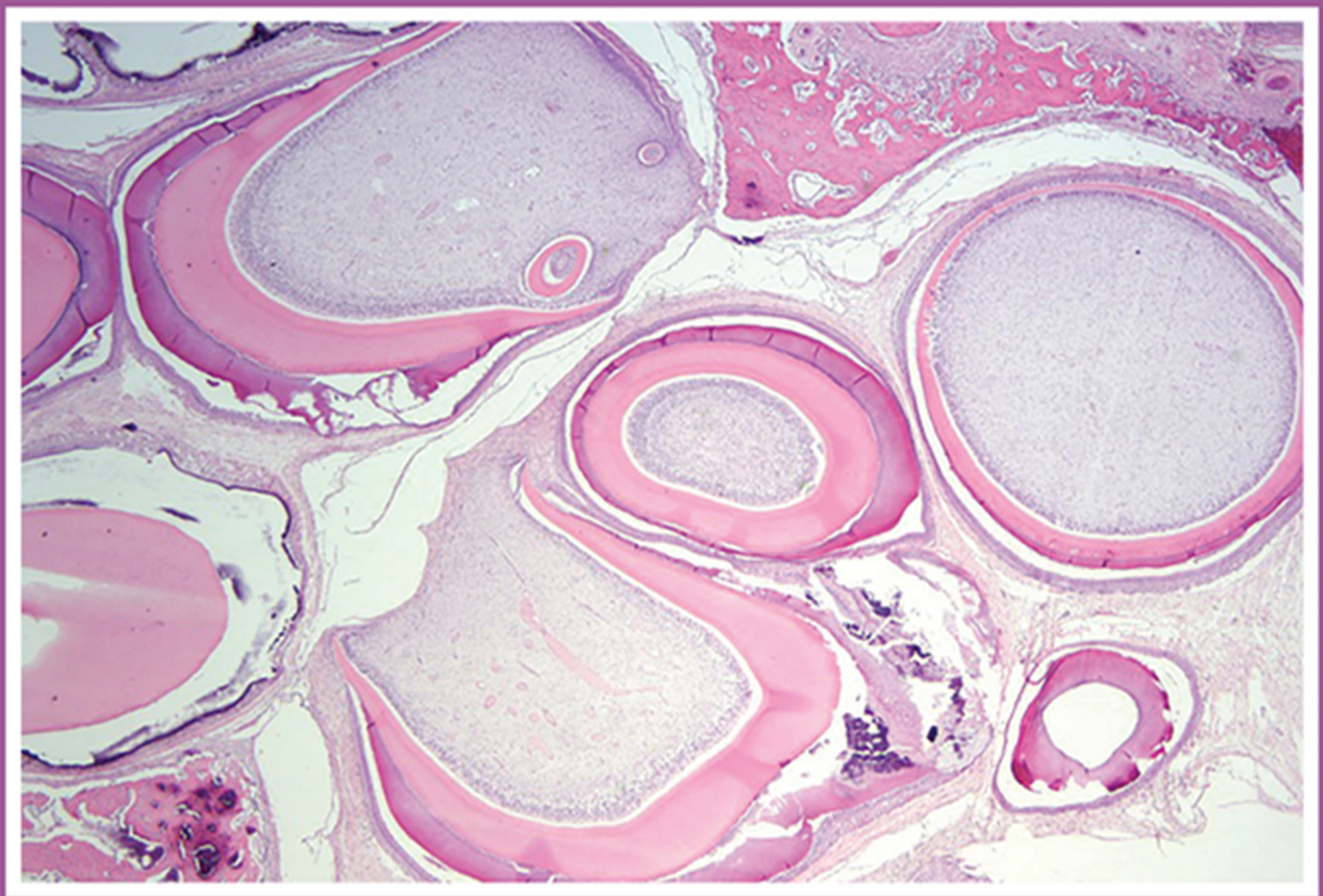
Veterinary Oral and Maxillofacial Pathology

Brian G. Murphy • Cynthia M. Bell • Jason W. Soukup



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Preface

This book is an attempt to address a perceived deficiency in the veterinary pathology literature and to provide a current and useful resource for diagnostic veterinary pathologists, veterinary dentists, oral surgeons, resident trainees and others with an interest in oral and maxillofacial pathology of veterinary species.

The text is *focused on methods for establishing a diagnosis and set of differential diagnoses*. Many oral lesions are unique (tooth-related lesions, fibrous lesions of the oral mucosa and jaws), and have their own nomenclature and embryologically informed pathogenesis. These lesions can be confusing to the non-specialist and are a central focus of this work.

Differential diagnoses for each lesion are a prominent feature of the text and expose the philosophy that lesion classification in oral pathology is ever- evolving. As much as possible, we have attempted to be up front with the reader concerning the often considerable ambiguity and morphologic overlap of oral lesion classification. The importance of a multi-modal approach to lesion classification is stressed throughout. We have attempted to directly address the controversies over lesion taxonomy and relationships between lesions, pathogenesis, and lesion nomenclature, and to not ignore or obfuscate these issues. Although examples of oral lesions are drawn from diverse species, the principal focus is on mammalian companion animals (dog, cat, horse) with less of an emphasis on ruminants, camelids and laboratory animal species (primate, rodent and rabbit).

Each chapter stresses the importance of a holistic approach in establishing a meaningful diagnosis, taking into consideration the patient signalment, lesion history, the often invaluable opinion of the submitting clinician, pre-biopsy imaging findings, and gross features of lesions, *in addition* to the histological features of the submitted specimen. In an attempt to clarify what is often perceived as an impenetrable subspecialty of veterinary pathology, the text has been richly illustrated with relevant radiographs, clinical, gross and histologic images (including special stains and IHC), as well as line drawings and diagrams. Key gross and histologic features, along with differential diagnoses to consider, have been provided for each lesion.

Although the focus of this work is on the establishment of a diagnosis and differential diagnoses, information has also been provided on lesion pathogenesis, prognosis, and treatment. It is *not the goal* of the authors to cover all of the oral and maxillofacial lesions which have been heretofore described in domestic animals, but rather to focus on complex and unique oral lesions, as well as those that a diagnostic veterinary pathologist would likely encounter in a surgical biopsy practice. It is important for the pathologist to recognize that what they see from day-to-day in their practice, even a busy specialist practice, may not represent the diversity of actual maxillofacial/oral pathology that occurs in veterinary species. Pathologists have a window on a subset of disease- those lesions that get biopsied or are present at the time of the animal's death (discovered during the necropsy examination).

Oral lesions that also occur in other systems and/or have been exhaustively described elsewhere will be less emphasized. Lesions encountered by clinical oral specialists (dentists) but rarely sampled or submitted for histological examination (palatal developmental disorders, malocclusions) will also be less emphasized. It is not the goal of this work to duplicate quality information available from other resources.

Brian G. Murphy
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Jason W. Soukup

Acknowledgments

Many people contributed their time, knowledge and creativity to this project. This is particularly true of our primary editor, Kirsten Murphy, who carefully read and considered every word of this work, often multiple versions of it. We are most grateful for her discerning eye.

Multiple people provided critical subject-specific expertise including Jennifer Luff, Nicola Pusterla, Stefan Keller, Richard Jordan, Peter Moore, Verena Affolter, Roy Pool, Santiago Diab, Boaz Arzi, Jamie Anderson, Denise Imai-Leonard, Richard Dubielzig, Mal Hoover, Donnell Hansen, Bonnie Shope, Liz Layne, Mary Bagladi-Swanson, and Melissa Behr. Alex Harvey, Kate Lieber, and Allison Klein all provided invaluable logistical support.

We are grateful for the numerous clinical and gross images provided by residents, veterinary clinicians, dentists and anatomic pathologists. Images are the backbone of this work; without them, the story would be greatly diminished. Each of these specific contributions has been acknowledged where it appears throughout the textbook.

We would also like to thank our families for their support, love and tolerance.

About the Companion Website

Don't forget to visit the companion website for this book:

www.wiley.com/go/murphy/pathology

We have created a companion website featuring a series of guided histological tours showcasing select oral pathology lesions (oral malignancies, odontogenic tumors, proliferative fibro-osseous lesions, oral inflammation, etc.). Microscopic images have been digitally captured using a slide scanner and appended to an annotated voice file (BGM and CMB) strategically walking the viewer through the lesions' salient diagnostic features. It is the authors' hope that the reader will find these annotated digital files to be useful.

1

A Philosophical Approach to Establishing a Diagnosis

Lesions in the oral cavity of veterinary species are common, and the pathologist's correct diagnosis can play an important role in the well-being of animals and owners alike. Unfortunately, multiple factors can conspire to make the diagnosis of oral and maxillofacial lesions difficult: some oral lesions can be rare and one-of-a-kind, lesions may require extensive decalcification, the existing literature is arguably less comprehensive for oral diseases than for other body systems, and perhaps most importantly, oral lesions with markedly different outcomes can demonstrate coalescing morphologic features. It is the authors' opinion that the factors that make these lesions challenging to diagnose can also make them intellectually attractive, and the pursuit of the most appropriate diagnosis a rewarding one. This book was written with this concept ever in mind.

While lesions in the oral cavity can share multiple morphologic features with lesions in other body systems, some oral lesions are absolutely unique and may be found nowhere else. In addition, pathologic lesions arising from the jaw can also be unique, as maxillary and mandibular bone tissue is embryologically and physiologically unlike bone of the appendicular skeleton. Perhaps most importantly, the oral cavity and jaws of higher vertebrates include teeth, the sole anatomic structures that bridge the skeletal and digestive systems.

One of the most important goals for a diagnostic pathologist is to establish the correct diagnosis – *to put the right lesion into the right categorical box*. To accomplish this, veterinary pathologists have long utilized the framework of human oral disease as a template for organizing the oral lesions of veterinary species. While humans and veterinary species share certain features of oral pathophysiology, it is the authors' opinion that oral lesions that occur in human beings do not fully capture the great diversity of pathology that occurs in veterinary species. Likewise, many clinicopathological entities in humans are defined or subclassified by specific demographic, behavioral, and/or environmental factors that are unlikely to be significant in animals.

Diagnosis is a form of *categorization,* and the process of categorization is a human construct. We created *categorization* as a means of dividing up the natural world. Making sense of veterinary oral pathology through categorization is a process that has been going on for more than a century, and many individuals have made important contributions to this effort. Unfortunately (or perhaps fortunately), nature is highly complex. Because this effort to diagnose and categorize is a difficult one, it is essentially an iterative process, and such attempts will always remain works in progress.

In order to establish a diagnosis, many pathologists adhere to a heuristic process of morphologic pattern recognition. For the experienced pathologist, this cognitive process may even occur at a level beyond conscious recognition. The diagnosis *just feels right*. Although the end goal of establishing a correct diagnosis may be met, a dependency on the process of pattern recognition alone remains an imperfect one, as oral lesions can and frequently do share overlapping morphologic features.

Bell curves can be constructed as simple, two-dimensional metaphors representing the diversity of morphologic types found within a particular type of lesion (Figure 1.1). For such curves, the diversity of a particular morphologic feature or collection of features within a lesion can be represented along the x-axis, while the frequency of occurrence of those features in a population of lesions is mapped along the y-axis. In such a system, a steep and narrow bell curve suggests that relatively little morphologic diversity exists within the lesion type, while a broad-based bell curve suggests the opposite. Superimposition of these curves graphically demonstrates this concept of overlapping morphologic features (Figure 1.2). Structural overlap between lesions presents a diagnostic challenge for the pathologist and is a concept that will be returned to throughout this book.

It is the opinion of the authors that the examination of histologic features frequently allows the designation of a principal diagnosis along with one or more differential diagnoses. These differential diagnoses are important

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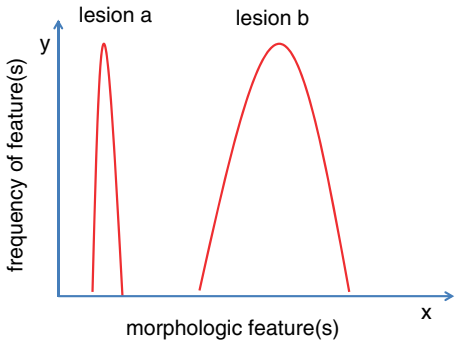

Figure 1.1 Bell curves representing lesion diversity and frequency. For a given lesion, the *x*-axis can represent a single morphologic feature or set of morphologic features that collectively comprise the lesion in question. The *y*-axis represents how common the particular morphologic feature(s) is/are within a group of similar lesions; lesions with a broad curve are morphologically diverse and therefore more difficult to diagnose.

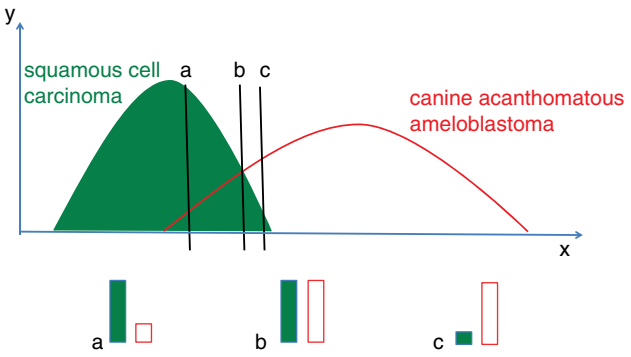

Figure 1.2 Superimposed bell curves are a metaphor for the morphologic overlap between related lesions. Some lesions, like squamous cell carcinoma (SCC) and canine acanthomatous ameloblastoma (CAA) can either be morphologically distinct lesions (extreme right and left edges of the two bell curves) or share multiple features (within the region of curve overlap). Sections a, b, and c represent lesions that are most likely to be SCC, equally likely to be SCC or CAA, or more likely to be CAA, respectively.

and should be included in the report sent to the submitting clinician. Assigning a principal diagnosis and accompanying set of differential diagnoses effectively conveys a measure of ambiguity, which may have great value for the clinician. For these reasons, histologically related lesions (differential diagnoses) have been included for each lesion type described in this book.

To assist in this difficult but ultimately rewarding endeavor, the judicious use of appropriate immunohistochemical assays and/or special stains can be invaluable to inform the final diagnosis. Perhaps even more importantly, clinical data, most typically available through the submitting clinician, should be sought out. Patient signalment, anatomic location, and lesion natural history can be invaluable facets of the final diagnosis. Radiographic imaging studies and/or three-dimensional imaging studies like computed tomography may be available. The opinion of the clinician/ radiologist regarding such studies, or better yet, the diagnostic images themselves, should be reviewed by the pathologist in conjunction with the gross and histological features of the submitted sample.

If not openly offered, the opinion of the submitting clinician should be sought out, as an astute clinician will often have made a preliminary clinical diagnosis prior to submission. This *clinical diagnosis* may be correct, based upon the clinician's experience, the anatomic location, results of diagnostic imaging studies, signalment of patient, clinical signs, and prior biopsy results. The diagnosis of relatively common oral lesions such as odontogenic cysts and equine cementomas (nodular hypercementosis) are highly dependent upon their anatomic relationship with teeth, jawbones, and/or the paranasal sinuses. Some clinicians have a curious policy of withholding such information from the pathologist in a dubious attempt to "not influence the diagnostic process." It is likely that these same clinicians would be at a loss if their own clients withheld important clinical information for the same reason.

There is also value in seeking out the opinions of colleagues or even trainees. At academic institutions, such opinions are typically readily available, and such advice may even be offered without asking for it! Useful discussions can also occur in the setting of private diagnostic labs, even in those laboratories staffed by a single pathologist. The common use of digital images facilitates rapid communication, and networks of colleagues around the world are often willing to lend a hand. Finally, following a challenging lesion *down the road* can be a valuable learning experience in itself. Does the eventual clinical outcome fit the diagnosis, and most importantly, can one learn from it?

2

Histological Features of Normal Oral Tissues

Histopathological evaluation of oral tissues requires a solid understanding and familiarity with the normal microscopic anatomy. Several tissues, such as teeth, are anatomically unique to the oral cavity. The authors hope that this brief chapter will assist readers with acquiring this basic understanding and enable them to interpret tissue changes accurately and meaningfully. We highly recommend Ten Cate's *Oral Histology* [1] as a highly detailed and authoritative resource for learning more about the unique histology, development, and physiology of oral tissues.

2.1 Oral Mucosa

Oral mucosa covers the entire surface of the oral cavity with the exception of the gingiva, which is a specialized form of mucoperiosteum (discussed below). The mucosa consists of surface epithelium and lamina propria. In most areas, there is also a distinct submucosa of fibrous connective tissues that is looser (usually) and supports other structures such as glands, muscle, and larger vessels and nerves. Depending on the location within the oral cavity, the mucosa varies in thickness and extent of keratinization. For example, particularly delicate buccal mucosa (also called vestibular mucosa) and sublingual mucosa line the inner surface of the cheeks and the floor of the mouth, respectively. In contrast, the palatal mucosa lining the hard palate is more durable, with thicker epithelium, occasional keratinization, and compact collagen within the lamina propria (Figure 2.1).

The non-keratinized epithelium (e.g. buccal and sublingual mucosa) has four layers that are distinguished by morphological differences – from deep to superficial: basal cell layer, prickle cell layer, intermediate cell layer, and superficial layer. Identification of layers is slightly different with keratinized epithelium (e.g. hard palate and dorsal tongue): basal cell layer, prickle cell layer, granular cell layer, and keratinized (usually parakeratinized) layer. In the oral cavity, unlike the epidermis, parakeratinization can be a normal pattern of squamous cell maturation/ differentiation. The lamina propria (also called mucosa propria) is divided into two layers – papillary and reticular. The papillary layer *interdigitates* with epithelial pegs and has capillary loops in close proximity to the epithelial basement membrane. With small vessels and bundles of collagen, the deeper reticular layer blends into the underlying submucosa (Figure 2.1).

The submucosa also varies in density and amount of collagen matrix. Minor salivary glands and their associated ducts are widely distributed throughout the oral submucosa (Figure 2.2). Occasionally, organized lymphoid tissue is present within the submucosa, particularly in the soft palate of young animals. As in the dermis, inflammation is often superficial, and cellular infiltrates are densely distributed within the lamina propria (see Figure 2.3).

Specialized mucosa of the tongue includes various types of papillae (filiform, fungiform, vellate). Some species, especially cats, also have filiform keratin projections on the hard palate mucosa. The rostral hard palate has an *incisive papilla* composed of cartilage that should not be mistaken for pathology.

2.2 Gingiva

The gingiva is a unique and distinct tissue that is characterized by surface epithelium and its underlying fibrous stroma which, together, comprise a mucoperiosteum. In the gingiva, there is no distinct lamina propria or submucosa, since the fibrous stroma extends from the epithelial basement membrane to the periosteal surface of the underlying alveolar bone of the jaw. The fibrous stroma is poorly cellular and overwhelmingly composed of densely organized, intersecting robust bundles of fibrillar collagen. Gingival stroma has an indistinct transition to periosteum – these two tissues are firmly connected by abundant extracellular fibers.

Like the oral mucosa, the gingiva has variation among specific anatomical sites. This variation is not as much a function of location along the dental arcades as it is

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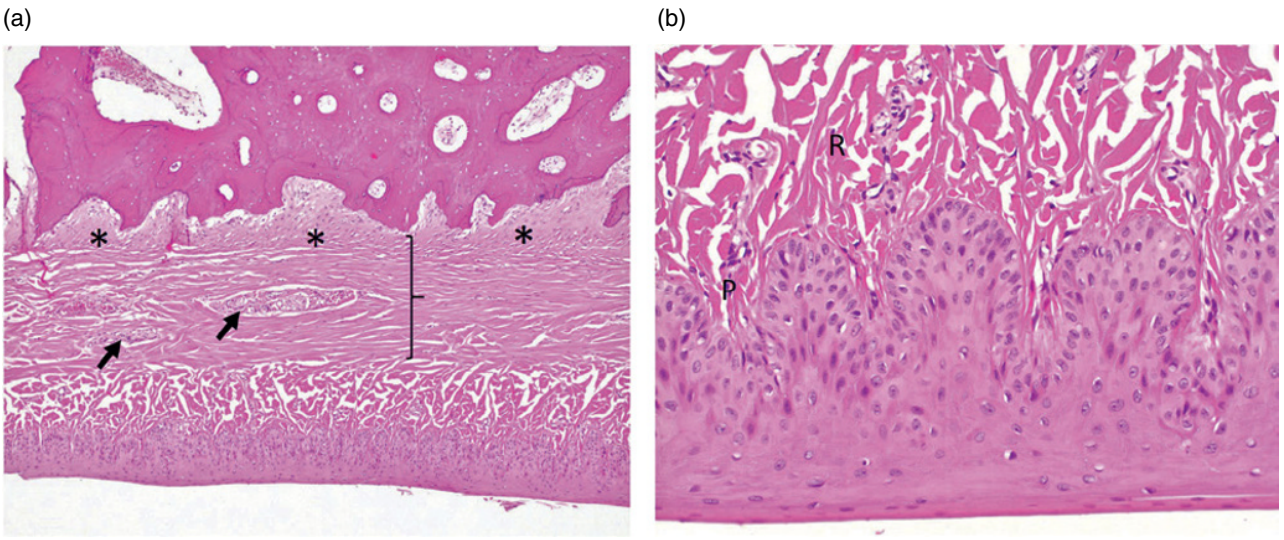

Figure 2.1 Histologic images of the hard palate of a five-month-old male boxer dog. (a) There is a compact fibrous submucosa (bracket) between the palatal mucosa and the periosteum (asterisks) of the palatine bone. Neurovascular bundles (arrows) course within this layer. (b) The mucosal epithelium of the hard palate is thick relative to many other area of the oral cavity, and the surface layers may be parakeratinized. The papillary (P) layer of the lamina propria interdigitates with the epithelium, and the reticular (R) layer contains more prominent vasculature.

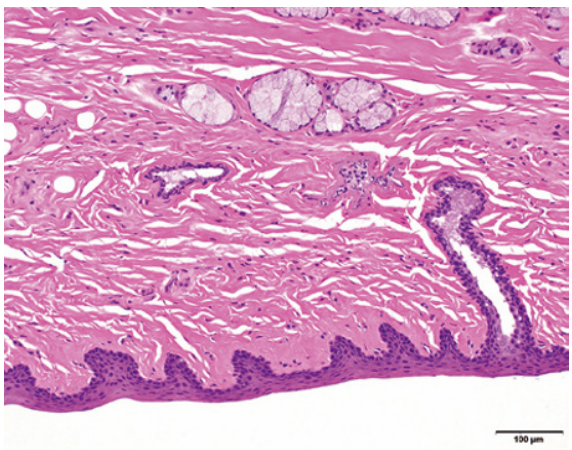

Figure 2.2 Histologic image of the soft palate mucosa from a seven year old, spayed female domestic short-haired (DSH) cat. Minor salivary glands are abundant throughout the oral mucosa. These glands open directly onto the mucosal surface via small ducts.

location with respect to individual teeth. The *attached gingiva* is a more or less flat layer that covers alveolar bone; it is mucoperiosteum and organized as described above. The *free gingiva* represents the unattached margin of this mucoperiosteum as it meets and transitions to tissues that line the sulcus, then attaches near the cementoenamel junction of the tooth (Figure 2.4).

The free gingiva is comprised of tissue from two different embryological sources, and this difference is readily appreciated in the mature animal. The outer surface is derived from gingiva, whereas the lining of the sulcus is derived from odontogenic origin, specifically the reduced enamel epithelium and dental follicle that once surrounded

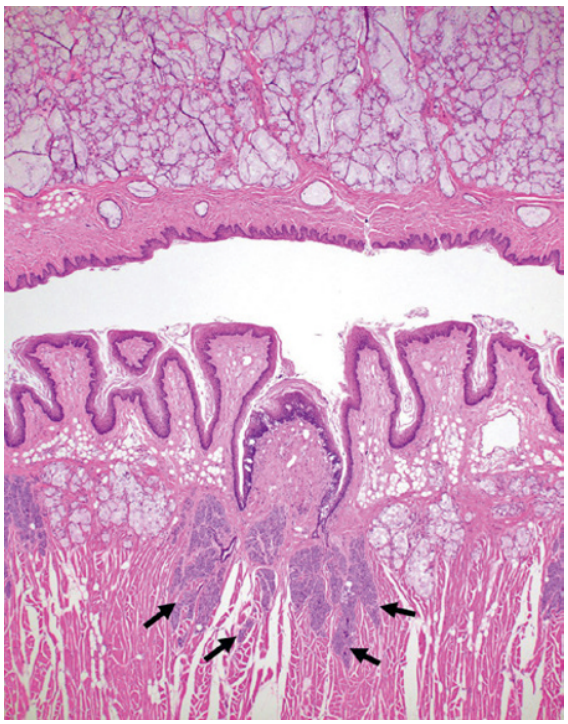

Figure 2.3 Histologic image of the tongue and soft palate of a seven-year-old, spayed female, DSH cat. At the level of the soft palate, the caudal oral soft tissues in the cat are very rich in salivary tissue. Mucous salivary glands are abundant dorsal to the palatal mucosa, and within the submucosa and superficial skeletal muscle of the tongue. The tongue has both pale-staining mucous salivary glands and more basophilic serous salivary glands (arrows). In the center of the image, the lingual mucosa forms a fungiform papilla. The lingual mucosa is otherwise undulant, which correlates with mucosal ridges that can be seen grossly on the caudal dorsal surface of cat tongues.

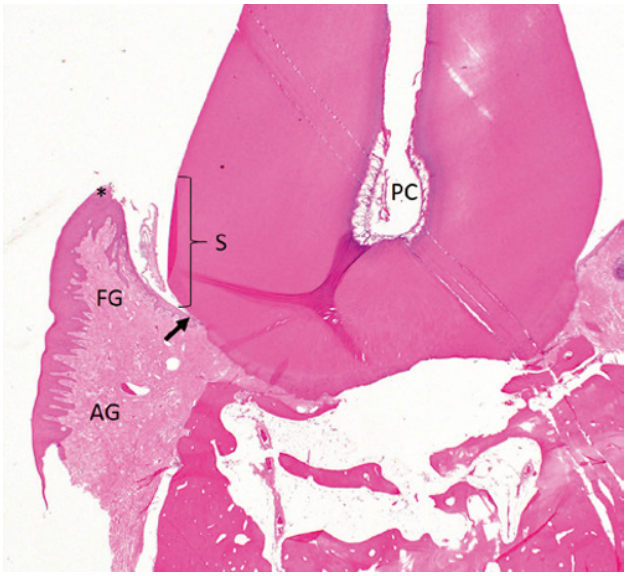

Figure 2.4 Histologic image of a normal premolar tooth from a seven year old dog. The free gingiva (FG) surrounds the base of the tooth crown, forming a sulcus (S). The depth of the sulcus (bracket) is from the gingival margin (asterisk) to the point where the sulcular epithelium attaches to the tooth (arrow). The attached gingiva (AG) covers alveolar bone. Tissues within the pulp canal (PC) are distorted due to artifact.

the crown of the tooth prior to eruption. As such, the free gingiva does not exist prior to tooth eruption. The sulcular epithelium has features of odontogenic epithelium, and the fibrovascular connective tissue under the sulcular epithelium is more similar to periodontal ligament than it is to fibrous gingival stroma. At the base of the sulcus, the site of attachment is particularly rich in fibers, similar to the attachment interface between gingival stroma and periosteum. The epithelium of the sulcus also attaches to the tooth at the base of the crown – this attachment is less obvious histologically, but some sections will show a thin epithelium reflecting onto the tooth surface (Figure 2.5). Loss of this epithelial attachment is an important step in the development of periodontal disease. To clarify, the attached gingiva is not the same as the attached epithelium. Attached gingiva covers alveolar bone and contrasts with the free gingiva. Attached epithelium is toward the base of the gingival sulcus where the gingiva anchors at the base of a tooth crown.

Gingival fiber bundles are abundant and unequally distributed within the tissues, tending to be most abundant where a ligamentous attachment is necessary between gingiva and bone, as well as between gingiva and the cervical portion of the tooth. Collagen fibers are by far most abundant (Figure 2.6). In addition to collagen

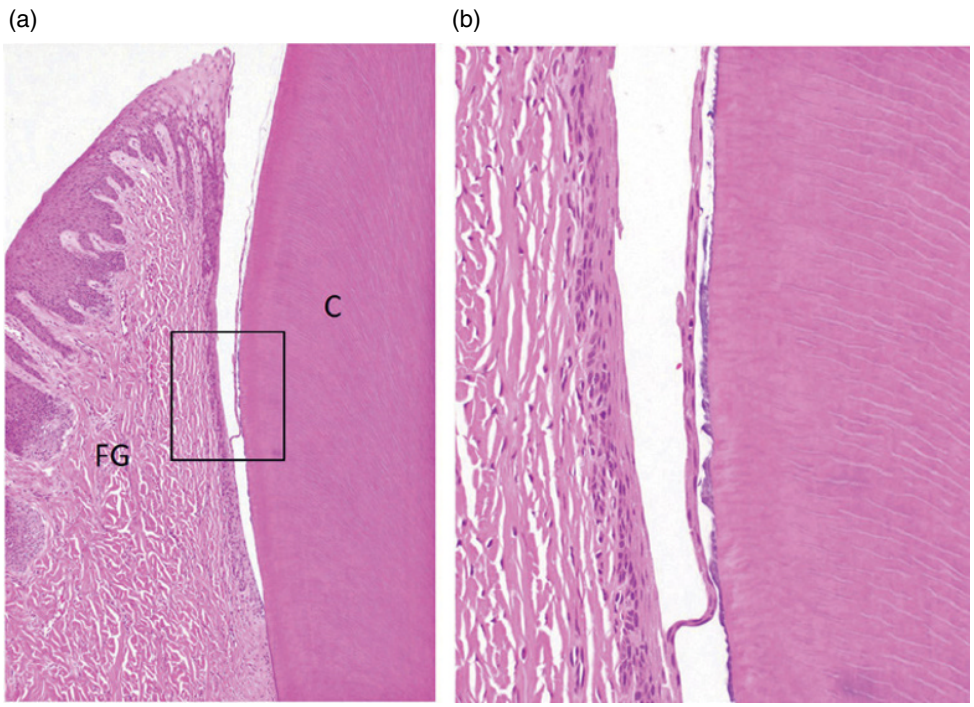

Figure 2.5 Histologic images of a normal tooth from a five-month-old, male Boxer dog. (a) A narrow cleft of clear space separates the free gingiva (FG) from the tooth crown (C), which is an artifact of processing. (b) Higher-magnification (area within the box of a) shows continuity between the sulcular epithelium and epithelium that attaches broadly and directly to the tooth surface. The broad zone of attachment is exaggerated in this case because the tooth is not fully erupted, but histological evidence of attachment is rarely seen in decalcified sections because, in the natural state, the epithelium adheres to enamel.

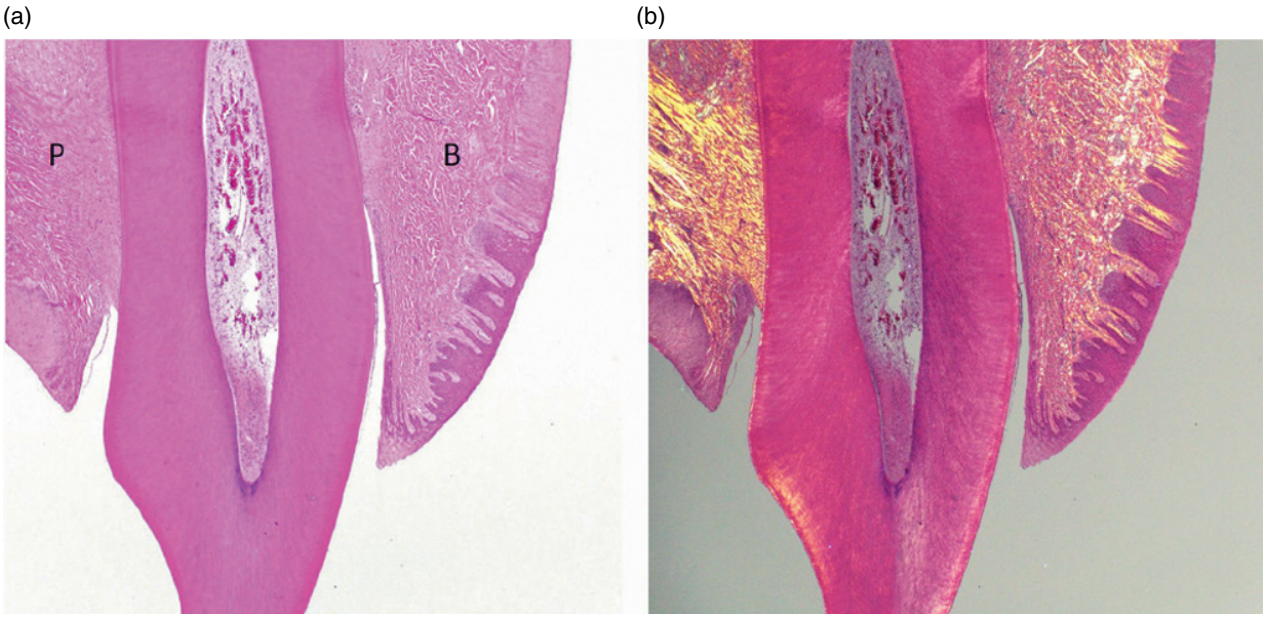

Figure 2.6 Histologic images of a normal maxillary premolar tooth from a five-month-old, male Boxer dog. Photomicrographs taken with (a) brightfield microscopy and (b) polarized light in order to demonstrate the abundance and orientation of gingival collagen fibers. There are obvious differences in the shape of the gingiva and the organization of fibers between the palatal (P) and buccal (B) sides of the tooth.

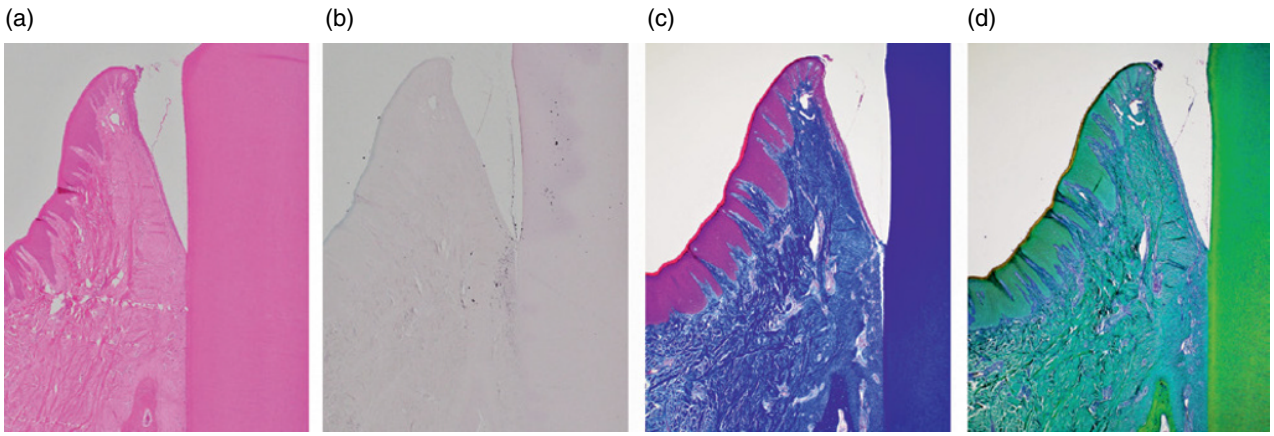

Figure 2.7 A series of low-magnification histologic images of free and attached gingiva adjacent to a tooth of a dog. (a) HE-stained section. (b) Acid Orcein–Giemsa stains elastin fibers black. (c) Masson's trichrome stains collagen blue. (d) Gomori's aldehyde fuchsin stains oxytalan fibers royal blue.

fibers, the gingiva has fibers with elastic properties, including both elastin fibers and oxytalan fibers. These fibers are abundant within the cervical portion of the attached gingiva and are often organized parallel to collagen fiber bundles (Figures 2.7 and 2.8).

2.3 Periodontal Apparatus

Periodontal apparatus refers to all those tissues and structures that anchor the tooth within the bony alveolus. The entire periodontal apparatus includes the periodontal ligament, its adjacent structures (i.e. cementum and alveolar bone), the attached gingival epithelium, and the fiber-rich gingiva that attaches to the cervical portion of a tooth. Cells within the periodontal ligament are assumed to regulate mineralization in some way that would allow a distinct fibrous layer to exist between two heavily mineralized tissues – cementum and bone. The mechanism of this regulation is not currently understood.

The periodontal ligament (PDL), or gomphosis, forms a sheath between the tooth root and surrounding alveolar bone; its functions include (i) holding the tooth in

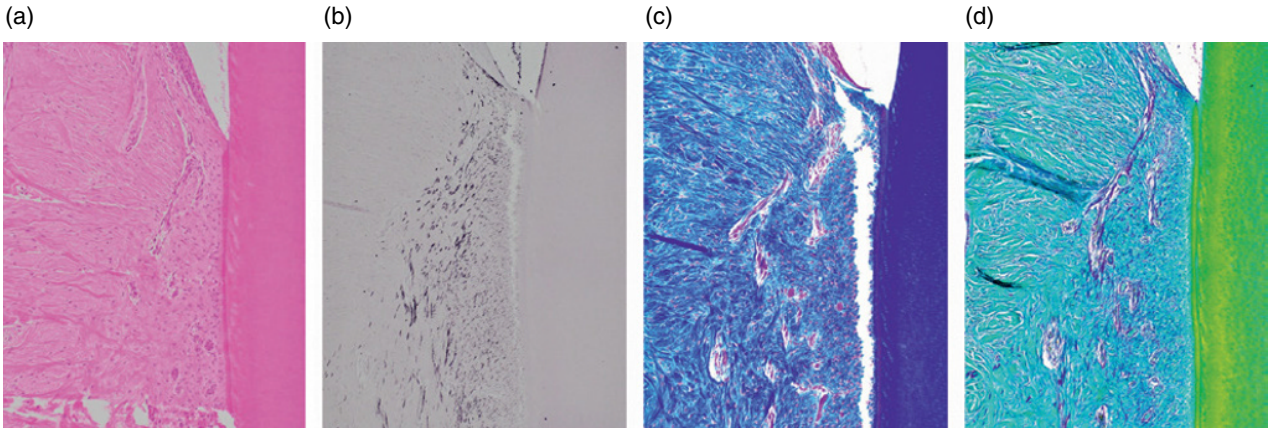

Figure 2.8 Histologic images taken at high magnification at the site of gingival attachment of the same sections shown in Figure 2.7. (a) The hematoxylin and eosin (HE)-stained tissue at the attachment site resembles PDL and is the junction between gingiva and PDL proper. (b) The acid Orcein–Giemsa stain reveals many fine elastin fibers in the attaching tissues, but elastin fibers are not present in the adjacent gingival fibrous tissue (left part of the image) or in the PDL proper (Figure 2.9b). (c) With Masson's trichrome stain, the short, fine collagen bundles near the attachment site contrast with the long, thick collagen bundles in the gingival fibrous tissue to the left. (d) The Gomori's aldehyde fuchsin stain shows that at the site of attachment, oxytalan fibers have approximately the same abundance and distribution as the elastin fibers.

Box 2.1 Components of PDL

Periodontal Ligament Components:

Mesenchymal Cells
- fibroblasts
- osteoblasts
- osteoclasts
- cementoblasts
- undifferentiated mesenchymal cells

Other Cells
- epithelial cells within odontogenic rests
- macrophages
- vessels and nerves

Extracellular Components
- collagen fiber bundles
- ground substance
- oxytalan fibers

place, (ii) acting as a sensory receptor, and (iii). providing a flexible cushion with limited movement when the tooth is subjected to forces. Lower vertebrates, like some reptiles, fish, and sharks, have teeth directly connected to the jawbone and completely lack a periodontal ligament (acrodont dentition). The periodontal ligament is a complex tissue composed of cellular and extracellular components (see Box 2.1). Undifferentiated cells are believed to have the capacity to differentiate into fibroblasts, cementoblasts, or osteoblasts. Fibroblasts produce collagen fibers that arrange in bundles and these are critically important to the structure and function of the periodontal apparatus. *Principal fibers* within the PDL are analogous to gingival fibers within the gingiva, as discussed previously. Principal fibers are composed of type I collagen fiber bundles that firmly attach tooth to bone by anchoring into cementum, spanning the PDL, and anchoring into adjacent alveolar bone. *Sharpey's fiber* refers to an end of a collagen fiber bundle where it embeds into either cementum or bone. Compared to the gingiva, the PDL has fewer oxytalan fibers, which tend to run vertically, parallel to the tooth root (Figure 2.9).

The periodontal tissues are constantly remodeling and the PDL in particular has a high rate of collagen turnover. The PDL is derived from tissues of the dental follicle that surround a forming tooth. The PDL of a young tooth can be difficult to distinguish from adjacent fibrous periosteum of the forming alveolar bone. The forces associated with a tooth in use influence modeling of a distinct PDL. In both disease and health, altered use of a tooth can significantly affect the structure and/or quality of the periodontal tissues. Increased use is expected to lead to increased width of the PDL, increased thickness of the collagen fiber bundles, and increased amount of alveolar bone. Conversely, disuse will lead to narrowing of the PDL, decreased fiber thickness and increased porosity of bone [1].

2.4 Enamel

The histological sections of decalcified teeth rarely retain enamel, which is approximately 96% inorganic mineral, 3–4% organic matrix, and less than 1% water (in comparison, bone is approximately 67% mineral and

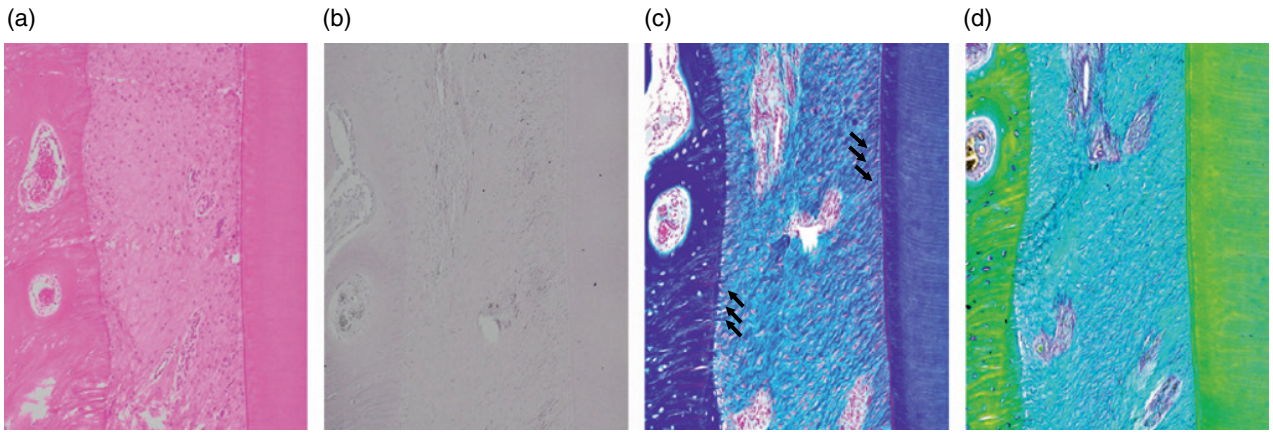

Figure 2.9 Histologic images taken at high magnification of the PDL of the same sections shown in Figure 2.7. (a) With HE stain, the PDL has a familiar pattern of stellate fibroblasts individually surrounded and separated by abundant fine collagen fibers. (b) The acid Orcein–Giemsa stain reveals nearly no elastin fibers within the PDL. (c) Masson's trichrome highlights the fine fibrillar structure of collagen and the Sharpey's fibers (arrows) that anchor PDL to bone (on the left) and PDL to cementum (on the right). (d) Gomori's aldehyde fuchsin stains fine oxytalan fibers that are interspersed throughout the collagen and considerably more abundantly around vessels.

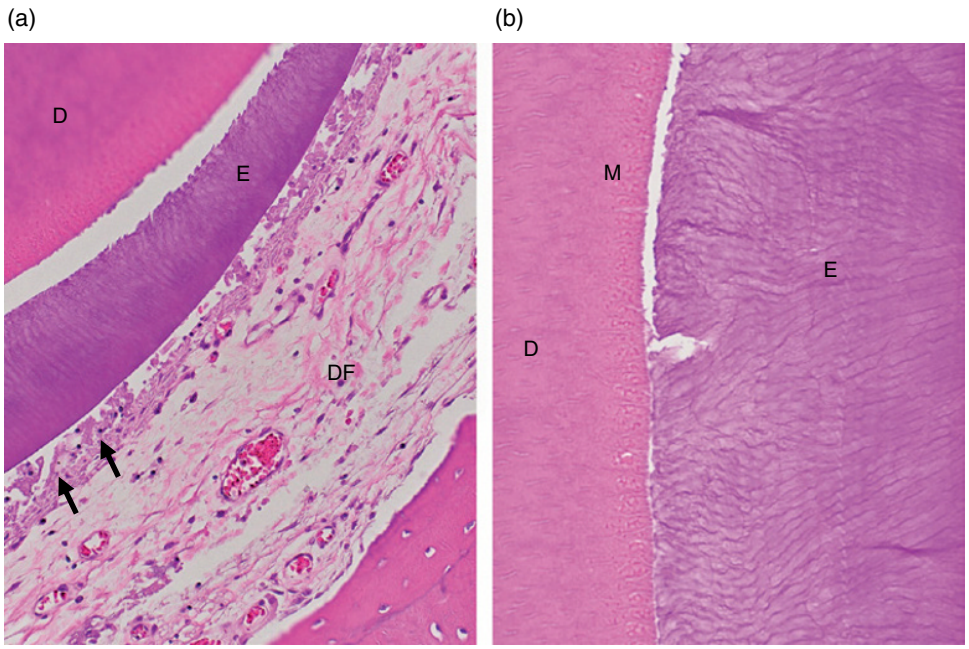

Figure 2.10 Histologic images of an unerupted tooth from a five-month-old, male Boxer dog. Because the tooth has not fully developed, the enamel has enough organic matrix to remain even in decalcified sections such as these. (a) Enamel (E) has been deposited directly onto dentin (D). A layer of degenerating ameloblasts (arrows) separates the enamel from the adjacent fibrovascular stroma of the dental follicle (DF). (b) At higher magnification, the rod (or prism) architecture of the enamel is highly organized and uniform. The mantle dentin (M) is subtly apparent as a thin, ragged outermost layer of dentin. Unlike primary dentin, this layer of mantle dentin is fibrillar rather than tubular.

33% organic) [1]. Ameloblasts secrete enamel matrix that provides the scaffold for mineralization. The matrix is produced in long tubular extensions, called rods (or prisms), that extend from the ameloblasts' basement membrane surface. Crystalline calcium phosphate (hydroxyapatite) is densely deposited within and between rods of matrix. Occasionally, a small amount of the organic enamel matrix will remain in a decalcified section. This residual enamel matrix shows the shape of the "rod sheath," which is a negative image of the regularly organized enamel rods that have been dissolved by acid demineralization (Figure 2.10). When enamel matrix remains in decalcified histological sections, there may be irregularities such as variably-sized vacuoles – these are thought to be an artifact of tissue processing. Occasionally, a *pellicle* (derived from salivary glycoproteins) is apparent

on the outer enamel surface. *Dental plaque* forms as the pellicle is colonized by oral bacteria, creating a biofilm. Subsequently, *dental calculus* (tartar) may form when inorganic salts are deposited within plaque.

2.5 Dentin

There are three main types of dentin (primary, secondary, and tertiary) that represent two different morphological patterns. In addition, the outermost dentin layer (mantle dentin) and the innermost dentin layer (predentin) are unique. *Mantle dentin* is the first layer of odontogenic matrix to be deposited and is the initial mineralization center at the interface of enamel and dentin. Mantle dentin is deposited at the outset of dentinogenesis crown formation. As such, the mantle dentin is a thin amorphous layer of matrix along the enamel–dentin interface that serves as the initial scaffold for secretion of tubular dentin matrix. Enamel is external to the mantle dentin and primary dentin is internal.

Primary dentin and *secondary dentin* have highly organized tubular architecture – these layers comprise the majority of the dentinal wall of a normal tooth. Primary and secondary dentin are histologically identical and are distinguished from one another only by the time of deposition – primary dentin is deposited until root formation is complete, then secondary dentin accounts for all subsequent dentinogenesis throughout the life of the animal (unless disrupted, in which case tertiary dentin may form). While there is no apparent microscopic difference between primary and secondary dentin, there is occasionally an artifactual cleft that separates the two in histological sections. Although primary and secondary dentin are produced in the same way by the same cells, it is intuitive that some physiological or developmental differences must exist in order to explain (i) the sharp line of demarcation between these layers, and (ii) the fact that some dentinal disorders affect secondary dentin but not primary dentin.

An innermost layer of non-mineralized *predentin* faces the layer of odontoblasts within the pulp chamber. Predentin represents the site of new matrix deposition by odontoblasts. Normal teeth, whether immature or mature, should have a distinct predentin layer since dentinogenesis is ongoing throughout the life of the tooth. See Chapter 3 on odontogenesis for more detail.

Finally, *tertiary dentin* is produced by damaged odontoblasts or replacement odontoblasts from the pulp. As opposed to organized tubules, the tertiary dentin matrix is deposited irregularly. While some wavy or disrupted tubules may occur, the majority of the matrix is amorphous and often bone-like due to entrapment of odontoblasts; thus, *osteodentin* is a term commonly used for tertiary dentin. Tertiary dentin forms when odontoblasts are disrupted or injured for any number of reasons; as such, tertiary dentin is pathological dentin. Pathologists beware – at sites of disrupted dentinogenesis, there is often also irregular deposition and remodeling of both cementum and alveolar bone. In these cases, distinguishing osteodentin from cemento-osseous matrix is a challenge (see Section 6.2.1, Disrupted tooth development).

2.6 Cementum

Cementum is a poorly cellular, bone-like tissue produced by cementoblasts. The origin of cementoblasts is controversial – they arise either from the fibrovascular tissue of the dental follicle or the epithelial root sheath [1]. It is known that the mature periodontal ligament contains cells capable of differentiating into fibroblasts, cementoblasts or osteoblasts. In the normal tooth, *acellular cementum* forms a narrow, relatively uniform seam along the lateral surfaces of the tooth roots, directly upon the outer dentin surface and facing the periodontal ligament on the opposite side. As discussed above, numerous extracellular fibers anchor cemental matrix to the fibrous periodontal ligament matrix.

A second type of *cellular cementum* allows the periodontal apparatus to adapt to wear and tooth movement, and to assist in the repair of the periodontal tissues [1]. As the name suggests, this tissue is more cellular and may be more porous than the cementum that broadly attaches the tooth to the periodontal ligament. Because of this, cellular cementum may be histologically indistinguishable from immature woven bone. In daily practice, the authors of this textbook rarely use the modifiers "acellular" or "cellular," preferring to say just "cementum." We also favor the term "cemento-osseous matrix," which is useful when describing lesions where ankylosis and remodeling make it impossible (or nearly so) to distinguish cementum from alveolar bone.

2.7 Odontoblasts and Pulp Stroma

In a normal vital tooth, the odontoblasts may range from a robust palisading layer of tall columnar cells with cytoplasmic extensions (tubules), to an attenuated cell layer that is scarcely visible in histological sections. The latter morphology is common in aged teeth. Intuitively, the morphology correlates with rate of dentin production. In a single maturing tooth, the morphology of the odontoblast layer can vary with location in order to maintain the appropriate tooth shape (Figure 2.11).

The dental pulp is loosely arranged fibrovascular connective tissue with rich innervation. Older teeth have less abundant pulp due to deposition of secondary or tertiary dentin that narrows the pulp canal (Figure 2.12).