*Lewis Menaker*

# THE BIOLOGIC BASIS OF DENTAL CARIES

*an oral biology textbook*

# The Biologic Basis of Dental Caries

## AN ORAL BIOLOGY TEXTBOOK



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*Biologic Basis of Dental Caries*
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# The Biologic Basis of Dental Caries

AN ORAL BIOLOGY TEXTBOOK

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*With 27 Contributors*

*To our parents*

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# Preface

The maturation of dentistry from a craft to a healing art and science has been made possible by the changes in, and growth of, our scientific knowledge base. A progression from emphasis on removing a focus of infection by extracting a diseased tooth, to the therapeutic repair by restoration with a filling material, to the prevention of disease has been a reflection of the information available and subsequently transferred to the clinician. What is important to understand is that the driving force for the advancement of patient care has been our expanding understanding of the disease itself and the translation of this information through the educational process.

The central role of dental caries in the clinical practice of dentistry establishes without question the importance of this subject to both the student and practitioner. The present explosion in our knowledge of this subject has underscored the increased complexity of this condition as a disease process, the essentiality of a multidisciplinary approach to the understanding of this problem, and the importance of a rationale of patient care centered on the concept of preventive interception. Accepting these premises, we see the threefold goal of this text: (1) to bring the reader to a new level of appreciation of the unity of knowledge too often segregated by dental educators into clinical and basic sciences; (2) to provide the reader with current scientific evidence upon which clinical judgment must be based; and (3) to introduce the reader to the field of caries research in a manner that will provide a basis for future understanding of the burgeoning scientific literature in this field.

To accomplish these objectives this book has been designed around a framework of host, vector, and environmental factors that not only bear on the disease itself but also on those aspects that determine caries prevention. The complexity of etiology, interactions, mechanisms, and principles presented here is testimony to the advances that dentistry has made as a scientifically based profession. The need for our profession to expand knowledge continually is not optional; the responsibility to expand, understand, and apply such knowledge is mandatory. It is hoped that this book will be an aid in meeting these obligations.

*Lewis Menaker*
*Robert E. Morhart*
*Juan M. Navia*

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PART ONE

# The Host

## A. Saliva and Salivary Glands

# 1 Microanatomy of Human Salivary Glands*

WALTER H. WILBORN
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## INTRODUCTION

Salivary glands are important glands of the digestive system that produce digestive enzymes, withdraw constituents from the plasma, and serve many other functions that directly or indirectly influence oral health in general and dental caries specifically. A knowledge of the microscopic anatomy of these glands is the keystone for understanding their function. This information also provides a basis for appreciating the multifaceted investigative work on salivary glands which includes a broad spectrum of inquiry and is reported in many scientific journals.

Because the salivary glands are convenient for extirpation, produce secretions that are easily collected, and are composed of fundamental tissues which respond to a variety of the same stimuli as other tissues of the body, they serve as ideal models to study many areas of modern biology. They have provided much new information related to protein synthesis (See Chap. 2 and 3), ion and water transfer (See Chap. 4), epithelial-mesenchymal interactions, tissue regeneration, uptake of radioactive substances, and the pathogenesis of tumors. Ablation of salivary glands or alterations of their secretions have given insight into the initial formative stages of caries, calculus, and peridontal disease. Many biologically active substances, including nerve growth factor, parotin, serotonin, kinin, and lysozyme, have been isolated from salivary glands and are of special interest to biologists.

Salivary glands also serve as models to study the effects of hormones, diet, and the autonomic nervous system on glandular structure and function. For example, thyroxine and sex

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hormones alter the metabolism, histology, and histochemistry of salivary glands; liquid diets result in major ultrastructural alterations of acinar cells of the parotid gland; and the autonomic nervous system maintains the functional and structural integrity of salivary glands and plays a role in regulating the development of immature glands.

Since most previous works on salivary glands have dealt with laboratory animals, the material presented here summarizes the most significant microscopic features of normal human salivary glands. A brief account of salivary glands in other forms is also included for comparative purposes. Inclusion of the major and minor salivary glands within a single chapter benefits the student, since a report of this type has not previously been published and the information available is spread throughout many books, symposia, and journals, where it is difficult to survey.

## PHYLOGENETIC CONSIDERATIONS

*Salivary glands* can be defined as glands that secrete into the anterior part of the digestive tract. On the basis of this broad definition, salivary glands are found in many groups of animals, invertebrates as well as vertebrates.

Among the invertebrates, salivary glands have been studied in worms, molluscs, and arthropods. The anticoagulant substances of leeches, tsetse flies, and mosquitos, the silk of certain insects, and the toxin of octopuses are examples of salivary gland secretions. In some forms, as in flatworms, the cells comprising the salivary glands are morphologically so simple that they can be distinguished from the surrounding epithelial cells only by their larger size. In contrast, salivary glands of certain insects attain marked structural and functional development and may secrete amylase, as in the case of the cockroach. The salivary glands of invertebrates and vertebrates are certainly not homologous, but in some cases, their functions of lubrication and initiation of the digestion of food are interestingly similar.

Fish, the earliest vertebrates, usually do not have salivary glands. Mucous secretions in their oral cavity are from unicellular glands constituting part of the epithelial lining of the oral cavity. One excepton is the lamprey eel, a parasite, which has large salivary glands that open by ducts into the sucker where the juice is added to the blood and flesh ripped from the prey. Other exceptions are found in at least two species of the salt water male catfish. These fish contain deep oral crypts, also called brood pouches, where fertilized eggs are carried and kept moist by goblet cell secretions.

Beginning with amphibians, terrestrial tetrapods have characteristically large numbers of oral glands, but the number is markedly reduced in practically all aquatic tetrapods. This is no handicap because salivary glands are unnecessary for lubrication in the aqueous environment. The salivary glands of amphibians are mucous glands with ducts lined by ciliated epithelium. Although lingual glands occur in all amphibians, only anurians have internasal glands whose ducts open into the anterior part of the oral cavity. These glands in frogs secrete a sticky substance that is deposited on the tongue and assists in the capture of insects.

The oral glands of reptiles (other than the aquatic forms such as turtles and crocodiles) are more highly developed than those of amphibians. They may contain serous cells, in addition to mucous cells, and are divided into groups: 1) palatal, 2) lingual, 3) sublingual, and 4) labial. Venom glands of poisonous snakes are serous salivary glands homologous to the parotid glands of mammals. The Gila monster, the only poisonous lizard, has lingual salivary glands that produce a poison. When biting a prey, the venom travels along fanglike grooved teeth into the wound.

Salivary glands of birds are poorly developed. There are, however, aggregations of mucous cells in the lingual, sublingual, and parotid regions; smaller collections of similar cells occur in the wall of the oral cavity. The glands, as in the chicken, produce a mucous secretion that lacks digestive enzymes.

Mammals, the only animals that chew their food, possess three pairs of major salivary glands in addition to the minor salivary glands of the lips, tongue, cheeks, and palate present in other terrestrial forms. Of the major salivary glands (parotid, submandibular, and sublingual glands), only the parotid and submandibular are characteristic of all mammals. Both glands secrete *ptyalin* or *amylase*, the enzyme that hydrolyzes starches to maltose.

The position of the major salivary glands is variable with the exception of the parotid which is closely related to the external ear. In general, submandibular glands lie near the angle of the mandible in animals with flattened faces, such as man; they are in the ventral cervical region in animals with elongated faces such as rodents. Sublingual glands of man occupy a position beneath the tongue in the floor of the oral cavity. They vary in anatomic position in other forms and may be absent.

Salivary glands have not been studied in all mammals, but enough information is available to illustrate the influence of environment and feeding habits on these glands. For example, the rudimentary salivary glands of aquatic mammals, such as seals and whales, are probably related to life in water and to a lack of starch in the diet. Parotid glands are usually larger than submandibular glands in herbivorous mammals (e.g., the cow and beaver). This fact is well illustrated among bats, in whom parotid glands are larger than submandibular glands in frugivorous forms and smaller in insectivorous forms. The variation in size of salivary glands is no doubt related functionally to the needs of the organism for a particular type of secretion.

The major salivary glands of most mammals are not essential for life, but sheep die when deprived of the secretion from their parotid glands; newborn rats also die after removal of submandibular and major sublingual glands. The submandibular, parotid, and sublingual glands of man function respectively in tasting, masticating, and swallowing food. In addition to these functions, secretions of the major salivary glands keep the mouth wet and help clean the teeth. They also produce amylase which begins the digestion of starches within the oral cavity.

## ANATOMIC CLASSIFICATION OF GLANDS

Salivary glands comprise an important group of glands of the digestive system. Like other glands, they are composed of specialized epithelial cells, referred to as *parenchyma*, and of connective tissue, called *stroma*. The stroma surrounds and supports the epithelial cells and serves as a passageway for nerves, blood vessels, and lymphatics. It contains collagenous fibers, fibroblasts, macrophages, plasma cells, and mast cells.

Differences in glandular morphology have given rise to various anatomic classifications of glands that must be understood to conceptualize glandular architecture. The simplest classification is based on the number of cells comprising the gland. Accordingly, glands are classified as unicellular or multicellular. The only unicellular gland in man is the goblet cell.

The terms *exocrine* and *endocrine* are used to classify glands according to the presence or absence of ducts. Salivary glands are exocrine glands because they have ducts in which the secretion is conveyed toward the oral cavity. Endocrine glands (*e.g.*, the hypophysis cerebri and the thyroid gland) lack ducts and secrete hormones directly into the blood or lymph. They are also called ductless glands or glands of internal secretion. Some glands, such as the pancreas, are both exocrine and endocrine. There is some evidence that the major salivary glands also produce hormones (e.g., parotin), but this concept remains to be firmly established before salivary glands can be classified as endocrine. Parotin is believed to stimulate growth of tissues derived from mesenchyme.

The terms *merocrine* or *eccrine*, *apocrine*, and *holocrine* are often used to classify glands according to the mode by which they liberate their secretory product. Most gland cells (e.g., parotid and pancreatic acinar cells) secrete by the merocrine method; (i.e., they discharge their secretion without any loss of cytoplasm). The process of discharging the secretion is referred to as *exocytosis*. It is the reverse of *endocytosis* or *pinocytosis*, in which a cell takes up raw materials for use within the cell, as for the synthesis of secretory products. Some gland cells, such as those of apocrine sweat glands, lose part of their apical cytoplasm during the process of discharging their secretion, and are said to secrete by the apocrine method. Electron microscopy shows that cells lining large excretory ducts also secrete by the apocrine method, and their apices have been identified in the saliva. Cells that secrete by the holocrine method are found, e.g., in sebaceous glands. Holocrine secretion requires that the cell fill itself with its own secretory product, which is liberated by the cell's breaking open and dying. Surviving cells must multiply to replace those lost if the gland is to continue its secretory activity.

Glands are also classified according to the nature of their secretion as serous, mucous, mixed, or seromucous. Serous glands contain only serous secretory cells, arranged in "grapelike" or "saclike" clusters called acini, which produce a thin, watery secretion rich in enzymes. The parotid gland and pancreas are examples of purely serous glands. Mucous glands contain only mucous secretory cells, which are usually arranged in elongated tubules, rather than as acini. The cells produce a viscid, slimy secretion. Minor salivary glands of the soft palate are examples of purely mucous glands. Mixed glands contain both serous and mucous secretory cells. Human submandibular and sublingual glands are examples of mixed glands. The consistency of the secretory product varies from thick to thin and depends on the proportion of mucous to serous cells within the gland. Seromucous glands, composed of seromucous secretory cells arranged as acini, produce a secretion intermediate between watery and viscous. Seromucous salivary glands are absent in man but are found in certain rodents. Although other glands of the seromucous type do occur in man, as in the nasal cavity, they show considerable histophysiologic variation among individuals.

Exocrine glands can be classified according to their duct system as simple or compound. Simple glands have an unbranched duct system that connects with one or more secretory end pieces (Fig. 1-1A–D). There may be slight branching of the duct at the point of origin of the secretory end pieces (tubules or acini). Compound glands have a highly branched duct system (Fig. 1-1E–F). Secretions pass from secretory end pieces into small ducts and then into larger ducts. The site of termination of the main duct represents the point where the gland arose embryologically.

Secretory end pieces of simple or compound glands resemble tubules, alveoli, or

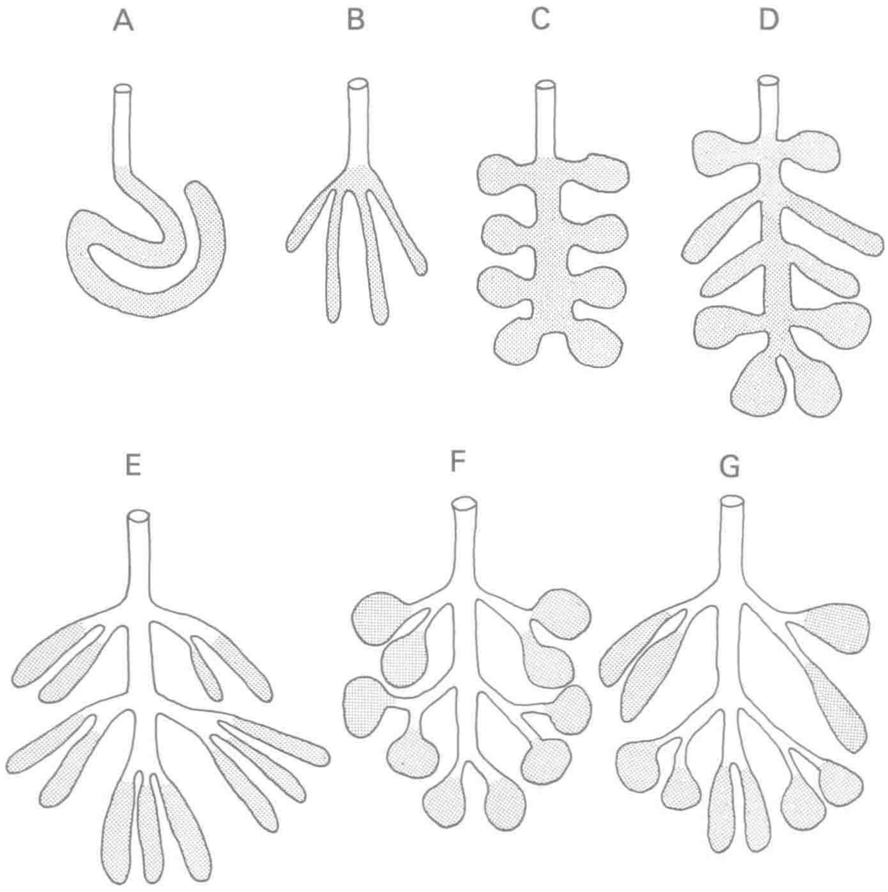


Fig. 1-1. Diagrams of various types of exocrine glands. **A–D.** Simple glands with unbranched ducts. **E–G.** Compound glands with branched ducts. **A.** Simple coiled tubular. **B.** Simple branched tubular. **C.** Simple alveolar. **D.** Simple tubuloalveolar. **E.** Compound tubular. **F.** Compound alveolar. **G.** Compound tubuloalveolar.