

Chapter 17: Salivary Glands

There are essentially three paired salivary glands: the parotid glands, submandibular glands, and the sublingual glands. In addition, the minor salivary glands, or accessory glands are present in the oral cavity. They can be split into 3 main categories: the anterolingual glands, the serous glands of Von Ebner, the lingual buccolabial and palatal glands.

Parotid Glands

Each parotid gland is pyramidal in shape and weighs approximately 25 g. The deep cervical fascia splits to enclose the parotid gland. The gland is serous in nature, with a few scattered mucous acini. Anatomically the gland can be split into two lobes: the larger superficial lobe and the deep lobe.

The superficial lobe lies wedged between the mastoid process and the posterior border of the mandible, extending forward over the masseter for a variable distance. Its anterior border is convex forward and from it emerges the parotid duct and the five divisions of the facial nerve. Posteriorly, the gland is related to the mandibular joint, the osseous and cartilagenous portions of the external auditory canal, the mastoid process, and sternomastoid muscle.

The deep lobe of the gland, a narrow edge of the wedge-shaped gland, lies in contact with the internal jugular vein. The gland contains the pes anserinus of the facial nerve within the substance of its superficial lobe. More deeply lies the retromandibular vein and deepest of all, the external carotid artery. The parotid duct passes forward across the masseter muscle, turns around its anterior border to pierce the buccinator. The duct opens on the mucous membrane of the cheek, opposite the second upper molar tooth. The bed of the parotid consists of the posterior belly of the digastric muscle, the styloid process, and the stylohyoid muscles. Deep to them are the internal jugular vein, crossed by the accessory nerve as it lies on the accessory nerve as it lies on the lateral mass of the atlas; further forward is the internal carotid artery. The blood supply is from branches of the external carotid artery, and the venous drainage is via the retromandibular vein.

Nerve Supply

The nerve supply is secretomotor fibers arising from cell bodies in the otic ganglion. These reach the gland by hitchhiking along the auriculotemporal nerve. The preganglionic fibers arise from cell bodies in the inferior salivatory nucleus in the medulla and travel by way of the glossopharyngeal nerve. They then travel by the tympanic branch and the tympanic plexus, and subsequently by the lesser superficial petrosal nerve to the otic ganglion. The sympathetic fibers reach the gland from the superior cervical ganglion by way of the plexus on the external carotid and middle meningeal arteries.

Submandibular Gland

This salivary gland, which is two-thirds serous, lies between the floor and the roof of the submandibular fossa, partly under the cover of the mandible. Its contact with the bone is responsible for the smooth enlarged concavity that lies below the mylohyoid line opposite the bicuspid and molar teeth. The gland, which is the size of a walnut, becomes narrow posteriorly and curves around the free posterior border of the mylohyoid muscle. A smaller deep part of the gland lies on the floor of the mouth between the mandible and the side of the tongue. The main duct within the gland thus curves around the posterior border of the mylohyoid muscle. The blood supply is via the main facial artery, and venous drainage is into the common facial vein.

Nerve Supply

Secretomotor fibers to the gland have their cell bodies in the submandibular ganglion, the preganglionic fibers pass through cell bodies in the superior salivatory nucleus in the pons by way of the nervus intermedius and travel with the facial nerve as far as the stylomastoid canal. They leave the facial nerve in the chorda tympani nerve, the company with the taste fibers, to the anterior two-thirds of the tongue, pass along the lateral wall of the middle ear, and leave the skull through the petrotympanic fissure. They join the lingual nerve from behind, a full inch below the base of the scalp.

Sublingual Glands

The sublingual glands are the smallest of the major glands. Each is the size and shape of an almond and weighs approximately 3-4 g. Each gland lies immediately beneath the oral mucous membrane, raising a fold beside the tongue. Below the gland is the mylohyoid muscle, laterally is the mandible and medially is the genioglossus muscle.

Histology and Ultrastructure

The salivary glands are described as being lobular and racemose, i.e. lobes or lobules having the separate appearance of a bunch of grapes. These lobules are the functional units of the glands. Each is built up from acini, intercalated ducts, and striated ducts, the stalks. Each acinus gives rise to an intercalated duct and these join to form larger ducts. Joining of ducts occurs throughout the intercalated and striated duct regions, until each lobule gives rise to a lobular excretory duct. Finally, after many further junctions of ducts, the glands' secretion passes out through the main duct (see Fig. 17.1). An acinus consists of a spherical group of cells, each polygonal in section, enclosed by a basement membrane and themselves enclosing a space which is the beginning of the duct system. The acinar cells are classified histologically into two types, according to their appearance after staining with haematoxylin and eosin. Predominantly pink-staining cells with large granules are found in the acini of the sublingual and the submandibular gland, but rarely in the parotid gland. Since their staining properties resemble those of other cells elsewhere which produce mucoid substances, and since the secretion of sublingual and submandibular glands is viscous and rich in protein-carbohydrate complexes, they have been referred to as mucous cells. Cells which stained pale blue and contained much smaller granules than those in the mucous cells make up most of the acini of the parotid gland and the glands of Von Ebner. Similar cells are found in the

anterior lingual glands and the submandibular glands, where they are raised as a layer on the outer surface of acini, composed of the mucous-type cells. In these glands they represent, in section, a crescent shape or demilune. In the parotid, the secretion of this type of cell can reach the acinus directly, but in other glands it must pass through fine canaliculi between the mucous cells. As these cells are the dominant ones in the parotid gland, and produce a secretion much less viscid and more serous than the secretions of other glands, they are termed serous cells. Despite this histologic distinction these cells do produce mucoproteins. However, their characteristic product in man is the starch-splitting enzyme, amylase. The cells of the intercalated duct are small cuboidal cells with large nuclei and few organelles. The intercalated duct is relatively short and the small cells soon give way to large cuboidal cells. From the striated duct there is an abrupt transition to the excretory ducts with a two-layered epithelium, the superficial layer columnar, and the deep layer flat cuboidal. Finally, near the termination of the main ducts there is another abrupt transition to a multilayered stratified squamous epithelium like that of the oral mucosa. In addition to these cells another cell is found in the major salivary glands. This is the myoepithelial cell, a cell with a regular orientation of fibers like that of smooth muscle. It is believed that the contraction of these fibers causes the expulsion of formed saliva.

Stimulus to Secretion

The stimulus to secretion can be classified the three separate categories: local, interorgan, and psychic stimuli.

Psychic Stimuli

Stimuli to sense organs of the head and specifically the mouth, often are associated with food intake. The stimulation of sight or hearing causes salivation only by a condition reflex, i.e. the sight of food or the sound of cooking, while the hearing or a verbal description of food is a psychic stimulus rather than a local or direct stimulus.

Local Stimuli

Stimuli upon the sensory organs of the head often are termed cephalic. The term normally also includes psychic stimuli. In considering stimuli causing secretion of saliva, local stimuli may be taken as the cephalic stimuli with the exclusion of the psychic or condition stimuli. Local stimuli include:

Smell

Olfactory irritants cause a direct salivary reflex. It is uncertain, however, whether or not nonirritating olfactory stimuli also can do so, or whether the salivary response to nonirritating smell is a conditioned reflex.

Taste

There is an increase in the salivary flow whenever the sense of taste is stimulated. Acid stimuli are the most effective in stimulating salivary flow, sweet and salt are less so, and bitter least of all.

Touch and Irritation of the Oral Mucosa

The proprioceptive impulses arise from the masseter muscles, the temporomandibular joint, and impulses from pressure sensors in peridental membranes of the teeth. There is evidence that unilateral stimulation of smell, taste, touch, or proprioceptive sensors cause predominantly unilateral secretion of saliva.

Interorgan Stimuli

Inter-organ stimuli are not particularly apparent in the control of salivary secretion. Irritation of the esophagus is said to cause reflex salivation.

Composition of Saliva

Saliva contains inorganic ions and organic molecules of various sizes dissolved in water. More than 99% of saliva is water. In mixed saliva the total organic content amounts to a little over 5 g/L and the total inorganic to about half of this.

Organic Compounds

Protein

The total protein content of mixed saliva is around 2.2 g/L. At higher flow rates the amount of protein increases. Analysis of saliva collected over a variety of conditions give a protein concentration of 2.3 g/L. The amount of protein in saliva depends on the flow rate. In general, the protein concentration increases with increased flow rate. The proteins of saliva have been classified as serum proteins, proteins of glandular origin, including glycoproteins and enzymes, and blood group substances. In all, more than 20 proteins have been separated in analysis of saliva.

Serum Protein

Amylases of saliva by electrophoresis and immunochemical methods have demonstrated seven or eight proteins which show antigenic properties similar to those of blood proteins. These include serum albumin and gamma globulin with beta globulins. The total proportion of serum proteins may be as much as 20%. Gamma globulins in saliva have interested dental research workers, since they may include antibodies against oral disease. No correlation has been shown between susceptibility to dental caries and gamma globulin concentrations in saliva.

Proteins Similar to Those in Serum

The question of the origin of gamma globulins and of serum albumin already has been discussed. The number of proteins similar to action to some of the blood-clotting factors has been described in saliva: proactivator, Christmas factor, antihemophilic globulin, and a platelet factor. All have their analogues in saliva.

Enzymes

Amylase

The characteristic enzyme of saliva is an alpha-amylase capable of splitting cooked starch down to maltose. It has an optimum pH of 6.8 and needs chloride ions present for full activity.

Lysozyme

This enzyme which splits the carbohydrate of the cell walls of certain bacteria is present in most body secretions. In parotid saliva it comprises about 10% of the total protein. Its concentration is high in submaxillary gland saliva.

Phospholipase, Cholinesterase and Ribonuclease

These are present in similar concentrations in plasma and saliva.

Lipase

A specific lipase has been described in saliva.

Peroxidase

An antibacterial peroxidase system is found in saliva.

Other Enzymes

In mixed saliva an enormous range of enzymes is present. These enzymes include those produced in the glands and also from plasma.

Kallikrein

This enzyme which produces bradykinin by splitting a serum beta globulin is produced in the salivary glands. Most of the early work on bradykinin was carried out with saliva-serum mixtures. It is thought that this enzyme passes back into the gland to reach the blood vessel, causing the functional dilatation necessary to supply the totally secreting gland with sufficient blood flow.

Mucoproteins and Glycoproteins

Most salivary proteins contain a large portion of carbohydrate in their molecules. In parotid saliva about 35% of the total protein contains appreciable amounts of carbohydrates. These carbohydrate-proteins contain about 75% protein, with proline, glycine, and glutamic acid as the major amino acids.

Blood Group Substance

Blood group substances are carbohydrate-protein complexes present on the cell walls of the red blood cells. Normally the red cells are characterized by the presence or absence of two antigens, A and B, which differ in their terminal sugar chains. About 80% of the population exhibit, in their tissue fluids and secretions, the antigens corresponding to their blood group, or the glycoprotein H substance which lacks the terminal polysaccharide groups. These substances are secreted in the submandibular and sublingual salivary glands, but not in parotid saliva. The only blood group antigens which have been described in saliva are those of the Lewis group.

Hormones

A substance having hormonal activity has been isolated as a protein compound of the parotid saliva termed parotin. It is said to maintain serum calcium levels and promote calcification.

Inorganic Compounds

The total inorganic content of saliva is about 2.5 g/L.

Sodium

Sodium is the most abundant ion in extracellular fluids and appears in the secretion at 140-150 micromol/L.

Potassium

Extracellular fluids normally contain low concentrations of potassium. However, all parts of the salivary and ductal system, except for the terminal duct, appear to transport potassium into the secretion at flow rates above 0.2 mL/min. The potassium concentration of the saliva stays constant at around 20 micromol/L.

Chloride

Chloride is the major anion of extracellular fluids. Its concentration in the secretion mirrors that in the plasma at around 100 mEq/L.

Bicarbonate

Bicarbonate appears to be in very low concentration in resting saliva. As the gland cells become active, their carbon dioxide production, due to metabolism, increases the enzyme carbonic anhydrase, made from the formation of carbonic acid and bicarbonate, is secreted into the saliva. The concentration of bicarbonate increases with the flow rate to reach as high as 60 mEq/L.

Hydrogen Ions

The pH of saliva is low in the resting secretions but rises as high as 8 in fast-flowing saliva. This is largely due to the bicarbonate content.

Iodine

The salivary gland actually transports iodine so the concentration is higher in saliva than in plasma. The concentration increases with flow rate.

Fluoride

Saliva contains 0.1 ppm or 5.2 micromol/L of fluoride. This concentration is of the same order of magnitude as that in plasma.

Thiocyanate

Thiocyanate is present in saliva in a higher concentration than in serum. It has been suggested that the salivary glands have an excretory function for this ion. There is some evidence that the concentration is higher in the saliva of cigarette smokers.

Calcium

The calcium content of the submandibular saliva is approximately twice that of parotid saliva. The concentration is high in resting saliva. Levels in submandibular saliva may exceed blood levels. This probably is due to active secretion of calcium. As the flow rate rises above resting rates, the concentration at first falls, but in fast-flowing saliva the concentration rises.

Phosphate

Almost all the phosphate present in saliva is inorganic.

Factors Affecting the Concentration of Salivary Constituents

Flow Rate in Individual Salivary Glands

These can be briefly summarized as follows:

1. Substances whose concentration increase with flow rate: total protein, amylase, sodium bicarbonate.
2. Substances whose concentration does not change with changes in flow rate: potassium, possibly fluoride.
3. Substances whose concentration falls as the flow rate increases: phosphate, urea, amino acids, uric acid, ammonia, serum albumin, magnesium.
4. Substances whose concentration falls at first but rises as flow rate increases: chloride, calcium, protein, bicarbonate.

Maintenance of Stimulus

Maintenance of stimulation to the glands for periods briefer than 3 minutes results in their reduced concentration of many components. After an initial fall, concentrations of calcium bicarbonate and protein again begin to rise. Sodium and iodine concentrations are not affected by duration of stimulation. After the first few minutes, phosphate and potassium concentrations fall and then remain steady.

Nature of Stimulus

Protein concentration in the parotid and submandibular saliva may vary with the stimulating agent. Variations in composition of whole saliva may arise from different proportions of the major secretions, either due to the greater maximum flow from the larger parotid glands or difference in stimuli susceptibility among the glands.

Time of Day

Circadian rhythms have been reported in the concentrations of protein, amylase, potassium, chloride, phosphate, organic phosphates, cortisone, and thiocyanate. In general, protein concentrations seem to be high in the afternoon and related to mealtimes. Sodium and chloride concentrations are high in the early hours of the morning. Plasma concentrations: The concentration in salivary urea, uric acid, amino acids, sodium, and chloride are related to plasma concentrations.

Hormonal Effects

Antidiuretic Hormone

The water content of saliva is affected by secretion of antidiuretic hormone. This appears to affect the permeability of striated duct cells and permits more water to be reabsorbed.

Aldosterone

Transportation of sodium and potassium in striated ducts is controlled by aldosterone, causing increased reabsorption of sodium.

Systemic Hormones

Hypophysectomy reduces secretion in animals. Testosterone and thyroxine both increase salivation. In pregnancy salivation increases, and at the menopause there is often xerostomia.

Local Hormones

Bradykinin and its precursor kallidin stimulate secretion by increased blood flow.

Influence of Diet

It is known that the size and activity of salivary glands are influenced by the degree of stimulation, either mechanical or gustatory, to which they are subjected. Increases in phosphate or calcium in the diet do not appear to affect salivary levels.

Functions of Saliva

The function of saliva may be classified as follows:

Protective Function

As a Fluid:

Saliva acts as a protective medium for the cells of the mucous membrane, preventing them from drying. The oral mucosal cells differ from squamous epithelium elsewhere, being much less protected against evaporation. Production of saliva in large quantities allows it to act as a mechanical medium, washing away particles from around the teeth.

As a Lubricant:

The lubricant action of the water of saliva is enhanced by its protein and mucoprotein content. The mouth is subjected to abrasive food substances and this abrasive action is moderated by the covering of the tissues by a viscous solution. This lubricating fluid assists in the formation of a food bolus suitable for swallowing. It is also necessary for adjustments of air flow to produce speech.

As a Solution with Antibacterial Activity:

Saliva has several components which afford protection against bacterial attack. The cells of saliva include leukocytes which may contribute to its protective activity against bacteria and the substances synthesized by them. The bacteria normally present in saliva establishes a close, interwoven ecology that foreign invading bacteria are unable to penetrate. Lysozyme is specifically active against bacteria whose cell walls contain muramic acid. The antibodies of saliva, the gamma globulins, are able to react with the antigens in the presence of some oral bacteria. An antibacterial system consisting of the globulin and thiocyanate ions has been described. Peroxidases also act as antibacterial enzymes.

As an Accelerator of Blood Clotting

A number of blood-clotting factors have already been described.

As a Factor in Maturation of Teeth

The tooth surfaces are composed of apatite crystals which can acquire ions from, or exchange ions with, saliva. The susceptibility of newly erupted teeth to solution in acid is much greater than that with which have been exposed to saliva for some time.

As a Protection to Tooth Decay/Solution in Acid

Saliva is effectively supersaturated with respect to the apatite of dental enamel. This means that only if the pH drops markedly will apatite begin to dissolve. Furthermore, saliva contains the buffer bicarbonate.

Digestive Functions

Saliva has little digestive function in the mouth, its role as a lubricant being much more important. Amylase is the main digestive enzyme.

Water Balance

The digestive secretions, including saliva, consist largely of water. This water, about 8 L/day in all, passes into the lumen of the digestive tract, which is functionally outside the body. It must therefore be reabsorbed. If this amount of water is lost, either by vomiting or diarrhea, the total body water will be depleted. Loss of water can occur due to panting or hyperpnea. Reduction in extracellular fluid volume leads to reduction in salivary volume.

Excretory Function

Saliva has been described as an excretory route for several blood components. Since saliva and its constituents usually are reabsorbed in the lower part of the gut, it would not appear to be a very efficient excretory route. Urea, uric acid, and ammonia pass into saliva. Their small size enables them to cross the membranes of the cells of the salivary glands. Thiocyanate also has been described as an excreted substance. Heavy metals including lead, mercury, and bismuth appear in saliva if blood levels are raised.

Solvent Function

Saliva dissolves foodstuffs and aids in their comminution and digestion. In addition, solubilization is essential for perception of taste.

Iodine Balance

Secretion of iodine into saliva has already been mentioned.

The Importance of Saliva in Relation to Oral Disease

Many studies have been performed on saliva with the object of linking its composition or changes in composition with oral disease, particularly dental caries. The important interactions of saliva may be summarized as its antibacterial activity, its role in plaque formation, the equilibrium between saliva and plaque constituents, and its possible effects on dental calculus formation.

Antibacterial Activity

This has already been discussed as a protective function of saliva.

Formation of Dental Plaque

The pellicle formed on clean tooth surfaces exposed to saliva is similar in composition to the glycoproteins of saliva. Saliva contains a glycoprotein which binds to apatite and therefore to the dental enamel. Saliva contains proteins which spontaneously may precipitate out of solutions or on drying. The enzyme neuraminidase is found in saliva. It is capable of changing the properties of glycoproteins by splitting off sialic acid end groups. The changed glycoproteins may precipitate on the tooth surfaces. Some salivary bacteria are capable of producing sticky polysaccharidic coats which cause them to aggregate and stick to surfaces. The layer of bacteria could then function as an initial layer of plaque.

Salivary Gland Pathology

Classification

Congenital Disease.

1. Dermoid cysts.
2. First cleft anomalies (type 1, type 2).
3. Branchial pouch.

Traumatic.

Laceration.

Inflammatory Disease.

Acute

1. Viral.
2. Bacterial (acute suppurative disease).
3. Allergic.
4. Drugs.

Chronic

1. Obstructive (calculi, stricture, sialadenitis, sialectasis).
2. Nonobstructive (postmumps sialectasis, nonspecific sialadenitis).
3. Tuberculosis, actinomycosis.
4. Benign lymphoepithelial disease (sialectasis).
5. Drugs (iodine, lead, copper).

Metabolic

Benign Hypertrophy

1. Hyperthyroidism.
2. Diabetes.
3. Alcoholism.
4. Endocrinopathies.

Benign Atrophy

1. Fatty replacement.
2. Menopausal.
3. Malnutrition.
4. Gouty parotitis.

Immunologic Disease

Sjögren's Syndrome.

Neoplastic Disease Classification

Benign

1. Benign mixed tumor (pleomorphic adenoma).
2. Papillary cyst adenoma (Warthin's tumor).
3. Oncocytoma.
4. Monomorphic adenoma.

Malignant Tumors

1. Malignant mixed tumor.
2. Mucooid epidermoid tumor (low- or high-grade).
3. Adenoid cystic carcinoma.
4. Acinous cell carcinoma.
5. Adenocarcinoma.
6. Oncocytic carcinoma.
7. Clear cell carcinoma.
8. Squamous cell carcinoma.

Cysts and Congenital Lesions of the Parotid Gland

The parotid glands are affected more frequently by congenital lesions than any other of the salivary glands. Ranules affect the sublingual gland area, and lesser salivary glands are sites for the development of retention cysts.

Cysts of the Gland

Cysts of the parotid gland account for 2-5% of all parotid gland lesions. A cystic lesion can occur in the parotid gland presenting difficulties in diagnosis. Patients may be affected at any period of life.

Acquired Cysts

The etiology includes: Obstruction of the duct or ducts (postinflammatory), neoplasms, calculi associated with benign lymphoepithelial disease, and trauma. Intermittent obstruction from stricture, calculi, or mucous plugs may lead to dilatation and cyst formation. If there is no superimposed inflammation, a retention cyst may develop. The cells lining the cysts may be cuboidal, columnar, or squamous. They develop during years of intermittent obstruction. Once obstruction is complete the secreting membrane continues to function, thus accounting for the increase in size. Treatment of the patient with obstructive cysts usually is correction by surgical excision of the whole gland, with preservation of the facial nerve.

Congenital Cysts

Congenital cystic lesions of the salivary glands also occur mainly in the parotid glands. For the most part these lesions are ectodermal in origin. The congenital lesion of the parotid glands may be divided into dermoid cysts, branchial cleft cysts (type 1 and type 2), branchial pouch cysts, and congenital ductal cysts. Clinically these cysts can present as benign lesions within the parotid gland. For convenience, congenital first cleft lesions are classified as types 1 and 2. Both have different clinical behavior. Type 1 first cleft lesions appear as sinus tracts or swelling in the region of the posterior crease of the pinna, concha, or anterior to the tragus. They are a duplication anomaly of the membranous external auditory canal. They can be positioned above, inferior, or medial to the facial nerve. The type 2 defect is also a duplication anomaly forming an anomalous external auditory canal and rudimentary pinna. Treatment of these lesions is surgical with preservation of the facial nerve.

Traumatic Lesions of the Salivary Glands

Injury to Ducts

Lacerations to the face posterior to the edge of the masseter muscle may result in damage to the parotid duct. Neglect of parotid duct injury in all probability will result in swelling of the face and salivary accumulation in a recently sutured wound. Diagnosis is made by the appearance of saliva in the wound during manual expression of the gland. Cannulation of the duct through the mouth will confirm the diagnosis. Every wound suspected of duct injury should be checked for facial nerve damage. When the duct is severed, repair over a catheter using fine, interrupted sutures. The catheter which leads into the mouth is sutured to the oral mucosa and removed in approximately 14 days. Suturing the duct is more easily accomplished using the operating microscope.

Injuries to the Facial Nerve

Laceration of the parotid duct should inevitably result in a check for facial nerve function. The main tract of the facial nerve can be damaged at the stylomastoid foramen, within the gland itself, or at the anterior edge of the parotid gland. When injury to the nerve is suspected, each division of the nerve is checked clinically. Early repair of the nerve is desirable. If delayed repair is considered necessary because of concomitant wound infection, marking of distal branches with metal clips at the time of original wound treatment is imperative.

Injuries to the Parenchyma

Damage to the parenchyma of a major salivary gland should be treated with careful debridement and layered closure of the gland. Complications include chronic extraoral fistula or salivary gland cyst.

Acute and Chronic Inflammatory Diseases of the Salivary Glands

Acute Disease

Acute suppurative sialadenitis is largely confined to the parotid and submaxillary glands. Clinically, it presents with sudden painful swelling of the gland and periglandular soft tissues, with a fever and leukocytosis. Examination reveals a firm indurated tender salivary gland, with pus expressible from the ductal orifice. The most common causative organism is the coagulase-positive staphylococcus. Approximately one-third of all cases of acute suppurative disease of the parotid gland are associated with the postoperative state. Surgical parotitis has been estimated to occur in 1:1000 postoperative patients, with bilateral presentation in 20%. Other predisposing factors include debilitation, dehydration, and poor fluid and electrolyte management. The disease may occur in children. A culture from the duct should be undertaken. A blood culture also may be obtained. Treatment is with an appropriate antibiotic and rehydration.

Chronic Recurrent Bacterial Sialadenitis

This is more characteristically seen in the parotid gland. It occasionally may be bilateral. The most common cause is duct obstruction. Other causes include debilitation or intense fluid restriction for cardiac or renal disease. Clinically it presents with a history of recurrent mildly painful gland enlargement which the patient often associated with eating. A decreased rate of salivary secretion and an alteration in the character of secretions occur. There appears to be an interrelationship between acute and chronic inflammatory disease. Sialectasis, duct ectasia, and low-grade progressive acinar destruction result. These result in further reduction in salivary flow and stasis. The advanced cases of chronic sialadenitis and fibrosis are accompanied by lymphocytic infiltration. Sialography may demonstrate duct ectasia or dilatation, with atrophy of the acinar elements. Treatment should be conservative. Sialogogues such as lemon or chewing gum may stimulate salivary flow and ductal irrigation. Periodic massage of a gland may assist. Treatment alternatives other than conservative management include tympanic neurectomy or superficial parotidectomy.

The end result of chronic sialadenitis may include sialectasia, Kussmaul's disease, and local duct obstruction by stricture. In chronic sialectasia the patient complains of diffuse swelling of one parotid gland which may slowly increase over several months or years. Histologically, saculation of the ductal and acinar elements is found with lymphocytic infiltration.

Kussmaul's Disease

As a result of mucous plugs in one or more of the collecting salivary ducts, this disease typically occurs in dehydrated patients. Recurrent swellings are common and extremely painful on eating. The most serious complication is recurrent acute suppurative sialadenitis. The treatment consists of gentle pressure and sialogogues.

Local Duct Obstruction by Stricture

The etiology of ductal stricture involving Stenson's duct includes ill-fitting dentures and poor oral hygiene. Internal stricture formation is due to calculus, infection, trauma, neoplasm, or congenital failure of development. In any event, the patients complain of periodic painful swelling. Signs and symptoms of acute infection may occur, reaching the stage of abscess formation and sepsis. Probing of the duct and sialography will outline the stricture. Treatment consists of ductal ligation, fistulization of the duct into the mouth, or gland excision. Sialolithiasis is both a cause and consequence of recurrent sialoadenitis. Stones are composed of inorganic calcium and sodium phosphate salts, and are thought to arise around a small mucous plug or debris. The sequence of events includes initial stasis of secretions with ductal metaplasia and static cellular ductal debris. Ascending bacterial infection promotes further ductal metaplasia and the formation of calcareous debris. The cycle results in progressive stone enlargement contributing to duct obstruction and low-grade recurrent sialadenitis. Complete obstruction leads to marked tissue edema and secondary acute infection. The patient complains of painful swelling when eating. A repeated history of spontaneous extrusion of small calculi from the ducts may occur. Complications include acute abscess formation, sinus tract, and salivary fistulas. Treatment consists of intraoral removal of stones. Repeated stone formation may require excision of the affected gland.

Specific Granulomatous Disease

Mycobacterium Tuberculosis

The primary tuberculosis in salivary tissue occurs most commonly in the parotid gland. Although primary infection of the parotid tissue is seen, it would seem more likely to occur from infection of the tonsils or elsewhere in the oral cavity. Treatment consists of specific antitubercula chemotherapy.

Cat-Scratch Disease

The causal agent in cat-scratch disease is thought to be a virus found in many household pets. The disease results in necrotizing granulomatous infection.

Sarcoidosis (Heerfordt's Disease)

Sarcoidosis of the uveal tract, and lacrimal and salivary glands is fairly uncommon. Parotid gland and parotid lymph node involvement is estimated to occur in approximately 6% of all cases. Diagnosis is made by biopsy. Facial nerve paralysis may occur.

Fungal Disease

Actinomycosis of the parotid gland has been reported rarely in suppurative parotitis. This infection usually follows dental extraction. Progressive symptoms are fever, weight loss, and trismus. High doses of intravenous penicillin are administered over a prolonged period of treatment.

Inflammatory Disorders of Viral Etiology

Mumps (Epidemic Parotitis)

Mumps is the most common of all salivary gland diseases. It causes an acute febrile illness with a prodrome of approximately 2-3 weeks. It primarily infects young adults and children, classically 4-7 years of age. The onset of such a disease is typified with fever, headaches, and painful swelling of the parotid glands. Serum antibodies to mumps S and V antigens with a titer of greater than 1:920 indicates recent infection. Complications of the disease include parotid gland sialectasia, recurrent chronic suppurations, unilateral hearing loss, diabetes secondary to pancreatic fibrosis, sterility secondary to gonadal involvement, and meningoencephalitis.

Salivary Gland Inclusion Disease

This is a disease occurring in neonates and is a form of cytomegalic inclusion disease. Infection occurs transplacentally, without evidence of maternal disease. Hepatosplenomegaly, jaundice, thrombocytopenic purpura, and involvement of the nervous system can occur. Other variants may produce local parotitis. The diagnosis rests on viral isolation.

Secondary Inflammatory Disorders of the Salivary Glands

Radiation

Radiotherapy for lesions of the head and neck causes acute tender swelling of the major salivary glands. A resultant destruction and atrophy of the minor salivary glands occurs. Dryness of the mouth will develop. Drug effects on salivary glands are of two distinct types:

Idiosyncratic and Direct Effects: Direct effects include clinical sialadenitis following injection of certain heavy metals, including mercury and bismuth. Iodine causes diffuse and tender swelling of the salivary glands within 2-3 days of injection. Salivary gland enlargement also has been noted as an idiosyncratic effect. Atropine derivatives cause enlargement of the glands because of the side effect of making saliva more viscid and thick. Phenylbutazone has been noted to produce xerostoma in 20% of the patients. Phenothiazine derivatives all exert

an atropine-like effect. Other drugs noted to cause gland enlargement include methimazole, thiocyanates, and thiourea.

Immunological Diseases of Salivary Glands

Sjögren's Syndrome

Sjögren's syndrome is characterized by a triad of symptoms: xerostoma, keratoconjunctivitis sicca, and a connective tissue disorder. The latter is more commonly rheumatoid arthritis in over 50% of the cases, but systemic lupus, polyarteritis nodosa, dermatomyositis, or scleroderma may accompany the other features. Sjögren's syndrome should be distinguished from Mikulicz's disease, an enlargement of the lacrimal and parotid glands of unknown origin. Women are affected by Sjögren's syndrome more frequently than men. The first signs are seen in early middle-age.

Manifestations in the oral cavity are always present, but may only be elicited on careful examination. Dry lips or mouth and diminished salivary flow are the two most common symptoms, often accompanied by difficulty in masticating food and by dental problems. A routine oral examination reveals dryness and cracking of the oral mucosa. The parotid glands generally are enlarged bilaterally and the patient may have noticed a chronic progressive enlargement. Major histopathologic features are atrophy and loss of acinar tissue, with distortion of lobular architecture. Lymphoid infiltration occurs.

The serum proteins in Sjögren's syndrome include a rise in the gamma globulin fraction. Hypergammaglobulinemia usually is broad-based with the IgG fraction being particularly elevated. The rheumatoid factor in Sjögren's syndrome is significantly increased. Antinuclear antibodies are common in Sjögren's syndrome, with most investigators reporting their presence in more than 50% of the patients.

Tumors of the Parotid Gland

Management of Benign Parotid Tumors

Benign Mixed Tumor (Pleomorphic Adenoma)

Benign mixed tumors of the parotid gland account for up to 75% of all parotid tumors. Treatment is surgical excision of the parotid gland with preservation of the facial nerve.

Warthin's Tumor (Adenocystoma Lymphomatosum)

Warthin's tumor accounts for approximately 20% of the benign tumors involving the salivary glands, occurring most commonly in males in the fifth decade. It is notable for its tendency toward multiplicity, bilateral tumors of this type being common. This occasionally makes evaluation of tumor recurrence somewhat difficult. It is interesting to note that of 120 patients studied in Barnes Hospital, eight lesions (approximately 6%) were discovered as occult tumors in the radical neck dissections that were done to control reasonable extension of another tumor. As Warthin's tumors have a low incidence of recurrence, parotidectomy with facial nerve preservation is the treatment of choice.

Management of Malignant Parotid Tumors

It should be remembered that while a consensus of opinion exists concerning the management of facial nerve in the treatment of benign tumors of the parotid gland, this is not the case with malignant tumors. A disparity of opinion exists in the relationship with reference to definitive treatment.

Diagnosis

When considering treatment for the management of malignant tumors of the parotid gland, histologic diagnosis is important. Hamberger has stated that the prerequisite for adequate treatment of parotid tumors is the correct diagnosis based on a well delineated histologic type of tumor. It seems that the histologic type, the biologic behavior, and the size of the tumor all may influence the proposed treatment regimen. In view of this, each of the major histologic types will be discussed in relation to facial nerve preservation, and whether or not radical neck dissection would be of benefit to the patient.

Mucoepidermoid Carcinoma

The most common type of malignant tumor found in the parotid gland is the mucoepidermoid carcinoma. This tumor accounts for 50% of all malignant tumors reported in a major series. It is a tumor of varying malignant potential, usually separate into three major grades: low grade, intermediate grade, and high grade. By far the most common is the low-grade malignancy, occurring in approximately 70-95% of the series presented. In low-grade mucoepidermoid carcinoma (female/male ratio is 2:1) it would appear that unless the facial nerve is affected, parotidectomy with facial nerve preservation, without radical neck dissection, is the treatment of choice.

In high-grade mucoepidermoid carcinoma a wide en bloc excision with a radical neck dissection should be done. The facial nerve would be sacrificed if it in any way compromised a surgical margin. It is felt that because of the high recurrence rate and low 5-year survival rate (41%), a total radical parotidectomy with sacrifice of the facial nerve should be performed, with an accompanying radical neck dissection. Intermediate-grade tumors present difficulty in management, but probably can be managed similar to low-grade lesions, reserving radical neck dissection for those patients showing clinical evidence of cervical lymph node involvement.

Acinar Cell Carcinoma

Acinar cell carcinoma has been described as an uncommon low-grade, slow-growing malignant tumor. It is said to constitute approximately 10% of all malignancies of the parotid gland. There is a low incidence of tumor spread to regional lymph nodes (8%). In view of this, treatment for acinar cell carcinoma of the parotid gland should be total excision of the gland with preservation of the facial nerve unless to do so would compromise the surgical margins. In view of the limited number of node metastases reported, elective radical neck dissection is probably not indicated.

Adenocystic Carcinoma (Cylindromas)

These tumors are relatively rare in the parotid gland, constituting 2% of the parotid neoplasms reported. Although slow growing, adenocystic carcinoma is characterized by its propensity for nerve invasion and late recurrence. Because of this tendency for late metastasis it is difficult to analyze the effectiveness of various treatment regimens. Surgical survival based on 5-year observations are inadequate for proper evaluation. A reasonable treatment for patients with adenocystic carcinoma should consist of a total parotidectomy including a wide cuff of parotid tissue, with dissection of the upper jugular and subparotid lymph nodes. The facial nerve probably should be sacrificed because of the propensity of this tumor for perineural invasion. Frozen section biopsies of the severed nerve should be obtained until clear margins are reported. There seems to be no advantage to performing elective radical neck dissection because of the low instance of metastatic involvement of the cervical nodes. Postoperative irradiation also should be considered. The 5-year survival is 30%.

Malignant Mixed Tumor

The treatment of a mixed malignant tumor is difficult based on current reports and literature. Although far from conclusive, the evidence points to treatment of these tumors with a total parotidectomy, plus dissection of the subparotid nodes and upper jugular nodes, with sacrifice of the facial nerve whenever necessary to preserve the surgical margins. With the rate of documented cervical metastases ranging from 20-25%, the overall benefit to the patient of a radical neck dissection is open to question, especially in view of the high incidence of recurrence following radical neck dissection. Most authors agree that radical neck dissection is indicated when positive lymph nodes are apparent. The benefit of elective dissection is in doubt.

Adenocarcinoma

Adenocarcinoma appears histologically to be of two types: Type 1 exhibiting low-grade characteristics and responding to a treatment regimen of subtotal parotidectomy and partial resection of the facial nerve as necessary. Type 2 is a high-grade tumor, where treatment with radical parotidectomy and neck dissection appears imperative. In the treatment of low-grade adenocarcinoma with subtotal parotidectomy and partial resection of the facial nerve where necessary, radical neck dissection appears probably of no benefit. Such treatment leads to a survival rate of approximately 95%. In the treatment of high-grade adenocarcinoma, total parotidectomy and facial nerve sacrifice appears to be the treatment of choice. Even so, a survival rate of 40% appears to be the normal range.

Squamous Cell Carcinoma

Squamous cell carcinoma of the parotid gland occurs in approximately 3-20% of all malignancies of the parotid gland. With a determined 5-year survival rate in the range of 20%, total parotidectomy with excision of a wide margin of normal tissue and a radical neck dissection with facial nerve sacrifice appears to be the treatment of choice.

Since metastases to the cervical lymph nodes range from 50-75% it seems reasonable that a radical neck dissection should be part of the primary treatment plan.

Undifferentiated Carcinoma

Undifferentiated carcinoma constitutes a small portion of malignant tumors of the parotid gland. It appears that no matter what treatment regimen is selected, prognosis for the patient with undifferentiated carcinoma is poor. The accepted treatment consists of radical parotidectomy with facial nerve sacrifice and a radical neck dissection.

Management of Severed Facial Nerve

After the decision has been made to sacrifice the facial nerve, the surgeon immediately faces the question of how to deal with the consequences of his treatment. It would seem reasonable that if no contraindications exist, repair of the severed facial nerve should be accomplished wherever possible. Surgical repair is rarely possible or indicated when the main trunk and its branch were excised. Such resection usually extend from the stylomastoid foramen, sacrificing most of the peripheral branches and leaving little to graft. Therefore, surgical repair and nerve grafting are considered unrealistic in patients requiring radical ablative surgery, radiation, and with a poor prognostic post-treatment.

On the other hand, patients with low-grade mucoepidermoid mixed tumors or adenocystic carcinoma can and may be treated with immediated nerve grafts.

In general, the direct immediate autograft of a free nerve graft, when feasible, gives results superior to those of cross-over anastomosis.

Tumors of the Minor Salivary Glands and Submaxillary Glands

Treatment of tumors of these two areas in no way differs from that of treatment of the parotid gland. In the submaxillary gland, benign tumors account for 50% of the tumors found.

Of carcinomas in the submaxillary gland, adenocystic carcinoma is the most common. In minor salivary glands and the sublingual glands the incidence of malignancy is 80% while in parotid glands it is 20%.

Oncocytoma (Oxyphil Adenoma)

This benign tumor is a well-encapsulated circumscribed lesion with cystic areas. The predominant cell type is the eosinophilic oncocyte. The peak age for this tumor is the sixth or seventh decade. The treatment of choice is a superficial parotidectomy to include good margins of the tumor mass.

Recurrence is possible with incomplete excision.

Survival for Malignant Tumors of the Salivary Gland

Survival for malignant tumors of the salivary gland appears not to follow the rules that are normally set for cancers of the head and neck. Survival in terms of 5 years may not be appropriate for many of these lesions in view of their propensity for slow growth and ultimate

reappearance up to 20 years after the initial diagnosis. Successful treatment is dependent upon an accurate pathologic diagnosis with appropriate management.

Factors Affecting Cure Rate

Facial Nerve Paralysis

Facial nerve paralysis in association with a parotid gland mass is generally believed to carry an adverse prognosis. The survival rate after the onset of facial nerve paralysis appears to be 2.7 years. The instance of metastases in patients with facial nerve paralysis is high.

Pain

Pain does not appear to be a useful criteria for malignancy. There appears to be an equal instance of pain in both benign and malignant tumors.

Other Facts

It would appear that the younger the patient the better the prognosis probably related to the high instance of low-grade tumors in the younger age group. Fixation to a deep structure with extension beyond the confines of the parotid and with neck metastases obviously reduce the survival figures.

Tumors of the deep portion of the gland appear to have a survival rate similar to those in the body or tail.

Survival rate obviously depends on the pathologic diagnosis with low-grade mucoepidermoid and acinous cell carcinoma, allowing excellent survivals. Malignant mixed, undifferentiated carcinoma, squamous cell carcinoma, and adenocarcinoma would appear to have a much poorer survival rate.

At this time, the clinical staging (TNM) system of classification of salivary gland neoplasms is not widely used or accepted. The American Joint Committee for Cancer Staging end results were reported in 1976 and a clinical classification system proposed for major salivary gland tumors. This system has not been tried.

T1: Solitary nodule, freely mobile, 0-3 cm. Facial nerve intact.

T2: 3-6 cm, solitary, freely mobile or reduced mobility of nodule or with skin fixation. Facial nerve intact.

T3: Greater than 6 cm, multiple nodules, ulceration, or deep fixation. Facial nerve dysfunction.

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