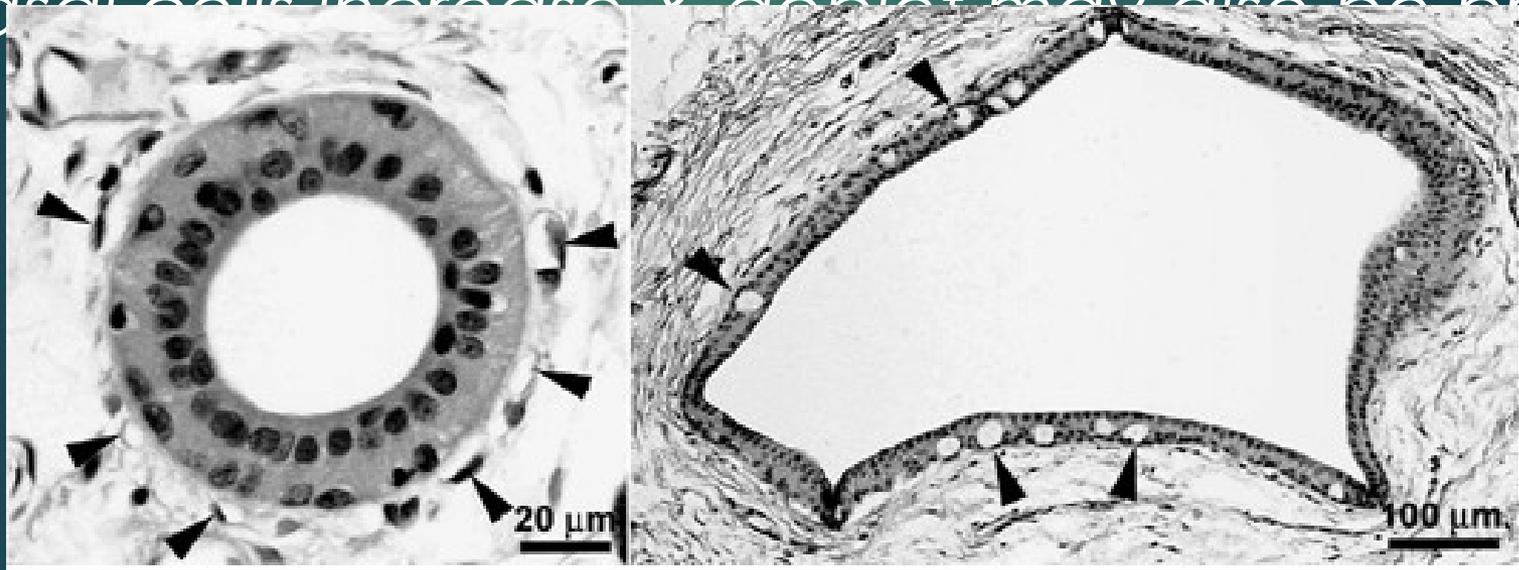
- ▶ *Short stubby microvilli at the luminal surface.*
- ▶ *Joined to adjacent cells by junctional complexes and tight junction but lack gap junctions.*
- ▶ **Function:**
 - Modify the salivary secretion-Changes from isotonic to hypotonic.*
 - Na⁺ reabsorption & K⁺ excretion.*

Terminal Excretory Ducts:

- ▶ As the striated ducts leave the individual glandular lobules and enter the inter lobular connective tissue, they join to form **excretory ducts**.
- ▶ Larger than striated ducts
- ▶ **Main excretory ducts** leading from the gland to the oral cavity is formed by the continued confluence of the



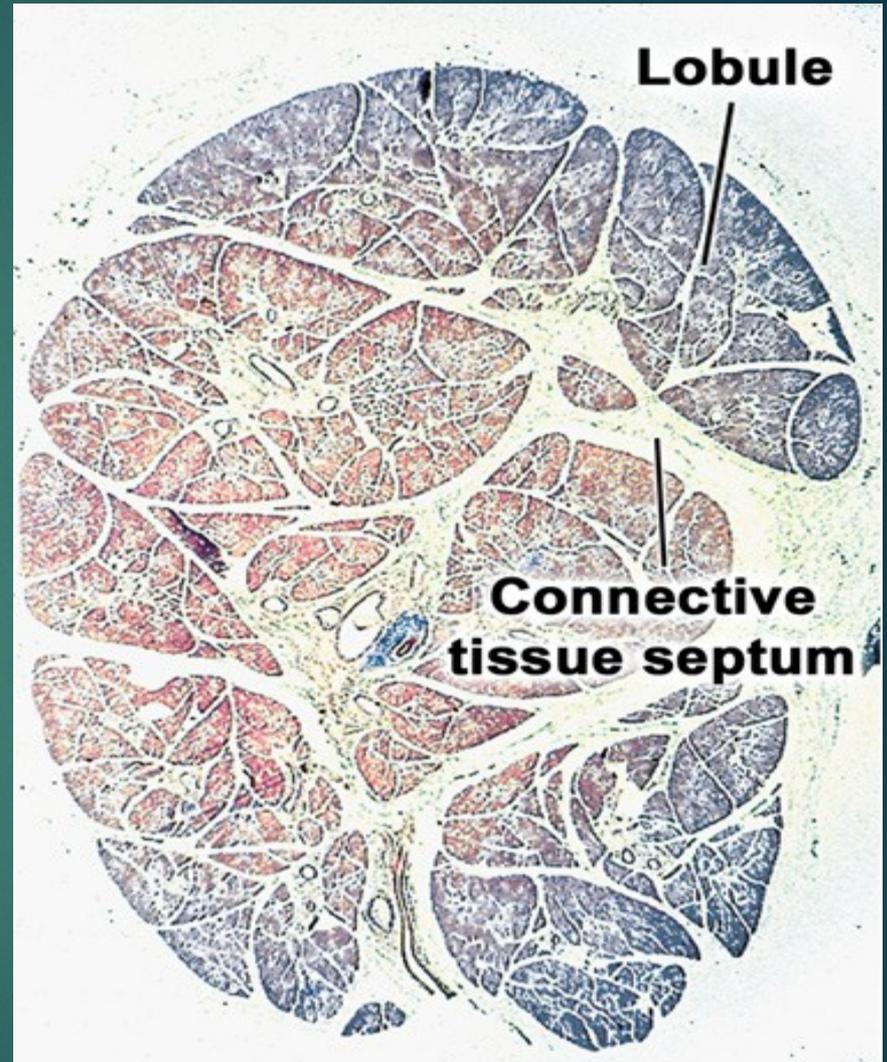
- ▶ Near the striated ducts they are lined by pseudostratified with columnar cells admix with small basal cells and goblet cells.
- ▶ As the smaller duct join to form larger duct, no. of basal cells increase & goblet may also be present.



- As they approach oral cavity epithelium changes to a stratified epithelium.
- **Function:** Modify the final saliva by altering its electrolyte concentration.

CONNECTIVE TISSUE:

- ▶ Capsule –demarcate gland from adjacent structures.
- ▶ Septa –divide gland into lobes and lobules
 - Carry the nerves and blood vessels and excretory ducts.
- ▶ Fibroblast, Macrophages, Dendritic cells, Mast cells, Plasma Cells, Adipose tissue.
- ▶ Collagen fibers and elastic fibers along with glycoprotein and proteoglycans of the Ground substances



Nerve Supply:

▶ Follow the course of vessels

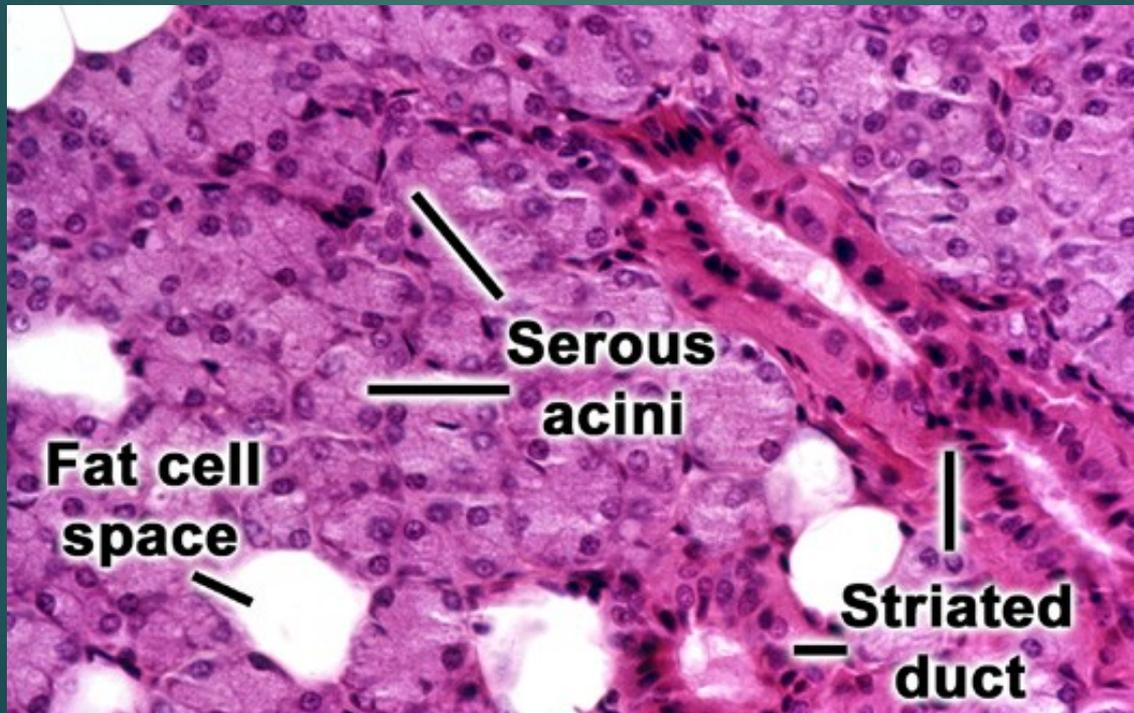
▶ 2 patterns :

- I. Intrapanietal type : Axons leaves the nerve bundle, loses its schwann cell investment, penetrate the basal lamina and form an expanded swelling or varicosity in close contact (10 to 20 nm) to basolateral membrane or between epithelial cells.
e.g., submandibular gland & minor salivary gland of lip.
- II. Extrapanietal Type: Axons remain associated with the nerve bundle in the connective tissue-100 to 200 nm from epithelial cells.
e.g., parotid gland

Histology of major salivary glands

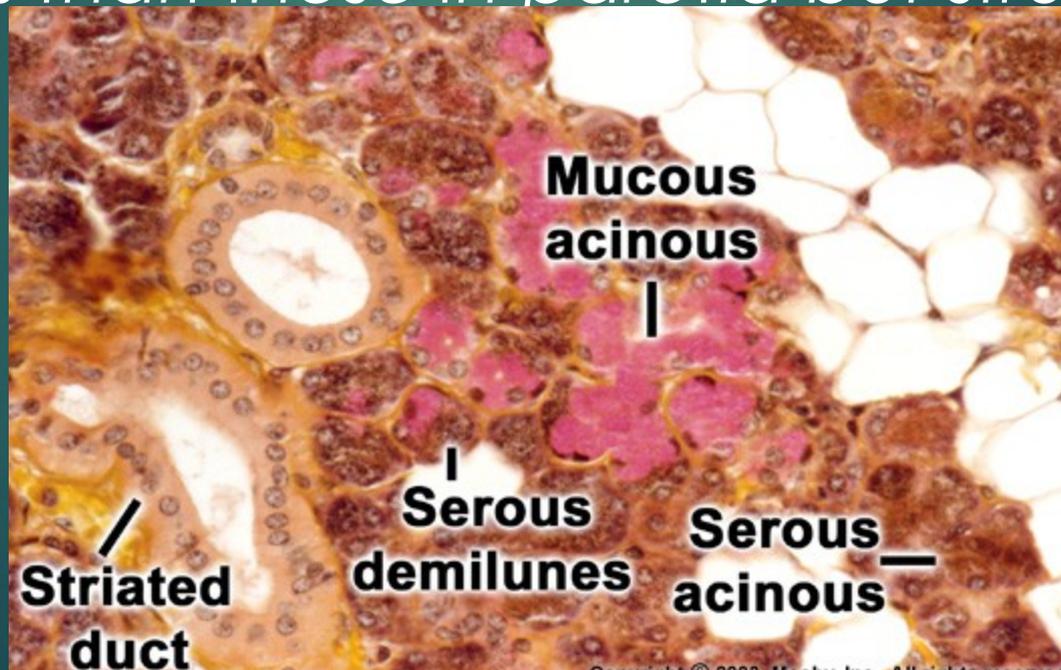
Parotid gland:

- ▶ glands All serous
- ▶ Fat cells may be seen.
- ▶ Long intercalated ducts are seen.



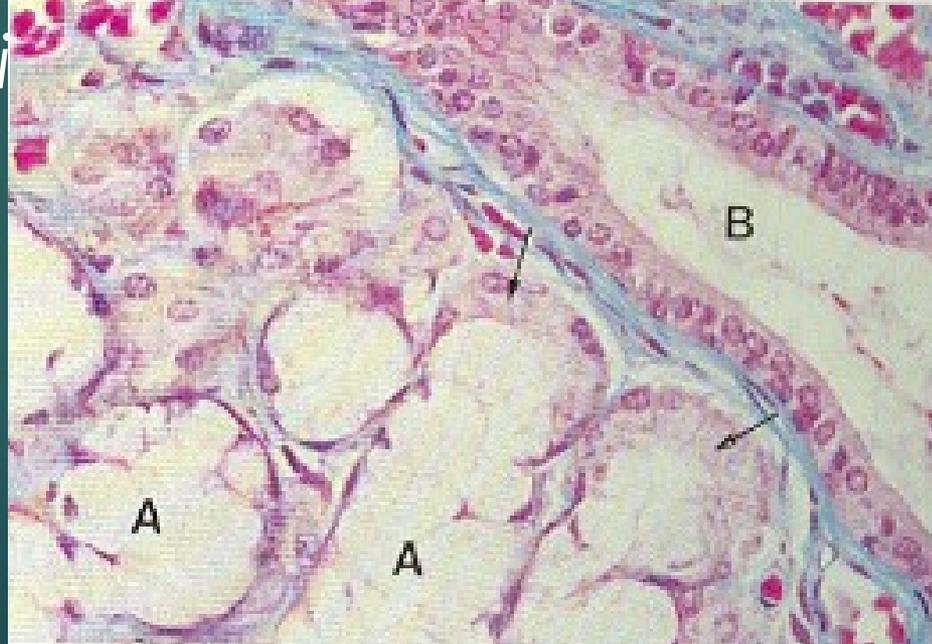
Submandibular gland:

- ▶ Consists of serous end pieces & mucous tubules capped with serous demilunes.
- ▶ Serous cells significantly outnumber the mucous cells (pale staining).
- ▶ The intercalated & striated ducts are less numerous than those in parotid but structurally similar.



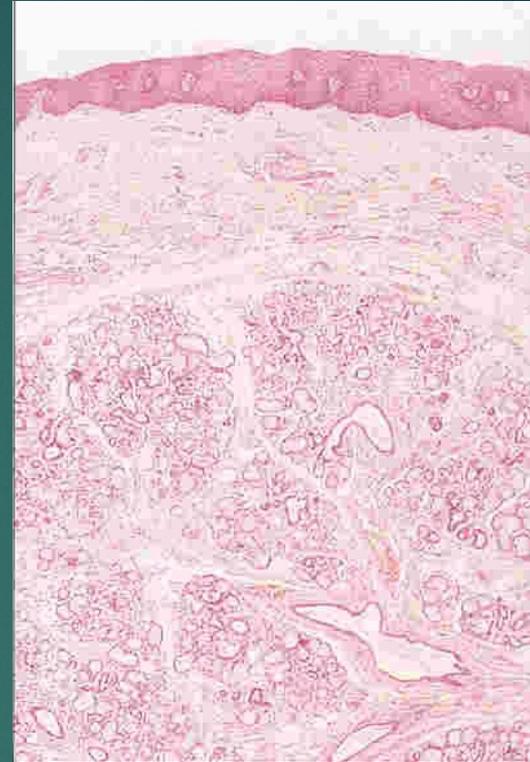
Sublingual salivary gland :

- ▶ Mixed, with mucous cells more.
- ▶ Intercalated ducts are short & difficult to recognise.
- ▶ Intralobular ducts are fewer in no. than in the parotid or submandibular gland
- ▶ Some ducts may lack the infoldings characteri



Minor salivary glands:

- ▶ Consists of aggregates of secretory end pieces and ducts, organised into lobule like structure in the submucosa or between muscle fibers of tongue.
- ▶ Mostly mucous
- ▶ Occasional demilunes.



SALIVA

Thin, watery, slightly viscid fluid secreted by the salivary glands.

- Composition
- Functions
- Formation & Secretion Of Saliva

Composition

Water: 94 to 99.5%

Solids: 0.5 to 0.6%

Organic:

Glycoproteins

Enzymes: α - amylase

Lysozyme

Lactoperoxidase

Kallikrein

Esterase

Acid phosphatase

Mucins

Lactoferrin

Blood clotting factors

Hormones - Parotin

Secretory Immunoglobulin-

IgA, IgG, IgM

Inorganic Substances:

Sodium

Calcium

Chloride

Bicarbonate

Phosphate

Potassium

Less Amounts:

Fluoride

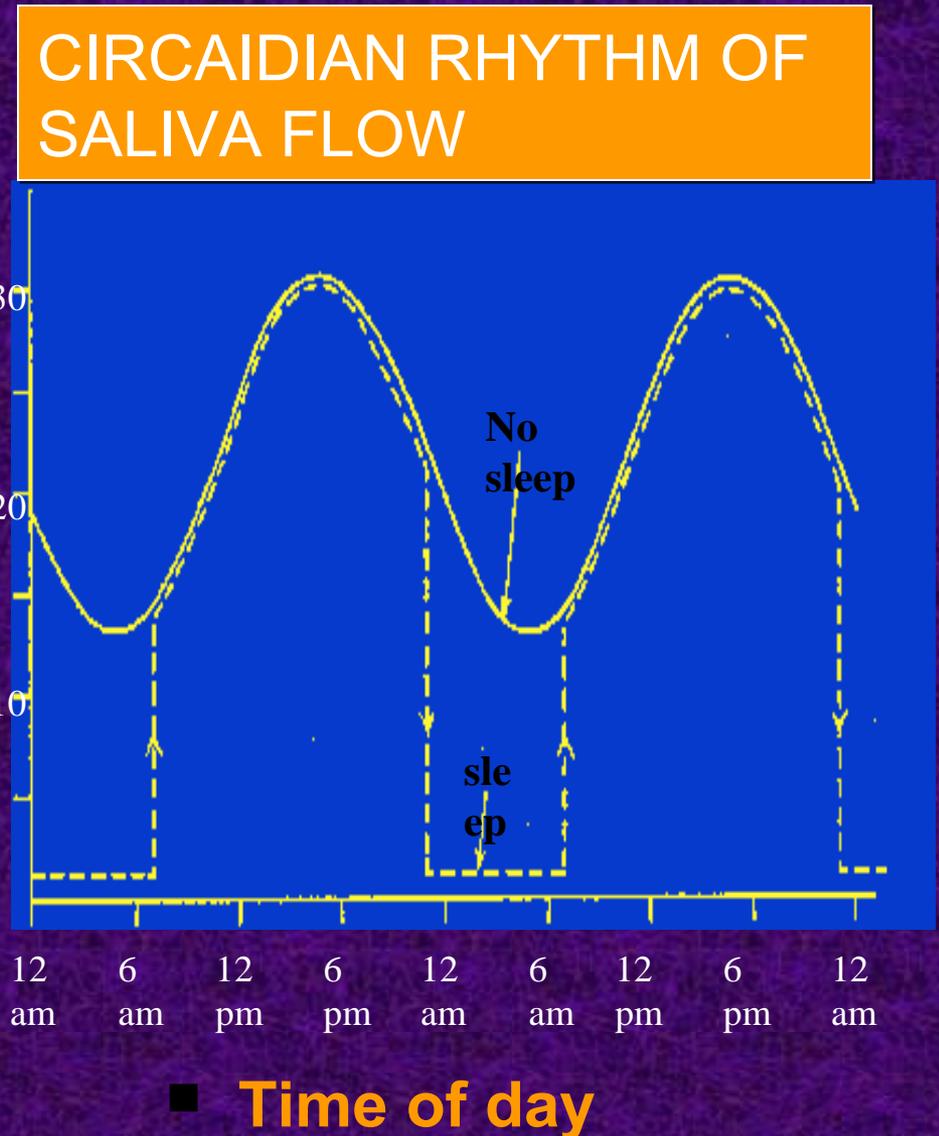
Magnesium

Iodides

- ▶ *More than a litre* of saliva is secreted per day.
- ▶ Specific Gravity : **1.002 to 1.008**
- ▶ pH: **6.2 to 7.6 (6.7)**
- ▶ Water : **99.4%** (unstimulated) & **99.5%** (stimulated)
Solids: **0.6%** (unstimulated) & **0.5%** (stimulated)

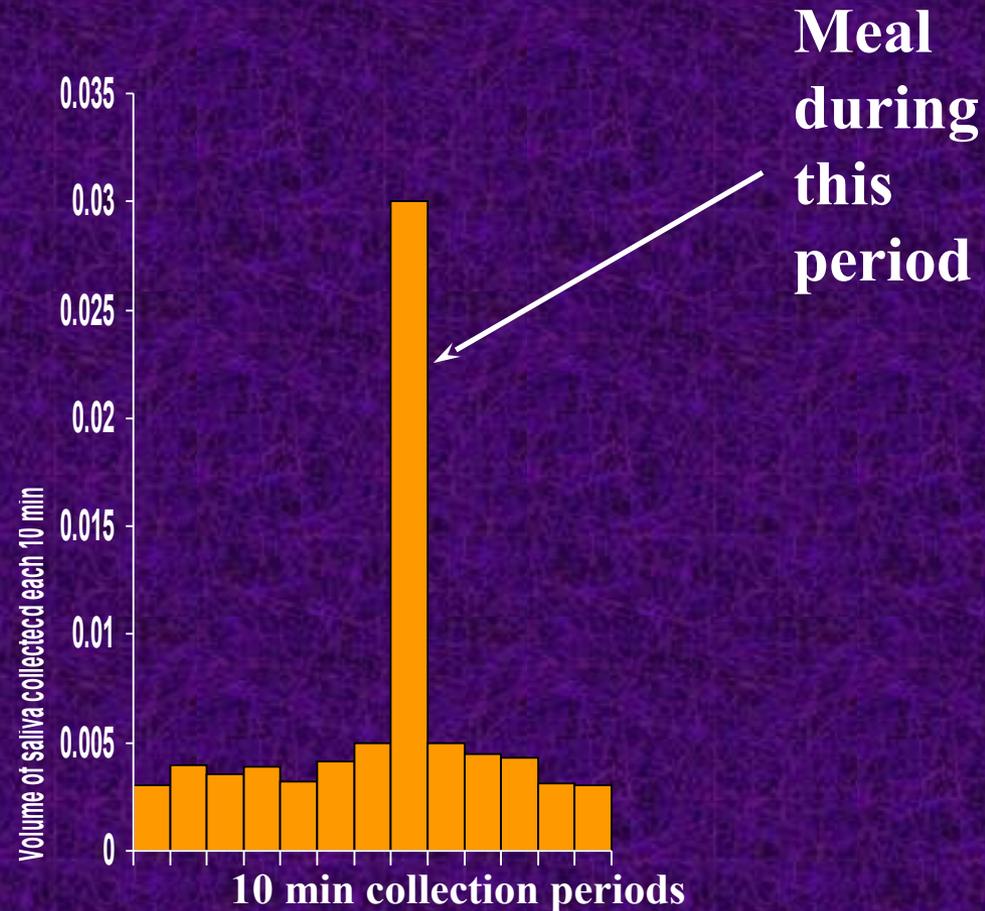
Salivary flow rate

- Normal salivary flow rate:
0.3ml/min(unstimulated)
2.0 – 5.0 (stimulated)
- Exhibit diurnal and seasonal variations
Peak : Mid afternoon
Spring
- Negligible: During sleep flow



Effect of feeding on salivary secretion

- Unstimulated flow
 - Whole 0.2 – 0.4 ml/min
 - Submandibular g. 0.1 ml/min
 - Parotid g. 0.04 ml/min
- Stimulation
 - Whole 2.0 – 5.0 ml/min
 - Submandibular g. 0.8 ml/min
 - Parotid g. 1.0 – 2.0 ml/min



▶ **Parotid glands:**

-Watery saliva.

-Rich in enzymes such as amylase, proteins such as proline rich proteins and other glycoproteins.

▶ **Submandibular glands:**

-In addition to above component, contains highly glycosalated substance called mucins

▶ **Sublingual glands:**

-Viscous rich in saliva

Organic components

Mucins:

▶ Glycoproteins - protein core with many oligosaccharide side chains attached by **O-glycosidic bond**.

Two major mucins (**MG1 and MG2**).

▶ Lubrication

Hydrophilic-resists dehydration.

Amylases:

▶ **30%** of total protein in parotid saliva

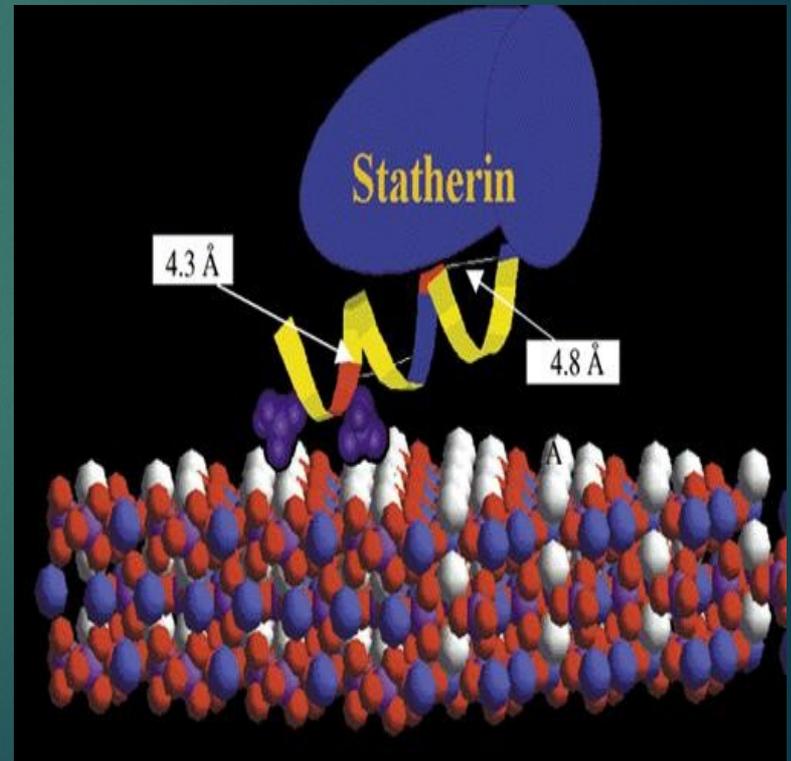
▶ Hydrolyzes **$\alpha(1-4)$ bonds** of starches such as amylose and amylopectin

Lingual Lipase:

- Secreted by lingual glands and parotid.
- Involved in **fat digestion**-Important in digestion of milk fat in new-born.

▶ Statherins:

- ▶ *Statherins prevent precipitation or crystallization of supersaturated calcium phosphate in ductal saliva and oral fluid.*
- ▶ *Also an effective lubricant*



Lactoferrin:

Iron-binding protein

Lysozyme:

- Also called **muramidase**
- Hydrolysis of $\alpha(1-4)$ bond between N-acetylmuramic acid and N-acetylglucosamine in the peptidoglycan layer of bacteria.

Proline-rich Proteins (PRPs):

- Inhibitors of calcium phosphate crystal growth
- Subdivided into three groups
 - Acidic 45%
 - Basic 30%
 - Glycosylated 25%

Salivary peroxidase systems

- ▶ Sialoperoxidase (SP, salivary peroxidase)
 - ▶ Produced mainly by parotid gland
- ▶ Myeloperoxidase (MP)
 - ▶ From leukocytes entering via gingival crevice

Histatins

- Potent inhibitors of *Candida albicans* growth

Cystatins:

- Considered to be protective against unwanted **proteolysis** caused by bacteria - inhibit proteases in periodontal tissues
- Also have an effect on calcium phosphate precipitation

Inorganic Content

Calcium and phosphate:

▶ *Help to prevent dissolution of dental enamel*

▶ Calcium

- ▶ *1.4 mmol/l (unstimulated saliva)*
- ▶ *1.7 mmol/l (stimulated saliva)*
- ▶ *50% in ionic form*
- ▶ *sublingual > submandibular > parotid*

▶ Phosphate

- ▶ *6 mmol/l (unstimulated saliva)*
- ▶ *4 mmol/l (stimulated saliva)*
- ▶ *90% in ionic form*

Bicarbonate:

- ▶ *Buffer - Defence against acids produced by cariogenic bacteria*
- ▶ *Derived actively from CO₂ by carbonic anhydrase*

Thiocyanate:

- ▶ *Antibacterial*
- ▶ *Higher conc. => lower incidence of caries*
- ▶ *Smokers - increased conc.*

Lead, cadmium, copper:

- ▶ *May reflect systemic concentrations - diagnostics*

FUNCTIONS

1. PROTECTION:

▶ Mechanical washing action:

- Flushes away non-adherent bacterial and acellular debris from the mouth.
- Clearance of sugars from the mouth limits their availability to acidogenic plaque microorganisms.

▶ Lubricant: (mucin)

- Protects the lining mucosa by forming a barrier against noxious stimuli, microbial toxins and minor trauma.
- Allows the oral surface to move one another with minimal friction during function.

2. BUFFERING:

▶ Bicarbonate ,phosphate, some salivary proteins.

Metabolism of salivary proteins and peptides produce ammonia and urea which help in increase of pH.

3. Pellicle formation:

- ▶ Salivary proteins bind to surface of the teeth and oral mucosa, thus forming **salivary pellicle** which behaves as a protective membrane .
- ▶ Binding site for bacteria – **plaque**.

4. MAINTAINENCE OF TOOTH INTEGRITY:

- ▶ Saliva is saturated with Ca^+ & PO_4^- : **acidic protein rich proteins & statherin**
- ▶ High concentration of these ions ensures that ionic exchange with the tooth surface results in post eruptive enamel maturation, increase in surface hardness, decrease in permeability and increase in resistance to demineralization.
- ▶ Remineralization of initial caries

5.ANTIMICROBIAL ACTION:

- ▶ Lysozyme is an enzyme that can hydrolyse the cell wall of some bacteria.
- ▶ Lactoferrin binds free iron & in doing so deprives bacteria of this essential element.
- ▶ Antibodies present in saliva (IgA)
 - has the capacity to agglutinate microorganisms that are swallowed.
 - prevent their agglutination to oral tissue.
- ▶ Mucin and specific agglutins: aggregate microorganisms.
- ▶ Histatin and peroxidase

6.ROLE OF SALIVA IN TISSUE REPAIR:

- ▶ *Bleeding time of oral tissues is shorter than other tissues.*
- ▶ *Experiment have shown that wound healing is faster & wound contraction is also increased in the presence of saliva.*

7.DIGESTION:

- ▶ *Forms the food bolus-preparation of the ingested food for deglutition.*
- ▶ *Breaks down starch (Amylase).*
- ▶ *Lipase*
- ▶ *Dilutes gastric chyme.*

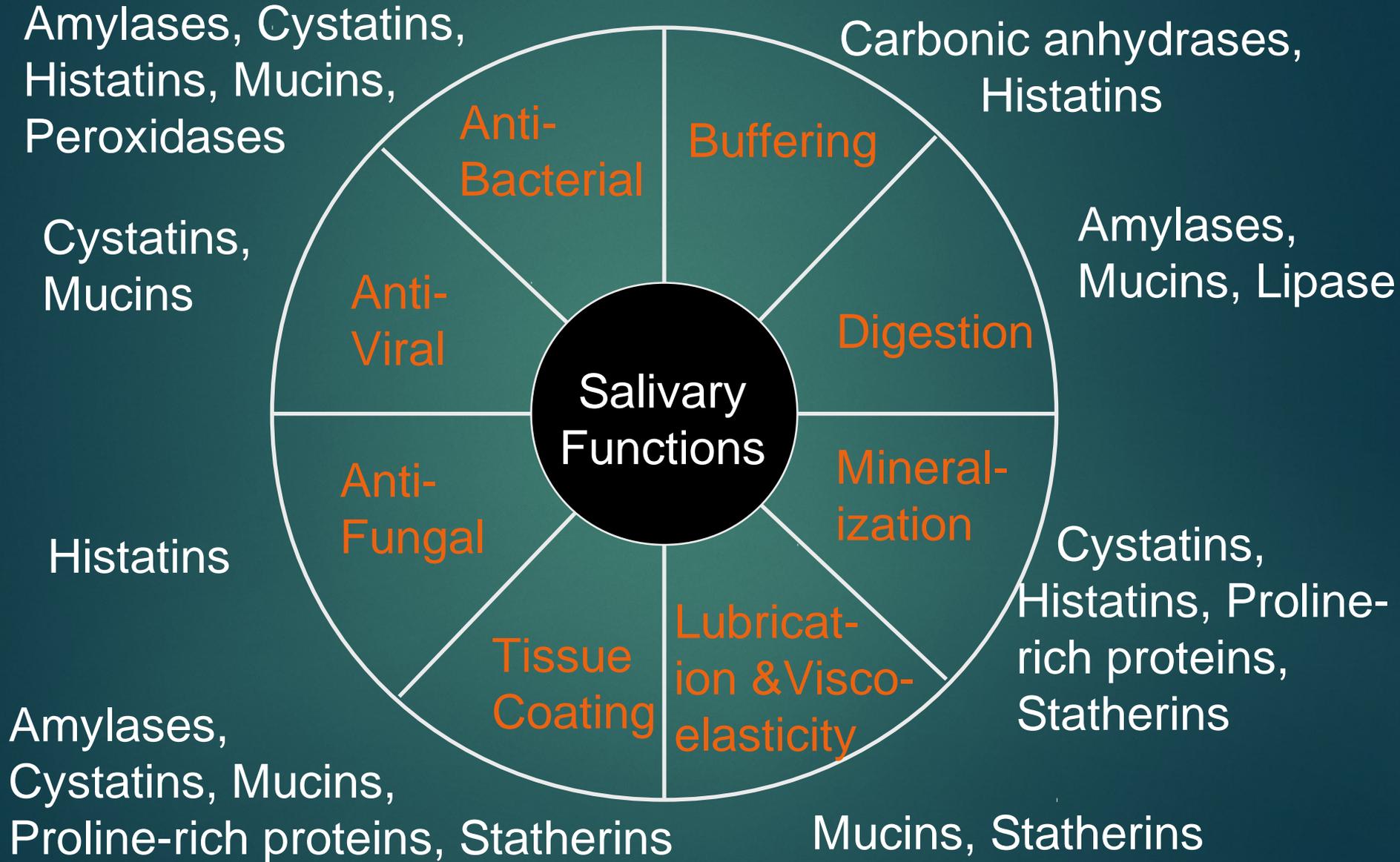
8.TASTE:

- ▶ *Saliva is required to dissolve substance to be tasted & carry them to the taste buds.*
- ▶ *It also contains a protein called **gustin** that is thought to be necessary for growth & maturation*

8. Salivary anticaries activity:

- ▶ Carbohydrate & microbial clearance from the oral cavity.
- ▶ Buffering action - Salivary bicarbonates.
- ▶ Remineralization of incipient carious lesion-
 Ca^+ , PO_4^+ , F^-
- ▶ Increase enamel resistance to acid decalcification- F^-
- ▶ Salivary urea and bicarbonate can increase rate of glycolysis, thus leading to faster carbohydrate metabolization, which in turn leads to reduced duration of the enamel

Multifunctionality



FORMATION & SECRETION OF SALIVA

Two Stage Hypothesis Of Saliva Formation:

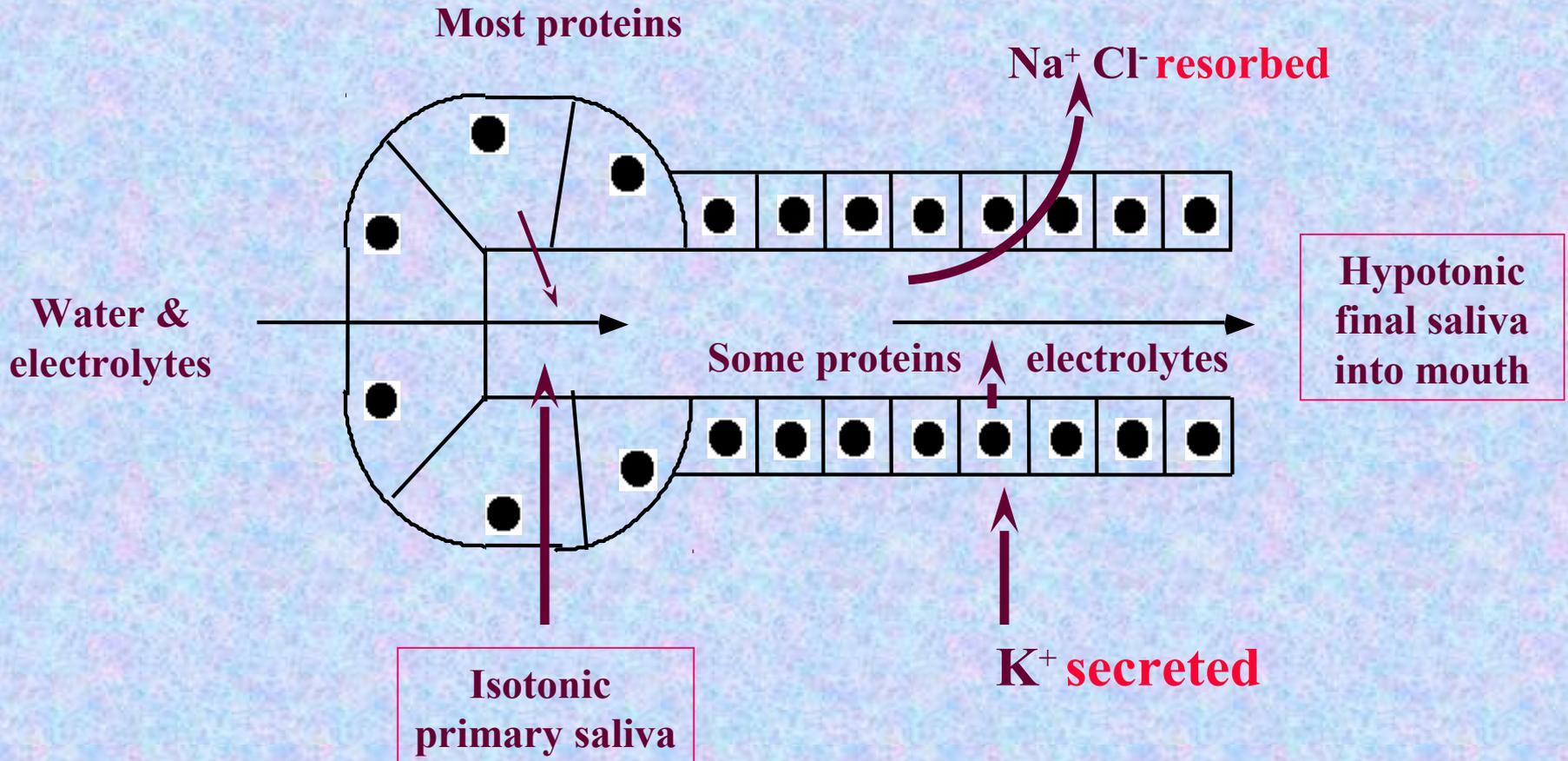
First stage:

- ▶ *Primary saliva is produced by secretory end piece & intercalated ducts.*
- ▶ *Isotonic - most of the organic components & water.*

Second stage:

- ▶ *Primary saliva is modified as it passes striated & excretory ducts - reabsorption & secretion of electrolyte.*

TWO STAGE HYPOTHESIS OF SALIVA FORMATION



First stage:

- ▶ *Formation of macromolecular component*
- ▶ *Fluid & Electrolyte release*

Formation of macromolecular component

Proteins synthesis in ribosomes associated with RER



Translocated to lumen of RER



Folding of protein & Posttranscriptional modification such as disulphide bond formation & N- and O-glycosylation.



Transferred as small vesicles to golgi complex



Further modification followed by condensation & packing into secretory granules (stored in apical cytoplasm).



Secretory signals (via sympathetic neurotransmitters)



Fused to luminal surface [Exostosis]



Released to external surface

Role of Secretory signals in exostosis

The binding of the sympathetic transmitter norepinephrine (*NE*) to (β -adrenergic (β) receptors on the basolateral membrane activates adenylyl cyclase (*AC*)



Catalyzes the formation of cyclic adenosine monophosphate (*cAMP*) from adenosine triphosphate (*ATP*)



Cyclic adenosine monophosphate activates protein kinase A (*PKA*)



Phosphorylates other proteins in a cascade



Fusion of secretory granules with the luminal surface to release their contents into the lumen



Exocytosis

Fluid & Electrolyte

Parasympathetic stimulation, Noradrenaline, and substance P



ER releases Ca^{++}



Free cytoplasm Ca^{++}



Opens Cl^- channel in apical & K^+ channel in basolateral membrane



Apical Efflux of Cl^-



Extracellular Na^+ draws into lumen probably through tight junction to balance the electrochemical gradient



Efflux of water-aquaporin & tight Junction

Role of Stimulatory signals in Fluid & Electrolyte release

Binding of the parasympathetic transmitter, acetylcholine (*ACh*), to muscarinic cholinergic (*MC*) receptors, and by norepinephrine binding to (α -adrenergic receptors (α)).

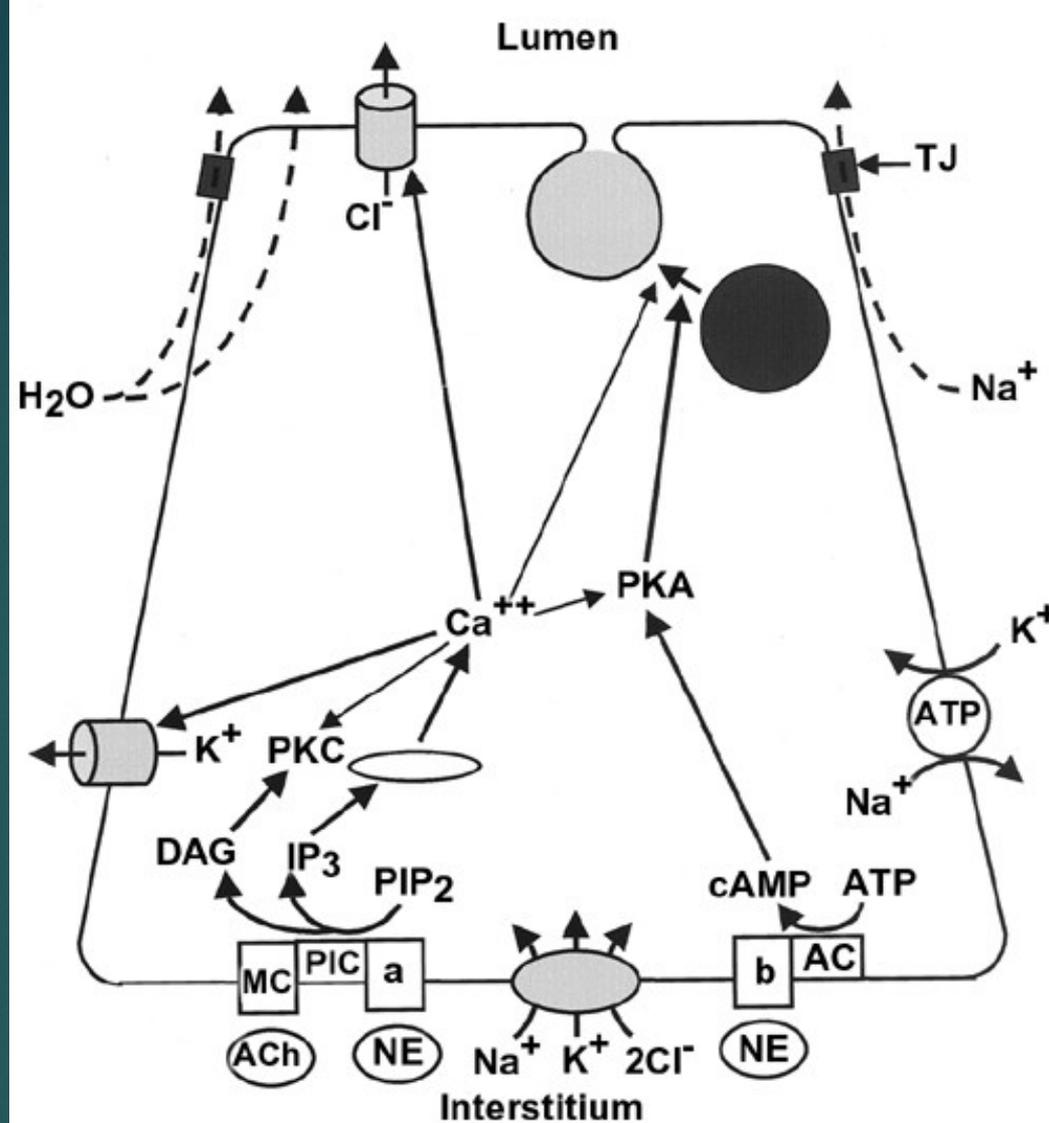
↓
Activate phospholipase C (*PLC*),

↓
Converts phosphatidylinositol bisphosphate (*PIP2*) to inositol trisphosphate (*IP3*) and diacylglycerol (*DAG*).

↓
Inositol trisphosphate causes the release of Ca^{2+} from intracellular stores, probably the endoplasmic reticulum.

↓
The increased Ca^{2+} concentration opens Cl^- channels in the luminal membrane and K^+ channels in the basolateral membrane, and activates the basolateral $\text{Na}^+/\text{K}^+ / 2\text{Cl}^-$ cotransporter.

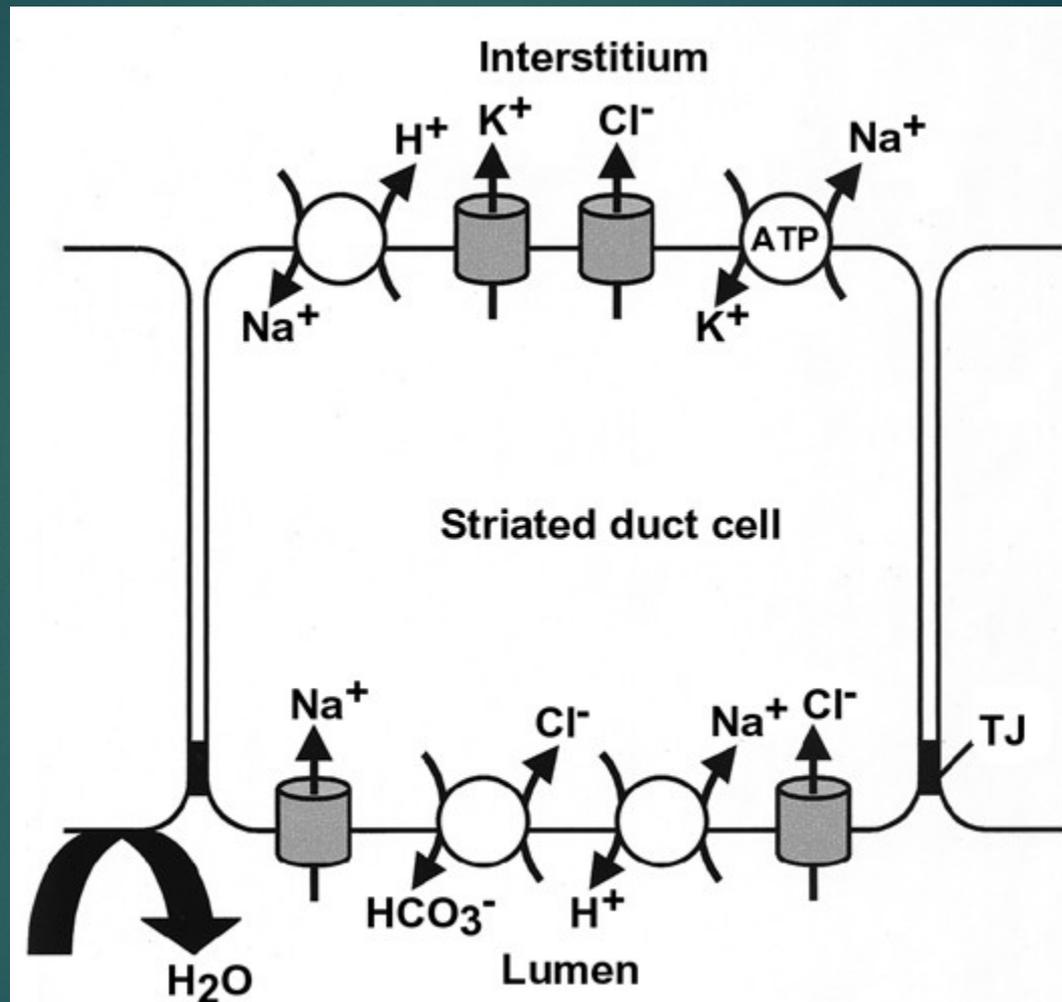
↓
The increased luminal Cl^- is balanced by the movement of extracellular Na^+ across the tight junctions (*TJ*), and the resulting osmotic gradient pulls water into the lumen through the cell and probably through the tight junction.



- *Calcium also modulates the activity of protein kinase A and protein kinase C (PKC). Protein kinase C, in turn, modulates exocytosis and intracellular Ca^{2+} concentrations.*

Ductal Modification of saliva:

- ▶ *Net reabsorption of Na^+ and Cl^- by luminal & basolateral membranes-hypotonic final saliva.*
- ▶ *Secretion of K^+ and HCO_3^- .*
- ▶ *Flow rate is directly related to Na^+ and Cl^- in saliva and inversely related to K^+ in saliva*
- ▶ *Flow rate is directly related to HCO_3^- in saliva.*

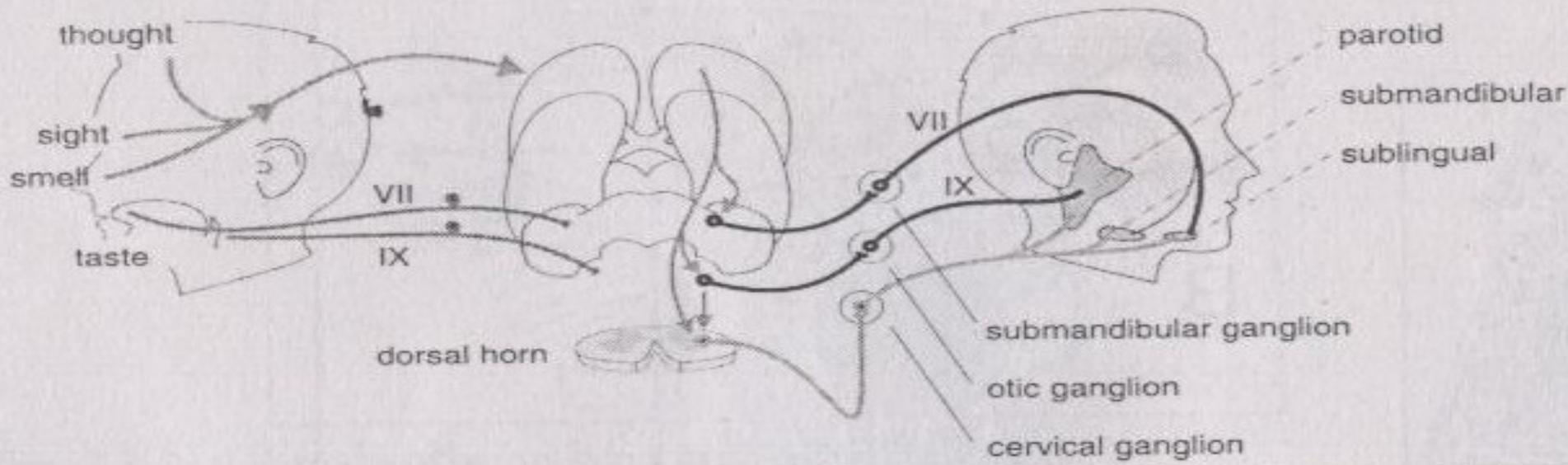


Neural control of Salivation:

- ▶ The afferent pathways: *via the facial & Glossopharyngeal nerves to a solitary nucleus in the medulla.*
- ▶ *There is also an input from higher centers in response to smell, sight etc.*
- ▶ Efferent pathways:
- ▶ The Parasympathetic efferent pathways
 - for the S.L&S.M. from the Facial nerve (chord tympani to reach the lingual nerve) via S.M. ganglion;*
 - the parotid gland from the glossopharyngeal N which pass through the tympanic and lesser superficial petrosal nerves to reach the otic ganglion where they synapse with post ganglionic fibres of the auriculotemporal nerve which supply*

AFFERENT

EFFERENT



Clinical considerations

Xerostomia:

- ▶ *Drugs- central or peripheral inhibition of salivary secretion.*
- ▶ *Destruction of salivary gland:*
 - Radiotherapy to H & N region*
 - Chemotherapy*
 - Bone marrow transplant*
 - Autoimmune diseases (**sjogren's syndrome**)-*
invasion of
lymphocytes & destruction of epithelial cells.
- ▶ *Psychological factors*

- ▶ *Loss of protective effect of salivary buffers, proteins, and mucins- increased susceptibility to infections.*
- ▶ *Difficulty & pain on eating, speech and swallowing.*
- ▶ *Temporary saliva*

Oral pharmacosympathomimetic drugs like Pilocarpine.

Sialorrhea:

Refers to excess saliva production.

Causes:

- Gastrointestinal irritants*
- Drugs (Pilocarpine)*
- Cerebro vascular accident*
- Pt. with a severe neurologic deficit*
- Pt. who have undergone extensive oral surgical procedures.*

Blockage of duct:

1. *Sialolith (stones)*

Mostly in submandibular gland

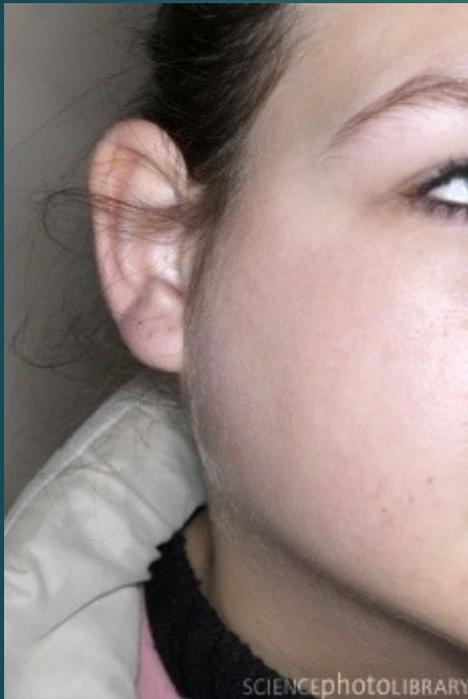
2. *Mucous plugging in minor salivary glands due to trauma.*

Age changes:

- ▶ *Parenchymal cells are replaced by adipose tissue.*
- ▶ *Decreased saliva production*
- ▶ *Resting saliva (unstimulated) is in normal range, while stimulated saliva is less.*

Diseases:

- ▶ Viral(mumps) & bacterial infections- painful swelling .



Endocrine:

- ▶ *Diabetes :*
Parotid gland swelling may occur
Salivary flow is reduced.
Changes in salivary proteins.

Autoimmune diseases *may cause destruction of salivary glands & reduced salivary flow.*

- ▶ *Sjogren's syndrome*
- ▶ *Rheumatoid arthritis*
- ▶ *Graft-versus host diseases*

Patients with adrenal disease *may have altered electrolyte composition.*

Immune deficiency syndrome:

- ▶ *Decreased flow rates.*
- ▶ *Lower levels of immunoglobulins in saliva*
- ▶ *Parotid enlargement – lymphadenopathy and lymphoepithelial cysts*

Genetic diseases:

- ▶ *Cystic fibrosis: Na^+ & Cl^- conc. are increased and mucous secreting glands may develop mucous plugs.*

Benign & malignant tumours.

Saliva as a diagnostic aid:

▶ Oral diseases

High risk caries patient, Patient susceptible to candidiasis

▶ Diagnostic aid for clinical problems

Psychological problems, smoking, poisoning

▶ Systemic diseases affecting saliva

Sjogren's syndrome, Cystic fibrosis

▶ Steroid hormone determination:

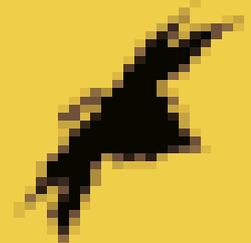
Functional efficiency of corpus luteum in case of defect in hypothalamic-pituitary-ovarian axis, Pregnant status, Ovulation time

▶ Monitoring of certain drugs that exhibit consistent saliva : plasma ratio. e.g., phenytoin, carbamazepine, theophylline

▶ For detection of marijuana smoking & cocaine

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THANK YOU

