Sixth Edition

Jubb, Kennedy, and Palmer's

Pathology of DOMESTIC ANIMALS

Volume 2

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Volume 2

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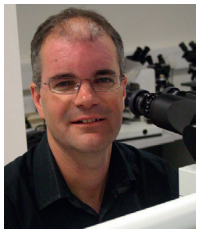

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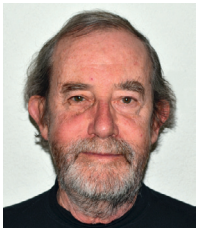

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Preface

In this sixth edition of *Pathology of Domestic Animals*, we continue the long tradition of surveying the literature and updating the information in this reference textbook in light of our own practical experience in the pathology of the major domestic mammals. True to the spirit of the first edition, this text is designed to explain the pathogenesis of common and not-so-common diseases, define the distinguishing features of these various conditions, and put them in a context relevant to both students and working pathologists. Knowledge has been generated incrementally since the publication of the fifth edition, particularly with respect to improved understanding of pathogenesis at the molecular level, as well as through the use of improved diagnostic tools, including the frontier of whole genome sequencing. My thanks to the contributors to this edition for their rigorous perusal of the literature in their areas of interest, for their addition of insightful information to their chapters, and for their inclusion of many new figures.

NEW TO THE SIXTH EDITION

The most noticeable, and I think very welcome, change in the sixth edition is the addition of full-color figures throughout the text. Nearly all of the images from prior editions have been replaced. These new images clearly depict the diagnostic features of hundreds of conditions.

We have also added a new chapter, "Introduction to the Diagnostic Process," to the usual lineup of chapters in these 3 volumes. The goal of this new chapter is to illustrate the whole-animal perspective and detail the approaches to systemic, multi-system, and polymicrobial disease.

The complete index is again printed in each volume as an aid to readers. "Further reading" lists have been pruned in the print book to save space. All references are available on any electronic version of the text as well as on the companion website that accompanies the purchase of any print book. These online references link to abstracts on PubMed.com.

COMPANION WEBSITE

In addition to updating the graphic design of these volumes, the print version of *Pathology of Domestic Animals* now has a companion website, accessible at:
PathologyofDomesticAnimals.com

Included on the companion website are:

- A complete image collection, including 325 bonus, electronic-only figures that have been called out in the text. These figures are identified in the printed version as "eFigs."
- An expanded list of useful references, each linked to the original abstract on PubMed.com.

I hope that we have captured significant changes and have synthesized this new knowledge to provide a balanced overview of all topics covered. Keeping pace with evolving agents and their changing impacts is a never-ending challenge. We have used current anatomical and microbial terminology, based on internationally accepted reference sources, such as the Universal Virus Database of the International Committee on Taxonomy of Viruses (http://www.ncbi.nlm.nih.gov/ICTVdb/index.htm). Microbial taxonomy is, of course, continually evolving, and classifications and names of organisms can be expected to be updated as newer phylogenetic analyses are reported. Debate continues, for example, over the taxonomy of *Chlamydophila/Chlamydia* spp. And change will continue.

We have attempted to contact all contributors of figures from previous editions and from various archives and apologize to any whom we were unable to contact or who were overlooked. If any individual recognizes an image as one of his/her own or as belonging to a colleague, we would be happy to correct the attribution in a future printing.

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Grant Maxie
Guelph, Ontario, 2015

These volumes are dedicated to Drs. Kenneth V.F. Jubb (1928-2013)[1], *Peter C. Kennedy (1923-2006)*[2], *and Nigel C. Palmer, and to my family—Laura, Kevin, and Andrea.*

Drs. Palmer, Jubb, and Kennedy while working on the third edition in Melbourne, 1983. (Courtesy, University of Melbourne.)

[1]http://www.vet.unimelb.edu.au/news/2013/memorial.html
[2]http://senate.universityofcalifornia.edu/inmemoriam/peterckennedy.htm

CHAPTER 1

Alimentary System

Francisco A. Uzal • Brandon L. Plattner • Jesse M. Hostetter

ACKNOWLEDGMENTS

We gratefully acknowledge the contributions of all previous authors of this chapter, including Drs. Ken Jubb, Peter Kennedy, Nigel Palmer, Ian Barker, Corrie Brown, and Dale Baker.

ORAL CAVITY

Examination of the oral cavity should be standard procedure during any postmortem examination. To obtain a clear view of the mucous membranes of the buccal and oral cavities, teeth, tongue, gums, and tonsils, it is essential to split the mandibular symphysis and separate the mandibles as far as possible. A thorough examination of all structures will reveal not only local lesions, but often those that may be due to systemic disease. Lesions may be associated with congenital anomalies (genetic and nongenetic); trauma (physical and chemical); bacterial, mycotic, viral, and parasitic infections; metabolic and toxic diseases; and immune-mediated, dysplastic, or neoplastic disease. The poor physical condition of an animal may be directly related to oral lesions that result in difficulties of prehension, mastication, or swallowing of food.

Congenital anomalies

Congenital anomalies may occur as heritable conditions or be the result of nongenetic factors, including toxicity and infectious agents. The development of normal face, jaws, and the oral cavity requires the integration of many embryonic processes, most importantly the frontonasal, maxillary, and mandibular processes. The complexity and duration of this development may lead to a great variety of aberrations. These are usually expressed in the newborn in the form of *clefts resulting from failures of integrated growth and fusion of these processes*. A common failure of fusion is that of the maxillary processes to the frontonasal process. This may leave facial fissures, cleft lip (harelip, cheiloschisis) and unilateral or bilateral primary cleft palate involving the area rostral to the incisive papilla.

Facial clefts may involve the skin only, or the deeper tissues as well. They are variously located, and not all are obviously related to normal lines of fusion. All are rare. The most common is a complete cleft from one angle of the mouth to the ear of that side. This results from failure of fusion of the lateral portions of the maxillary and mandibular processes. A defect extending from a cleft lip to the eye results from failure

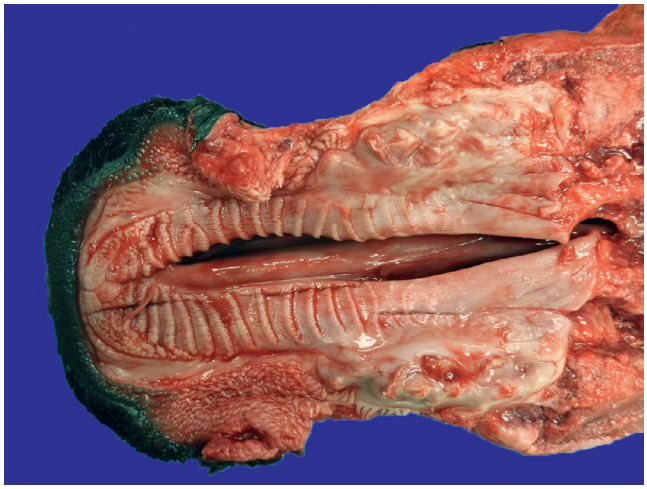

Figure 1-1 Secondary cleft palate exposing the nasal cavity in a calf. (Courtesy J. Caswell.)

of fusion of the maxillary and frontonasal processes, which may be a superficial defect with failure of closure of the nasolacrimal duct.

Primary cleft palate (harelip, cheiloschisis) includes developmental anomalies of the upper lips rostral to the nasal septum, columella, and premaxilla. They may be unilateral or bilateral and superficial or extend into the nostril. The defect arises from incomplete fusion of the frontonasal process with the maxillary processes.

Secondary cleft palate (cleft palate, palatoschisis) (Fig. 1-1) is often associated with primary cleft palate. The normal hard palate is formed, except for a small rostral contribution from the frontonasal process, and by the bilateral ingrowth of the lateral palatine shelves from the maxillary processes. At the midline, they fuse with each other and with the nasal septum, and undergo intramembranous ossification, except in their caudal part, which becomes the soft palate. Inadequate growth of the palatine shelves leaves a central defect, in either or both of the hard and soft palates, which communicates between the oral and nasal cavities. Other manifestations of disordered palato-genesis include unilateral defects in the soft palate; bilateral hypoplasia of the soft palate; or dorsal displacement of the soft palate, with excess soft tissue on the caudal portion. Affected animals have difficulty sucking, may have nasal regurgitation, and usually die within the first few days of life from aspiration pneumonia. In dogs, malformation of the soft palate has also been associated with alterations in the tympanic bulla and middle ear dysfunction.

Cleft palates have been reported in most species of domestic animals. In one extensive survey of Thoroughbred foals, 4% of congenital defects were secondary cleft palates. Most of these foals had a complete cleft of the hard palate; a few had clefts or hypoplasia of the soft palate only. In calves, cleft palate is one of the most common anomalies, but is very uncommon in sheep. Primary cleft palate is less common than secondary cleft palate in swine, although the two anomalies often occur together. In dogs and cats, cleft palate is often associated with certain breeds, suggesting that these are heritable traits.

The etiology of cleft palate is usually unknown, but examples of *hereditary causes*, maternal ingestion of certain *drugs*, or maternal consumption of *teratogenic plants* during pregnancy have been demonstrated. Secondary cleft palate and arthrogryposis frequently occur together in Charolais calves, and appear to be hereditary (probably simple autosomal recessive), as in Hereford cattle. Cleft palate in lambs may be genetic in origin, but also is associated with the ingestion of *Veratrum californicum*. Secondary cleft palates have been induced experimentally in newborn pigs by feeding gilts seeds or plants of poison hemlock (*Conium maculatum*) during gestational days 30-45. Both tree tobacco (*Nicotiana glauca*) in the western United States and tobacco stalks (*N. tabacum*) when fed to gilts early in pregnancy can induce a high incidence of cleft palate and arthrogryposis in newborn pigs. Piperidine alkaloids (coniine, coniceine, and anabasine) in hemlock and tobacco plants are responsible for the teratogenic effects of these plants. Lupines (*Lupinus formosus, L. arbustus*) produce piperidine alkaloids, including the teratogen ammodendrine, which can cause cleft palate and arthrogryposis (crooked calf disease) in calves born of dams fed the lupine at days 40-50 of gestation. Palatoschisis in piglets has also been associated with consumption of feed contaminated with *Crotalaria retusa* seed by sows during gestation. Primary and secondary cleft palate of German Boxer dogs appear to be hereditary, probably because of a single autosomal recessive gene. A single autosomal recessive gene has been associated with cleft palate in Pyrenees Shepherd dogs. Secondary cleft palate occurs in Siamese and Abyssinian cats and is likely hereditary. Griseofulvin treatment of the pregnant queen and mare will result in palatoschisis in the offspring. The defect has also been reported in both parts of the doubled face in diprosopus cats.

Anomalies in the growth of jaws are quite common. **Brachygnathia superior,** *shortness of the maxillae,* is an inherited breed characteristic among dogs and swine. It has been reported in the Large White or Yorkshire breed. The condition is progressive with age, resulting in malapposition of the incisor and cheek teeth, which interferes with prehension and mastication. In swine, brachygnathia superior may be confused with atrophic rhinitis. In Angus and Jersey cattle, brachygnathia superior occurs as a hereditary trait. In any species, it may be associated with chondrodysplasia and is also present with other facial defects.

Brachygnathia inferior or micrognathia, *shortness of the mandibles,* may be a mild to lethal defect in cattle and sheep and is a breed characteristic of long-nosed dogs. Brachygnathia inferior is a common defect in calves. It is inherited, probably as a simple autosomal recessive trait. There is a higher incidence in males. This condition in calves has been associated with cerebellar hypoplasia. In Aberdeen Angus cattle, the defect may occur concurrently with cerebellar hypoplasia, and with osteopetrosis in this and other breeds (see Vol. 1, Bones and joints). In Merino sheep, brachygnathia is associated with a cardiomegaly and renal hypoplasia syndrome that has an autosomal recessive inheritance pattern. Transplacental infection with Schmallenberg virus, an orthobunyavirus, will lead to brachygnathia among other congenital malformations in lambs and calves. Mild brachygnathia inferior, termed *parrot mouth*, is a common conformational defect in horses.

Prognathism refers to *abnormal prolongation of the mandibles.* It is rather common, especially in sheep. It may develop with recovery from calcium deficiency in this species (see Vol. 1, Bones and joints). The malformation is relative, and it is not always easy to determine whether the jaw is absolutely long or merely apparently so, relative to a mild brachygnathia superior.

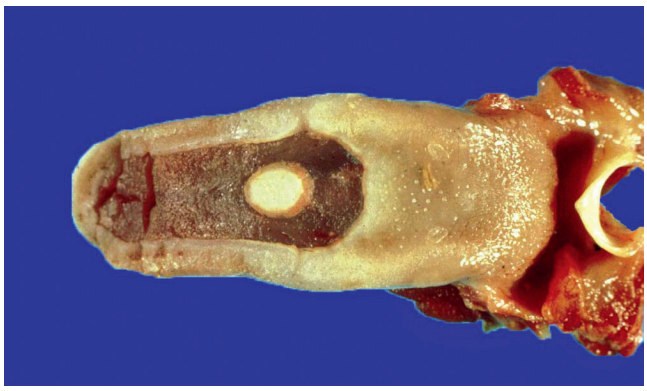

Figure 1-2 Epitheliogenesis imperfecta of the tongue of a pig. (Courtesy Noah's Arkives.)

Agnathia is a mandibulofacial malformation characterized by *absence of the lower jaw,* caused by failure of development of the first branchial arch and associated structures. The defect is one of the most common anomalies in lambs but is rare in cattle. Associated malformations in lambs may include atelosprosopia (incomplete development of the face), microglossia or aglossia, and atresia of the oropharynx. Concurrent anomalies affecting other body systems also may be evident.

A lethal glossopharyngeal hereditary defect, termed **bird tongue** and caused by a simple autosomal recessive gene, has been reported in dogs. Affected pups have a narrow tongue, especially the rostral half, where the margins are folded medially onto the dorsal surface. The pups are unable to swallow. The muscle fibers of the affected tongues are normal histologically. In dogs, there is a congenital defect leading to a thickened short lingual frenulum called **ankyloglossia**. This lesion may be most pronounced at the rostral tongue, and the tip of the tongue may be notched. **Hypertrophy of the tongue** occurs as a congenital anomaly in pigs.

Epitheliogenesis imperfecta is an anomaly that causes *widespread defects in cutaneous epithelium, and also affects the epithelial lining of the oral cavity, especially the tongue* (Fig. 1-2) (see Vol. 1, Integumentary system). The condition is characterized by irregular, well-demarcated, red areas from which the epithelium of the oral mucosa is absent. Histologically, these consist of abruptly defective areas in the squamous mucosa with inflammation of the submucosal connective tissues. The anomaly occurs in most species and is inherited as a simple autosomal recessive character in cattle, horses, and pigs; the mode of inheritance is unknown in the other species. There are several hereditary skin conditions in animals, such as epidermolysis bullosa simplex in Collie dogs, ovine epidermolysis bullosa in Suffolk and South Dorset Down sheep, and familial acantholysis of Aberdeen Angus calves, which have minor involvement of the lips and oral mucosa (see Vol. 1, Integumentary system).

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Diseases of teeth and dental tissues

Dental disease is common and often is a factor that limits the useful life-span of the animal, especially sheep. Evaluation of dental disease necessitates a thorough examination of the oral cavity. The comments on dental development and anatomy are intended to provide a brief overview and assist the understanding of dental disease.

Teeth develop from a band of ectoderm deep to the mucosal epithelium that spans the length of the gingiva. This ectodermal band is called the *dental lamina*. In the initial stage of tooth development, neural crest cells beneath the dental laminae induce multiple nodular thickenings along the length of the dental lamina. These are the *tooth buds*. Next, ectomesenchymal cells aggregate at the base of each tooth bud. The tooth bud then becomes a bell-shaped structure that grows down over the ectomesenchymal cells and becomes the *enamel organ*, which will give rise to enamel-producing *ameloblasts*. The ectomesenchyme below the enamel organ develops into the *dental papilla*, which will give rise to dentin-producing *odontoblasts* and also the tooth pulp. Ectomesenchyme cells also move around the periphery of the enamel organ to form a limiting sac called the *dental follicle* or *dental sac.* The dental sac will ultimately give rise to cementum-producing cells (*cementoblasts*), the periodontal ligament, and alveolar bone.

The cells of the enamel organ differentiate into 3 layers: outer epithelium, stellate reticulum, and inner epithelium. The *cervical loop* forms where the outer and inner epithelium of the enamel organ join. As the enamel organ develops, the dental lamina begins to disintegrate, leaving the tooth separate from the overlying oral mucosa. Remnants of the dental lamina can persist and give rise to dental cysts or neoplasms.

Hard tissues (dentin and enamel) are deposited on the developing tooth. The *inner enamel epithelium* of the enamel organ induces differentiation of odontoblasts from the ectomesenchyme of the dental papilla. Odontoblasts produce *dentin*, which in turn induces differentiation and enamel formation by the ameloblasts of the inner enamel epithelium. Thus formation of dentin is essential for the formation of enamel. These inductive interactions of epithelium and ectomesenchyme are considered important in the histodifferentiation of some tumors of dental tissues.

The crown of the tooth will ultimately be shaped by the inner enamel epithelium. The shape of the tooth roots will be determined by the cervical loop through epithelial extensions called *Hertwig's epithelial root sheath (HERS)*. The HERS guides the formation of the developing root by inciting differentiation of odontoblasts from the dental papilla. Typically the HERS will disintegrate after it initiates dentin formation. As the HERS fragments, it allows ectomesenchymal cells from the dental sac to contact the root dentin, differentiate into

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cementoblasts, and deposit cementum on the dentin of the root. Remnants of the HERS can persist and are called *epithelial rests of Malassez*. They persist in the periodontal ligament, and may give rise to tumors or cysts. They may be important in the induction or repair of cementum, and in periodontal reattachment following injury. In pigs and sheep, the rests may be incorporated into the junctional epithelium as it migrates apically in chronic periodontal disease. HERS cells of the root sheath that adhere to the dentin can produce *enamel pearls.*

As tooth development progresses, the crown of the tooth is covered by enamel, whereas the roots are covered by cementum. Dentin is present throughout the tooth. Fibroblasts in the dental follicle (sac) generate collagen that forms the *periodontal ligament*. The collagen of the periodontal ligament is intertwined with the cementum of the root surface and extends to the adjacent alveolar bone along the length of the root. The periodontal ligament is continually modified and reshaped with orientation of fibers in different directions during the life of the tooth.

The tooth will begin erupting while the roots are still developing. The mechanisms of tooth eruption are not fully understood. It is likely that the dental follicle plays a critical role in alveolar bone resorption and remodeling needed to allow the tooth to erupt. The inner enamel epithelium merges with the cells of the overlying stratum intermedium and the outer enamel epithelium to form the *reduced enamel epithelium*. This protects the enamel of the formed tooth before eruption. The reduced enamel epithelium will fuse with the mucosal epithelium as the tooth erupts, and after eruption a portion of the reduced enamel epithelium will persist along the gingival margin of the tooth as *junctional epithelium*. The process of tooth development is similar for *deciduous* and permanent teeth. Tooth germ for permanent teeth begins to develop along with the deciduous teeth. However, the permanent tooth germ is held dormant until later in life when the permanent teeth proceed with development and the deciduous teeth are lost.

There are important differences between the **brachydont teeth** of humans, carnivores, and swine, in which the enamel is restricted to the tooth crown, and the **hypsodont teeth** of herbivores. In hypsodont teeth, enamel extends far down on the roots, and is invaginated into the dentin to form *infundibula*. Also, the hypsodont teeth of herbivores, except the mandibular premolars of ruminants, are covered by cementum, which more or less fills the infundibula. Exceptions to these rules are provided by the tusks of boars, which are hypsodont, but not covered by cementum, and by ruminant incisors, which are brachydont but do have enamel covering part of the root dentin and cementum covering the root enamel.

The 3 hard tissues of teeth are dentin, enamel, and cementum. **Dentin** is light yellow and constitutes most of the tooth. It consists of ~35% organic matter and ~65% mineral. Thus its composition is similar to that of bone, and like bone, it contains type I collagen. Dentin is produced by columnar cells with basal nuclei called *odontoblasts,* which differentiate from ectomesenchyme of the dental papilla. It is formed as unmineralized predentin. The odontoblasts move away from the dentin-enamel junction, gradually encroaching on the pulp cavity as they produce dentin. Each odontoblast has a process extending into the dentin, encased in a dentinal tubule, which arborizes at the dentin-enamel junction. The process also anastomoses with the processes of other odontoblasts. Dentinal tubules are visible in histologic sections, but the anastomoses are not. Except for the processes, and nerve endings in the dentinal tubules near the pulp, dentin is acellular.

Normal dentin contains incremental or *imbrication lines of von Ebner,* which are fine basophilic lines running at right angles to the dentinal tubules. They represent normal variations in the structure and mineralization of dentin. Sublethal injury caused by certain infections, metabolic stresses, or toxic states may injure the odontoblasts, which then produce accentuated incremental lines known as the *contour lines of Owen*. Sometimes irregular zones of unmineralized or poorly mineralized dentin form between foci of normal mineralization. These are zones of *interglobular dentin,* which may be caused by hypophosphatemia.

There are 3 types of dentin. *Primary dentin* is produced by odontoblasts before tooth eruption. *Secondary dentin* is produced after root formation is complete by odontoblasts that remain active throughout life. Generation of secondary dentin is much slower than primary dentin. *Tertiary dentin* is produced in response to injury to the tooth. Tertiary dentin is called *reactionary* when it is produced by pre-existing odontoblasts. *Reparative dentin* is another type of tertiary dentin that is produced by newly differentiated odontoblasts. Reparative dentin may resemble bone and is sometimes called *osteodentin*. *Sclerotic* (*transparent*) *dentin* is formed when dentinal tubules are occluded by calcium salts. The junctions between primary, secondary, and reparative dentin are usually demarcated by basophilic lines.

Enamel has ~5% organic matter and ~95% mineral. It is produced by the tall columnar *ameloblasts* of the inner enamel epithelium. Enamel is produced in the form of prisms or rods, cemented together by a matrix. Mineralization begins as soon as it is formed and is a 2-stage process, somewhat similar to that in bone, but much more rapid. The cells of the inner enamel epithelium also move away from the dentin-enamel junction as the tooth is formed, but unlike odontoblasts, they do not have processes. Formation of enamel ends before tooth eruption. Enamel is hard, dense, brittle, and permeable, and is translucent and white. Mature enamel is not present in demineralized sections, but some of the matrix of immature enamel may be visible near ameloblasts of developing teeth.

Ameloblasts are very sensitive to environmental changes. Normal enamel contains *incremental lines of Retzius,* which are analogous to the incremental lines of von Ebner in dentin, and also reflect variations in structure and mineralization. The incremental lines are accentuated during periods of metabolic stress. More severe injury, as in fluorosis, or infections by some viruses can produce focal **hypoplasia or aplasia of enamel.** The *reduced enamel epithelium* protects the enamel of the formed tooth before eruption. Degeneration of this protective layer permits connective tissue to contact the enamel, and there may be resorption of enamel or deposition of a layer of cementum on it. This normally occurs during odontogenesis in horses.

Cementum is an avascular, bone-like substance, produced by *cementoblasts*; it contains ~55% organic and ~45% inorganic matter. In general the dentin of brachydont teeth is covered by cementum wherever it is not covered by enamel. When dentin formation has begun in the root, degeneration of Hertwig's epithelial root sheath begins and permits mesenchymal cells from the dental sac to contact dentin. They differentiate into cementoblasts, which produce *cementoid*, and later

mineralize it. Some layers of cementum do not contain cells (acellular cementum), but in other layers, *cementocytes* are enclosed in lacunae. Sharpey's fibers from alveolar bone are embedded in the cementum. Cementum is more resistant to resorption than is bone, and unlike bone, normally is not resorbed and replaced as it ages; instead a new layer of cementum is deposited on top of the old layer. In some pathologic conditions, cementum is resorbed; subsequently, cellular or acellular cementum is deposited, and more or less repairs the defect.

Hypercementosis is abnormal thickening of cementum and may involve part or all of one or many teeth. When extra cementum improves the functional properties of teeth, it is called *cementum hypertrophy;* if not, it is called *cementum hyperplasia*. Extensive hyperplasia is often associated with chronic inflammation of the dental root.

The **periodontal ligament** is derived from the dental follicle. It is well vascularized and very cellular containing fibroblasts, cementoblasts, undifferentiated mesenchymal cells, and epithelial cells. The periodontal ligament contains type I collagen fibers with complex orientation. The **periodontium** comprises the periodontal ligament, gingival lamina propria, cementum, and alveolar bone. The ligament supports the tooth and adjusts to its movement during growth. It is well supplied with nerves and lymphatics, which drain into alveolar bone. The periodontal ligament is also a source of the cells that remodel alveolar bone and, in disease, cementum.

Epithelial rests of Malassez are present in the periodontal ligament and are particularly numerous in the incisor region of sheep. In all species, they may proliferate and become cystic when there is inflammation of the periodontium. The periodontium is also a site of origin of tumors. The periodontal ligament is normally visible in radiographs as a radiolucent line between tooth and alveolar bone. In prolonged hyperparathyroidism, alveolar bone is resorbed, and the ligament is no longer outlined radiographically, a change referred to as *loss of the lamina dura*.

Developmental anomalies of teeth

Anodontia, *absence of teeth*, is inherited in calves, probably as a sex-linked recessive trait in males, and is associated with skin defects. **Oligodontia**, *fewer teeth than normal*, occurs sporadically in horses, cats, and dogs, and also as an inherited trait in dogs. In brachycephalic breeds, the cheek teeth are deficient; in toy breeds, the incisors are deficient. *Pseudo-oligodontia* and *pseudoanodontia* result from failed eruption. Delayed eruption of permanent teeth occurs in Lhasa Apso and Shih Tzu dogs. *X-linked hypohidrotic ectodermal dysplasia* is a heritable condition in dogs that also has been reported in horses, humans, mice, and cattle. In affected individuals, structures of ectodermal origin may be absent or abnormally formed, including teeth.

Polyodontia, *excessive teeth*, occurs in brachycephalic dogs; the incisors are involved, and the defect is probably related to breeding for broad muzzles. A high incidence of canine polyodontia, involving particularly an extra maxillary premolar, is reported from the Netherlands. Polyodontia also occurs in horses and cats, involving either incisors or cheek teeth (molars and premolars). **Pseudopolyodontia** *is retention of deciduous teeth after eruption of the permanent dentition*. It occurs in horses, cats, and dogs, especially in the miniature breeds. Retention of deciduous teeth can be problematic as it may lead to malocclusion.

Heterotopic polyodontia *is an extra tooth, or teeth, outside the dental arcades.* The best-known example is the *ear tooth of horses,* which develops in a branchiogenic cyst. The cysts originate from failure of closure of the first branchial cleft, or from the inclusion of cellular rests in this area. They are lined by a stratified mucous or cutaneous-type epithelium, and may contain one or more teeth, either loosely attached in the cyst wall or deeply embedded in the petrous temporal bone. The tooth is derived from misplaced tooth germ of the first branchial arch, which is displaced toward the ear with the first branchial cleft. The cysts eventually form in the parotid region near the ear and may fistulate to the exterior. They are occasionally bilateral. Rarely the tooth may form a pedunculated mass enclosed by skin, and attached by a pedicle to the skin of the head. Heterotopic polyodontia also occurs in cattle, dogs, pigs, and sheep.

Developmentally **misshapen teeth** are classified as **geminous** (dichotomous) when there is a single root and partially or completely separate crowns; **fused** when the dentin of 2 teeth is confluent; and **concrescent** when the dentin is separate but the roots are joined by cementum. Gemination represents the embryologic partial division of a tooth primordium. It occurs in dogs, usually involving the incisors, and the affected tooth usually has a groove dividing the crowns, whose pulp chambers can be seen radiographically to merge in a common root. Misshapen teeth and missing teeth have also been reported in dogs as an X-linked recessive trait of ectodermal dysplasia. Fusion and concrescence represent the joining of 2 adjacent tooth primordia, one of which may be supernumerary. *Malformation and malpositioning of teeth* accompany abnormalities of the jaw bones. Aberdeen Angus and Hereford calves with congenital osteopetrosis have brachygnathia inferior, malformed mandibles, and impacted cheek teeth. Impacted molars occur as an inherited lethal defect in Shorthorns; an association with osteopetrosis apparently has not been investigated in this breed.

Odontogenic cysts are epithelium-lined cysts derived from epithelium associated with tooth development. This includes rests of Malassez, cell rests of dental laminae, reduced enamel epithelium, or malformed enamel organs. By definition, **dentigerous cysts** are *cysts that contain part or all of a tooth*. Dentigerous cysts usually are associated with permanent teeth. The cyst often forms over the developing tooth and the affected tooth then erupts into the preformed cysts. Dentigerous cysts enclose at least the crown of the tooth, but may include it all. Of the odontogenic cysts, all except those derived from cell rests of Malassez are potentially dentigerous (the rests of Malassez are the probable source of periodontal cysts). Dentigerous cysts originating in malformed enamel organs usually include malformed teeth. Teeth in cysts of reduced enamel epithelium or rests of dental laminae are also often abnormal. The most common forms of odontogenic dentigerous cysts in animals are those involving the *vestigial wolf teeth* of horses and the *vestigial canines,* especially of mares. The smaller cysts appear as tumors of the gums, whereas some of the larger ones may cause swelling of the jaw or adjacent maxillary sinus. In dogs, brachycephalic breeds often develop dentigerous cysts, which can be bilateral. The first premolar is often affected. Dentigerous cysts of animals are not as destructive as those in humans, in which species they are regarded as the most common benign destructive lesion of the skeleton. In dogs, a cyst that resembles *odontogenic keratocyst* of humans has been reported. This cyst is lined

by keratinized epithelium and has a high rate of reoccurrence after removal.

The ear tooth of horses is probably the most common nonodontogenic dentigerous cyst. Occasionally true dentigerous cysts form when normal tooth eruption fails or when there is maleruption resulting from odontodystrophy. Tooth eruption can be interrupted by trauma, including fractures to the mandible and maxilla.

Cystic dental inclusions about vestigial supernumerary teeth also occur in juxtamolar positions in cattle, but are insignificant. These too may be dentigerous, or they may be primordial cysts developed before the stage of enamel formation, and hence contain no mineralized tooth structures. Either type of cyst may give rise to ameloblastomas.

A high incidence of dentigerous cysts involving incisors occurs in some sheep flocks in Scotland, Australia, and New Zealand. A congenital disease involving the jaws and teeth of calves in Germany (*odontodysplasia cystica congenita*) is characterized by massive fibro-osseous enlargement of the maxillae and horizontal rami of the mandibles. Some teeth are malformed, misshapen, or absent. Cystic spaces in the jaws are lined by fibrous tissue or epithelium, the latter probably derived from enamel organs. The dental changes are thought to be secondary to those in bone. Most affected calves are aborted or stillborn, and many have ascites and hydrocephalus. The disease may be caused by environmental influences.

The permanent teeth are unique in that they continue to develop for a long time after birth. Thus, inflammatory and metabolic disease of postnatal life, for instance canine distemper virus infection (Fig. 1-3A), can produce hypoplasia of dentin and enamel. Hypoplasia of the enamel of deciduous teeth occurs in some calves with intrauterine bovine viral diarrhea virus infection (Fig. 1-3B). It has also been described in calves and pigs following irradiation of the dam during gestation. Dysplastic proliferation of dentin and enamel involving mandibular premolars and molars has been seen in young uremic dogs. Extreme fragility of deciduous teeth is a feature of *bovine osteogenesis imperfecta* (see Vol. 1, Bones and joints). Dental dysplasia, characterized by normal dentin, absence of enamel matrix, and excess irregular cementum, was described in a foal with epitheliogenesis imperfecta involving the oral mucosa.

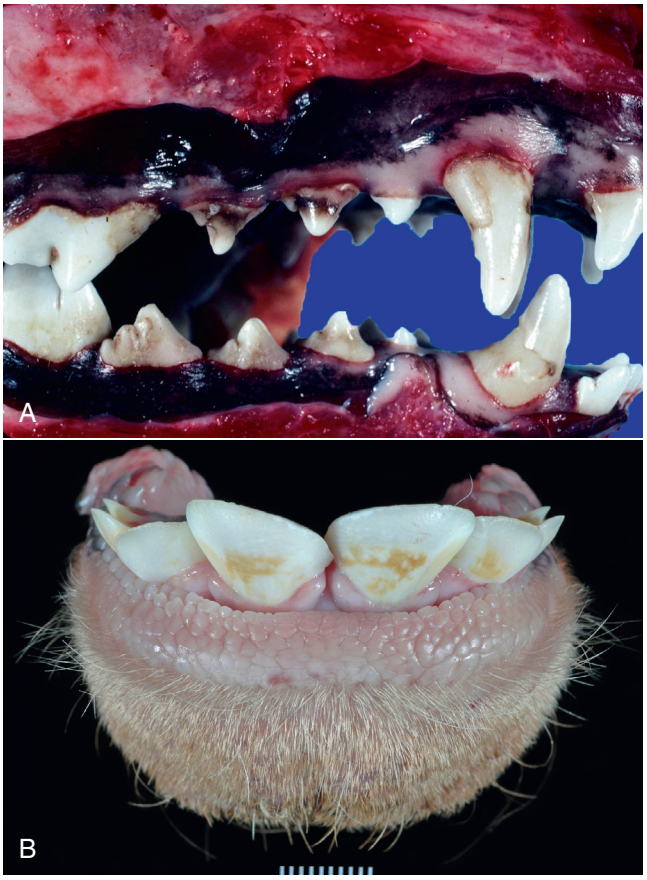

Figure 1-3 Enamel hypoplasia. A. A sequel to canine distemper virus infection in a dog. **B.** Subsequent to intrauterine infection by bovine viral diarrhea virus in a calf. (Courtesy Noah's Arkives.)

Degenerative conditions of teeth and dental tissue

Pigmentation of the teeth. Normal enamel is white and shiny, but normal cementum is off-white to light yellow, and normal dentin is slightly darker yellow. Depending on the tooth, or the part of the tooth being examined, the normal color may be any one of these. Normal enamel is never discolored. Hypoplastic enamel of chronic fluorosis is discolored yellow through brown to almost black. Discoloration of brachydont teeth results from pigmentation of dentin, which is then visible through the semitransparent enamel, or pigmentation of the cementum of the root. Dentin may be colored red-brown by pulpal hemorrhages or inflammation, gray-green in putrid pulpitis, and yellow in icterus. *Amelogenesis imperfecta* is a disorder of enamel formation that leads to inadequate mineralization of enamel and usually yellow discoloration of teeth. This condition has been reported in cattle and in Standard Poodle dogs. *Congenital erythropoietic porphyria* of calves, cats, and swine discolors the dentin red in young animals (pink tooth) and darker brown in adults, although in swine, the discoloration may disappear with aging.

Yellow to brown discoloration of teeth, and bright yellow fluorescence in ultraviolet light, caused by deposition of *tetracycline* antibiotics in mineralizing dentin, enamel, and probably cementum, occurs in all species. Treatment of the pregnant dam may cause staining of deciduous teeth in the offspring. Tetracyclines are toxic to ameloblasts in late differentiation and early secretory stages and, at high dose rates, may produce enamel hypoplasia. Black discoloration of ruminant cheek teeth is extremely common, and is caused by impregnation of mineral salts with chlorophyll and porphyrin pigments from herbage.

Dental attrition. *Dental attrition is loss of tooth structure caused by mastication.* The mature conformation of teeth is largely the outcome of opposed growth and wear, and the degree of wear depends on the type of tooth, the species of animal, and the material chewed. Wear is most evident in herbivores, and irregularities of wear are perhaps the most common dental abnormalities, especially in horses. In general, with normal occlusion and use, the extraalveolar portion of the tooth does not shorten. Its length is maintained initially by growth, the period of growth depending on the species, then by hypertrophy of the root cementum and/or dentin and by proliferation of alveolar bone, which serves to push the tooth out. Finally, senile atrophy of the alveolar processes and gingival recession may maintain or increase the length of the clinical crown. Cementum hypertrophy and alveolar atrophy may also result in loss of teeth in senility, or, if combined with subnormal wear, produce teeth that in old age are excessively

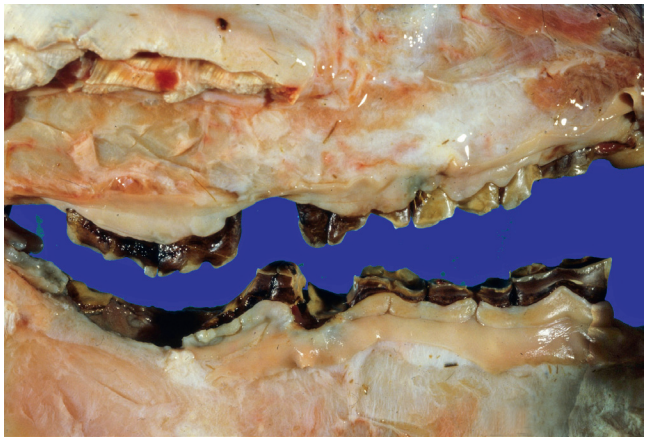

Figure 1-4 **Irregular wear** of the teeth of a horse.

long. Normal wear of the complicated cheek teeth (premolars and molars) of horses and cattle causes smoothing of the occlusal surfaces. As soon as wear of enamel exposes the dentin, which, being softer, wears more rapidly, secondary or tertiary dentin is deposited to protect the pulp. In time, this may fill the pulp cavity and cause death of the tooth. Abnormalities of wear are most common in herbivores (Fig. 1-4). Excessive wear of the deciduous and permanent central incisors occurs in certain sheep flocks in New Zealand. The wear is intermittent and may be severe enough to expose the pulp cavity. The cause is unknown but may be related to delayed eruption of adjacent teeth, leading to increased use of the affected pairs.

Subnormal wear, caused by loss of the opposing tooth, occurs in oligodontia, abnormal spacing of adjacent teeth, and acquired loss of teeth; it results in *abnormal lengthening*. Such elongated teeth may grow against the opposing gum or, if deviated, into an adjacent soft structure such as cheek or lip. These teeth usually wear in abnormal places because complete loss of antagonism is unusual, and, because the upper and lower arcades do not coincide exactly, the coincidence is further reduced by the displacement of chewing.

Abnormal wear resulting from abnormal chewing is caused by voluntary (as in painful conditions) or mechanical impairment of jaw movement. Incomplete longitudinal alignment of the molar arcades allows irregular wear and hook formation on the first and last cheek teeth. Lateral movements of the jaws without the normal rotary grinding movements allow the ridges of the teeth of herbivores to become accentuated. Steep angulation of the occlusal surfaces results from inadequate lateral movement of the jaws, and sharp edges form on the buccal aspect of the maxillary teeth and the lingual aspect of the mandibular teeth. This may be unilateral when the animal chews with only one side of its mouth, the other side then being affected. The teeth wear progressively sharper, and can result in the teeth passing each other like shear blades; hence the term **shear mouth**. Subnormal resistance to wear on the part of the molar teeth is common, and results in **wave mouth** (weave mouth) or **step mouth**, in which successive teeth in an arcade wear at different rates. The wave or step form of the antagonistic arcade is reversed, so that the teeth of the 2 arcades interdigitate. This pattern of attrition is caused by variation in the hardness of opposing teeth, and is usually caused by intermittent odontodystrophy. Opposing teeth of the upper and lower jaws do not develop at the same time; thus discontinuous nutritional deficiencies often result in unequal wear. Certain vices, such as crib biting, also produce abnormal wear. In severely worn ruminant incisors, a central black core may be visible, which is secondary dentin deposited in the pulp cavity. It is not carious, but stains darker than the surrounding primary dentin.

Odontodystrophies. *Odontodystrophies are diseases of teeth caused by nutritional, metabolic, and toxic insults.* They are manifest by changes in the hard tissues of the teeth and their supporting structures and often occur during the period of tooth development. Lesions of enamel and dentin are emphasized here. The most prominent effects of odontodystrophies appear in enamel, and lesions of enamel are most significant because they are irreparable.

Formation of enamel occurs in a set pattern. It begins at the occlusal surface and progresses toward the root. Mineral maturation occurs in the same sequence, but for each level, it begins at the dentin-enamel junction and moves toward the ameloblast. Deleterious influences have their most severe effects on those ameloblasts that are forming and mineralizing enamel. Depending on the severity on the insult, ameloblasts may produce no enamel, a little enamel, or poorly mineralized enamel. Removal of the insult permits those ameloblasts that were not yet active to begin making normal enamel. Thus enamel defects vary in severity from isolated opaque spots or pits on the surface to deep and irregular horizontal indentations. These defects are most clearly seen on the incisor teeth and canine teeth and are usually bilaterally symmetrical. Similar lesions are also produced by infectious agents that injure ameloblasts, such as canine distemper virus and bovine viral diarrhea virus (see Fig. 1-3).

Odontoblasts are susceptible to many of the same influences as ameloblasts, but they can be replenished from the undifferentiated cells of the dental pulp. Thus lesions in actively forming dentin may be repaired, whereas those in enamel are permanent.

Because of their close anatomical association with the bones of the jaws, teeth are very susceptible to disruption in the harmony of growth. This harmonious arrangement is often upset in the odontodystrophies and osteodystrophies, which may lead to malocclusion, anomalous development of teeth, and tooth loss.

Several nutritional and toxic conditions produce odontodystrophy. **Fluorine poisoning** is exemplary (see Vol. 1, Bones and joints). In **vitamin A deficiency,** ameloblasts do not differentiate normally, and their organizing ability is disturbed. As a result, odontoblastic differentiation is abnormal. Several lesions develop, including enamel hypoplasia and hypomineralization, vascularized dentin (osteodentin), and retarded or failed tooth eruption.

Calcium deficiency retards eruption and causes enamel hypoplasia and mild dentin hypoplasia. Teeth formed during the period of deficiency are very susceptible to wear. In sheep, recovery from prolonged calcium deficiency results in malocclusion caused by inferior prognathia. This reflects inadequate maxillary but normal mandibular repair during the recovery phase.

Phosphorus deficiency, combined with vitamin D deficiency, depresses dentin formation slightly, but has virtually no effect on enamel, at least not in sheep. Hypophosphatemia is associated with formation of interglobular dentin in humans. Malocclusion and abnormalities of bite in rachitic sheep are secondary to mandibular deformity.

Severe, experimental **malnutrition** also produces malocclusion. Recovery from malnutrition does not correct the lesion, and in addition, is associated with misshapen, malformed teeth, oligodontia, and polyodontia.

The major **effects of odontodystrophies** in herbivores are *malocclusion*, and/or accelerated *attrition*. Sometimes a high incidence of these abnormalities is attributable to one of the causes previously discussed, but often they are idiopathic.

A syndrome of dental abnormalities of sheep in the North Island of New Zealand is characterized by excessive wear of deciduous teeth, maleruption and excessive wear of permanent teeth, periodontal disease involving permanent teeth, and development of dentigerous cysts involving permanent incisors. Mandibular osteopathy is also present. Animals older than 5 years are culled for dental problems. The odontodystrophy (and osteodystrophy) is possibly caused by deficiencies of calcium and copper, and perhaps other nutrients, such as protein, and energy. This syndrome exemplifies the naturally occurring odontodystrophies, in that it probably has a complex pathogenesis, and is associated with an osteodystrophy. The latter association is to be expected, because bones and teeth are usually susceptible to the same insults.

Although dental lesions are not described, tooth loss caused by periosteal dysplasia and osteopenia occurs in Salers cattle afflicted with hereditary hemochromatosis.

Infectious and inflammatory diseases of teeth and periodontium

The role of viruses in enamel hypoplasia is mentioned previously. Bacterial plaque, along with other tooth-accumulated materials, is discussed here.

Bacterial diseases involving tooth surfaces are caused by the development of supragingival and subgingival **plaque**. *Supragingival plaque* is located on the exposed crown of the tooth and causes dental caries. *Subgingival plaque* is found in the crevicular groove and causes periodontal disease. Tooth enamel is covered by a translucent pellicle, the *acquired enamel pellicle,* which is formed by selective adsorption of complex salivary proteins, and that is essential to the development of supragingival plaque. This is a dense, nonmineralized, bacterial mass, firmly adherent to tooth surfaces, which resists removal by salivary flow and prevents the buffering capacity of saliva from influencing plaque metabolites. Formation of this plaque involves adhesion of bacteria to the pellicle, and adhesion of bacteria to each other, producing a *biofilm*. Initial bacterial binding to the tooth surface is reversible through electrostatic and hydrophobic interactions, but this transitions to permanent receptor mediated binding.

Only organisms with the ability to adhere to the pellicle can initiate the formation of supragingival plaque; those that cannot are removed by oral secretions and mechanical action. Pathologic reduction of salivary flow, or regions of teeth where flow is reduced (interproximal regions and areas of pits or fissures) increases the prevalence of caries in some species.

The bacteria in supragingival plaque are members of the indigenous oral flora and are usually gram-positive aerobes. Most are streptococci and *Actinomyces* spp., which form an organized array on the tooth surface. Some plaque-forming bacteria synthesize extracellular polymers, which constitute the matrix of the plaque and permit adhesion between organisms of the same species. Some utilize polymers derived from host secretions to adhere to the pellicle, whereas others attach to bacteria of a different species that are already fixed to the tooth. Plaque increases in mass with time, and its composition becomes more complex as anaerobic gram-negative bacteria join the streptococci and actinomycetes that initiated plaque formation.

Supragingival plaque is metabolically active. It utilizes dietary carbohydrates to produce the adhesive polymers and the acids needed to demineralize enamel, and as energy sources for maintenance and for production of various enzymes and stimuli for inflammation. Extensive deposits of supragingival plaque are virtually invisible unless treated with a disclosing solution.

Subgingival plaque is less organized than supragingival plaque, and many of the organisms involved are gram-negative anaerobes that are asaccharolytic, weakly adherent, and motile. They derive their nutrients from the crevicular fluid. The flora of subgingival plaque is less well characterized than that of supragingival plaque. Culture results vary with sample collection technique, site of collection, and selectivity of media, and appear to under-represent the flora detected by molecular means in humans. A number of species including *Bacteroides* spp., *Actinomyces* spp., *Porphyromonas* spp., *Tannerella forsythia*, and spirochetes have been associated with gingivitis and periodontal disease in animals.

Dental calculus (*tartar*) *is mineralized supragingival and subgingival plaque.* In supragingival plaque it is formed by the deposition of mineral, mainly from saliva, in dead bacteria. In subgingival plaque, mineral is generated from gingival crevicular fluid. In horses and dogs, calculus is predominantly calcium carbonate. Calculus is often found in old dogs and cats, occasionally in horses and sheep, and rarely in other species. The distribution is often uneven, but it is *usually most abundant next to the orifices of salivary ducts.* Calculus on horses' teeth is chalky and easily removed. In dogs, it is hard, firmly attached, and often discolored. Red-brown to black calculus with a metallic sheen develops in pastured sheep and goats. It usually involves all the incisors, principally on the neck of the buccal surface. Minor amounts are common along the gum-tooth junction of the molar teeth, but occasionally larger (up to 2 cm) hard, black, rounded concretions may protrude from between opposed surfaces of the premolars. A high prevalence of calculus in sheep on the Scottish island of North Ronaldsay was related to their predominantly seaweed diet. Calculus was most severe around the cranial cheek teeth, increased in severity with age, was associated with periodontal disease, and contained large amounts of calcium, magnesium, and phosphorus.

Materia alba, which adheres to teeth, is a mixture of salivary proteins, desquamated epithelial cells, disintegrating leukocytes, and bacteria. The bacteria are not organized, and materia alba is easily removed. It is distinct from dental plaque, and from food debris, which also accumulates between uncleaned teeth.

Dental caries. Dental caries is a disease of the hard tissues of teeth, characterized by *demineralization of the inorganic part and enzymatic degradation of the organic matrix*. **Erosions** of teeth are characterized by removal of hard tissues layer by layer. These definitions permit the inclusion of equine infundibular necrosis as a form of caries (see following sections). Caries is common in horses and sheep but rare in dogs. Cats are commonly subject to caries-like odontoclastic resorptive lesions of uncertain etiopathogenesis.

There are 2 types of caries:

1. **Pit or fissure caries** develops in irregularities or indentations, which trap food and bacteria, usually on the occlusal surface of the tooth. Plaque is not essential for initiation of this form of caries, of which *equine infundibular necrosis* is an example.
2. **Smooth-surface caries** usually occurs on proximal (adjacent) surfaces of teeth, typically just below contact points, or around the neck, and requires dental plaque for its initiation.

The organic acids, principally lactic, which initiate demineralization, are produced by bacterial fermentation of dietary carbohydrates. In smooth-surface caries, plaque produces the acid and maintains a low pH on the surface of the tooth. Progression of lesions depends on various factors such as salivary pH, hardness and resistance to demineralization of enamel, and frequency of access to carbohydrate. Demineralization of enamel often occurs in the subsurface enamel but progresses to caries only with prolonged exposure to acid. Infrequent exposure allows remineralization of enamel between meals. The enzymes that lyse the organic matrix are probably produced by plaque, but may be derived from leukocytes, for which plaque is chemotactic. Carious enamel loses its sheen and becomes dull, white, and pocked. When dentin is exposed, it becomes brown or black. Dentin is softer and more readily demineralized than enamel, and a pinpoint lesion in enamel may lead to a large defect when the carious process reaches the dentin. Enamel loss to caries is permanent, whereas odontoblasts at the pulp/dentin junction can generate tertiary dentin in response to dentin damage and loss. Nerve endings have not been identified at the enamel-dentin junction, and the pain of caries is thought to be caused by chemical or pressure changes in the dentinal tubules. Neuropeptides, including substance P, are generated in the pulp and may enhance pain during caries. Spread of infection along the dental tubules to the pulp cavity may result in formation of reparative dentin, pulpitis, or periapical inflammation and tooth loss.

In **horses, infundibular necrosis** is the most common form of caries. It develops most often on the occlusal surface of the maxillary first molar. The enamel invaginations (infundibula) in the cheek teeth of horses are normally filled with cementum before the teeth erupt. Filling proceeds from the occlusal surface toward the apex, but often is not completed before eruption. At this time the blood supply is cut off, and ischemic necrosis of any residual cementogenic tissue in the infundibula occurs (Fig. 1-5A). The deficiency of cementum is called *hypoplasia*.

Teeth with incompletely filled infundibula may accumulate food material and bacteria. This can lead to bacterial fermentation and lactic acid production that demineralizes the cementum over the infundibulum (Fig. 1-5B). In some animals, the cavitated area expands to involve all the cementum and the adjacent enamel and dentin. This may result in coalescence of adjacent infundibulum and creation of a large defect in the occlusal surface. Decay of the mineralized tissues and coalescence of infundibula may progress to fracture of the tooth, root abscess, and empyema of the paranasal sinuses. The incidence of infundibular necrosis increases with age, and 80-100% of horses older than 12 years may have the lesion. Most are without signs, and in most, the lesion does not progress. Inflammation of the dental pulp, in horses and in other species, may result from direct expansion of caries from penetration of bacteria and bacterial degradation products along the dentinal tubules. Production of reparative dentin in the pulp cavity is expected. Horses may also develop *peripheral caries* outside of the infundibulum. This typically occurs in the caudal cheek teeth and leads to loss of cementum that may contribute to irregular wear and periodontal disease.

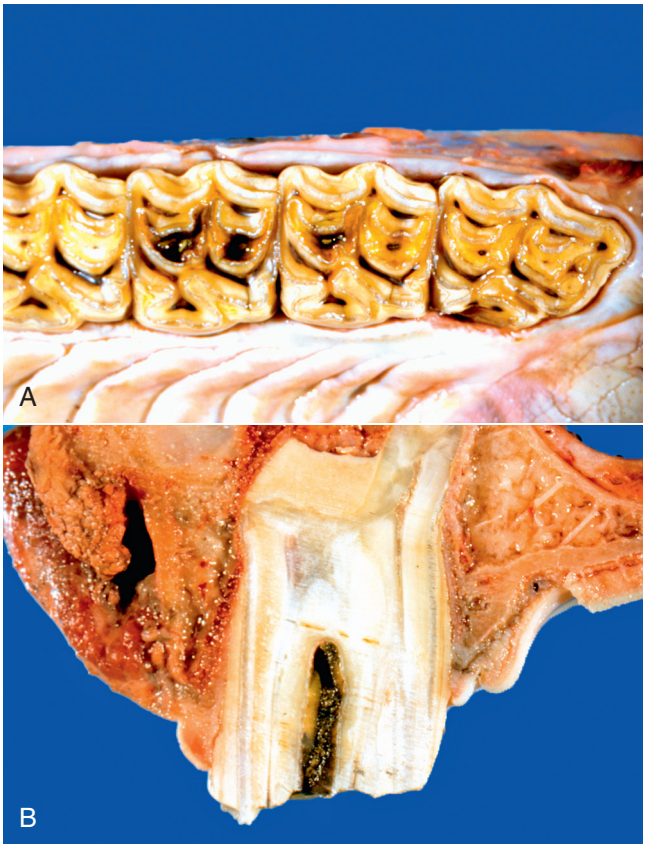

Figure 1-5 **A. Infundibular necrosis** of first and second maxillary molars in a horse. Necrosis is confined to cement lakes. **B.** Section through (**A**) showing black discoloration of infundibulum.

In **sheep**, the proximal surfaces of mandibular teeth are usually affected by caries, which is commonly accompanied by periodontitis. Erosions of the neck region of the deciduous teeth occurred in sheep in New Zealand. The lesions were mainly located apical to the enamel-dentin junction on the labial or lingual surface. They did not seem to be related to the usual causes of localized tooth destruction.

Cattle develop loss of dentin just below the crown of incisor teeth at increasing frequency with age. This usually follows recession of the gingiva, and is not considered to be a form of caries, but proteolytic digestion of dentin by chyme in an alkaline pH.

In **dogs,** caries most commonly involves the fourth premolar and the first and second molars. Although relatively uncommon, when caries occurs, defects are often multiple and advanced, leading to therapeutic extraction.

Cats, whose teeth do not have centers where food can collect, very commonly develop multiple caries-like **odontoclastic resorptive lesions,** initially involving the subgingival neck or upper root, most often of cheek teeth, and increasing in prevalence with age. This is not a true caries lesion. Odontoclasts are similar to osteoclasts and participate in absorption of roots of deciduous teeth. For reasons that are not entirely clear, they are recruited or form at the tooth and begin to

resorb enamel and eventually dentin. A reddened swollen area of gingiva or granulation tissue often lies over the lesion, which may be on the labial or buccal aspect, and frequently is painful to touch. The resorptive lesions begin as shallow defects in the cementum, lined by odontoclasts, facing a somewhat disorganized periodontal ligament. They progress into the underlying dentin, and, with time, into the root canal. Either or both coronal and apical extension of lesions may occur. Extension of the process coronally more superficially undermines the enamel, which is resorbed or breaks off, causing destruction or loss of the crown. Extension of the dentinal lesion apically leads to resorption of the root. Remnants of the root may persist, often overgrown by gingiva, following loss of the crown. Conversely, destruction primarily of the root may result in obliteration of the periodontal ligament, resorption of adjacent alveolar bone, but with odontoalveolar ankylosis by reparative hard tissues, retaining the crown in the dental arcade. In addition to the odontoclasts that line the resorbing cementum or dentinal surfaces of the lesion, more advanced defects contain a mixed leukocyte population, macrophages, and disordered granulation tissue. Repair is often superimposed, with cementoblastic or osteoblastic cells producing new mineralized tissue of varied osteoid, bone, cementum, or osteodentin morphology. Pulpitis may occur in the affected root canal, and reparative dentin may be deposited there. The prevalence of such lesions has increased markedly in the past 40 years, suggesting an association with changes in form of diet, but the lesion is idiopathic, with no clear relationship to periodontitis, mechanical trauma, viral infections, or nutritional or metabolic disturbances. A number of factors have been proposed to be involved with feline resorptive lesions, including local inflammatory mediators, increased vitamin D intake, and local pH.

Pulpitis. The dental pulp is derived from the dental papilla. It is surrounded by odontoblasts and dentin, except at the apical foramen, through which vessels and nerves pass. Pulp is a loose syncytium of stellate fibroblasts, and contains histiocytes and undifferentiated mesenchymal cells. The latter are odontoblastic precursors.

The apical foramen is located at the apex of the root and is where blood vessels and nerves enter the tooth. The apical foramen is narrow, and this predisposes to vascular occlusion, ischemic necrosis of the pulp, and death of the tooth. Production of abundant secondary dentin and reparative dentin can cause occlusion, but the usual cause is inflammation. Normally, pulp is the only vascular tissue of the tooth, and, along with the periodontium, the only site of conventional inflammation. *Pulpitis is always related to infection*, the effect of bacteria or their products entering through the surface of fractured teeth, carious perforations (especially in teeth with enamel defects), perforations resulting from abnormal wear or trimming, from periodontitis, and possibly hematogenously. In herbivores, in which the pulp is divided by enamel foldings, inflammation is usually limited to one division, and is usually purulent. Very mild pulpitis may heal, but usually it terminates in tooth necrosis, periapical abscessation, perhaps with fistula formation, osteomyelitis, or gangrene as inflammation of the pulp extends to the periodontium and the jaws.

Periapical abscess and osteomyelitis of the jaws are complications of pulpitis that may follow clipping the tusks ("needle teeth") of piglets. Trimming of the incisor teeth of sheep to avoid the effects of broken mouth often exposes the pulp cavity, but the pulpitis that ensues is rarely chronic. The exposed pulp canal is healed in 30-50 days by deposition of reparative dentin and secondary dentin. Similar healing presumably occurs in most piglets. Maxillary (malar) abscess of dogs involves the periapical tissues usually of the carnassial tooth, and may cause a discharging sinus beneath the eye. The pathogenesis of the abscess is obscure, but it may be a sequel to crown fractures or to pressure necrosis of periapical tissues. Some chronic inflammations of the pulp become slowly expansive spherical granulomas about the root apex (root granulomas). Occasionally these granulomas are enclosed by an epithelial cyst (periodontal cyst) derived from cell rests of Malassez. The epithelium contains plasma cells, and the combination may have a protective role in periapical sepsis.

Periodontal disease. Periodontal disease is the *most common dental disease of dogs and sheep*, and an important problem in other ruminants, horses, and cats. Although there are minor differences among species, in general, periodontal disease *begins as gingivitis associated with subgingival plaque*, and may progress through gingival recession and loss of alveolar bone to chronic periodontitis and exfoliation of teeth.

The gingival sulcus, or crevice, is an invagination formed by the gingiva as it joins with the tooth surface at the time of eruption. Clinically normal animals have a few lymphocytes, plasma cells, and macrophages under the crevicular epithelium of the gingiva, which forms the outer wall of the crevice. Low numbers of lymphocytes, plasma cells, and macrophages are also present under the junctional epithelium, which is apposed to the enamel of the tooth.

Clinical **gingivitis** is usually initiated by accumulation of plaque in the crevice, but may be associated with impaction of feed, especially seeds, between teeth. Gingivitis is initially characterized by increased numbers of leukocytes and fluid in the gingival crevice, and then by acute exudative inflammation and accumulation of neutrophils, plasma cells, lymphocytes, and macrophages in the marginal gingiva. If the disease progresses, marked loss of gingival collagen fibers, which hold the gingiva to the adjacent tooth, occurs in a few days. This is probably related to the activity of prostaglandins and matrix metalloproteinases generated in inflamed tissue, or possibly enzymes from plaque bacteria, such as *Porphyromonas gingivalis*, which also produce enzymes (gingipains) thought to damage junctional epithelium. *Porphyromonas* spp. are implicated as obligate pathogens for canine gingivitis, and as probable participants in feline gingivitis/periodontitis. Grossly the gingiva is red and swollen because of the hyperemia and edema of inflammation. Acute gingivitis may become quiescent, with lymphocyte aggregations beneath the junctional epithelium. Halitosis is associated with gingivitis in small animals.

Continuation and exacerbations of the inflammation cause apical recession of the tooth-gingiva junction, and resorption of alveolar bone (Fig. 1-6). Alterations in the periodontal flora may be responsible for these exacerbations. A major part of chronic periodontal disease is *resorption of alveolar bone,* which modifies the attachment site of the periodontal ligament. If concomitant bone loss precedes gingival recession, the sulcus is deepened to form a periodontal pocket, which is lined by transformed junctional "pocket" epithelium, and becomes the site of chronic active inflammation. When gingival recession precedes loss of alveolar bone and gingival collagen, pockets do not form, but tooth roots are exposed. In either case, destruction of the periodontium and periodontal ligament,

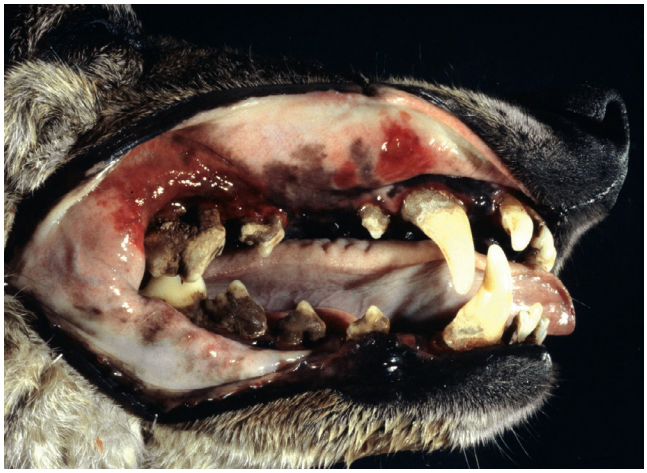

Figure 1-6 Marked gingival recession with exposure of roots of the molar teeth in advanced **periodontal disease** in a dog.

and resorption of alveolar bone, cementum, and root dentin, *lead to exfoliation of teeth*.

Gingivitis is common in **dogs.** Usually it is proliferative, the gingiva being replaced by collagen-poor, highly vascular granulation tissue, which appears as a red, rolled edge next to the tooth. In dogs, gingival pocket formation is quite unpredictable and may be present on one root of a tooth and absent on the other. Bone loss in dogs is often more severe at the bifurcation of two-rooted teeth than in interproximal areas (gingiva between teeth). Resorption of bone is associated with osteitis as the inflammation extends from the periodontium into alveolar bone. In dogs, the premolars and, to a lesser extent, the first molars and central incisors are most severely affected, whereas the second molars and mandibular canines are quite resistant.

Gingivitis is among the most common veterinary problems in **cats**. In general, it resembles that in dogs. Gingivitis in cats is also associated with the feline stomatitis/glossitis complex addressed in the following sections.

In **sheep,** periodontal disease may involve all teeth, but the effects are most severe on the incisors, and periodontal disease is a major cause of premature exfoliation. Sheep develop acute gingivitis during tooth eruption, in association with accumulation of subgingival plaque around the tooth. In some sheep, chronic gingivitis involving the lingual aspect of the incisors ensues, and on farms with a high incidence of broken mouth (lengthening of the incisor crown, forward protrusion, and loosening of the teeth), this progresses to chronic active periodontal disease.

Cara inchada (swollen face) is an epidemic periodontitis of **cattle**, formerly common in the west-central part of Brazil. Animals of 2-14 months were mostly affected, and herd prevalences of more than 50% were recorded. When progressive, cara inchada causes loss of teeth, leading to malnutrition. It is associated with dental eruption, and ingestion of forage thought to contain low levels of antibiotics derived from soil actinomycetes that permit colonization of the periodontal space by a variety of gram-negative bacteria, including *Prevotella* (*Bacteroides*) *melaninogenica*.

Severe periodontitis and tooth loss are an important part of the syndrome associated with *bovine leukocyte adhesion deficiency.*

The sequelae of suppurative periodontitis are many, being mainly variations on a theme of *osteomyelitis.* The osteomyelitis of actinomycosis is discussed in Vol. 1, Bones and joints. If the mandible is involved, the fistula usually develops on the ventral margin. If the maxillary molars are involved, fistulation may occur into the maxillary sinus. If the premolars are involved, fistulation may develop into the nasal cavity or externally. In dogs, involvement of the canine teeth may produce internal or external fistulae, and involvement of the maxillary carnassials usually produces a fistula beneath the eye, and orbital inflammation. Fistulation may be prevented for some time, or permanently, by ossifying periostitis over the involved bone. Fistulae in the upper jaw tend to be persistent. In the lower jaw, they may heal, usually with extensive deposition of new bone. Occasionally, especially in horses, chronic mild periodontitis may be confined by the periodontium, which is, however, expanded by granulation tissue to form a root granuloma. Under the same circumstances, there may be hyperplastic exostosis of the cementum.

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Diseases of the buccal cavity and mucosa

Pigmentation

Melanotic pigmentation is normal and common in most breeds of animals and increases with age. It may be irregular, or the mucosa may be entirely pigmented. Diffuse yellow discoloration may be seen in icterus.

Circulatory disturbances

Examination of the mucous membranes is an essential detail in any clinical or postmortem examination. Pallor may indicate anemia. In cyanosis, the mucosa is dark red-blue. The mucosa are muddy in methemoglobinemia. Acute congestion and cyanosis, associated with ulceration, are common in dogs and sometimes in cats with chronic uremia. Hemorrhages are

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indicative of septicemia, and larger ones may accompany local inflammation, trauma, and the hemorrhagic diatheses. Petechiae on the ventral surface of the tongue and frenulum in horses are consistent with equine infectious anemia, or other thrombocytopenic or purpuric conditions. The active hyperemia that gives the diffuse pink coloration to the mucosa in diffuse stomatitis disappears immediately at death, so that at autopsy the inflamed mucosa is disappointingly blanched.

Foreign bodies in the oral cavity

The presence of feed in the mouth of a cadaver is abnormal, except in ruminants, which may eructate and have feed in the caudal pharynx at the time of death. In most cases it is attributable to disease, which results in paralysis of deglutition or semiconsciousness. It is common in horses with encephalitis, leukoencephalomalacia, and hepatic encephalopathy. The food in such cases is usually poorly masticated and readily differentiated from that refluxed postmortem. Bones or other large foreign bodies lodged in the pharynx of cattle suggest pica of phosphorus deficiency. They may cause asphyxiation or pressure necrosis in the wall of the pharynx. Large portions of root crops may also lodge in the pharynx. Dogs often have bones and sticks that tend to be wedged across the palate behind the carnassial teeth.

In dogs, **foreign-body stomatitis** occurs, caused by plant fibers, burrs, or quills (Fig. 1-7). In mild cases, gingivitis surrounds the incisors and canine teeth. Small papules or vesicles and shallow ulcers may be evident on the tongue. Plant fibers may protrude from the lesions. Chronic cases are characterized by *exuberant granulomas* associated with lingual ulceration and gingival hyperplasia with plant fibers deeply embedded in these lesions. Long-haired dogs are especially prone to develop this type of lesion when they attempt to remove plant material that is trapped in their hair coat. The granulomas must be differentiated from neoplasms.

Sharp foreign bodies that cause laceration of the mucosa predispose to necrotic and deep stomatitis. Grass seeds and awns frequently impact between the retracted gingival margin and teeth in periodontitis of ruminants and exacerbate the local initial lesion, perhaps predisposing to the development of osteomyelitis. Metallic objects, including wire, may lacerate the oral mucosa, especially in cattle. Horses fed dry triticale hay may develop severe oral ulceration, with masses of awns embedded in the ulcers. The ulcers vary in size from 1 mm to 5 cm in diameter and are mainly located at the junction of the labial and gingival mucosa adjacent to the upper corner incisors, the lingual frenulum, the sublingual folds, the base of the dorsum of the tongue, and the soft palate. Similar lesions in horses have been associated with contamination of hay by foxtail.

Swine have a diverticulum of the pharynx in the caudal wall immediately above the esophagus, and barley awns and other rough plant fibers occasionally lodge here and penetrate the pharynx. This occurs mainly in young pigs, and death follows pharyngeal cellulitis. Similar problems occur in sheep following improper use of drenching guns, and in cattle injured by balling guns.

Inflammation of the oral cavity

Inflammatory processes of the oral cavity (*stomatitis*) may be diffuse or focal and they may predominantly affect certain regions to produce, if (1) the pharynx is involved, *pharyngitis*; (2) the tongue, *glossitis*; (3) the gums, *gingivitis*; (4) the tonsils, *tonsillitis* (Fig. 1-8); and (5) the soft palate, *angina*. Lesions limited to the mucosa of the oral cavity are termed *superficial stomatitides*. Processes seated in connective tissues of the mouth, the *deep stomatitides*, are usually sequelae to transient superficial lesions.

Superficial stomatitis. Inflammatory changes may be associated with ingestion of irritating chemicals such as caustic or toxic compounds. An example is paraquat, a herbicide that may cause severe erosive stomatitis in dogs. Dogs and cats that chew on the plant *Dieffenbachia* may develop oral erosions and ulcers. Electrical burns are occasionally seen in puppies or kittens that chew through electrical wires. It is often not possible to differentiate the cause of diffuse stomatitis, but an attempt to do so is important because it may indicate a systemic disease state. Viral diseases causing stomatitis will be considered in detail in the section on Infectious and parasitic diseases of the alimentary tract later in this chapter.

Inflammatory disease, localized to the buccal cavity and not part of systemic viral disease, is also common and important. It is generally caused by the indigenous bacterial flora. The oral microbiota ordinarily contains many microbial species,

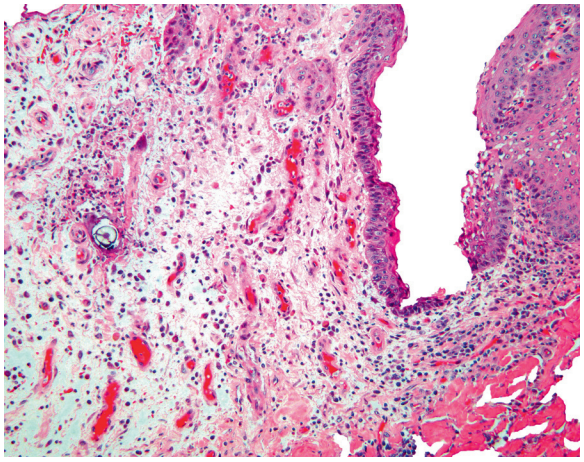

Figure 1-7 Granulomatous reaction to plant material and hair in the tongue of a dog; **foreign-body glossitis**.

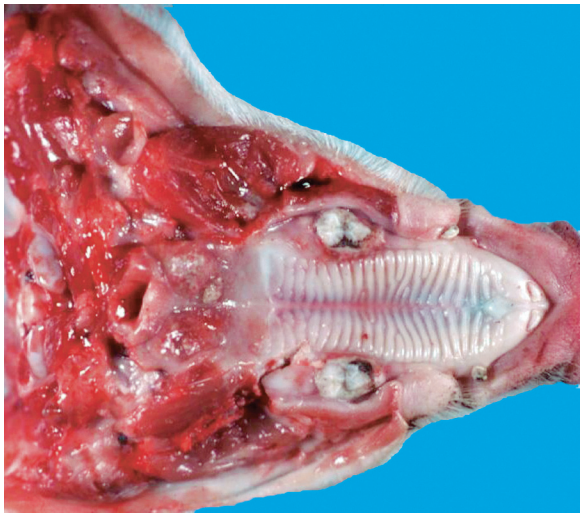

Figure 1-8 Necrotic palatine **tonsillitis** in a pig. (Courtesy Noah's Arkives and A. Doster.)

mainly anaerobes such as *Actinomyces*, *Fusobacterium*, and spirochetes, which exist in balance with each other and in harmony with the host. Disruption of this microfloral balance may lead to stomatitis. The oral mucosa is quite resistant to microbial invasion for several reasons. These include the squamous mucosal lining; antibacterial constituents of saliva such as lysozyme; immunoglobulins, especially immunoglobulin A (IgA), in oral secretions; and the presence of a rich submucosal vascular network and inflammatory cells. Factors altering the balance of indigenous organisms are not well delineated. Systemic illness, stress, and nutritional and hormonal imbalances may alter the microbial population by altering the amount, composition, and pH of saliva. The integrity of the oral epithelium depends on a high rate of epithelial regeneration to balance loss resulting from a high rate of abrasion and desquamation. Rapid epithelial replication promotes quick healing of superficial lesions.

The lamina propria of the oral epithelium is well vascularized, but generally dense and relatively inelastic. For this reason, there is little distention of lymphatics and tissue spaces with fluid exudate, and therefore swelling resulting from edema is not a significant part of stomatitis involving hard palate and gums, with the exception of the gingival margins.

Catarrhal stomatitis. *Catarrhal stomatitis is superficial inflammation of the oral mucosa*, which usually involves the caudal fauces and may be associated with mild gingivitis. It is a common nonspecific lesion, which often develops in the course of debilitating diseases. The mucosae are hyperemic, and the loose texture of the submucosa in the fauces permits development of edema. The swelling is aggravated by edema and hyperplasia of the abundant lymphoid tissues of the soft palate, tonsil, and pharyngeal mucosa. The epithelium accumulates, producing a dull gray mucosal surface. Palatine glands produce excessive mucus. Catarrhal stomatitis resolves with the return of normal oral function.

Thrush, or **oral candidiasis,** occurs most commonly in foals, pigs, and dogs. It involves the proliferation of yeasts and hyphae in the parakeratotic superficial layers of the oral epithelium. It appears grossly as patchy pale-gray pseudomembranous material on the oral mucosa and back of the tongue, and probably reflects alterations in epithelial turnover and oral microbiota (see section on Infectious and parasitic diseases of the alimentary tract, later in this chapter). Mold products of *Stachybotrys alternans* cause catarrhal and necrotizing stomatitis, as well as colitis, if feed is contaminated. Gingivitis and ulceration of the oral mucosa may rarely be associated with infection caused by *Nocardia* spp. in dogs.

Vesicular stomatitides. Stomatitis characterized by the formation of *vesicles* occurs in most species of domestic animals. The vesicles develop as accumulations of serous fluid within the epithelium or between the epithelium and the lamina propria. These may coalesce to form *bullae,* and the elevated epithelium is easily rubbed off during chewing to leave raw eroded patches with bits of epithelium adherent. *The transition from vesicle to erosion occurs rapidly,* so that, in individual animals, vesicles may not be seen. This is especially so in dogs and cats because the oral mucosa is very thin. Because the basal epithelium or basement membrane remains intact, regeneration and healing are complete in a few days unless the local lesions are complicated by bacterial or mycotic infections. However, foci of previous erosion may be identifiable for some months by their slight depression and lack of pigmentation.

Traditionally, vesicular stomatitides in animals were associated with *viral infections,* and these are still important causes. Vesicular stomatitis and foot-and-mouth disease are associated initially with vesicle formation; however, rinderpest, bovine viral diarrhea, and malignant catarrhal fever produce sharply demarcated erosive/ulcerative lesions without initial vesicle formation. *Oral erosions and ulcers in horses, ruminants, and swine should be regarded as indicating one of the vesicular diseases to which the species is susceptible, until proved otherwise* (see section on Infectious and parasitic diseases of the alimentary tract, later in this chapter). Sunburn, photoirritation associated with grazing on celery and related crops, and lesions associated with parvovirus infection in swine may cause lesions of the snout resembling vesicular diseases. Animals exposed to irritant chemicals in feed or bedding may develop vesicles and erosions of the face and oral cavity, for example, toxicity in horses and dogs associated with irritant quassinoids found in wood shavings derived from *Simaroubaceae* species.

Bullous immune skin diseases are recognized with increased frequency, especially in dogs, and some of these have severe oral lesions, which are described here (see also Vol. 1, Integumentary system).

Pemphigus vulgaris is a severe, acute or chronic, vesiculobullous autoimmune disease mediated by autoantibodies to the desmosome protein desmoglein 3, which is involved in joining adjacent epithelial cells to each other. Desmoglein is highly expressed in suprabasal oral epithelium. Pemphigus vulgaris is most common in dogs and cats with rare reports in horses. It is characterized by acantholysis of the epidermis, which results in formation of flaccid bullae and erosions involving mainly mucocutaneous junctions, oral mucosa and, to a lesser extent, skin. Canine pemphigus vulgaris follows a similar pathogenesis to that of humans with overexpression of the proto-oncogene *c-Myc* before acantholysis and bullae formation. *c-Myc* overexpression is likely a consequence of anti-desmoglein 3 antibody binding to its target on basal keratinocytes. Clinically affected dogs and cats have erosions/ulcerations of the oral mucosa and may drool. The oral lesions are generally more prominent than, and precede, the skin lesions. They are most obvious on the dorsal surface of the tongue, which is bright red, with a few scattered pink raised areas representing islands of normal mucosa. The lesions vary greatly in severity and distribution, although the hard palate is often severely ulcerated. Bullae are rarely seen in the oral cavity, because they ulcerate rapidly. Oral pemphigus vulgaris lesions have also been associated with drug reactions in dogs and cats.

Microscopically, the earliest lesion consists of *suprabasilar acantholysis,* which is followed by the formation of clefts. These lead to ulceration of the mucosa. The basal cells of the epidermis remain attached to the basement membrane and form a so-called "row of tombstones." A few neutrophils and eosinophils may infiltrate the epithelium. There is a variable lymphocytic and plasmacytic lichenoid reaction in the propria. *The presence of suprabasilar clefts and bullae caused by acantholysis is considered to be diagnostic of pemphigus vulgaris*. However, extensive erosion and ulceration of the mucosa and secondary bacterial infections frequently obscure these clefts and bullae. Several biopsies from different areas of the oral mucosa may be required to demonstrate the characteristic lesions. A presumptive histologic diagnosis should be supported by direct immunofluorescence tests that show

autoantibodies (usually IgG) and complement in the intercellular spaces of stratified squamous epithelium.

Bullous pemphigoid is a term that has been applied generically to superficial autoimmune vesiculobullous or ulcerative disease of mucous membranes (including the oral mucosa) and skin, characterized by subepithelial clefting; acantholysis is not a feature. It has been reported in humans, horses, dogs, and cats. It is now recognized that there is a *complex of autoimmune subepidermal blistering diseases,* varying in their target antigen, clinical manifestations, and prognosis. Those involving the oral cavity of cats and dogs include bullous pemphigoid, mucous membrane (cicatricial) pemphigoid, and canine epidermolysis bullosa acquisita. All are characterized by circulation of IgG and IgE autoantibodies against specific basement membrane antigens. The characteristic microscopic lesions of all are transient subepidermal blisters, which may contain fibrinocellular exudates with variable numbers of neutrophils and eosinophils. Differentiation and diagnosis of each is by the detection of circulating antibody directed at appropriate antigens, using ELISA or immunofluorescent tests, or by identification of immunoglobulin fixed to basement membrane. Paraneoplastic bullous stomatitis characterized by subepithelial clefting has been reported in a horse with a hemangiosarcoma.

Bullous pemphigoid is retained as the name for the second most common of the autoimmune subepidermal blistering disease in dogs and cats. The lesions mainly occur on haired skin, and a minority of cases involve the mucocutaneous junctions or mucosae, including the mouth, which is affected about one-third of the time. Microscopically, there is a rich neutrophilic and eosinophilic dermal infiltrate adjacent to, and sometimes spilling into the subepidermal bullae. The targets for the autoimmune response are epitopes on canine collagen XVII (also called bullous pemphigoid antigen 2 or BPAg2). Collagen XVII is an epithelial transmembrane protein that is a component of the hemidesmosome that joins basal keratinocytes to the lamina densa of the basement membrane.

Mucous membrane pemphigoid is the most common autoimmune subepidermal blistering disease of small animals, causing about half of all cases. Adults are predominantly affected, and among dogs, German Shepherds are overrepresented. The oral mucosa is a common site for lesion development, including gingiva, palate, and tongue. Typically, subepidermal vesicles in mucous membrane pemphigoid are associated with a relatively sparse inflammatory infiltrate. The antigen targeted by autoantibodies is collagen XVII or, in a low number of cases, laminin-5. Basement membrane–fixed immunoglobulin is detected by direct immunofluorescent or immunoperoxidase staining of formalin-fixed paraffin-embedded tissue.

Epidermolysis bullosa acquisita is a rare disease of dogs, representing about 25% of cases of autoimmune basement membrane diseases, with a poor prognosis. The associated autoantibodies are directed against collagen VII, which makes up the anchoring fibrils that join the lamina densa of the basement membrane to the type I collagen of the dermis. The lesions are most common on skin, and advance rapidly to erosions at points of friction, but the oral epithelium often sloughs extensively. Intact subepidermal vesicles may contain no inflammatory cells, or neutrophils may accumulate at the basement membrane, sometimes forming subepidermal microabscesses. The results of serum or cutaneous immunofluorescent tests resemble those in bullous pemphigoid or mucous membrane pemphigoid, but the autoantibodies may be recognized binding to the lower part of the basement membrane.

The oral lesions of pemphigus vulgaris and of the subepidermal blistering diseases must be differentiated from lesions caused by trauma, toxic epidermal necrolysis, drug eruptions, chronic uremia, mucocutaneous candidiasis, and lymphoreticular malignancies.

Feline calicivirus causes mainly a respiratory infection in cats. The disease is complicated by lingual and oropharyngeal ulcers, which start out as vesicles. They are 5-10 mm in diameter, smooth, and well demarcated from the surrounding normal mucosa. They occur mainly on the rostrodorsal and lateral surfaces of the tongue and each side of the midline of the hard palate. The palatine lesions are apparently more severe in cats fed dry food. Microscopically, the earliest lesions consist of foci of pyknotic cells in the stratum corneum and superficial stratum spinosum. They progress to foci of necrosis with vesicle formation and subsequent erosion and ulceration of the mucosa. Regeneration of the oral mucosa in the ulcerated areas generally occurs within 10-12 days. A single layer of squamous epithelial cells extends from the margins of the ulcer beneath a layer of exudate. Active viral replication also takes place in the tonsillar crypt epithelial cells, and virus may be recovered from these areas for weeks postinfection. Viral inclusions have not been observed in oral epithelial cells. The virus is isolated from a high percentage of cats with chronic stomatitis. Concurrent infection with felid herpesvirus 1 may also occur.

Erosive and ulcerative stomatitides. This form of stomatitis is characterized by local epithelial defects of the oral mucosa and nasolabium and is usually associated with acute diffuse stomatitis and pharyngitis. *Erosions* are circumscribed areas of loss of epithelium, which leave the stratum germinativum and basement membrane more or less intact. They are usually associated with acute inflammation in the underlying propria. The erosions vary in size and shape. Although they are often a nonspecific development in a wide variety of conditions, they are also an essential part of a number of important diseases. They heal cleanly and quickly, but if secondarily infected or complicated, may develop into ulcers.

Ulcers, in contrast to erosions, are deeper deficiencies that extend into the substantia propria. They too vary greatly in size and shape; the edges tend to be elevated and ragged, and when they heal, it is with scar formation.

The causes of ulcerative stomatitis are in general those of erosive stomatitis. There are, however, a number of recognized syndromes and specific diseases in which the predominant change is ulceration. Phenylbutazone intoxication in horses may cause oral ulcers in concert with ulcers of the stomach, intestine, and colon; the syndrome is discussed with ischemic diseases of the gut.

Chronic gingivostomatitis—a progressive stomatitis that involves the palatoglossal arches, gingiva, palate, and tongue—is most common in cats, but occurs at a lower frequency in dogs. A number of terms have been used to describe these clinical entities, including *lymphoplasmacytic stomatitis* and *plasma cell gingivitis-stomatitis-pharyngitis*. There are commonalities and differences among the manifestations of these entities, and it is likely that they represent a continuum of disease processes. Two broad categories are described in the following, with the understanding of their overlapping clinical signs, gross and microscopic pathology, and potential etiologies.

Feline ulcerative stomatitis and glossitis or lymphocytic-plasmacytic stomatitis, is an ulcerative and chronic inflammation of the mucosa of the fauces, the angle of the jaws and, less commonly, the hard palate, gingiva, and tongue. Microscopically, there is diffuse inflammation of the oral mucosa and submucosal connective tissues, dominated by lymphocytes and plasma cells. The syndrome is more common in older cats and may accompany periodontitis. The cause is unknown, but is probably multifactorial, involving imbalance in the oral microbiota, with predominance of gram-negative anaerobes and spirochetes, leading to an overall decrease in the microbial diversity at inflammatory lesion sites. Some have reported the isolation of feline calicivirus and felid herpesvirus 1 from more cats with lesions of chronic stomatitis compared with those without, but the role of these viruses in the etiology is unresolved. Feline calicivirus can persist as a sequel to previous disease episodes and in the face of prior vaccination. Feline leukemia virus and feline immunodeficiency virus may predispose some cats to chronic stomatitis because of their immunosuppressive effects, but evidence of infection is not consistently found.

Feline plasma cell gingivitis-pharyngitis or **feline chronic gingivostomatitis** is characterized by raised erythematous, proliferative lesions, mainly in the glossopalatine arches, extending caudally to the palatopharyngeal arch and rostrally to the gingiva. The lesions may involve Eustachian tubes and also can affect the conjunctiva. Histologically the mucosa is hyperplastic and frequently ulcerated, with a marked submucosal inflammatory cell reaction, mainly plasmacytes, including binucleate cells and cells containing Russell bodies. Neutrophils, lymphocytes, and histiocytes are scattered among the plasma cells. Inflammation is most intense at the epidermal-lamina propria junction. Affected cats have elevated polyclonal serum gamma-globulin levels. The polyclonal gammopathy and the plasmacytic, lymphocytic reaction are suggestive of an immune-mediated lesion, and differentiation from mucosally associated lymphoid neoplasia may be challenging. The etiology and the relationship of this syndrome to feline ulcerative stomatitis and glossitis (see previous section) are unclear; the 2 syndromes probably form a continuum, although the plasma cell predominance and the hypergammaglobulinemia attributed to plasma cell gingivitis–stomatitis are distinguishing. Similar stomatitis occurs in dogs.

Eosinophilic ulcer (eosinophilic granuloma, lick granuloma, labial ulcer, rodent ulcer) is a chronic, superficial ulcerative lesion of the mucocutaneous junctions of the lips, and, to a lesser extent, the oral mucosa and skin, in cats of all ages. The cause is unknown. A number of etiologies have been considered, including allergic disease and primary eosinophil dysfunction. The lesions may respond to corticosteroid, oral progestagens, cryosurgery, or radiation therapy, although recurrences are common. Typically, well-demarcated, red-brown, shallow ulcers, often with elevated margins, occur on the *upper lip on either side of the midline.* They are usually a few millimeters wide and several centimeters long. Occasionally, ulcers are present elsewhere in the mouth, such as on the gums, palate, pharynx, and tongue. Skin lesions are located in those areas that are frequently licked, such as the neck, lumbar area, and abdomen. Microscopically, the squamous mucosa is ulcerated, with large areas of necrosis of the underlying connective tissues and accompanied by a marked inflammatory cell reaction. The cellular reaction consists predominantly of neutrophils at the periphery of the ulcers, with plasma cells and mast cells in the lamina propria. Eosinophils and macrophages may not be prominent, especially in the chronic stages of the lesion.

Eosinophilic ulcer is one of the 3 different types of lesions that have been associated with the so-called *eosinophilic granuloma complex*. The other 2 conditions, *eosinophilic plaque* and *linear granuloma*, cause mainly skin lesions, which are different clinically and morphologically from eosinophilic ulcer (see Vol. 1, Integumentary system).

Oral eosinophilic granuloma (collagenolytic granuloma) in dogs occurs as a familial disease in young Siberian Huskies. Sporadic cases have been reported in other breeds, especially Cavalier King Charles Spaniels. Affected dogs have single or multiple firm, often ulcerated, raised plaques, which are covered by yellow-brown exudate, on the *lateral or ventral surfaces of the tongue.* Lesions on the soft palate are less common, and here they tend to be oval to circular ulcers with slightly elevated borders.

Microscopically, *foci of collagenolysis* in the mid and deep zones of the lingual submucosa are surrounded by a mainly granulomatous inflammatory reaction, with macrophages, giant cells, lymphocytes, plasma cells, and mast cells. *Eosinophils* are a constant feature, but their numbers vary from few to many. The lesions are identical to those seen in linear granuloma of cats.

The cause is unknown, although the morphology of the lesion and the response to corticosteroid therapy suggest hypersensitivity. The familial tendency in Siberian huskies indicates that hereditary factors are involved. *Eosinophilic granuloma must be differentiated from oral mast cell tumors,* which also affect the tongue in dogs. Degeneration of collagen fibers is often a feature of mast cell tumors; however, in mastocytoma, the characteristic mixture of mast cells and eosinophils infiltrates the tongue and connective tissues more diffusely. The mast cells may be in various stages of degranulation, and inflammation is minimal or absent in mast cell tumors.

Horses with **eosinophilic epitheliotropic disease** (see Vol. 1, Integumentary system and the later section on Eosinophilic enteritis in cats and horses) may also have eosinophilic stomatitis and lingual ulceration.

Ulcerative stomatitis can be a presenting lesion in *erythema multiforme* in dogs, and must be differentiated from oral epitheliotropic T-cell lymphoma.

In dogs there may be foci of ulceration in the mucosa of the lip or cheek that overlies areas of severe periodontal inflammation. This has been termed **chronic ulcerative stomatitis** or **chronic ulcerative paradental syndrome**.

Feline viral rhinotracheitis is a common upper respiratory tract infection of cats caused by felid herpesvirus 1 (see Vol. 2, Respiratory system). This virus may cause ulcerative lesions in the mouth, especially on the tongue. Rarely, oral and skin ulcers may occur, without evidence of concurrent respiratory tract infection. Microscopically, foci of cytoplasmic vacuolation in squamous epithelium evolve into areas of necrosis and ulceration. The ulcers are often covered by a layer of fibrinocellular exudate. Herpetic inclusions may be present in epithelial cells at the periphery of the ulcers.

Uremia associated with chronic renal disease often causes fetid *ulcerative stomatitis* in dogs, and less commonly in cats. Dirty gray-brown ulcers occur on the gums, lateral surface, and margin of the tongue, and on the inner surface of the lips

and cheeks, often adjacent to the openings of salivary ducts. The margins of the ulcers are swollen and hyperemic.

The pathogenesis of the oral lesions in uremia is poorly understood. Elevations in blood and salivary urea in combination with urease-producing bacteria, normally present in the oral microflora, may generate ammonia from salivary urea. Ammonia has a caustic effect on the oral mucous membranes. Experimental antibody production against urease renders some intestinal bacteria nonpathogenic and prevents uremic colitis, providing evidence of the importance of urease. However, there is poor correlation between the levels of blood urea and the development of uremic stomatitis, suggesting other important factors. Uremic vasculitis and impaired microvascular perfusion may contribute to the pathogenesis of uremic stomatitis.

Salivary glucose levels may be elevated in dogs and cats with *diabetes mellitus,* resulting in an imbalance of the oral microflora and predisposing to chronic gingivitis in diabetic animals.

Ulcerative glossitis and stomatitis in **swine** is commonly part of **exudative epidermitis** (greasy pig disease) of preweaning pigs (see Vol. 1, Integumentary system). In addition to the characteristic skin lesions, about a third of the piglets may develop ulcers on the dorsum of the tongue. Erosions and ulcers of the hard palate occur in a small number of piglets. Microscopically, there is ulceration of the squamous mucosa with coagulative necrosis, and vesicle and pustule formation in the superficial epithelium over the rete pegs. A pleocellular inflammatory reaction is evident in the connective tissue below the ulcers.

Further reading

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Deep stomatitides. Lesions of the oral mucosa may permit the entry of pyogenic bacteria, often normal oral flora, into the connective tissues of the submucosa and muscle. Purulent inflammation or cellulitis may develop in the lips, tongue, cheek, soft palate, and pharynx. Abscesses may form and may fistulate through the mucosa or skin. Abscesses in the wall of the pharynx may result from necrosis of retropharyngeal lymph nodes. Necrotic stomatitis with simple necrosis of the epithelium and lamina propria may be produced by thermal or chemical agencies, but in animals, it is usually caused by *Fusobacterium necrophorum* and other anaerobes.

Fusobacterium necrophorum is the principal cause of **oral necrobacillosis** or **necrotic stomatitis** in animals. It is also associated with necrotizing lesions elsewhere in the upper and lower alimentary tract, and liver. Wherever it occurs, it is usually a secondary invader following previous mucosal damage (Fig. 1-9A). The organism produces a variety of exotoxins and endotoxins; among the latter are leukocidins, hemolysins, and a cytoplasmic toxin, all of which probably enhance the necrotizing ability of the organism. Once established in a suitable focus, *F. necrophorum* proliferates, causing extensive coagulative necrosis.

The best-known form of necrobacillary stomatitis is **calf diphtheria,** an acute necrotizing ulcerative inflammation of the buccal and pharyngeal mucosa, and also of the laryngeal mucosa (**necrotic laryngitis**). The predisposing lesions may include trauma, infectious bovine rhinotracheitis, and papular stomatitis. Necrosis of palatine and pharyngeal tonsils may be seen. The incidence of diphtheria in slaughtered beef cattle may be as high as 1.4%. The same syndrome is rather common in housed lambs as a complication of contagious ecthyma. The infection also may be initiated in the gums about erupting teeth in any species, and by the trauma produced in baby pigs by removing the needle teeth. It is frequently fatal in young animals, in which extension often occurs to other organs. In adults, oral necrobacillosis tends to remain localized to the oral cavity, where it may complicate vesicular and ulcerative stomatitides. It is not unusual, however, for the infection to spread down the alimentary tract.

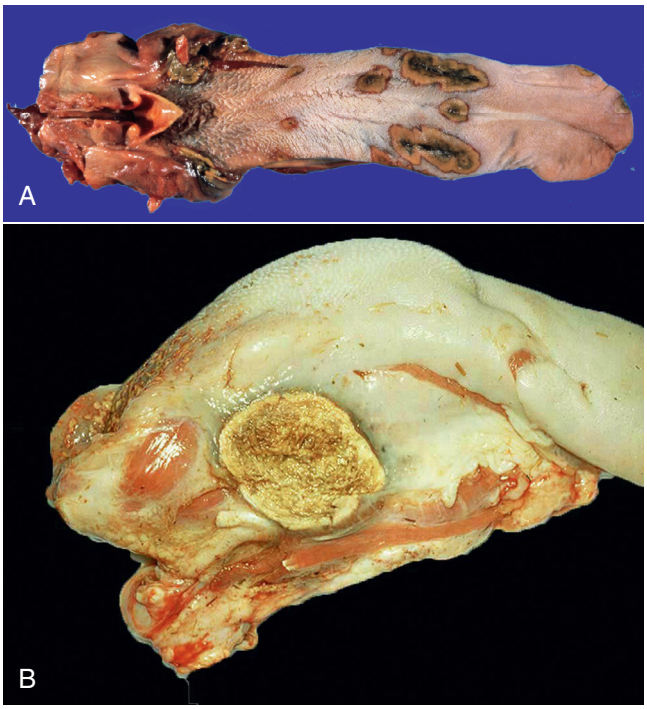

Figure 1-9 **A.** Necrotic **glossitis and stomatitis** in a dog. **B. Oral necrobacillosis** in a calf. (Courtesy Noah's Arkives.)