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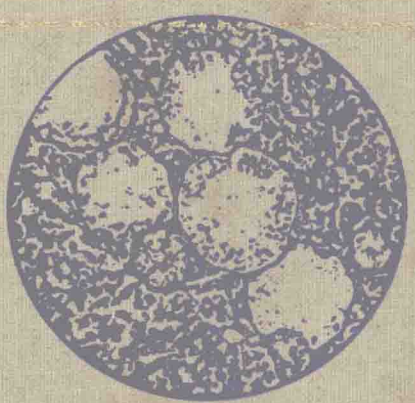
ANDERSON'S PATHOLOGY

EDITED BY

JOHN M. KISSANE



EIGHTH EDITION

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ANDERSON'S PATHOLOGY

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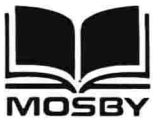

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ANDERSON'S
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Preface to eighth edition

Readers and followers of this book will have noticed that this is the first edition in which Dr. W.A.D. Anderson ("Wad" to his innumerable friends) has not actively participated. He remains vigorous and active, however, and has offered welcome encouragement and advice. We all wish him well.

Since the preparation of the seventh edition, spectacular advances have occurred in the basic sciences and in clinical medicine, on which pathology depends and to which it contributes. Advances in immunopathology and hematopathology, to mention only two general areas, and in diseases of the breast and of somatic soft tissues, to mention only two organ systems, have compelled revision of the text.

My first responsibility as editor was to examine the organization of the book to see if major structural revision was in order. I have retained the initial presentation of mechanisms both as a didactically effective transition between the basic sciences and pathology and as a review for readers whose exposure to the basic sciences has not been recent. This section of the book is followed by considerations of diseases of the various organ systems. The emphasis throughout is on the mechanisms whereby normal phenomena and processes become disturbed, giving rise to diseases and lesions.

The seventh edition introduced a chapter on geographic pathology. Even by that time, however, the Jet Age had made geographic pathology an authentic subspecialty with a language and information base of its own. It deserves separate consideration without the duplication of language and concepts that its introduction in a primary pathology text would impose. Thus, with some regret, I decided to remove the chapter on geographic pathology and rely on contributors of organ-system chapters to include geographic factors in their discussions of the epidemiology of various disorders. This effort I believe has been effectively addressed in this edition.

I chose also not to include a separate chapter on venereal diseases. Such a chapter has, over several decades, come to include sociologic and public health considerations that transcend the mechanisms and morphologic expressions of the venereal diseases. These aspects are more appropriately dealt with in works directed to public health or preventive medicine than in a work on pathology. In this edition venereally transmitted diseases are considered along with other agent-mediated diseases.

In the preparation of this edition I have been fortunate in being able to recruit several new contributors. I welcome their contributions and at the same time express my appreciation to previous contributors.

Finally, I would like to express my gratitude to the generation of supporters of *Anderson's Pathology*. I hope the eighth edition continues to merit their support.

John M. Kissane

Preface to first edition

Pathology should form the basis of every physician's thinking about his patients. The study of the nature of disease, which constitutes pathology in the broad sense, has many facets. Any science or technique which contributes to our knowledge of the nature and constitution of disease belongs in the broad realm of pathology. Different aspects of a disease may be stressed by the geneticist, the cytologist, the biochemist, the clinical diagnostician, etc., and it is the difficult function of the pathologist to attempt to bring about a synthesis, and to present disease in as whole or as true an aspect as can be done with present knowledge. Pathologists often have been accused, and sometimes justly, of stressing the morphologic changes in disease to the neglect of functional effects. Nevertheless, pathologic anatomy and histology remain as an essential foundation of knowledge about disease, without which basis the concepts of many diseases are easily distorted.

In this volume is brought together the specialized knowledge of a number of pathologists in particular aspects or fields of pathology. A time-tested order of presentation is maintained, both because it has been found logical and effective in teaching medical students and because it facilitates study and reference by graduates. Although presented in an order and form to serve as a textbook, it is intended also to have sufficient comprehensiveness and completeness to be useful to the practicing or graduate physician. It is hoped that this book will be both a foundation and a useful tool for those who deal with the problems of disease.

For obvious reasons, the nature and effects of radiation have been given unusual relative prominence. The changing order of things, with increase of rapid, worldwide travel and communication, necessitates increased attention to certain viral, protozoal, parasitic, and other conditions often dismissed as "tropical," to bring them nearer their true relative importance. Also, given more than usual attention are diseases of the skin, of the organs of special senses, of the nervous system, and of the skeletal system. These are fields which often have not been given sufficient consideration in accordance with their true relative importance among diseases.

The Editor is highly appreciative of the spirit of the various contributors to this book. They are busy people, who, at the sacrifice of other duties and of leisure, freely cooperated in its production, uncomplainingly tolerated delays and difficulties, and were understanding in their willingness to work together for the good of the book as a whole. Particular thanks are due the directors of the Army Institute of Pathology and the American Registry of Pathology, for making available many illustrations. Dr. G.L. Duff, Strathcona Professor of Pathology, McGill University, Dr. H.A. Edmondson, Department of Pathology of the University of Southern California School of Medicine, Dr. J.S. Hirschboeck, Dean, and Dr. Harry Beckman, Professor of Pharmacology, Marquette University School of Medicine, all generously gave advice and assistance with certain parts.

To the members of the Department of Pathology and Bacteriology at Marquette University, the Editor wishes to express gratitude, both for tolerance and for assistance. Especially valuable has been the help of Dr. R.S. Haukohl, Dr. J.F. Kuzma, Dr. S.B. Pessin, and Dr. H. Everett. A large burden was assumed by the Editor's secretaries, Miss Charlotte Skacel and Miss Ann Cassady. Miss Patricia Blakeslee also assisted at various stages and with the index. To all of these the Editor's thanks, and also to the many others who at some time assisted by helpful and kindly acts, or by words of encouragement or interest.

W.A.D. Anderson

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CHAPTER 25

Face, Lips, Tongue, Teeth, Oral Soft Tissues, Jaws, Salivary Glands, and Neck

ROBERT J. GORLIN

FACE AND LIPS

Developmental anomalies including minor variations from normal

Facial clefts. Facial cleft, occurring in approximately 1 of every 800 births in whites, may exist as an isolated anomaly or in combination with other developmental disturbances (about 15% of clefts are so associated). Clefts have a racial predilection. They are most common in Native Americans (about 1 in 250) and least common in blacks (about 1 in 2500). Clefts in combination with other developmental disturbances may be so well known as to constitute a syndrome. Over 200 cleft syndromes are known[14]; only a few will be discussed here. Similarly, details of lateral and oblique facial clefts, cleft uvula, and microforms are left for comprehensive discussions elsewhere.[3,10]

Facial clefts arise from the failure of the ectomesenchyme to cross the junction of fusion of facial processes about the seventh week in utero. Thus cleft upper lip (harelip), the most common facial cleft, results from failure of fusion of the lower part of the median nasal (globular) process with the maxillary process. Unilateral cleft is about eight times more common than bilateral involvement. It is more common in males (about 60%) and on the left side (about 2:1). The degree of cleavage may vary from a slight notch at the lateral border of the philtrum to a complete separation extending into the nostril.

Commonly (in about 50% of cases), cleft lip is associated with cleft palate. When the cleft extends through the line of fusion between the primary and secondary palates, the area subsequently to be occupied by the developing lateral incisor frequently is disturbed. Supernumerary, impacted, or (most commonly) missing maxillary lateral incisors often are observed.

Cleft palate also may exist to varying degrees, ranging from bifid uvula to complete cleft. Not uncommonly, a submucous palatal cleft may remain undetected. Cleft palate unassociated with cleft lip (about 25%) is seen more commonly in females. Associated with abnormally small mandible (micrognathia) and tongue (microglossia) and posterior displacement of the tongue (glossoptosis), it is known as Pierre Robin syndrome. Cleft lip and cleft palate are commonly associated with chromosomal abnormalities; for example, cleft lip or cleft palate or both are seen in about 65% of infants with trisomy 13 and 4p-syndrome and in about 15% of the cases of trisomy 18.[2,3,13]

The tongue is cleft into two to four lobes in association with asymmetric cleft palate, pseudocleft of the upper lip, and digital anomalies in the orofaciodigital syndrome.[16]

Congenital lip pits. Congenital paramedian pits of the lower lip vary in size from small bilateral dimples on the vermilion border to large snoutlike structures in the midline (Fig. 25-1). Resulting fistulas are lined by stratified squamous epithelium and are connected at the base with the mucous glands of the lip by means of communicating ducts. Mucus may exude from the openings.

The pits may occur alone or in combination with cleft palate or cleft lip and agenesis of second premolars as part of a syndrome. Inheritance is autosomal dominant with variable expressivity.[18] An unrelated condition, commissural lip pits, is observed on one or both sides in up to 15% of those examined.[12]

Fordyce's granules. Fordyce's granules are collections of sebaceous glands symmetrically located on the lateral vermilion part of the upper lip and on the buccal mucosa of approximately 65% of adults. They increase in number during mature adult life. The most common oral mucosal sites are lateral to the angle of the mouth about Stensen's papilla and lateral to the anterior pillar of the fauces.[17]

TONGUE

Developmental anomalies

Aglossia, microglossia, and macroglossia. Aglossia and its modification, microglossia, are rare congenital anomalies. Often, severe hypoglossia is associated with other defects, especially diminution of the extremities (hypo-

glossia-hypodactylia syndrome). The tongue, although apparently absent, is present as a small nubbin located posteriorly in the mouth and consisting essentially of that part normally developed from the copula. Cleft palate and bony fusion of the jaws have been associated with aglossia and microglossia.[3]

The term *macroglossia* is rather nonspecific, referring only to the presence of an enlarged tongue. In cases observed at birth or in the neonatal period, the usual cause is lymphangioma or hemangiolymphangioma, although rarely there may be true muscular hypertrophy or enlargement caused by congenital neurofibromatosis. Enlargement of half the tongue occurs in congenital hemifacial hypertrophy. The tongue may protude from the mouth in trisomy 21 syndrome, congenital hypothyroidism, Hurler's syndrome, Beckwith-Wiedemann syndrome, glycogen storage disease type 2 (Pompe's disease), and many other conditions.[20]

Lingual thyroid gland. The presence of thyroid tissue within the tongue indicates arrested, partial, or incomplete embryologic descent of the gland. Approximately 10% of patients at autopsy have ectopic lingual thyroid tissue. Although the heterotopic tissue may occur anywhere along the normal path of the thyroglossal tract, the most frequent location is the base of the tongue at the foramen cecum. When superficial, the tissue is often raised, purplish, and crenulated and may be associated with hemorrhage. About 25% of patients are hypothyroid. The incidence appears to be about 1 in 3000 patients with thyroid disease. Grossly, the heterotopic nodule measures about 2 to 3 cm and resembles the normal thyroid gland, although encapsulation is often less well defined.[21]

Median rhomboid "glossitis." Median rhomboid "glossitis" is manifest as a roughly diamond-shaped reddish pattern on the dorsum of the tongue, immediately anterior to the circumvallate papillae. Occurring in somewhat less than 1% of individuals, it reportedly represents developmental failure of coverage of the tuberculum impar by the lateral tubercles of the tongue. *Candida albicans* infection has also been suggested as playing an etiologic role, but a cause-and-effect relationship has not been proved. It may arouse suspicion of malignant neoplasm in the minds of clinicians unaware of the nature of this condition.[19]

Fissured tongue. Fissured tongue occurs in about 5% of the population, with the frequency increasing with age. It is noted more commonly in trisomy 21, being present in about 30% of affected individuals, and is also part of the Melkersson-Rosenthal syndrome (upper facial edema, facial palsy, cheilitis granulomatosa, buccal mucosal plication).[94]

TEETH

Developmental anomalies

Anomalies of number. Rarely is there complete absence of teeth (anodontia) or noticeable suppression in tooth formation (oligodontia). More commonly, a mild reduction in number (hypodontia) is observed.[10,31] The third molars, and less commonly the maxillary lateral incisors and second premolars, are the teeth most likely to be missing. Irradiation of the jaws may injure or inhibit developing tooth buds. Supernumerary teeth occasionally are observed—most commonly mesiodens in the midline of the maxilla and extra molars posterior to the third molars.

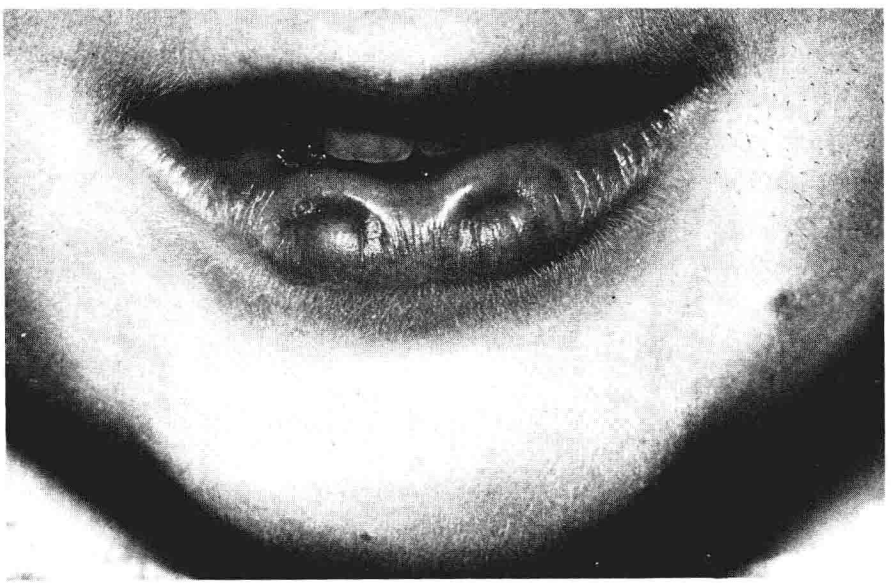

Fig. 25-1. Congenital lip pits (fistulas). Usually bilateral, frequently associated with facial clefts, and symmetrically situated on vermilion border of lower lip, fistulas represent failure of closure of evanescent sulci that appear in 10 to 14 mm embryo.

Anomalies of size. Rarely are all the teeth too large or too small. More frequently a single tooth is reduced in size (microdontia) or disproportionately enlarged (macrodontia).

Anomalies of shape. An anomaly called "dens invaginatus (dens in dente)" is manifest most commonly in the maxillary lateral permanent incisor.[10]

Anomalies of eruption. Rarely (1 in 2000 white infants) are teeth present at birth (natal teeth). This condition may occur idiopathically or occasionally in association with other anomalies (chondroectodermal dysplasia, pachyonychia congenita, oculomandibulodyscephaly) in the neonatal period. Delay in eruption may be related to physical obstruction (impaction), endocrine disturbances (cretinism), or a multitude of other causes (cleidocranial dysplasia, fibromatosis gingivae, and so on).[2,3,10]

Anomalies of dental pigmentation. The teeth may be discolored as a result of exogenous factors (usually chromogenic bacteria) or endogenous factors (usually altered blood pigments resulting from internal hemorrhage from trauma, congenital porphyria, erythroblastosis fetalis, and so on). Tetracyclines administered to the mother during the last trimester of pregnancy or to the infant are also incorporated in developing teeth, producing a yellow to gray color.[5,7,8] Their presence may be demonstrated by a noticeable yellow fluorescence under ultraviolet light.[10]

Premature loss of teeth. Premature loss of a tooth or teeth may be attributable to trauma, histiocytosis X, or various genetic disorders such as hypophosphatasia, cyclic or chronic neutropenia, or premature periodontoclasia with hyperkeratosis of palms and soles (Papillon-Lefèvre syndrome).[3]

Hereditary enamel defects. Hereditary enamel defects occur in about 1 in 16,000 children, affecting both dentitions. According to Witkop and Rao,[34] there appear to be at least 10 distinct types.

In the hereditary enamel dysplasias, the teeth are frequently brown and the enamel has a tendency to flake off, but the enamel varies in hardness and thickness according to the specific type. The underlying dentin and the root formation are entirely normal, in contrast to dentinogenesis imperfecta and dentin dysplasia.

Hereditary dentin defects. Only two dentin defects are considered here: dentinogenesis imperfecta (hereditary opalescent dentin) and radicular dentin dysplasia. Both are transmitted as autosomal dominant traits.[9,34]

Dentinogenesis imperfecta usually occurs as an isolated phenomenon (1 in 8000 individuals). A somewhat similar condition may occur as a component of osteogenesis imperfecta. Both deciduous and permanent teeth have an opalescent blue to brown color. Because of poor attachment at or near the dentinoenamel junction, the enamel fractures off. The roots are frequently thin and short and the canals obliterated. Microscopically, irregularly arranged dentinal tubules and defective matrix formation are noted.

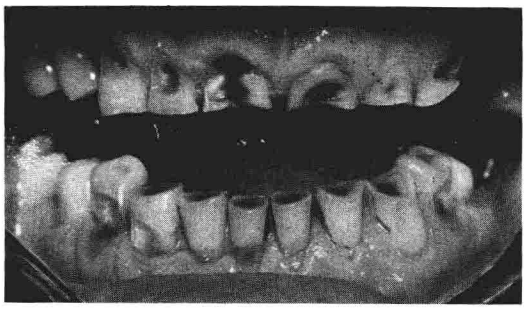

Fig. 25-2. Dental erosion. Characterized by smooth surface dissolution of enamel, especially at cervical portion, condition is of unknown etiology.

Radicular dentin dysplasia is characterized by rootless teeth, generally exhibiting an absence of pulp chambers and canals but normal-appearing crowns.[9] Many teeth exhibit large periapical radiolucencies, and a pathognomonic half moon–shaped pulp chamber may be seen on radiographic examination.

Other enamel disturbances. Nonhereditary enamel disturbances may affect either dentition, and they may be widespread or involve only a single tooth. The disturbance may be severe, causing deep pitted grooves, or so mild as to be manifest by only a small chalky spot. Defective enamel may result from injury to the enamel organ at any time from the earliest period of matrix formation to the last stage when calcification is taking place or may result from acquired abnormalities as in dental erosion (Fig. 25-2).

Nutritional deficiencies (of calcium, phosphorus, vitamin D), endocrine and related disorders (hypoparathyroidism, pseudohypoparathyroidism, hypophosphatasia, rickets), congenital syphilis, infection of the deciduous precursor (Turner's tooth), ingestion of excessive fluoride (in excess of 1.5 ppm), and many miscellaneous conditions can injure the developing ameloblast, producing enamel hypoplasia.[10]

Other dentin disturbances. In rickets the developing dentin is hypocalcified, with a wide margin of predentin analogous to the wide osteoid seams in forming bone.

Vitamin D–resistant rickets, an X-linked dominant trait, is associated with defective dentin formation and resultant periapical abscess development. Similar changes have been reported in a variety of related metabolic disorders.[10]

Diseases of teeth

Dental caries. Dental caries is a disease of the enamel, dentin, and cementum that produces progressive demineralization of the calcified component and eventual destruction of the organic component, with the forma-

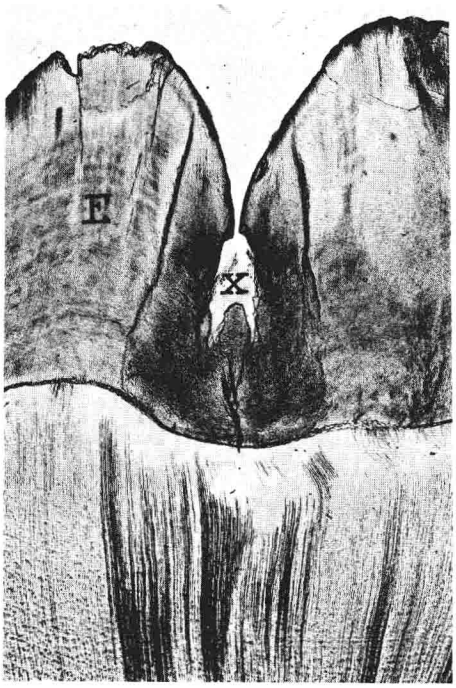

Fig. 25-3. Dental caries. Fissure lesion resulted in establishment of cavity, *X*, in enamel, *E*. Ground section of molar.

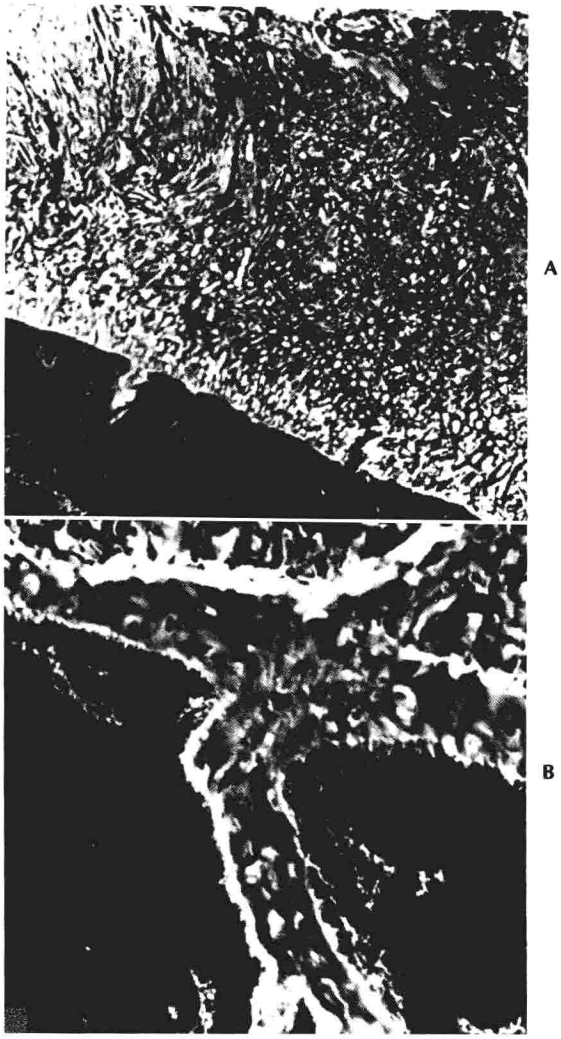

Fig. 25-4. A, Bacterial plaque isolated by acid flotation from clinically noncarious enamel. **B,** Mass of bacteria at enamel surface extending from plaque into lamella. (**A,** 2000×; **B,** 6000×; **A** and **B,** from Scott, D.B., and Albright, J.T.: Oral Surg. 7:64, 1954.)

tion of a cavity in the tooth (Fig. 25-3). Microorganisms are present at all stages of the disease and, from the results of animal experiments, appear to be essential etiologic factors.[24,26,30] Specific strains of streptococci, especially *Streptococcus mutans* in its various serotypes, have been shown to induce dental caries in rats and hamsters. The etiologic process involves the metabolism of fermentable carbohydrates by these bacteria with the production of organic acids, which demineralize the tooth surface. Destruction of tooth structure by caries is easily differentiated from dental erosion and abrasion.

Tooth decay occurs or has occurred in the majority of individuals living in the United States, Canada, and Europe. Once a carious cavity has formed, the defect is permanent. The designation DMF (decayed, missing, filled) has proved useful in comparative studies of the frequency of dental caries, particularly in children and young adults.

Caries occurs in areas on tooth surfaces where saliva, food debris, and bacterial plaques accumulate. These areas are chiefly the pits and fissures, cervical part of the tooth, and interproximal surfaces. Surfaces that are cleansed by the excursion of food and the action of the tongue and cheeks are usually free of caries. If this process is disrupted (for example, by prosthetic appliances or lack of saliva), caries may develop rapidly.

The formation of bacterial plaques in areas of stagnation precedes cavity formation, especially in smooth dental surfaces. Acidogenic and aciduric bacteria, together with filamentous forms, are present in such plaques (Fig. 25-4).[26,32]

Studies throughout the world have given striking evidence of the efficiency of fluoridation of communal water supplies in reducing the rate of tooth decay in children.[22] After the introduction of fluoride to the drinking water (1 ppm) the DMF rate has generally decreased over a period of years by more than 50%.[27] Partial control of tooth decay by this method constitutes an important public health achievement. Topical applications of fluoride solutions to tooth surfaces and brushing the teeth with dentifrices containing fluoride appear to be effective in further reducing susceptibility to dental caries.

Excessive amounts of fluoride cause a condition called

mottled enamel. It occurs in children who have consumed drinking water containing 1.5 ppm fluoride or more during the time when tooth enamel is being formed in the developing, unerupted teeth.

Pulp and periapical periodontal disease. The tooth, projecting into the oral cavity through the mucous membrane and extending deep into the jawbone, affords a surprisingly direct pathway for infection after exposure and infection of the dental pulp and after ulceration or breakdown of the epithelial attachments.

Carious destruction of dental hard tissues frequently produces pulpitis or inflammation of dental soft tissues, including, by way of extension, those surrounding the apex of the tooth. An alternative, yet equally dentally threatening, pathway exists through the gingival attachment (see following discussion concerning periodontal disease).

Inflammation of the dental pulp may be noninfective. Trauma to the tooth from a blow, which may or may not fracture the tooth, from dental operations, or from excessive thermal changes may also induce inflammation. This may be minimal with recovery, particularly in teeth with incompletely formed roots, or it may be severe leading to necrosis.

Pulpitis, regardless of the etiologic agent, may be acute or chronic. In acute pulpitis, pain is usually severe and increased by heat or cold. Pulpitis, acute or chronic, may be asymptomatic or accompanied by a mild fever and leukocytosis. Periapical tissues become involved by extension.

Acute alveolar or periapical abscess is usually the result of spread of suppurative infection from the tooth pulp through the root canals to the periodontal ligament about the tooth root apices. Drainage through the oral mucosa or to the adjacent skin of the face or neck may follow.

A more common sequela to dental pulp infection is the dental granuloma. Clinically, this may be completely symptomless. Radiographic examination frequently discloses an area of bone rarefaction about a tooth root apex, with a chronically infected or partially obliterated root canal. This area is usually spherical and well demarcated. Histologically, the tissue consists of fibrous connective tissue, often heavily infiltrated by lymphocytes and plasma cells, surounding necrotic tissue at the apex of the root canal foramen or within the pulp canal. Peripherally, loose and dense connective tissue merges into the surrounding bone, which may develop a definite cortical layer (Fig. 25-5).

Remnants of epithelium (rests of Malassez) are found in the periodontal ligament, surrounding the teeth. In granulomas this epithelium may proliferate. The root end may become surrounded by fluid with epithelium lining the surface, thus forming a cyst. The cyst may enlarge to a considerable size. Although epithelium is present in practically all granulomas and often proliferates to line small cystic cavities, the development of large cysts is relatively uncommon (see also section on odontogenic cysts).

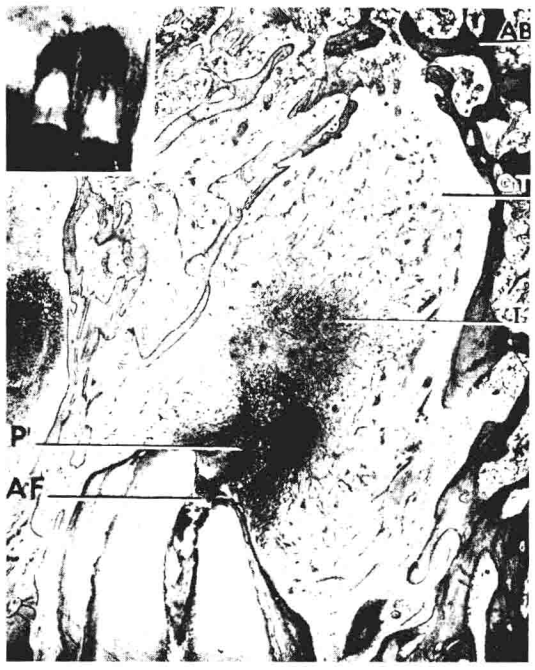

Fig. 25-5. Mesiodistal section through apex of maxillary first premolar with granuloma. *Inset,* Radiograph of specimen shows large areas of bone destruction around root ends of both maxillary premolars. *AB,* Alveolar bone; *AF,* apical foramen; *GT,* granulation tissue; *I,* dense cellular infiltration next to foramen; *P,* breaking down of tissue and formation of pus at foramen. (From Boyle, P.E., editor: Kronfeld's histopathology of the teeth and their surrounding structures, Philadelphia, 1955, Lea & Febiger.)

Periodontal disease. The inflammatory and degenerative processes that develop at the gingival margin and progress until the tooth-supporting structures are lost have much in common with periapical periodontal disease. In both instances, chronic asymptomatic infection by a variety of oral pathogens is usual, although episodes of acute suppuration may occur.

Strict anaerobes are primary etiologic agents, but the destructive process if thought to be mediated in large part by immunologic reactions of the host.[29,33] The tissue response involves a walling-off process with a pronounced chronic inflammatory cell infiltration. The proliferation of epithelium is always present in the marginal form of periodontal disease. It represents an attempt to cover the surface of the chronic ulcer that develops about the involved tooth root area (Figs. 25-6 and 25-7).[23,25,28]

The disease commonly begins as a gingivitis. Deposits of plaque and calculus on the tooth surfaces, impaction of food, decayed teeth, overhanging margins of dental res-