

PART 1

The Normal Periodontium

Michael G. Newman

The periodontium consists of the investing and supporting tissues of the tooth: gingiva, periodontal ligament, cementum, and alveolar bone. It has been divided into two parts: the *gingiva*, the main function of which is protecting the underlying tissues, and the *attachment apparatus*, composed of the periodontal ligament, cementum, and alveolar bone. The cementum is considered a part of the periodontium because, with the bone, it serves as the support for the fibers of the periodontal ligament.

The periodontium is subject to morphologic and functional variations, as well as changes associated with age. This section deals with the normal features of the tissues of the periodontium, since this knowledge is necessary for an understanding of periodontal diseases.

The soft and hard tissues surrounding dental implants have many similar features and some important differences with the periodontal tissues, as discussed in Chapter 68.

CHAPTER 2

Anatomy of the Periodontium

Joseph P. Fiorellini, Daniel W.K. Kao, David M. Kim, and N. Guzin Uzel

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Refer to the **Expert CONSULT** companion website at www.expertconsult.com for additional content. Some text and figures may be out of numeric order in this printed chapter.

The normal periodontium provides the support necessary to maintain teeth in function. It consists of four principal components: gingiva, periodontal ligament, cementum, and alveolar bone. Each of these periodontal components is distinct in its location, tissue architecture, biochemical composition, and chemical composition, but all of these components function together as a single unit. Recent research has revealed that the extracellular matrix components of one periodontal compartment can influence the cellular activities of adjacent structures. Therefore the pathologic changes occurring in one periodontal component may have significant ramifications for the maintenance, repair, or regeneration of other components of the periodontium.¹⁸

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This chapter first discusses the structural components of the normal periodontium, then describes their development, vascularization, innervation, and functions.

ORAL MUCOSA

The *oral mucosa* consists of the following three zones:

1. The gingiva and the covering of the hard palate, termed the *masticatory mucosa*
2. The dorsum of the tongue, covered by *specialized mucosa*
3. The oral mucous membrane lining the remainder of the oral cavity. The *gingiva* is the part of the oral mucosa that covers

the alveolar processes of the jaws and surrounds the necks of the teeth.

GINGIVA

Clinical Features

In an adult, normal gingiva covers the alveolar bone and tooth root to a level just coronal to the cementoenamel junction. The gingiva is divided anatomically into *marginal*, *attached*, and *interdental* areas. Although each type of gingiva exhibits considerable variation in differentiation, histology, and thickness according to its functional demands, all types are specifically structured to function appropriately against mechanical and microbial damage.⁷ That is, the specific structure of different gingiva reflects its effectiveness as a barrier to the penetration by microbes and noxious agents into the deeper tissue.

Marginal Gingiva. The marginal, or *unattached*, gingiva is the terminal edge or border of the gingiva surrounding the teeth in collarlike fashion (Figures 2-1 and 2-2).⁶ In about 50% of cases, it is demarcated from the adjacent attached gingiva by a shallow linear depression, the *free gingival groove*.⁶ Usually about 1 mm

wide, the marginal gingiva forms the soft tissue wall of the gingival sulcus. It may be separated from the tooth surface with a periodontal probe.

The most apical point of the marginal gingival scallop is called the *gingival zenith*. Its apicocoronal and mesiodistal dimensions varied between 0.06 and 0.96 mm.¹⁷³

For more information on marginal gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

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Gingival Sulcus. The gingival sulcus is the shallow crevice or space around the tooth bounded by the surface of the tooth on one side and the epithelium lining the free margin of the gingiva on the other side. It is V shaped and barely permits the entrance of a periodontal probe. The clinical determination of the depth of the gingival sulcus is an important diagnostic parameter. Under absolutely normal or ideal conditions, the depth of the gingival sulcus is 0 mm or close to 0 mm.¹⁰⁷ These strict conditions of normalcy can be produced experimentally only in germ-free animals or after intense, prolonged plaque control.^{13,50}

In clinically healthy human gingiva, a sulcus of some depth can be found. The depth of this sulcus, as determined in histologic sections, has been reported as 1.8 mm, with variations from 0 to 6 mm¹⁹⁹; other studies have reported 1.5 mm²⁹⁴ and 0.69 mm.⁹⁵ The clinical evaluation used to determine the depth of the sulcus involves the introduction of a metallic instrument, the periodontal probe, and the estimation of the distance it penetrates. The histologic depth of a sulcus does not need to be exactly equal to the depth of penetration of the probe. The so-called probing depth of a clinically normal gingival sulcus in humans is 2 to 3 mm (see Chapter 30).

Attached Gingiva. The attached gingiva is continuous with the marginal gingiva. It is firm, resilient, and tightly bound to the underlying periosteum of alveolar bone. The facial aspect of the attached gingiva extends to the relatively loose and movable alveolar mucosa and is demarcated by the *mucogingival junction* (see Figure 2-2).

The *width of the attached gingiva* is another important clinical parameter.⁷ It is the distance between the mucogingival junction and the projection on the external surface of the bottom of the gingival sulcus or the periodontal pocket. It should not be confused with the *width of the keratinized gingiva* because the latter also includes the marginal gingiva (see Figure 2-2).

The width of the attached gingiva on the facial aspect differs in different areas of the mouth.⁴¹ It is generally greatest in the incisor region (3.5 to 4.5 mm in maxilla, 3.3 to 3.9 mm in mandible), and narrower in the posterior segments (1.9 mm in maxillary and 1.8 mm in mandibular first premolars)⁶ (Figure 2-3).

For more information on attached gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

Interdental Gingiva. The interdental gingiva occupies the gingival embrasure, which is the interproximal space beneath the area of tooth contact. The interdental gingiva can be pyramidal or can have a “col” shape. In the former the tip of one papilla is located immediately beneath the contact point; the latter presents



Figure 2-1 Normal gingiva in a young adult. Note the demarcation (mucogingival line) (arrows) between the attached gingiva and the darker alveolar mucosa.

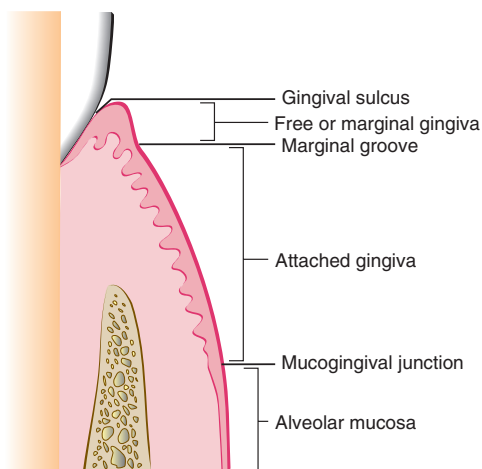


Figure 2-2 Diagram showing anatomic landmarks of the gingiva.

a valleylike depression that connects a facial and lingual papilla and conforms to the shape of the interproximal contact⁶³ (Figures 2-4 and 2-5).

The shape of the gingiva in a given interdental space depends on the contact point between the two adjoining teeth and the presence or absence of some degree of recession. Figure 2-6 depicts the variations in normal interdental gingiva.



Figure 2-3 Mean width of attached gingiva in human permanent dentition.



Figure 2-4 Site of extraction showing the facial and palatal interdental papillae and the intervening col (arrow).

The facial and lingual surfaces are tapered toward the interproximal contact area, whereas the mesial and distal surfaces are slightly concave. The lateral borders and tips of the interdental papillae are formed by the marginal gingiva of the adjoining teeth. The intervening portion consists of attached gingiva (Figure 2-7).

If a diastema is present, the gingiva is firmly bound over the interdental bone and forms a smooth, rounded surface without interdental papillae (Figure 2-8).

Microscopic Features

Microscopic examination reveals that gingiva is composed of the overlying stratified squamous epithelium and the underlying central core of connective tissue. Although the epithelium is predominantly cellular in nature, the connective tissue is less cellular and composed primarily of collagen fibers and ground substance. These two tissues are considered separately.*

*A detailed description of gingival histology can be found in Schroeder HE: *The periodontium*, New York, 1986, Springer-Verlag; and in Biological structure of the normal and diseased periodontium, *Periodontology* 2000 13, 1997.

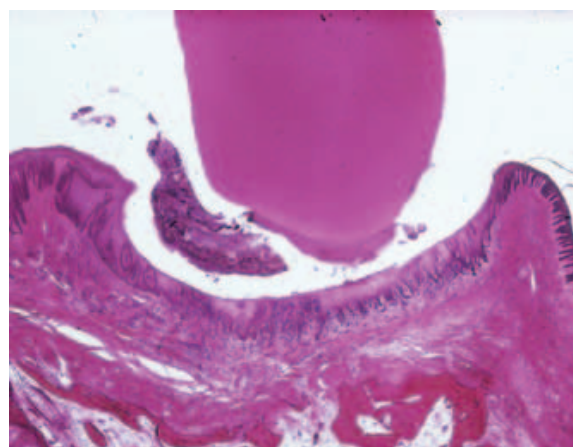


Figure 2-5 Faciolingual section (monkey) showing col between the facial and lingual interdental papillae. The col is covered with nonkeratinized stratified squamous epithelium.

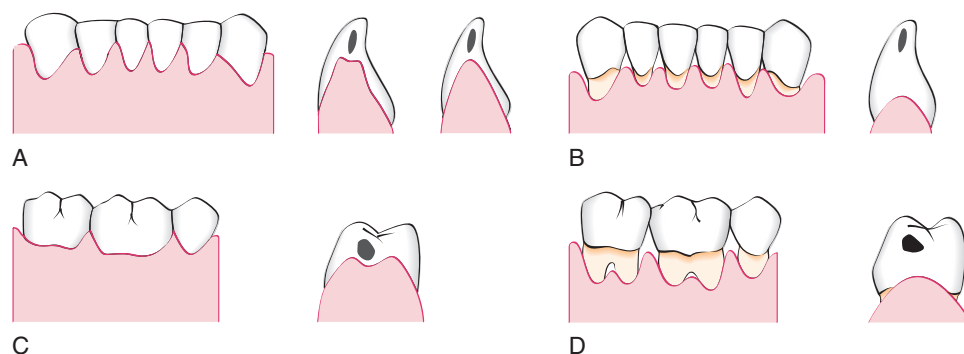


Figure 2-6 Diagram comparing anatomic variations of the interdental col in the normal gingiva (left side) and after gingival recession (right side). A and B, Mandibular anterior segment, facial and buccolingual views, respectively. C and D, Mandibular posterior region, facial and buccolingual views, respectively. Tooth contact points are shown by black marks in lower individual teeth.

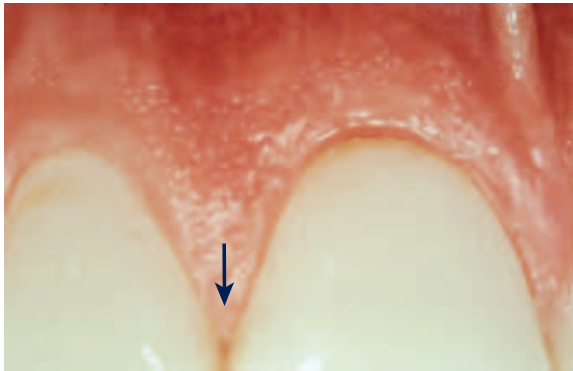


Figure 2-7 Interdenal papillae (arrow) with central portion formed by attached gingiva. The shape of the papillae varies according to the dimension of the gingival embrasure. (Courtesy Dr. Osvaldo Costa.)



Figure 2-8 Absence of interdenal papillae and col where proximal tooth contact is missing. (Courtesy Dr. Osvaldo Costa.)

Gingival Epithelium.

To view Box 22-1 and for more information on general aspects of gingival epithelium biology, please visit the companion Expert CONSULT website at www.expertconsult.com.

The gingival epithelium consists of a continuous lining of stratified squamous epithelium, and the three different areas can be defined from the morphologic and functional points of view: the oral or outer epithelium, sulcular epithelium, and junctional epithelium.

The principal cell type of the gingival epithelium, as well as of other stratified squamous epithelia, is the *keratinocyte*. Other cells found in the epithelium are the clear cells or nonkeratinocytes, which include the Langerhans cells, Merkel cells, and melanocytes.

The main function of the gingival epithelium is to protect the deep structures, while allowing a selective interchange with the oral environment. This is achieved by proliferation and differentiation of the keratinocytes.

Proliferation of keratinocytes takes place by mitosis in the basal layer and less frequently in the suprabasal layers, in which a small proportion of cells remain as a proliferative compartment while a larger number begin to migrate to the surface.

Differentiation involves the process of keratinization, which consists of progressions of biochemical and morphologic events that occur in the cell as they migrate from the basal layer (Figure 2-9). The main morphologic changes are (1) progressive flattening of the cell with an increasing prevalence of tonofilaments, (2) intercellular junctions coupled to the production of keratohyaline granules, and (3) disappearance of the nucleus. (See Schroeder²³⁶ for further details.)

A complete keratinization process leads to the production of an *orthokeratinized* superficial horny layer similar to that of the skin,

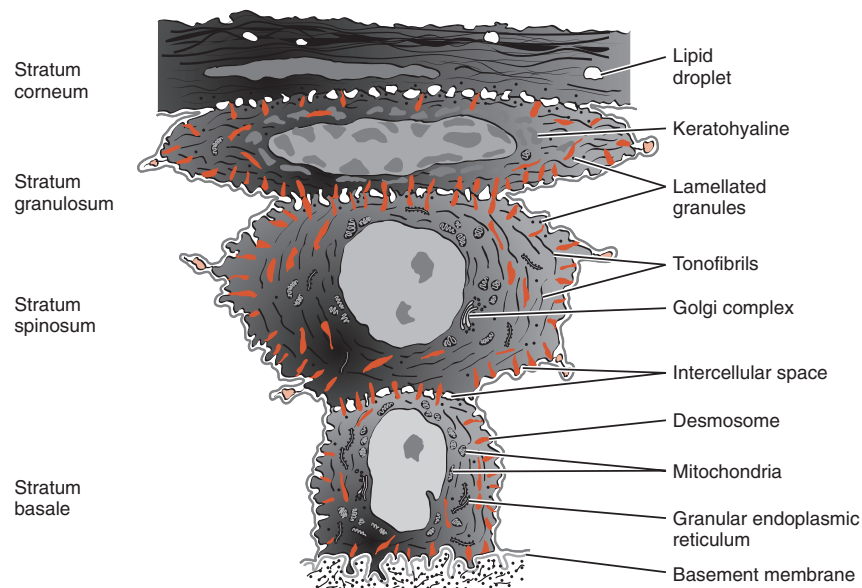


Figure 2-9 Diagram showing representative cells from the various layers of stratified squamous epithelium as seen by electron microscopy. (Modified from Weinstock A: In Ham AW: Histology, ed 7, Philadelphia, 1974, Lippincott.)

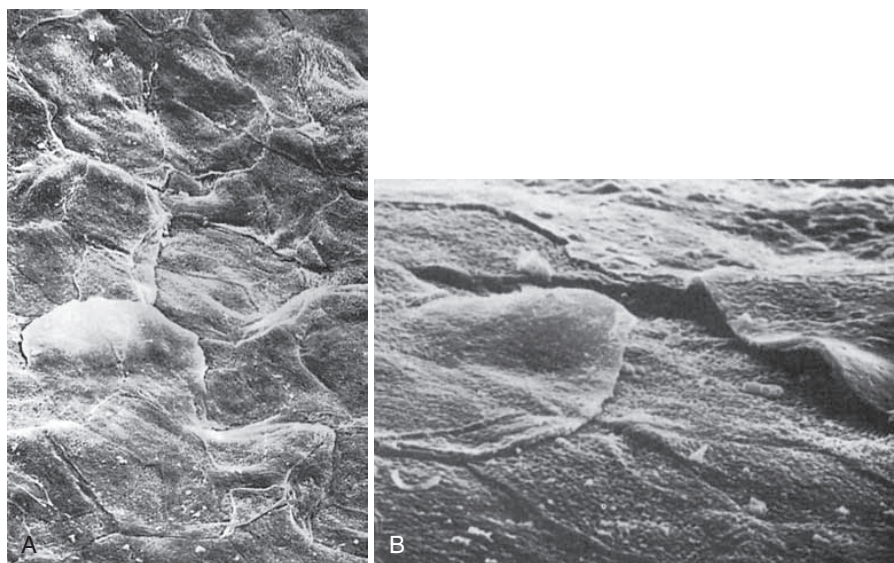


Figure 2-10 A, Scanning electron micrograph of keratinized gingiva showing the flattened keratinocytes and their boundaries on the surface of the gingiva ($\times 1000$). B, Scanning electron micrograph of gingival margin at edge of gingival sulcus showing several keratinocytes about to be exfoliated ($\times 3000$). (From Kaplan GB, Pameijer CH, Ruben MP: J Periodontol 48:446, 1977.)

with no nuclei in the stratum corneum and a well-defined stratum granulosum (Figure 2-10). Only some areas of the outer gingival epithelium are orthokeratinized; the other gingival areas are covered by parakeratinized or nonkeratinized epithelium⁴⁶ and considered to be at intermediate stages of keratinization. These areas can progress to maturity or dedifferentiate under different physiologic or pathologic conditions.

In *parakeratinized epithelia* the stratum corneum retains pyknotic nuclei, and the keratohyalin granules are dispersed, not giving rise to a stratum granulosum. The *nonkeratinized epithelium* (although cytokeratins are the major component, as in all epithelia) has neither granulosum nor corneum strata, whereas superficial cells have viable nuclei.

For more information on general aspects of gingival epithelium biology, please visit the companion Expert CONSULT website at www.expertconsult.com.

Electron microscopy reveals that keratinocytes are interconnected by structures on the cell periphery called *desmosomes*.¹⁵⁶ These desmosomes have a typical structure consisting of two dense attachment plaques into which tonofibrils insert and an intermediate, electron-dense line in the extracellular compartment. Tonofilaments, which are the morphologic expression of the cytoskeleton of keratin proteins, radiate in brushlike fashion from the attachment plaques into the cytoplasm of the cells. The space between the cells shows cytoplasmic projections resembling microvilli that extend into the intercellular space and often interdigitate.

Less frequently observed forms of epithelial cell connections are tight junctions (*zonae occludens*), in which the membranes of the adjoining cells are believed to be fused.^{273,292} Evidence suggests that these structures allow ions and small molecules to pass from one cell to another.

Cytoplasmic organelle concentration varies among different epithelial strata. Mitochondria are more numerous in deeper strata and decrease toward the surface of the cell.

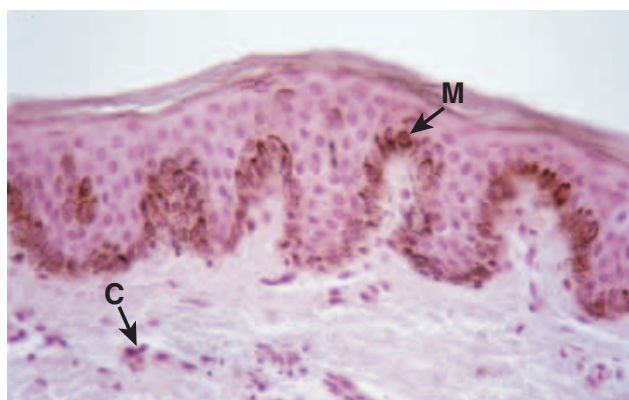


Figure 2-11 Pigmented gingiva of dog showing melanocytes (M) in the basal epithelial layer and melanophores (C) in the connective tissue (Glucksman technique).

For more information on general aspects of gingival epithelium biology, please visit the companion Expert CONSULT website at www.expertconsult.com.

The uppermost cells of the stratum spinosum contain numerous dense granules, *keratinosomes* or *Odland bodies*, which are modified lysosomes.

Nonkeratinocyte cells are present in gingival epithelium as in other malpighian epithelia. *Melanocytes* are dendritic cells located in the basal and spinous layers of the gingival epithelium. They synthesize melanin in organelles called *premelanosomes* or *melanosomes*.^{62,233,258} (Figure 2-11).

Langerhans cells are dendritic cells located among keratinocytes at all suprabasal levels (Figure 2-12). They belong to the mononuclear phagocyte system (reticuloendothelial system) as modified monocytes derived from the bone marrow. They contain elongated

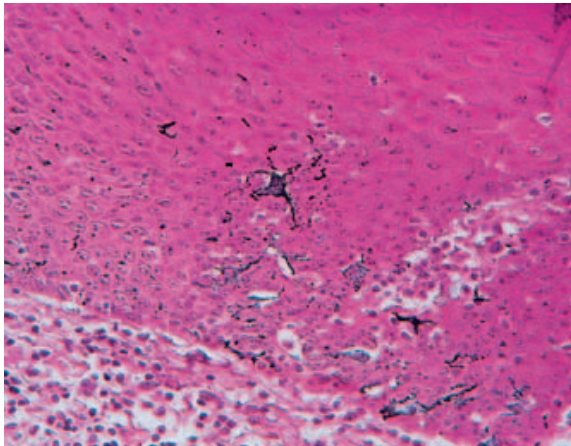


Figure 2-12 Human gingival epithelium, oral aspect. Immunoperoxidase technique showing Langerhans cells.

granules and are considered macrophages with possible antigenic properties.⁷⁴ Langerhans cells have an important role in the immune reaction as antigen-presenting cells for lymphocytes. They contain g-specific granules (Birbeck's granules) and have marked adenosine triphosphatase activity. They are found in oral epithelium of normal gingiva and in smaller amounts in the sulcular epithelium; they are probably absent from the junctional epithelium of normal gingiva.

Merkel cells are located in the deeper layers of the epithelium, harbor nerve endings, and are connected to adjacent cells by desmosomes. They have been identified as tactile receptors.¹⁹¹

The epithelium is joined to the underlying connective tissue by a *basal lamina* 300 to 400 Å thick, lying approximately 400 Å beneath the epithelial basal layer.^{149,241,260} The basal lamina consists of lamina lucida and lamina densa. Hemidesmosomes of the basal epithelial cells abut the lamina lucida, which is mainly composed of the glycoprotein laminin. The lamina densa is composed of type IV collagen. The basal lamina, clearly distinguishable at the ultrastructural level, is connected to a reticular condensation of the underlying connective tissue fibrils (mainly collagen type IV) by the anchoring fibrils.^{186,218,263} Anchoring fibrils have been measured at 750 nm in length from their epithelial end to their connective tissue end, where they appear to form loops around collagen fibers. The complex of basal lamina and fibrils is the periodic acid-Schiff (PAS)-positive and argyrophilic line observed at the optical level.^{243,264} (Figure 2-13). The basal lamina is permeable to fluids but acts as a barrier to particulate matter.

Structural and Metabolic Characteristics of Different Areas of Gingival Epithelium.

The gingiva shows regional morphologic variations that reflect tissue adaptation to the tooth and alveolar bone.²³⁷ These variations include the oral epithelium, sulcular epithelium, and junctional epithelium. Whereas the oral epithelium and sulcular epithelium are largely protective in function, the junctional epithelium serves many more roles and is of considerable importance in regulating tissue health.¹⁸ It is now recognized that epithelial cells are not “passive bystanders” in the gingival tissues; rather, they are metabolically active and capable of reacting to external stimuli by synthesizing a number of cytokines, adhesion molecules, growth factors, and enzymes.¹⁸



Figure 2-13 Normal human gingiva stained with the periodic acid-Schiff (PAS) histochemical method. The basement membrane (B) is seen between the epithelium (E) and the underlying connective tissue (C). In the epithelium, glycoprotein material occurs in cells and cell membranes of the superficial hornified (H) and underlying granular layers (G). The connective tissue presents a diffuse, amorphous ground substance and collagen fibers. The blood vessel walls stand out clearly in the papillary projections of the connective tissue (P).

Oral (outer) Epithelium. The oral, or outer, epithelium covers the crest and outer surface of the marginal gingiva and the surface of the attached gingiva. On average, the oral epithelium is 0.2 to 0.3 mm in thickness. It is keratinized or parakeratinized or presents various combinations of these conditions (Figure 2-14). The prevalent surface, however, is parakeratinized.^{32,46,290}

The oral epithelium is composed of four layers: stratum basale (basal layer), stratum spinosum (prickle cell layer), stratum granulosum (granular layer), and stratum corneum (cornified layer).

For more information on oral (outer) epithelium, please visit the companion Expert CONSULT website at www.expertconsult.com.

Sulcular Epithelium. The sulcular epithelium lines the gingival sulcus (Figure 2-15). It is a thin, nonkeratinized stratified squamous epithelium without rete pegs, and it extends from the coronal limit of the junctional epithelium to the crest of the gingival margin (Figure 2-16). It usually shows many cells with hydropic degeneration.³²

For more information on sulcular epithelium, please visit the companion Expert CONSULT website at www.expertconsult.com.

The sulcular epithelium is extremely important because it may act as a semipermeable membrane through which injurious bacterial products pass into the gingiva and tissue fluid from the gingiva seeps into the sulcus.²⁷² Unlike the junctional epithelium, however, the sulcular epithelium is not heavily infiltrated by polymorphonuclear neutrophil leukocytes (PMNs), and it appears to be less permeable.¹⁸

Junctional Epithelium. The junctional epithelium consists of a collarlike band of stratified squamous nonkeratinizing epithelium. It is 3 to 4 layers thick in early life, but the number of layers increases with age to 10 or even 20 layers. Also, the junctional

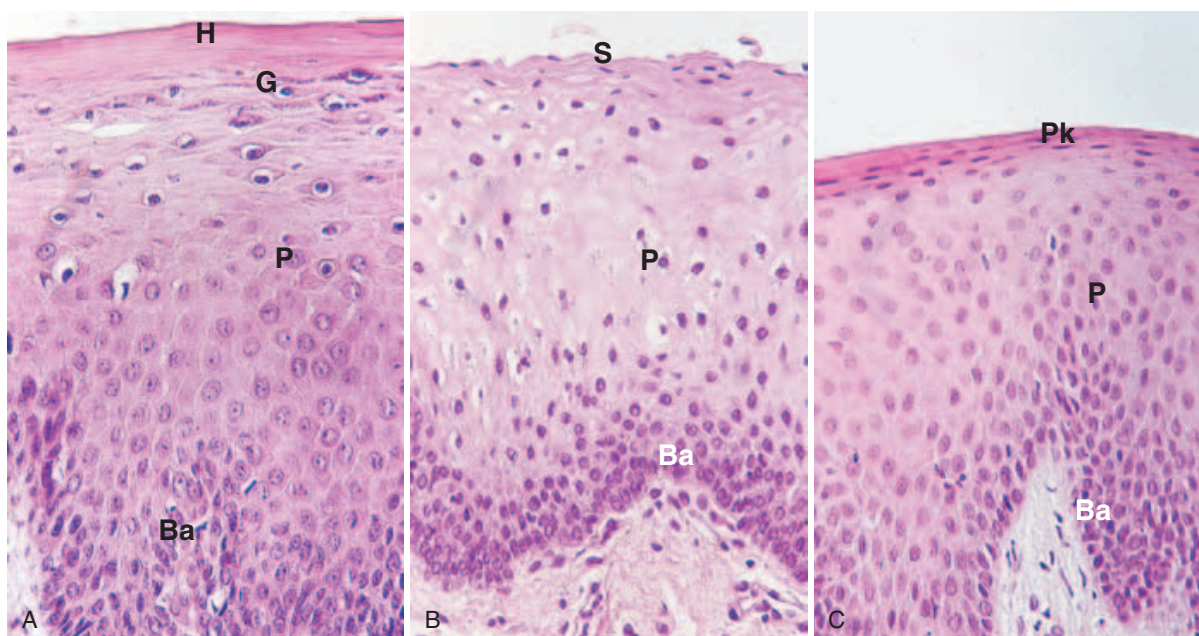


Figure 2-14 Variations in gingival epithelium. **A**, Keratinized. **B**, Nonkeratinized. **C**, Parakeratinized. Horny layer (*H*), granular layer (*G*), prickle cell layer (*P*), basal cell layer (*Ba*), flattened surface cells (*S*), parakeratotic layer (*Pk*).

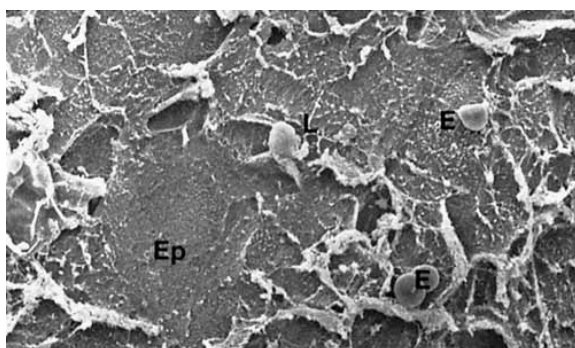


Figure 2-15 Scanning electron microscopic view of epithelial surface facing the tooth in a normal human gingival sulcus. The epithelium (*Ep*) shows desquamating cells, some scattered erythrocytes (*E*), and a few emerging leukocytes (*L*). (×1000.)

epithelium tapers from its coronal end, which may be 10 to 29 cells wide to 1 or 2 cells at its apical termination, located at the cemento-enamel junction in healthy tissue. These cells can be grouped in two strata: the basal layer facing the connective tissue and the suprabasal layer extending to the tooth surface. The length of the junctional epithelium ranges from 0.25 to 1.35 mm (Figure 2-17).

To view Figure 2-17 and for more information on junctional epithelium, please visit the companion Expert CONSULT website at www.expertconsult.com.

The junctional epithelium is attached to the tooth surface (epithelial attachment) by means of an internal basal lamina. It is



Figure 2-16 Epon-embedded human biopsy specimen showing a relatively normal gingival sulcus. The soft tissue wall of the gingival sulcus is made up of the oral sulcular epithelium (*ose*) and its underlying connective tissue (*ct*), whereas the base of the gingival sulcus is formed by the sloughing surface of the junctional epithelium (*je*). The enamel space is delineated by a dense cuticular structure (*dc*). A relatively sharp line of demarcation exists between the junctional epithelium and the oral sulcular epithelium (*arrow*), and several polymorphonuclear leukocytes (*pmn*) can be seen traversing the junctional epithelium. The sulcus contains red blood cells resulting from the hemorrhage occurring at the time of biopsy. (×391; inset ×55.) (From Schlager S, Youdelis R, Page RC: Periodontal disease, Philadelphia, 1977, Lea & Febiger.)

attached to the gingival connective tissue by an external basal lamina that has the same structure as other epithelial-connective tissue attachments elsewhere in the body.^{157,163}

The internal basal lamina consists of a lamina densa (adjacent to the enamel) and a lamina lucida to which hemidesmosomes are attached. Hemidesmosomes have a decisive role in the firm attachment of the cells to the internal basal lamina on the tooth surface.

For more information on junctional epithelium, please visit the companion Expert CONSULT website at www.expertconsult.com.

Histochemical evidence for the presence of neutral polysaccharides in the zone of the epithelial attachment has been reported.²⁷⁷ Data also have shown that the basal lamina of the junctional epithelium resembles that of endothelial and epithelial cells in its laminin content but differs in its internal basal lamina, which has no type IV collagen.^{144,228} These findings indicate that the cells of the junctional epithelium are involved in the production of laminin and play a key role in the adhesion mechanism.

The attachment of the junctional epithelium to the tooth is reinforced by the gingival fibers, which brace the marginal gingiva against the tooth surface. For this reason, the junctional epithelium and the gingival fibers are considered a functional unit, referred to as the *dentogingival unit*.¹⁶⁰

In conclusion, it is usually accepted that the junctional epithelium exhibits several unique structural and functional features that contribute to preventing pathogenic bacterial flora from colonizing the subgingival tooth surface.²⁰⁹ First, junctional epithelium is firmly attached to the tooth surface, forming an epithelial barrier against plaque bacteria. Second, it allows access of gingival fluid, inflammatory cells, and components of the immunologic host defense to the gingival margin. Third, junctional epithelial cells exhibit rapid turnover, which contributes to the host-parasite equilibrium and rapid repair of damaged tissue. Also, some investigators indicate that the cells of the junctional epithelium have an endocytic capacity equal to that of macrophages and neutrophils and that this activity might be protective in nature.⁵⁸

Development of Gingival Sulcus. After enamel formation is complete, the enamel is covered with *reduced enamel epithelium* (REE), which is attached to the tooth by a basal lamina and hemidesmosomes.^{158,261} When the tooth penetrates the oral mucosa, the REE unites with the oral epithelium and transforms into the junctional epithelium. As the tooth erupts, this united epithelium condenses along the crown, and the ameloblasts, which form the inner layer of the REE (see Figure 2-17), gradually become squamous epithelial cells. The transformation of the REE into a junctional epithelium proceeds in an apical direction without interrupting the attachment to the tooth. According to Schroeder and Listgarten,²³⁹ this process takes between 1 and 2 years.

The junctional epithelium is a continually self-renewing structure, with mitotic activity occurring in all cell layers.^{158,261}

To view Figure 2-18 and for more information on the development of the gingival sulcus, please visit the companion Expert CONSULT website at www.expertconsult.com.

The gingival sulcus is formed when the tooth erupts into the oral cavity. At that time, the junctional epithelium and REE form

a broad band attached to the tooth surface from near the tip of the crown to the cemento-enamel junction.

The gingival sulcus is the shallow, V-shaped space or groove between the tooth and gingiva that encircles the newly erupted tip of the crown. In the fully erupted tooth, only the junctional epithelium persists. *The sulcus consists of the shallow space that is coronal to the attachment of the junctional epithelium and bounded by the tooth on one side and the sulcular epithelium on the other. The coronal extent of the gingival sulcus is the gingival margin.*

Renewal of Gingival Epithelium. The oral epithelium undergoes continuous renewal. Its thickness is maintained by a balance between new cell formation in the basal and spinous layers and the shedding of old cells at the surface. The mitotic activity exhibits a 24-hour periodicity, with the highest and lowest rates occurring in the morning and evening, respectively.²⁶² The mitotic rate is higher in nonkeratinized areas and is increased in gingivitis, without significant gender differences. Opinions differ as to whether the mitotic rate is increased^{162,163,181} or decreased¹⁵ with age.

For more information on renewal of gingival epithelium, please visit the companion Expert CONSULT Web site at www.expertconsult.com.

Cuticular Structures on the Tooth. The term *cuticle* describes a thin, acellular structure with a homogeneous matrix, sometimes enclosed within clearly demarcated, linear borders.

Listgarten¹⁶¹ has classified cuticular structures into coatings of developmental origin and acquired coatings. *Acquired coatings* include those of exogenous origin such as saliva, bacteria, calculus, and surface stains (see Chapters 21 and 22 *Coatings of developmental origin* are those normally formed as part of tooth development. They include the REE, coronal cementum, and dental cuticle.

For more information on cuticular structures on the tooth, please visit the companion Expert CONSULT website at www.expertconsult.com.

Electron microscopy has shown a *dental cuticle* consisting of a layer of homogeneous organic material of variable thickness (approximately 0.25 μm) overlying the enamel surface. It is non-mineralized and not always present. In some cases near the cemento-enamel junction, it is deposited over a layer of afibrillar cementum, which in turn overlies enamel. The cuticle may be present between the junctional epithelium and the tooth. Ultrastructural histochemical studies have shown that the dental cuticle is proteinaceous,¹⁴⁵ and it may be an accumulation of tissue fluid components.^{90,238}

Gingival Fluid (Sulcular Fluid). The value of the gingival fluid is that it can be represented as either a transudate or an exudate. The gingival fluid contains a vast array of biochemical factors, offering potential use as a diagnostic or prognostic biomarker of the biologic state of the periodontium in health and disease.⁸⁴ (see Chapter 6).

For more information on gingival fluid (sulcular fluid), please visit the companion Expert CONSULT website at www.expertconsult.com.

Gingival Connective Tissue. The major components of the gingival connective tissue are collagen fibers (about 60% by volume), fibroblasts (5%), vessels, nerves, and matrix (about 35%).

The connective tissue of the gingiva is known as the *lamina propria* and consists of two layers: (1) a *papillary layer* subjacent to the epithelium, which consists of papillary projections between the epithelial rete pegs; and (2) a *reticular layer* contiguous with the periosteum of the alveolar bone.

For more information on gingival connective tissue, please visit the companion Expert CONSULT website at www.expertconsult.com.

The *ground substance* fills the space between fibers and cells, is amorphous, and has a high content of water. It is composed of proteoglycans, mainly hyaluronic acid and chondroitin sulfate, and glycoproteins, mainly fibronectin. Glycoproteins account for the faint PAS-positive reaction of the ground substance.⁸⁵ Fibronectin binds fibroblasts to the fibers and many other components of the intercellular matrix, helping mediate cell adhesion and migration. Laminin, another glycoprotein found in the basal lamina, serves to attach it to epithelial cells.

The three types of connective tissue fibers are collagen, reticular, and elastic. Collagen type I forms the bulk of the lamina propria and provides the tensile strength to the gingival tissue. Type IV collagen (argyrophilic reticulum fiber) branches between the collagen type I bundles and is continuous with fibers of the basement membrane and blood vessel walls.¹⁶³

The elastic fiber system is composed of oxytalan, elaunin, and elastin fibers distributed among collagen fibers.⁵⁷

Therefore densely packed collagen bundles that are anchored into the acellular extrinsic fiber cementum just below the terminal point of the junctional epithelium form the connective tissue attachment. The stability of this attachment is a key factor in limiting the migration of junctional epithelium.⁵⁸

Gingival Fibers. The connective tissue of the marginal gingiva is densely collagenous, containing a prominent system of collagen fiber bundles called the *gingival fibers*. They consist of type I collagen.²¹⁸ The gingival fibers have the following functions:

1. To brace the marginal gingiva firmly against the tooth.
2. To provide the rigidity necessary to withstand the forces of mastication without being deflected away from the tooth surface.
3. To unite the free marginal gingiva with the cementum of the root and the adjacent attached gingiva.

The gingival fibers are arranged in three groups: gingivodental, circular, and transseptal.¹⁴⁸

Gingivodental Group. The gingivodental fibers are those on the facial, lingual, and interproximal surfaces. They are embedded in the cementum just beneath the epithelium at the base of the gingival sulcus. On the facial and lingual surfaces, they project from the cementum in fanlike conformation toward the crest and outer surface of the marginal gingiva, terminating short of the epithelium (Figures 2-19 and 2-20). They also extend externally to the periosteum of the facial and lingual alveolar bones, terminating in the attached gingiva or blending with the periosteum of the bone. Interproximally, the gingivodental fibers extend toward the crest of the interdental gingiva.

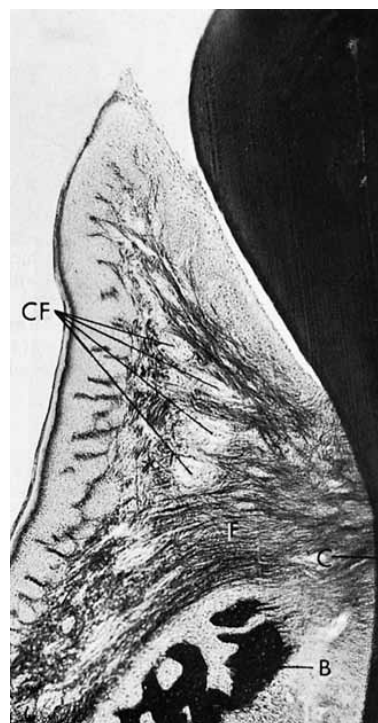


Figure 2-19 Faciolingual section of marginal gingiva showing gingival fibers (F) extending from the cementum (C) to the crest of the gingiva, to the outer gingival surface, and external to the periosteum of the bone (B). Circular fibers (CF) are shown in cross-section between the other groups. (Courtesy Sol Bernick.)

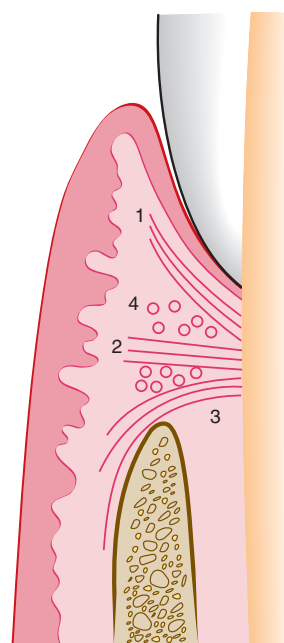


Figure 2-20 Diagram of the gingivodental fibers extending from the cementum (1) to the crest of the gingiva, (2) to the outer surface, and (3) external to the periosteum of the labial plate. Circular fibers (4) are shown in cross-section.

Circular Group. The circular fibers course through the connective tissue of the marginal and interdental gingivae and encircle the tooth in ringlike fashion.

Transseptal Group. Located interproximally, the transseptal fibers form horizontal bundles that extend between the cementum of approximating teeth into which they are embedded. They lie in the area between the epithelium at the base of the gingival sulcus and the crest of the interdental bone and are sometimes classified with the principal fibers of the periodontal ligament.

Page et al²⁰² also described (1) a group of *semicircular fibers* that attach at the proximal surface of a tooth, immediately below the cementoenamel junction, go around the facial or lingual marginal gingiva of the tooth, and attach on the other proximal surface of the same tooth; and (2) a group of *transgingival fibers* that attach in the proximal surface of one tooth, traverse the interdental space diagonally, go around the facial or lingual surface of the adjacent tooth, again traverse diagonally the interdental space, and attach in the proximal surface of the next tooth.

Tractional forces in the extracellular matrix produced by fibroblasts are believed to be the forces responsible for generating tension in the collagen. This keeps the teeth tightly bound to each other and to the alveolar bone.

Cellular Elements. The preponderant cellular element in the gingival connective tissue is the *fibroblast*. Numerous fibroblasts are found between the fiber bundles. Fibroblasts are of mesenchymal origin and play a major role in the development, maintenance, and repair of gingival connective tissue. As with connective tissue elsewhere in the body, fibroblasts synthesize collagen and elastic fibers, as well as the glycoproteins and glycosaminoglycans of the amorphous intercellular substance. Fibroblasts also regulate collagen degradation through phagocytosis and secretion of collagenases.

For more information on cellular elements, please visit the companion Expert CONSULT website at www.expertconsult.com.

Mast cells, which are distributed throughout the body, are numerous in the connective tissue of the oral mucosa and the gingiva.^{53,250,251,293} Fixed macrophages and histiocytes are present in the gingival connective tissue as components of the mononuclear phagocyte system (reticuloendothelial system) and are derived from blood monocytes. Adipose cells and eosinophils, although scarce, also are present in the lamina propria.

In clinically normal gingiva, small foci of plasma cells and lymphocytes are found in the connective tissue near the base of the sulcus (Figure 2-21). Neutrophils can be seen in relatively high numbers in both the gingival connective tissue and the sulcus. These inflammatory cells usually are present in small amounts in clinically normal gingiva.

For more information on cellular elements, please visit the companion Expert CONSULT website at www.expertconsult.com.

Repair of Gingival Connective Tissue. Because of the high turnover rate, the connective tissue of the gingiva has remarkably good healing and regenerative capacity. Indeed, it may be one of the best healing tissues in the body and generally shows little

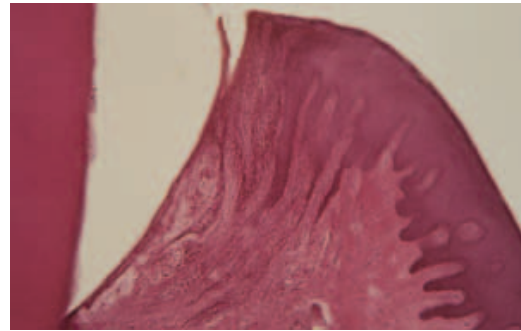


Figure 2-21 Section of clinically normal gingiva showing some degree of inflammation, which is almost always present near the base of the sulcus.

evidence of scarring after surgical procedures. This is likely caused by rapid reconstruction of the fibrous architecture of the tissues.¹⁸⁰ However, the reparative capacity of gingival connective tissue is not as great as that of the periodontal ligament or the epithelial tissue.

Blood Supply, Lymphatics, and Nerves. Microcirculatory tracts, blood vessels, and lymphatic vessels play an important role in drainage of tissue fluid and in the spread of inflammation. In gingivitis and periodontitis, the microcirculation and vascular formation change greatly in the vascular network directly under the gingival sulcular epithelium and junctional epithelium.¹⁷²

For more information on blood supply, lymphatics, and nerves, please visit the companion Expert CONSULT website at www.expertconsult.com.

Three sources of blood supply to the gingiva are as follows (Figures 2-22 and 2-23):

1. *Supraperiosteal arterioles* along the facial and lingual surfaces of the alveolar bone, from which capillaries extend along the sulcular epithelium and between the rete pegs of the external gingival surface.^{78,115,8} Occasional branches of the arterioles pass through the alveolar bone to the periodontal ligament or run over the crest of the alveolar bone.
2. *Vessels of the periodontal ligament*, which extend into the gingiva and anastomose with capillaries in the sulcus area.
3. *Arterioles*, which emerge from the crest of the interdental septa⁸⁷ and extend parallel to the crest of the bone to anastomose with vessels of the periodontal ligament, with capillaries in the gingival crevicular areas and vessels that run over the alveolar crest.

Beneath the epithelium on the outer gingival surface, capillaries extend into the papillary connective tissue between the epithelial rete pegs in the form of terminal hairpin loops with efferent and afferent branches, spirals, and varices^{55,115} (Figure 2-24; see Figure 2-23). The loops are sometimes linked by cross-communications,⁸⁹ and flattened capillaries serve as reserve vessels when the circulation is increased in response to irritation.¹⁰¹

For more information on blood supply, lymphatics, and nerves, please visit the companion Expert CONSULT website at www.expertconsult.com.

The role of the lymphatic system in removing excess fluids, cellular and protein debris, microorganisms, and other elements is



SCIENCE TRANSFER

The teeth are one of the few structures that penetrate the integument; that is, they go from inside the body to outside the body. As such, the gingival epithelium and connective tissue serve as a unique barrier to oral challenges. In addition, the shapes of the teeth are functionally adapted, and therefore the barrier morphology is adapted to correlate with the tooth shape. For example, the contact area varies between the teeth, as does the col shape of the interdental gingiva. Perhaps most important (and likely underestimated) are the functional qualities of the gingival barrier. The epithelium alone is a complex organ system with exquisite immune functions. Furthermore, the gingival fluid and connective tissues are complex and uniquely adaptive in the face of changes such as those associated with aging, disease, and trauma. Superimposed on these unique barrier and functional qualities is the consistent and predominantly successful response against persistent microbial challenge. The last response in this area is a complicated, intertwined system of tissue changes and cellular responses of the immune system.

The integrity of the dentogingival complex depends on having an intact epithelial covering, with junctional epithelium forming a seal in the gingival sulcus. This seal operates because of the function of the dense type I collagen gingival fibers, which provide the mass and tensile strength to hold the tissues in tight apposition to the neck of the tooth.

Dental procedures, such as root planing, subgingival restorative procedures, and crown and bridge gingival retraction techniques, all damage both the epithelium and the gingival connective tissue.

The oral sulcular epithelium and junctional epithelium have a great ability to replenish themselves in a short turnover time of 1 to 6 days, and fibroblasts can also produce new collagen fibers. It is essential that dental procedures be as atraumatic as possible so that sufficient volume of gingival collagen fibers are maintained to hold the healing gingiva close to the roots. This allows a new, intact epithelial lining of the gingival sulcus to be quickly reconstituted and thus heal without any loss of attachment.

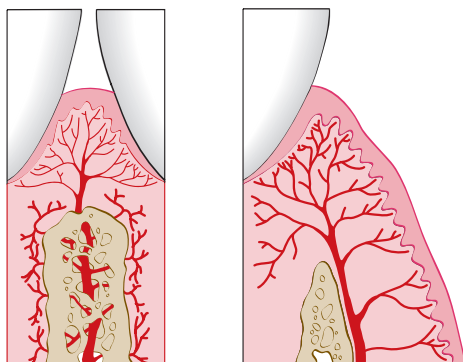


Figure 2-22 Diagram of arteriole penetrating the interdental alveolar bone to supply the interdental tissues (*left*) and a suprapariosteal arteriole overlying the facial alveolar bone, sending branches to the surrounding tissue (*right*).

important in controlling diffusion and the resolution of inflammatory processes.¹⁷⁰ The *lymphatic drainage of the gingiva* brings in the lymphatics of the connective tissue papillae.²⁴⁴ It progresses into the collecting network external to the periosteum of the alveolar process, then to the regional lymph nodes, particularly the submaxillary group. In addition, lymphatics just beneath the junctional epithelium extend into the periodontal ligament and accompany the blood vessels.

Neural elements are extensively distributed throughout the gingival tissues. Within the gingival connective tissues, most nerve fibers are myelinated and are closely associated with the blood vessels.¹⁶⁴ *Gingival innervation* is derived from fibers arising from nerves in the periodontal ligament and from the labial, buccal, and palatal nerves.³⁰ The following nerve structures are present in the connective tissue: a meshwork of terminal argyrophilic fibers, some of which extend into the epithelium; Meissner-type tactile corpuscles; Krause-type end bulbs, which are temperature receptors; and encapsulated spindles.¹⁴

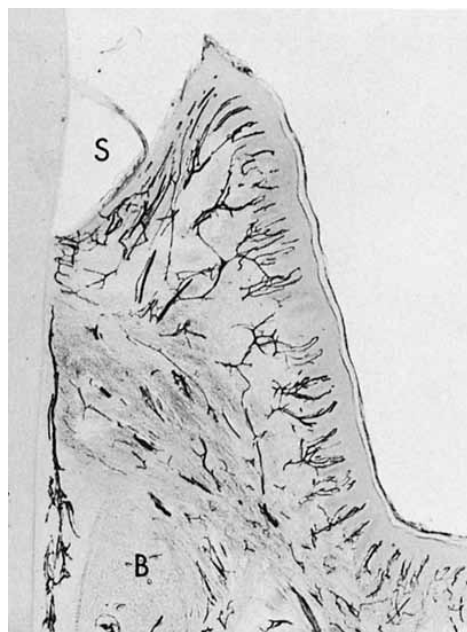


Figure 2-23 Blood supply and peripheral circulation of the gingiva. Tissues perfused with India ink. Note the capillary plexus parallel to the sulcus (*S*) and the capillary loops in the outer papillary layer. Note also the suprapariosteal vessels external to the bone (*B*), which supply the gingiva, and a periodontal ligament vessel anastomosing with the sulcus plexus. (Courtesy Sol Bernick.)

Correlation of Clinical and Microscopic Features

An understanding of the normal clinical features of the gingiva requires the ability to interpret them in terms of the microscopic structures they represent.

Color. The color of the attached and marginal gingiva is generally described as “coral pink” and is produced by the vascular supply, the thickness and degree of keratinization of the epithelium, and the presence of pigment-containing cells. The color varies among different persons and appears to be correlated with the cutaneous

pigmentation. It is lighter in blond individuals with fair complexion than in swarthy, dark-haired individuals (Figure 2-25).

To view Figure 2-26 and for more information on the color of attached and marginal gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

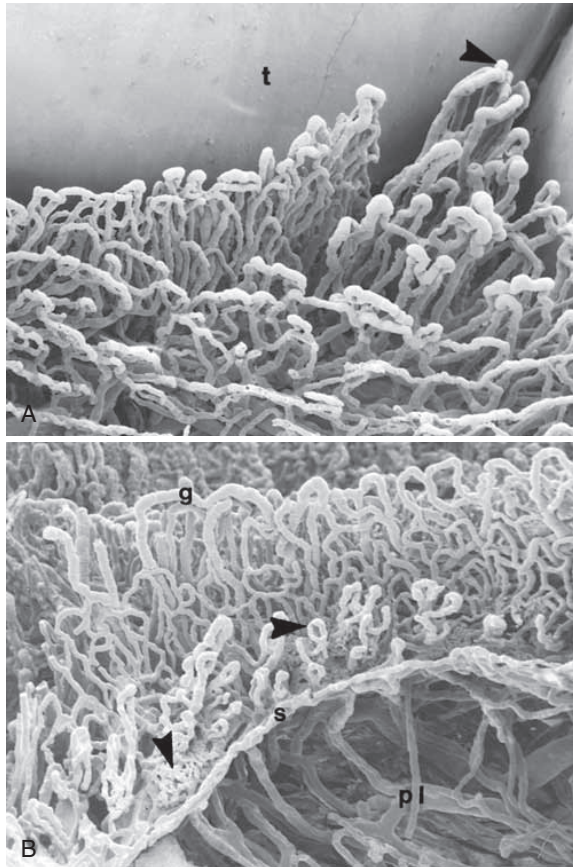


Figure 2-24 Scanning electron microscopic view of gingival tissues of rat molar palatal gingiva after vascular perfusion of plastic and corrosion of soft tissue. **A**, Oral view of gingival capillaries: *t*, tooth; interdental papilla (arrowhead) ($\times 180$). **B**, View from the tooth side. Note the vessels of the plexus next to the sulcular and junctional epithelium. The arrowheads point to vessels in sulcus area with mild inflammatory changes. *g*, Crest of marginal gingiva; *s*, bottom of gingival sulcus; *pl*, periodontal ligament vessels. ($\times 150$.) (Courtesy NJ Sellseth and K Selvig, University of Bergen, Norway.)

Physiologic Pigmentation (Melanin). Melanin is a non-hemoglobin-derived brown pigment with the following characteristics:

- Melanin is responsible for the normal pigmentation of the skin, gingiva, and remainder of the oral mucous membrane.
- Melanin is present in all normal individuals, often not in sufficient quantities to be detected clinically, but is absent or severely diminished in albinos.
- Melanin pigmentation in the oral cavity is prominent in black individuals (see Figure 2-25).
- Ascorbic acid directly downregulates melanin pigmentation in gingival tissues.²⁵²

For more information on physiologic pigmentation, please visit the companion Expert CONSULT website at www.expertconsult.com.

Size. The size of the gingiva corresponds with the sum total of the bulk of cellular and intercellular elements and their vascular supply. Alteration in size is a common feature of gingival disease.

Contour. The contour or shape of the gingiva varies considerably and depends on the shape of the teeth and their alignment in the arch, the location and size of the area of proximal contact, and the dimensions of the facial and lingual gingival embrasures.

To view Figure 2-27 and for more information on the contour of gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

Shape. The shape of the interdental gingiva is governed by the contour of the proximal tooth surfaces and the location and shape of gingival embrasures.



Figure 2-25 **A**, Clinically normal gingiva in a young adult. **B**, Heavily pigmented (melanotic) gingiva in a middle-aged adult. (From Glickman I, Smulow JB: Periodontal disease: clinical, radiographic, and histopathologic features, Philadelphia, 1974, Saunders.)

To view Figure 2-28 and for more information on the shape of the interdental gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

Consistency. The gingiva is firm and resilient and with the exception of the movable free margin, tightly bound to the underlying bone. The collagenous nature of the lamina propria and its contiguity with the mucoperiosteum of the alveolar bone determine the firmness of the attached gingiva. The gingival fibers contribute to the firmness of the gingival margin.

Surface Texture. The gingiva presents a textured surface similar to an orange peel and is referred to as *stippled* (see Figure 2-25). Stippling is best viewed by drying the gingiva. *The attached gingiva is stippled; the marginal gingiva is not.* The central portion of the interdental papillae is usually stippled, but the marginal borders are smooth. The pattern and extent of stippling vary among individuals and different areas of the same mouth.^{110,221} Stippling is less prominent on lingual than facial surfaces and may be absent in some persons.

Stippling varies with age. It is absent in infancy, appears in some children at about 5 years of age, increases until adulthood, and frequently begins to disappear in old age.

To view Figure 2-29 and for more information on gingival surface texture, please visit the companion Expert CONSULT website at www.expertconsult.com.

Position. The *position* of the gingiva refers to the level at which the gingival margin is attached to the tooth.

For more information on the position of the gingiva, please visit the companion Expert CONSULT website at www.expertconsult.com.

Continuous Tooth Eruption. According to the concept of continuous eruption,¹⁰⁷ eruption does not cease when teeth meet their functional antagonists but continues throughout life. Eruption consists of an active and a passive phase. *Active eruption* is the movement of the teeth in the direction of the occlusal plane, whereas *passive eruption* is the exposure of the teeth by apical migration of the gingiva.

This concept distinguishes between the *anatomic crown* (portion of the tooth covered by enamel) and the *anatomic root* (portion of the tooth covered by cementum) and between the *clinical crown* (part of the tooth that has been denuded of its gingiva and projects into the oral cavity) and *clinical root* (portion of the tooth covered by periodontal tissues). When the teeth reach their functional antagonists, the gingival sulcus and junctional epithelium are still on the enamel, and the clinical crown is approximately two-thirds of the anatomic crown.

To view Figure 2-30, and for more information on continuous tooth eruption, please visit the companion Expert CONSULT website at www.expertconsult.com.

PERIODONTAL LIGAMENT

The periodontal ligament is composed of a complex vascular and highly cellular connective tissue that surrounds the tooth root and connects it to the inner wall of the alveolar bone.¹⁷⁷ It is continuous with the connective tissue of the gingiva and communicates with the marrow spaces through vascular channels in the bone. Although the average width of the periodontal ligament space is documented to be about 0.2 mm, considerable variation exists. The periodontal space is diminished around teeth that are not in function and in unerupted teeth, but it is increased in teeth subjected to hyperfunction.

Periodontal Fibers

The most important elements of the periodontal ligament are the *principal fibers*, which are collagenous and arranged in bundles and follow a wavy course when viewed in longitudinal section (Figure 2-31). The terminal portions of the principal fibers that are inserted into cementum and bone are termed *Sharpey's fibers* (Figure 2-32). The principal fiber bundles consist of individual fibers that form a continuous anastomosing network between tooth and bone.^{25,59} Once embedded in the wall of the alveolus or in the tooth, Sharpey's fibers calcify to a significant degree. They are associated with abundant noncollagenous proteins typically found in bone and also recently identified in tooth cementum.^{33,134,177} Notable among these proteins are osteopontin and bone sialoprotein. These proteins are thought to contribute to the regulation of mineralization and to tissue cohesion at sites of increased biomechanical strain.¹⁷⁷

To view Figure 2-33 and for more information on periodontal fibers, please visit the companion Expert CONSULT website at www.expertconsult.com.

The principal fibers of the periodontal ligament are arranged in six groups that develop sequentially in the developing root: the transseptal, alveolar crest, horizontal, oblique, apical, and interradicular fibers (Figure 2-34).

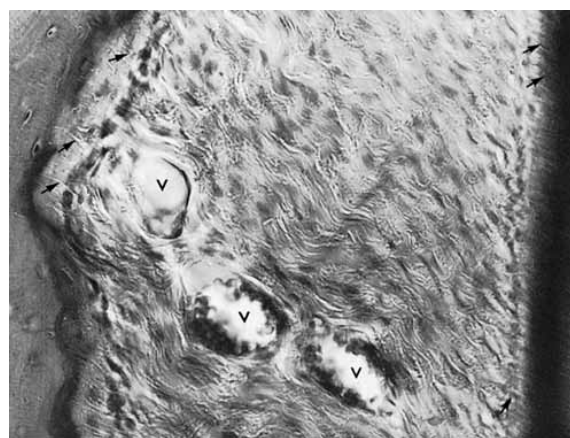


Figure 2-31 Principal fibers of the periodontal ligament follow a wavy course when sectioned longitudinally. The formative function of the periodontal ligament is illustrated by the newly formed osteoid and osteoblasts along a previously resorbed bone surface (*left*) and the cementoid and cementoblasts (*right*). Note the fibers embedded in the forming calcified tissues (*arrows*). V, Vascular channels.

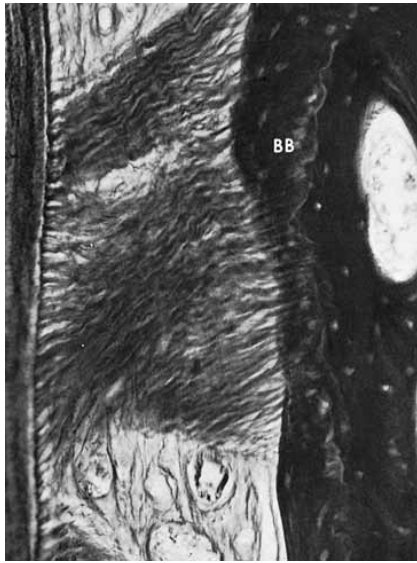


Figure 2-32 Collagen fibers embedded in the cementum (*left*) and bone (*right*) (silver stain). Note Sharpey's fibers within the bundle bone (*BB*) overlying lamellar bone.

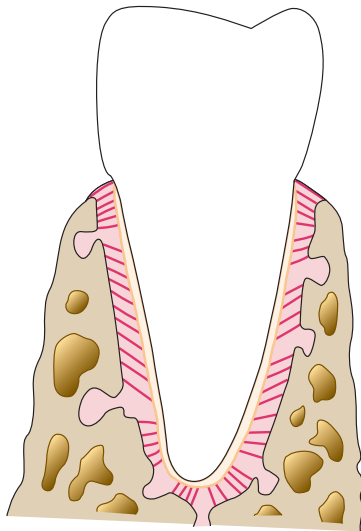


Figure 2-34 Diagram of principal fiber groups.

Transseptal Group. Transseptal fibers extend interproximally over the alveolar bone crest and are embedded in the cementum of adjacent teeth (Figure 2-35). They are reconstructed even after destruction of the alveolar bone resulting from periodontal disease. These fibers may be considered as belonging to the gingiva because they do not have osseous attachment.

Alveolar Crest Group. Alveolar crest fibers extend obliquely from the cementum just beneath the junctional epithelium to the alveolar crest (Figure 2-36). Fibers also run from the cementum over the alveolar crest and to the fibrous layer of the periosteum covering the alveolar bone. The alveolar crest fibers prevent the extrusion of the tooth⁵⁴ and resist lateral tooth movements. The

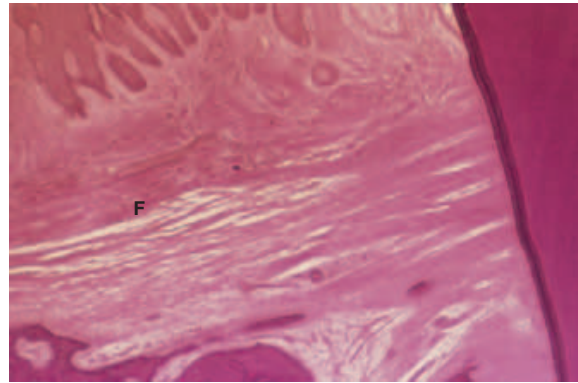


Figure 2-35 Transseptal fibers (*F*) at the crest of the interdental bone.

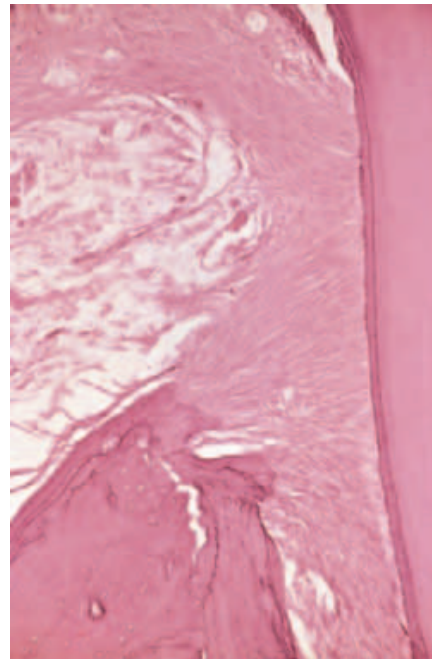


Figure 2-36 Rat molar section showing alveolar crest fibers radiating coronally.

incision of these fibers during periodontal surgery does not increase tooth mobility unless significant attachment loss has occurred.⁹⁹

Horizontal Group. Horizontal fibers extend at right angles to the long axis of the tooth from the cementum to the alveolar bone.

Oblique Group. Oblique fibers, the largest group in the periodontal ligament, extend from the cementum in a coronal direction obliquely to the bone (see Figure 2-34). They bear the brunt of vertical masticatory stresses and transform them into tension on the alveolar bone.

Apical Group. The apical fibers radiate in a rather irregular manner from the cementum to the bone at the apical region of the socket. They do not occur on incompletely formed roots.

Interradicular Group The interradicular fibers fan out from the cementum to the tooth in the furcation areas of multirooted teeth.

For more information on periodontal fibers, please visit the companion Expert CONSULT website at www.expertconsult.com.

Cellular Elements

Four types of cells have been identified in the periodontal ligament: connective tissue cells, epithelial rest cells, immune system cells, and cells associated with neurovascular elements.²⁶

Connective tissue cells include fibroblasts, cementoblasts, and osteoblasts. Fibroblasts are the most common cells in the periodontal ligament and appear as ovoid or elongated cells oriented along the principal fibers, exhibiting pseudopodia-like processes.²¹⁵ These cells synthesize collagen and possess the capacity to phagocytose “old” collagen fibers and degrade them²⁷⁰ by enzyme hydrolysis. Thus collagen turnover appears to be regulated by fibroblasts in a process of intracellular degradation of collagen not involving the action of collagenase.²⁴

For more information on cellular elements, please visit the companion Expert CONSULT website at www.expertconsult.com.

The *epithelial rests of Malassez* form a latticework in the periodontal ligament and appear as either isolated clusters of cells or interlacing strands (Figure 2-37), depending on the plane in which the microscopic section is cut. Continuity with the junctional epithelium has been suggested in experimental animals.¹⁰⁸ The epithelial rests are considered remnants of Hertwig’s root sheath, which disintegrates during root development (Figure 2-37, A).

For more information on cellular elements, please visit the companion Expert CONSULT website at www.expertconsult.com.

The *defense cells* in the periodontal ligament include neutrophils, lymphocytes, macrophages, mast cells, and eosinophils. These cells, as well as those associated with neurovascular elements, are similar to the cells in other connective tissues.

Ground Substance

The periodontal ligament also contains a large proportion of ground substance, filling the spaces between fibers and cells. It consists of two main components: *glycosaminoglycans*, such as hyaluronic acid and proteoglycans, and *glycoproteins*, such as fibronectin and laminin. Ground substance also has a high water content (70%).

For more information on ground substance, please visit the companion Expert CONSULT website at www.expertconsult.com.

The periodontal ligament may also contain calcified masses called *cementicles*, which are adherent to or detached from the root surfaces (Figure 2-38).

For more information on cellular elements, please visit the companion Expert CONSULT website at www.expertconsult.com.

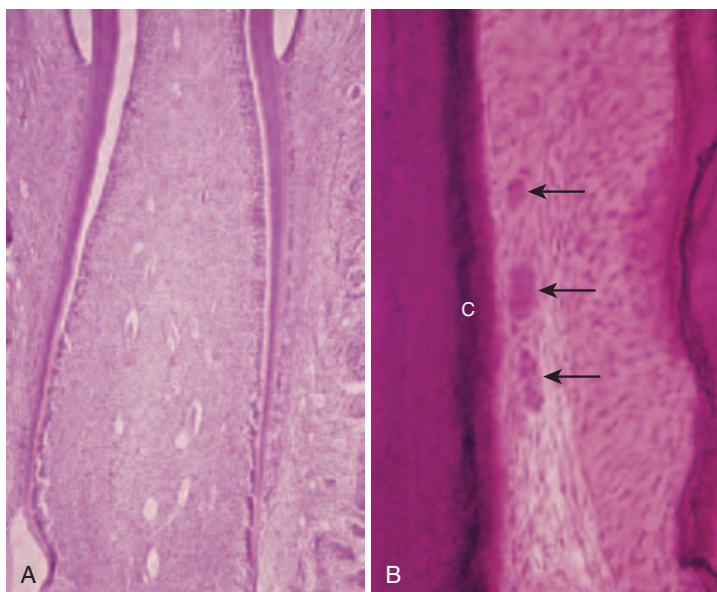
Functions of Periodontal Ligament

The functions of the periodontal ligament are categorized into physical, formative and remodeling, nutritional, and sensory.

Physical Functions. The physical functions of the periodontal ligament entail the following:

1. Provision of a soft tissue “casing” to protect the vessels and nerves from injury by mechanical forces.
2. Transmission of occlusal forces to the bone.
3. Attachment of the teeth to the bone.
4. Maintenance of the gingival tissues in their proper relationship to the teeth.

Figure 2-37 Epithelial rests of Malassez. **A**, Erupting tooth in a cat. Fragmentation of Hertwig’s epithelial root sheath giving rise to epithelial rests located along, and close to, the root surface. **B**, Human periodontal ligament with rosette-shaped epithelial rests (arrows) lying close to the cementum (C).



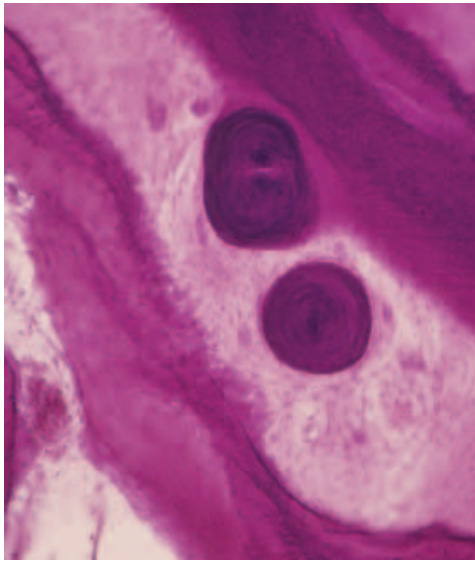


Figure 2-38 Cementicles in the periodontal ligament, one lying free and the other adherent to the tooth surface.

5. Resistance to the impact of occlusal forces (shock absorption).

To view Figures 2-39 to Figure 2-41 and Table 2-1 and for more information on physical functions of the periodontal ligament, please visit the companion Expert CONSULT website at www.expertconsult.com.

Formative and Remodeling Function. Periodontal ligament and alveolar bone cells are exposed to physical forces in response to mastication, parafunction, speech, and orthodontic tooth movement.¹⁷⁵ Cells of the periodontal ligament participate in the formation and resorption of cementum and bone, which occur in physiologic tooth movement; in the accommodation of the periodontium to occlusal forces; and in the repair of injuries.

For more information on formative and remodeling function, please visit the companion Expert CONSULT website at www.expertconsult.com.

Nutritional and Sensory Functions. The periodontal ligament supplies nutrients to the cementum, bone, and gingiva by way of the blood vessels and also provides lymphatic drainage (see later discussion).

For more information on nutritional and sensory functions, please visit the companion Expert CONSULT website at www.expertconsult.com.

Regulation of Periodontal Ligament Width. Some of the most interesting features of the periodontal ligament in animals are its adaptability to rapidly changing applied force and

its capacity to maintain its width at constant dimensions throughout its lifetime.¹⁷⁶ These are important measures of periodontal ligament homeostasis, providing insight into the function of the biologic mechanisms that tightly regulate the metabolism and spatial locations of the cell populations involved in the formation of bone, cementum, and periodontal ligament fibers. Also, the ability of periodontal ligament cells to synthesize and secrete a wide range of regulatory molecules is an essential component of tissue remodeling and periodontal ligament homeostasis.¹⁷⁵

CEMENTUM

Cementum is the calcified, avascular mesenchymal tissue that forms the outer covering of the anatomic root. The two main types of cementum are acellular (*primary*) and cellular (*secondary*) cementum.¹⁰⁶ Both consist of a calcified interfibrillar matrix and collagen fibrils.

The two main sources of collagen fibers in cementum are (1) Sharpey's fibers (*extrinsic*), which are the embedded portion of the principal fibers of the periodontal ligament²¹⁹ and are formed by the fibroblasts, and (2) fibers that belong to the cementum matrix (*intrinsic*) and are produced by the cementoblasts.²⁴⁶ Cementoblasts also form the noncollagenous components of the interfibrillar ground substance such as proteoglycans, glycoproteins, and phosphoproteins. Proteoglycans are most likely to play a role in regulating cell-cell and cell-matrix interactions, both in normal development, as well as in regeneration of the cementum.¹⁷ In addition, immunohistochemical studies have shown that the distribution of proteoglycans is closely associated with the cementoblasts and cementocytes.^{1,2}

To view Figures 2-42 and 2-43 and for more information on cementum, please visit the companion Expert CONSULT website at www.expertconsult.com.

Permeability of Cementum

In very young animals, acellular cementum and cellular cementum are very permeable and permit the diffusion of dyes from the pulp and external root surface. In cellular cementum the canaliculi in some areas are contiguous with the dentinal tubuli. The permeability of cementum diminishes with age.³⁶

Cementoenamel Junction

The cementum at and immediately subjacent to the *cementoenamel junction* (CEJ) is of particular clinical importance in root-scaling procedures. Three types of relationships involving the cementum may exist at the CEJ.¹⁹³ In about 60% to 65% of cases, cementum overlaps the enamel (Figure 2-44); in about 30%, an edge-to-edge butt joint exists; and in 5% to 10%, the cementum and enamel fail to meet. In the last case, gingival recession may result in accentuated sensitivity because of exposed dentin.

Cementodentinal Junction

The terminal apical area of the cementum where it joins the internal root canal dentin is known as the *cementodentinal junction* (CDJ). When root canal treatment is performed, the obturating material should be at the CDJ. There appears to be no increase or decrease in the width of the CDJ with age; its width appears to remain relatively stable.²⁵⁹ Scanning electron microscopy of the human teeth reveals that the CDJ is 2 to 3 μm wide. The fibril-poor layer contains a significant amount of proteoglycans, and fibrils intermingle between the cementum and dentin.^{298,299}

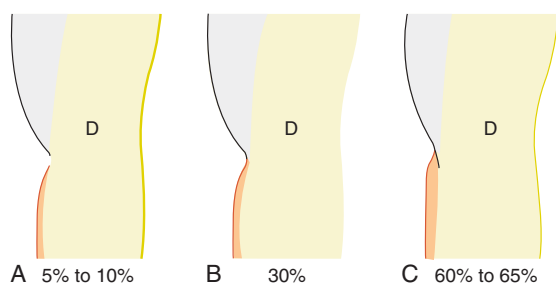


Figure 2-44 Normal variations in tooth morphology at the cementoenamel junction. **A**, Space between enamel and cementum with dentin (*D*) exposed. **B**, End-to-end relationship of enamel and cementum. **C**, Cementum overlapping the enamel.

To view Figures 2-45 to 2-48, and for more information on the thickness of cementum, resorption and repair, and exposure of cementum to the oral environment, please visit the companion Expert **CONSULT** website at www.expertconsult.com.

Thickness of Cementum

Cementum deposition is a continuous process that proceeds at varying rates throughout life. Cementum formation is most rapid in the apical regions, where it compensates for tooth eruption, which itself compensates for attrition.

For more information on the thickness of cementum, please visit the companion Expert **CONSULT** website at www.expertconsult.com.

Cementum Resorption and Repair

Permanent teeth do not undergo physiologic resorption as do primary teeth. However, the cementum of erupted, as well as unerupted teeth, is subject to resorptive changes that may be of microscopic proportion or sufficiently extensive to present a radiographically detectable alteration in the root contour.

For more information on cementum resorption and repair, please visit the companion Expert **CONSULT** website at www.expertconsult.com.

Ankylosis. Fusion of the cementum and alveolar bone with obliteration of the periodontal ligament is termed ankylosis. Ankylosis occurs in teeth with cemental resorption, which suggests that it may represent a form of abnormal repair. Ankylosis also may develop after chronic periapical inflammation, tooth replantation, and occlusal trauma and around embedded teeth.

For more information on ankylosis, please visit the companion Expert **CONSULT** brand here> website at www.expertconsult.com.

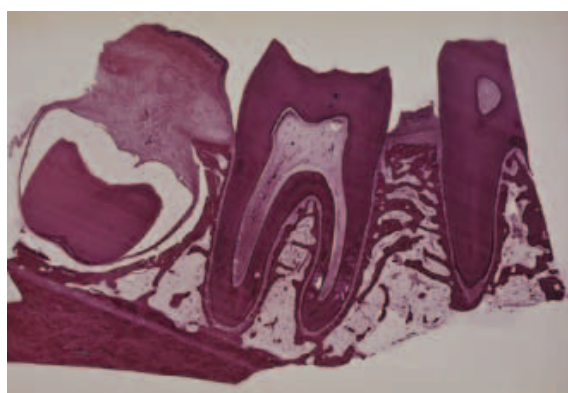


Figure 2-49 Mesiodistal section through mandibular molars of a 17-year-old female, obtained at autopsy. Note the interdentary bony septa between first and second molar. The dense cortical bony plates represent the alveolar bone proper (cribriform plates) and are supported by cancellous bony trabeculae. The third molar is still in early stages of root formation and eruption.

ALVEOLAR PROCESS

The alveolar process is the portion of the maxilla and mandible that forms and supports the tooth sockets (alveoli). It forms when the tooth erupts to provide the osseous attachment to the forming periodontal ligament; it disappears gradually after the tooth is lost.

Since the alveolar processes develop and undergo remodeling with the tooth formation and eruption, they are tooth-dependent bony structures.²³² Therefore the size, shape, location, and function of the teeth determine their morphology. Interestingly, although the growth and development of the bones of the jaw determine the position of the teeth, a certain degree of repositioning of teeth can be accomplished through occlusal forces and in response to orthodontic procedures that rely on the adaptability of the alveolar bone and associated periodontal tissues.²⁵⁷

The alveolar process consists of the following:

1. An external plate of cortical bone formed by haversian bone and compacted bone lamellae.
2. The inner socket wall of thin, compact bone called the *alveolar bone proper*, which is seen as the lamina dura in radiographs. Histologically, it contains a series of openings (*cribriform plate*) through which neurovascular bundles link the periodontal ligament with the central component of the alveolar bone, the cancellous bone.
3. Cancellous trabeculae, between these two compact layers, which act as supporting alveolar bone. The *interdentary septum* consists of cancellous supporting bone enclosed within a compact border (Figure 2-49).

To view Figures 2-50 to 2-55 and for more information on the alveolar process, please visit the companion Expert **CONSULT** website at www.expertconsult.com.

Periosteum and Endosteum

Layers of differentiated osteogenic connective tissue cover all the bone surfaces. The tissue covering the outer surface of bone is termed *periosteum*, whereas the tissue lining the internal bone cavity is called *endosteum*.

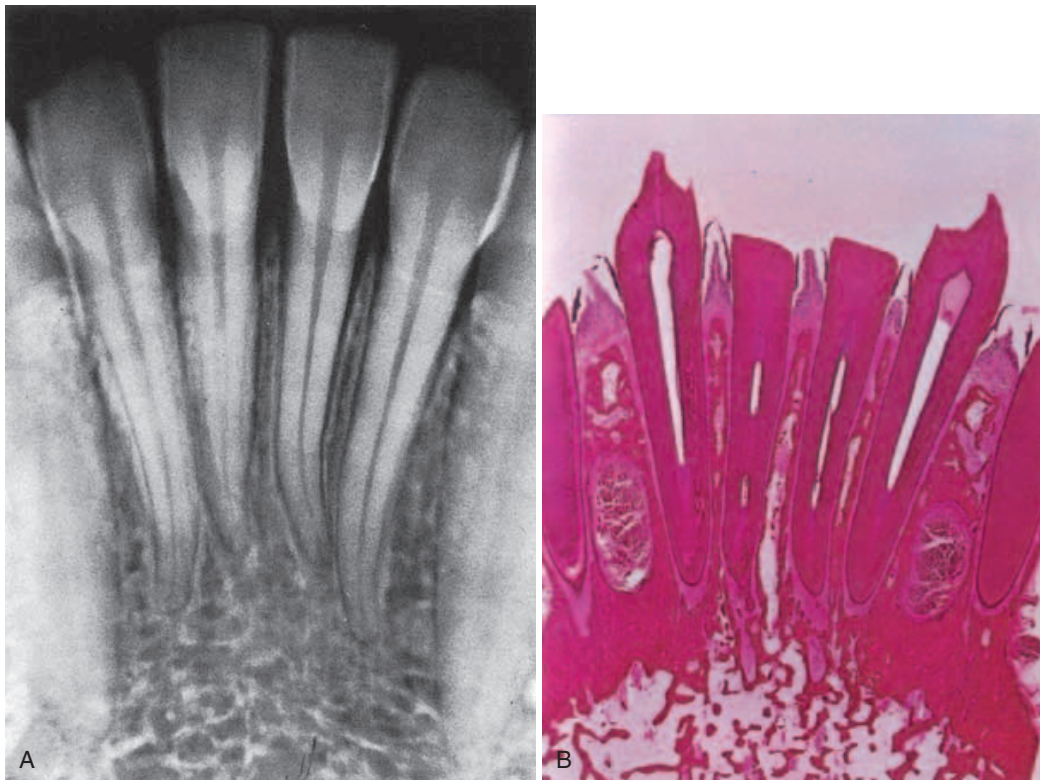


Figure 2-56 Interdental septa. **A**, Radiograph of mandibular incisor area. Note the prominent lamina dura. **B**, Interdental septa between the mandibular anterior teeth shown in **A**. There is a slight reduction in bone height with widening of the periodontal ligament in the coronal areas. The central cancellous portion is bordered by the dense bony cribriform plates of the socket, which form the lamina dura around the teeth in the radiograph. Attachments for the mentalis muscle are seen between the canine and lateral incisors. (From Glickman I, Smulow J: *Periodontal disease: clinical, radiographic, and histopathologic features*, Philadelphia, 1974, Saunders.)

The periosteum consists of an *inner layer* composed of osteoblasts surrounded by osteoprogenitor cells, which have the potential to differentiate into osteoblasts, and an *outer layer* rich in blood vessels and nerves and composed of collagen fibers and fibroblasts. Bundles of periosteal collagen fibers penetrate the bone, binding the periosteum to the bone. The endosteum is composed of a single layer of osteoblasts and sometimes a small amount of connective tissue. The inner layer is the osteogenic layer, and the outer layer is the fibrous layer.

For more information on the periosteum and endosteum, please visit the companion Expert CONSULT website at www.expertconsult.com.

Interdental Septum

The interdental septum consists of cancellous bone bordered by the socket wall cribriform plates (lamina dura or alveolar bone proper) of approximating teeth and the facial and lingual cortical plates (Figure 2-56). If the interdental space is narrow, the septum may consist of only the cribriform plate. In one study, for example, the space between mandibular second premolars and first molars consisted of cribriform plate and cancellous bone in 85% of the cases and only cribriform plate in the remaining 15%.¹¹⁸ If roots are too close together, an irregular “window” can appear in the bone between adjacent roots (Figure 2-57).

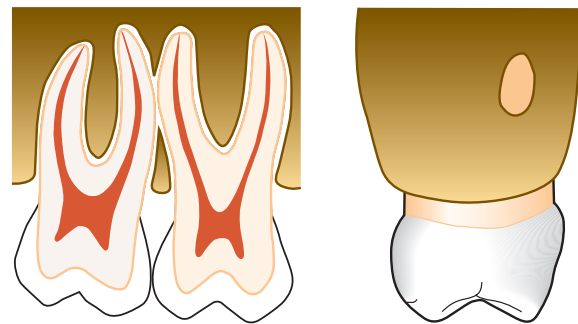


Figure 2-57 Boneless “window” between adjoining close roots of molars.

For more information on the interdental septum, please visit the companion Expert CONSULT website at www.expertconsult.com.

Osseous Topography

The bone contour normally conforms to the prominence of the roots, with intervening vertical depressions that taper toward the margin (Figure 2-58). Alveolar bone anatomy varies among patients



Figure 2-58 Normal bone contour conforms to the prominence of the roots.



Figure 2-60 Dehiscence on the canine and fenestration of the first premolar.

and has important clinical implications. The height and thickness of the facial and lingual bony plates are affected by the alignment of the teeth, angulation of the root to the bone, and occlusal forces.

To view Figure 2-59 and for more information on osseous topography, please visit the companion Expert CONSULT website at www.expertconsult.com.

Fenestration and Dehiscence

Isolated areas in which the root is denuded of bone and the root surface is covered only by periosteum and overlying gingiva are termed *fenestrations*. In these areas the marginal bone is intact.

When the denuded areas extend through the marginal bone, the defect is called a *dehiscence* (Figure 2-60).

For more information on fenestration and dehiscence, please visit the companion Expert CONSULT website at www.expertconsult.com.

DEVELOPMENT OF THE ATTACHMENT APPARATUS

For more information on development of the attachment apparatus, please visit the companion Expert CONSULT website at www.expertconsult.com.

EXTERNAL FORCES AND THE PERIODONTIUM

The periodontium exists for the purpose of supporting teeth during function and depends on the stimulation it receives from function for the preservation of its structure. Therefore a constant and sensitive balance is present between external forces and the periodontal structures.

Alveolar bone undergoes constant physiologic remodeling in response to external forces, particularly occlusal forces. Bone is removed from areas where it is no longer needed and added to areas where it is presently needed.

To view Figures 2-61 and 2-62 and Table 2-2 and for more information on external forces and the periodontium, please visit the companion Expert CONSULT website at www.expertconsult.com.

VASCULARIZATION OF THE SUPPORTING STRUCTURES

The blood supply to the supporting structures of the tooth is derived from the inferior and superior alveolar arteries to the mandible and maxilla, and it reaches the periodontal ligament from three sources: apical vessels, penetrating vessels from the alveolar bone, and anastomosing vessels from the gingiva.⁶⁴

To view Figures 2-63 and 2-64 and for more information on vascularization of the supporting structures, please visit the companion Expert CONSULT website at www.expertconsult.com.

References and suggested readings can be found on the companion Expert CONSULT website at www.expertconsult.com.



SCIENCE TRANSFER

The normal periodontium is a unique and complex dynamic structure. Each of its components (gingiva, periodontal ligament, cementum, and bone) has distinct functions that are capable of adaptation during the life of the structure. For example, as teeth respond to forces or migrate mesially with wear, the bone tissue is resorbed on the pressure side and added on the tension side. Cementum similarly adapts to wear on the occlusal surfaces of teeth by deposition in the apical area of the tooth root. The periodontal ligament itself is an area of high turnover, which allows the tooth not only to be suspended in the alveolar bone but also to respond to the intermediate forces. Thus, although seemingly static, the structure of tooth support is made up from components of the periodontium that are highly specialized, adaptive, and dynamic structures.

The function of the periodontal ligament is most similar to a viscoelastic system that absorbs the first movement of loading,

with collagen fibers then becoming important as a secondary phase of response to loading forces. This gives the periodontal ligament a shock-absorbing quality, as well as a hydraulic-like tendency to respond to axial loading with an increased pressure that counteracts the apically-directed tooth movement.

When a tooth is subjected to increased occlusal load, it will be slightly depressed, and when unloaded, it will have a rebound effect.

Therefore correction of “high” restorations by grinding may require 2 or more checks over 2 to 5 minutes. Also, the use of heavy-bodied materials for crown and bridge impressions with sustained pressure can cause intrusion of a tooth, followed by a rebound extrusion after the impression is removed. The result will be a restoration that is high.

Being aware of these properties of the periodontal ligament can allow clinicians to modify their clinical procedures.

Because the mucogingival junction remains stationary throughout adult life,⁴ changes in the width of the attached gingiva are caused by modifications in the position of its coronal portion. The width of the attached gingiva increases by age 4 and in supraerupted teeth.⁵ On the lingual aspect of the mandible, the attached gingiva terminates at the junction of the lingual alveolar mucosa, which is continuous with the mucous membrane lining the floor of the mouth. The palatal surface of the attached gingiva in the maxilla blends imperceptibly with the equally firm and resilient palatal mucosa.

General Aspects of Gingival Epithelium Biology.

Historically, the epithelial compartment was thought to provide only a physical barrier to infection and the underlying gingival attachment. However, we now believe that epithelial cells play an active role in innate host defense by responding to bacteria in an interactive manner,⁶⁹ which means the epithelium participates actively in responding to infection, in signaling further host reactions, and in integrating innate and acquired immune responses. For example, epithelial cells may respond to bacteria by increased proliferation, alteration of cell-signaling events, changes in differentiation and cell death, and ultimately, alteration of tissue homeostasis.⁶⁹ To understand this new perspective of the epithelial innate defense responses and the role of epithelium in gingival health and disease, it is important to understand its basic structure and function (Box 2-1).

BOX 2-1 Functions and Features of Gingival Epithelium**Functions**

Mechanical, chemical, water, and microbial barrier
Signaling functions

Architectural Integrity

Cell-cell attachments
Basal lamina
Keratin cytoskeleton

Major Cell Type

Keratinocyte

Other Cell Types

Langerhans cells
Melanocytes, Merkel cells

Constant Renewal

Replacement of damaged cells

Cell-Cell Attachments

Desmosomes, adherens junctions
Tight junctions, gap junctions

Cell-Basal Lamina

Synthesis of basal lamina components
Hemidesmosome

Modified from Dale BA: *Periodontal* 2000 30:71, 2002.

Immunohistochemistry, gel electrophoresis, and immunoblot techniques have made identification of the characteristic pattern of cytokeratins possible in each epithelial type. The keratin proteins are composed of different polypeptide subunits characterized by their isoelectric points and molecular weights. They are numbered in a sequence contrary to their molecular weight. Generally, basal cells begin synthesizing lower-molecular-weight keratins, such as K19 (40 kD), and express other higher-molecular-weight keratins as they migrate to the surface. K1 keratin polypeptide (68 kD) is the main component of the stratum corneum.⁶¹

Other proteins unrelated to keratins are synthesized during the maturation process. The most extensively studied are *keratolinin* and *involucrin*, which are precursors of a chemically resistant structure (the envelope) located below the cell membrane, and *filaggrin*, whose precursors are packed into the keratohyalin granules. In the sudden transition to the horny layer, the keratohyalin granules disappear and give rise to filaggrin, which forms the matrix of the most differentiated epithelial cell, the *corneocyte*.

Thus, in the fully differentiated state, the corneocytes are mainly formed by bundles of keratin tonofilaments embedded in an amorphous matrix of filaggrin and are surrounded by a resistant envelope under the cell membrane. The immunohistochemical patterns of the different keratin types, envelope proteins, and filaggrin change under normal or pathologic stimuli, modifying the keratinization process.^{130–132}

Accordingly, histochemical demonstration of succinic dehydrogenase, nicotinamide-adenine dinucleotide, cytochrome oxidase, and other mitochondrial enzymes reveals a more active tricarboxylic cycle in basal and parabasal cells, in which the proximity of the blood supply facilitates energy production through aerobic glycolysis.

Conversely, enzymes of the pentose shunt (an alternative pathway of glycolysis), such as glucose-6-phosphatase, increase their activity toward the surface. This pathway produces a larger amount of intermediate products for the production of ribonucleic acid (RNA), which in turn can be used for the synthesis of keratinization proteins. This histochemical pattern is in accordance with the increased volume and the amount of tonofilaments observed in cells reaching the surface; the intensity of the activity is proportional to the degree of differentiation.^{74,85,129,206}

They contain a large amount of acid phosphatase, an enzyme involved in the destruction of organelle membranes, which occurs suddenly between the granulosum and corneum strata and during the intercellular cementation of cornified cells. Thus acid phosphatase is another enzyme closely related to the degree of keratinization.^{47,127,289}

These contain tyrosinase, which hydroxylates tyrosine to dihydroxyphenylalanine (dopa), which in turn is progressively converted to melanin. Melanin granules are phagocytosed and contained within other cells of the epithelium and connective tissue called *melanophages* or *melanophores*.

The degree of gingival keratinization diminishes with age and the onset of menopause²⁰³ but is not necessarily related to the different phases of the menstrual cycle.¹³³ Keratinization of the oral mucosa varies in different areas in the following order: palate (most keratinized), gingiva, ventral aspect of the tongue, and cheek (least keratinized).¹⁸⁴

Keratins K1, K2, and K10 to K12, which are specific to epidermal-type differentiation, are immunohistochemically expressed with high intensity in orthokeratinized areas and with less intensity in parakeratinized areas. K6 and K16, characteristic of highly proliferative epithelia, and K5 and K14, stratification-specific cytokeratins, also are present. Parakeratinized areas express K19, which is usually absent from orthokeratinized normal epithelia.^{37,209}

In keeping with the complete or almost-complete maturation, histoenzyme reactions for acid phosphatase and pentose-shunt enzymes are very strong.^{48,129}

Glycogen can accumulate intracellularly when it is not completely degraded by any of the glycolytic pathways. Thus its concentration in normal gingiva is inversely related to the degree of keratinization^{242,290} and inflammation.^{73,278,281}

As with other nonkeratinized epithelia, the sulcular epithelium lacks granulosum and corneum strata and K1, K2, and K10 to K12 cytokeratins, but it contains K4 and K13, the so-called esophageal-type cytokeratins. It also expresses K19 and normally does not contain Merkel cells.

Histochemical studies of enzymes have consistently revealed a lower degree of activity in the sulcular than in the outer epithelium, particularly in the case of enzymes related to keratinization. Glucose-6-phosphate dehydrogenase expressed a faint and homogeneous reaction in all strata, unlike the increasing gradient toward the surface observed in cornified epithelia.¹²⁹ Acid phosphatase staining is negative,⁴⁷ although lysosomes have been described in exfoliated cells.¹⁵⁰

Despite these morphologic and chemical characteristics, the sulcular epithelium has the potential to keratinize if (1) it is reflected and exposed to the oral cavity^{45,49} or (2) the bacterial flora of the sulcus is totally eliminated.⁵¹ Conversely, the outer epithelium loses its keratinization when it is placed in contact with the tooth.⁵¹ These findings suggest that the local irritation of the sulcus prevents sulcular keratinization.

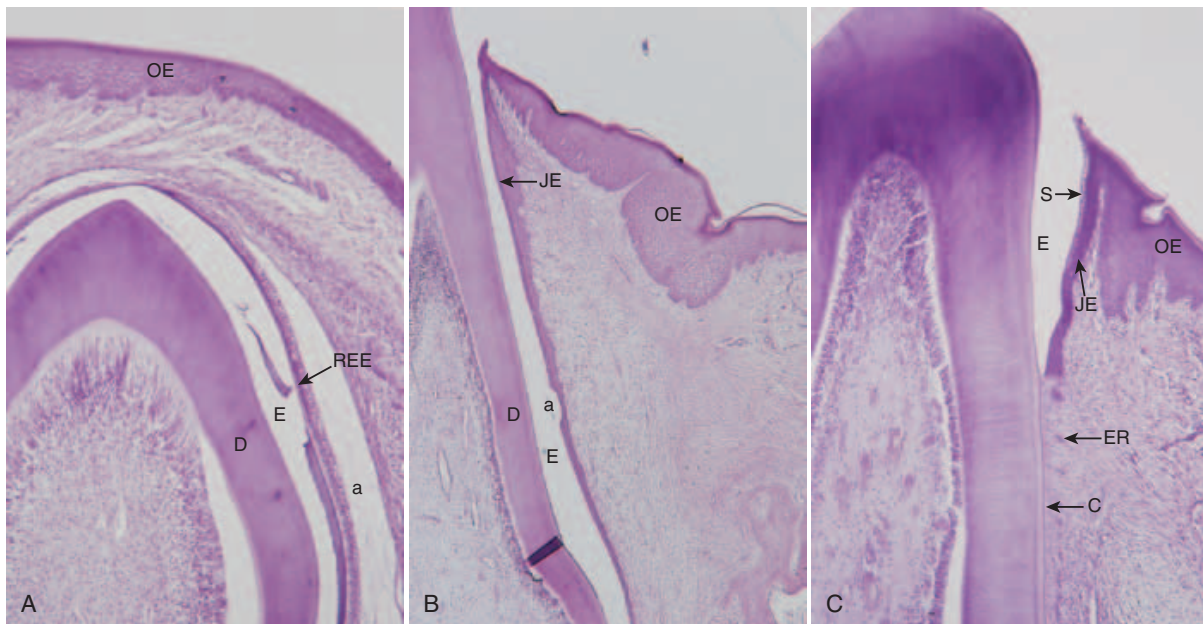


Figure 2-17 Eruption process in cat's tooth. **A**, Unerupted tooth. Dentin (*D*), remnants of enamel matrix (*E*), reduced enamel epithelium (*REE*), oral epithelium (*OE*), artifact (*a*). **B**, Erupting tooth forming junctional epithelium (*JE*). **C**, Completely erupted tooth. Sulcus with epithelial debris (*S*), cementum (*C*), and epithelial rests (*ER*).

The junctional epithelium is formed by the confluence of the oral epithelium and the reduced enamel epithelium during tooth eruption. However, the reduced enamel epithelium is not essential for its formation; in fact, the junctional epithelium is completely restored after pocket instrumentation or surgery, and it forms around an implant.¹⁵³

Cell layers not juxtaposed to the tooth exhibit numerous free ribosomes and prominent membrane-bound structures, such as Golgi complexes, and cytoplasmic vacuoles, presumably phagocytic. Lysosome-like bodies also are present, but the absence of keratinosomes (Odland bodies) and histochemically demonstrable acid phosphatase, correlated with the low degree of differentiation, may reflect a low defense power against microbial plaque accumulation in the gingival sulcus. Similar morphologic findings have been described in the gingiva of germ-free rats. PMNs are found routinely in the junctional epithelium of both conventional rats and germ-free rats.³⁰¹ Research has shown that although numerous migrating PMNs are evident and present around healthy junctional

epithelium, a considerable increase in PMN numbers can be expected with the accumulation of dental plaque and gingival inflammation.¹⁸

The different keratin polypeptides of junctional epithelium have a particular histochemical pattern. Junctional epithelium expresses K19, which is absent from keratinized epithelia, and the stratification-specific cytokeratins K5 and K14.²²⁹ Morgan et al¹⁸⁵ reported that reactions to demonstrate K4 or K13 reveal a sudden change between sulcular and junctional epithelia; the junctional area is the only stratified nonkeratinized epithelium in the oral cavity that does not synthesize these specific polypeptides. Another particular behavior of junctional epithelium is the lack of expression of K6 and K16, which is usually linked to highly proliferative epithelia, although the turnover of the cells is very high.

Similar to sulcular epithelium, junctional epithelium exhibits lower glycolytic enzyme activity than outer epithelium and lacks acid phosphatase activity.^{47,129}

Recent data suggest that the hemidesmosomes may also act as specific sites of signal transduction and thus may participate in regulation of gene expression, cell proliferation, and cell differentiation.¹³⁶ Organic strands from the enamel appear to extend into the lamina densa.²⁶² The junctional epithelium attaches to afibrillar cementum present on the crown (usually restricted to an area within 1 mm of the cementoenamel junction)²³⁹ and root cementum in a similar manner.

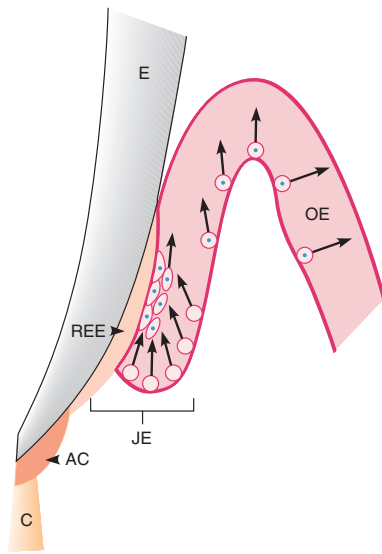


Figure 2-18 Junctional epithelium on an erupting tooth. The junctional epithelium (*JE*) is formed by the joining of the oral epithelium (*OE*) and the reduced enamel epithelium (*REE*). Afibrillar cementum (*AC*) is sometimes formed on enamel after degeneration of the *REE*. The arrows indicate the coronal movement of the regenerating epithelial cells, which multiply more rapidly in the *JE* than in the *OE*. *E*, Enamel; *C*, root cementum. A similar cell turnover pattern exists in the fully erupted tooth. (Modified from Listgarten MA: J Can Dent Assoc 36:70, 1970.)

The regenerating epithelial cells move toward the tooth surface and along it in a coronal direction to the gingival sulcus, where they are shed²² (Figure 2-18). The migrating daughter cells provide a continuous attachment to the tooth surface. The strength of the epithelial attachment to the tooth has not been measured.

The mitotic rate in experimental animals varies among different areas of the oral epithelium in descending order: buccal mucosa, hard palate, sulcular epithelium, junctional epithelium, outer surface of the marginal gingiva, and attached gingiva.^{9,114,162,279} The following have been reported as turnover times for different areas of the oral epithelium in experimental animals: palate, tongue, and cheek, 5 to 6 days; gingiva, 10 to 12 days, with the same or more time required with age; and junctional epithelium, 1 to 6 days.^{22,255}

Regarding junctional epithelium, it was previously thought that only epithelial cells facing the external basal lamina were rapidly dividing. However, evidence indicates that a significant number of the cells, such as the basal cells along the connective tissue, are capable of synthesizing deoxyribonucleic acid (DNA), demonstrating their mitotic activity.^{226,227} Rapid shedding of cells effectively removes bacteria adhering to the epithelial cells and therefore is an important part of the antimicrobial defense mechanisms at the dentogingival junction.²⁰⁹

After enamel formation is completed, the ameloblastic epithelium is reduced to one or two layers of cells that remain attached to the enamel surface by hemidesmosomes and a basal lamina. This REE consists of postsecretory ameloblasts and cells from the stratum intermedium of the enamel organ.

In some animal species the REE disappears entirely and very rapidly, thereby placing the enamel surface in contact with the connective tissue. Connective tissue cells then deposit a thin layer of cementum known as *coronal cementum* on the enamel. In humans, thin patches of afibrillar cementum sometimes may be seen in the cervical half of the crown.

The gingival fluid contains components of connective tissue, epithelium, inflammatory cells, serum, and microbial flora inhabiting the gingival margin or the sulcus (pocket).⁸² In the healthy sulcus the amount of the gingival fluid is very small. During inflammation, however, the gingival fluid flow increases, and its composition starts to resemble that of an inflammatory exudate.⁶⁰

The main route of the gingival fluid diffusion is through the basement membrane, through the relatively wide intracellular spaces of the junctional epithelium, and then into the sulcus.²⁰⁹ The gingival fluid is believed to (1) cleanse material from the sulcus, (2) contain plasma proteins that may improve adhesion of the epithelium to the tooth, (3) possess antimicrobial properties, and (4) exert antibody activity to defend the gingiva

Connective tissue has a cellular and an extracellular compartment composed of fibers and ground substance. Thus the gingival connective tissue is largely a fibrous connective tissue that has elements originating directly from the oral mucosal connective tissue, as well as some fibers (dentogingival) that originate from the developing dental follicle.¹⁸

Fibroblast heterogeneity is now a well-established feature of fibroblasts in the periodontium.²³¹ Although the biologic and clinical significance of such heterogeneity is not yet clear, it seems that this is necessary for the normal functioning of tissues in health, disease, and repair.¹⁸

Speculations about whether small amounts of leukocytes should be considered a normal component of the gingiva or an incipient inflammatory infiltrate without clinical expression are of theoretic rather than practical importance. Lymphocytes are absent when gingival normalcy is judged by strict clinical criteria or under special experimental conditions,^{13,196} but they are practically constant in healthy, normal gingiva, even before complete tooth eruption.^{152,169,235}

Immunohistochemical studies using monoclonal antibodies have identified the different lymphocyte subpopulations. The infiltrate in the area below the junctional epithelium of healthy gingiva in newly erupted teeth in children is mainly composed of T lymphocytes (helper, cytotoxic, suppressor, and natural killer)^{12,100,248} and thus could be interpreted as a normal lymphoid tissue involved in the early defense recognition system. As time elapses, B lymphocytes and plasma cells appear in greater proportions to elaborate specific antibodies against already-recognized antigens that are always present in the sulcus of clinically normal gingiva.²⁴⁰

Blood vessels are easily evidenced in tissue sections by means of immunohistochemical reactions against proteins of endothelial cells (factor VIII and adhesion molecules). Before these techniques were developed, vascularization patterns of periodontal tissues had been described using histoenzymatic reactions for alkaline phosphatase and adenosine triphosphatase because of the great activity of these enzymes in endothelial cells.^{55,302}

In experimental animals the perfusion with India ink also was used to study vascular distribution. The injection and subsequent demonstration of peroxidase allow blood vessel identification and permeability studies.²⁴⁵ The PAS reaction also outlines vascular walls by a positive line in their basal membrane.²⁴³ Endothelial cells express 5-nucleotidase activity as well.¹²⁸ Scanning electron microscopy can be used after injection of plastic into the vessels through the carotid artery, followed by corrosion of the soft tissues.⁸⁷ In addition, laser Doppler flow measurement provides a noninvasive means to observe blood flow modifications related to disease.⁸

Along the sulcular epithelium, capillaries are arranged in a flat, anastomosing plexus that extends parallel to the enamel from the base of the sulcus to the gingival margin.⁵⁵ In the col area, a mixed pattern of anastomosing capillaries and loops occurs.

As mentioned, anatomic and histologic changes have been shown to occur in the gingival microcirculation with gingivitis. Prospective studies of the gingival vasculature in animals have demonstrated that in the absence of inflammation, the vascular network is arranged in a regular, repetitive, and layered pattern.^{55,221} In contrast, the inflamed gingival vasculature exhibits an irregular vascular plexus pattern, with the microvessels exhibiting a looped, dilated, and convoluted appearance.²²¹

The attached gingiva is demarcated from the adjacent alveolar mucosa on the buccal aspect by a clearly defined mucogingival line. The alveolar mucosa is red, smooth, and shiny rather than pink and stippled. Comparison of the microscopic structure of the attached gingiva with that of the alveolar mucosa provides an explanation for the difference in appearance. The epithelium of the alveolar mucosa is thinner, is nonkeratinized, and contains no rete pegs (Figure 2-26). The connective tissue of the alveolar mucosa is loosely arranged, and the blood vessels are more numerous.

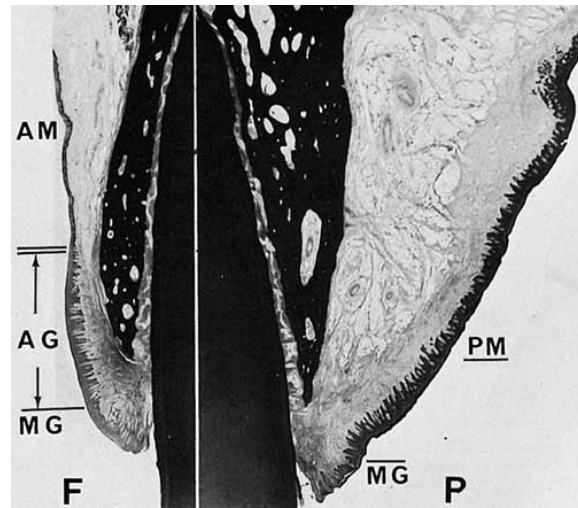


Figure 2-26 Oral mucosa, facial and palatal surfaces. The facial surface (*F*) shows the marginal gingiva (*MG*), attached gingiva (*AG*), and alveolar mucosa (*AM*). The double line marks the mucogingival junction. Note the differences in the epithelium and connective tissue in the attached gingiva and alveolar mucosa. The palatal surface (*P*) shows the marginal gingiva (*MG*) and thick, keratinized palatal mucosa (*PM*).

According to Dummett,⁷⁵ the distribution of oral pigmentation in black individuals is as follows: gingiva, 60%; hard palate, 61%; mucous membrane, 22%; and tongue, 15%. Gingival pigmentation occurs as a diffuse, deep-purplish discoloration or as irregularly shaped, brown and light-brown patches. It may appear in the gingiva as early as 3 hours after birth and often is the only evidence of pigmentation.⁷⁵

Oral *repigmentation* refers to the clinical reappearance of melanin pigment after a period of clinical *depigmentation* of the oral mucosa resulting from chemical, thermal, surgical, pharmacologic, or idiopathic factors.⁷⁶ Information on the repigmentation of oral tissues after surgical procedures is extremely limited, and no definitive treatment is offered at this time.

The marginal gingiva envelops the teeth in collarlike fashion and follows a scalloped outline on the facial and lingual surfaces. It forms a straight line along teeth with relatively flat surfaces. On teeth with pronounced mesiodistal convexity (e.g., maxillary canines) or teeth in labial version, the normal arcuate contour is accentuated, and the gingiva is located farther apically. On teeth in lingual version, the gingiva is horizontal and thickened (Figure 2-27). In addition, gingival tissue biotype varies significantly. A thin and clear gingiva is found in one-third of the population primarily in females with slender teeth with a narrow zone of keratinized tissue, while a clear thick gingiva with a broad zone of keratinized tissue is present in two-thirds of the population primarily in males.⁷²



Figure 2-27 Thickened shelflike contour of gingiva on tooth in lingual version aggravated by local irritation caused by plaque accumulation.

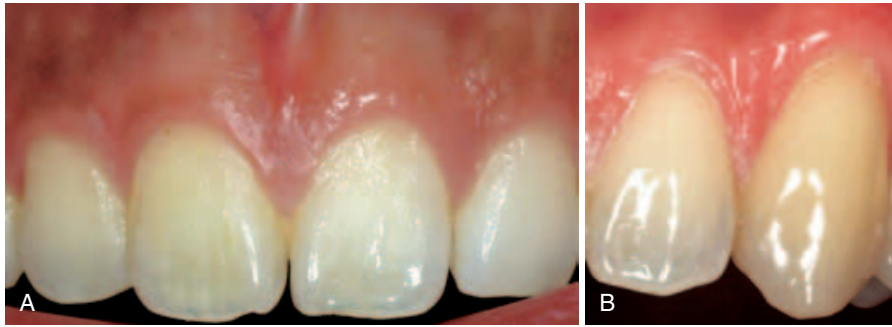


Figure 2-28 Shape of interdental gingival papillae correlated with shape of teeth and embrasures. **A**, Broad interdental papillae. **B**, Narrow interdental papillae.

When the proximal surfaces of the crowns are relatively flat faciolingually, the roots are close together, the interdental bone is thin mesiodistally, and the gingival embrasures and interdental gingiva are narrow mesiodistally. Conversely, with proximal surfaces that flare away from the area of contact, the mesiodistal diameter of the interdental gingiva is broad (Figure 2-28). The height of the interdental gingiva varies with the location of the proximal contact. Thus, in the anterior region of the dentition, the interdental papilla is pyramidal in form, whereas the papilla is more flattened in a buccolingual direction in the molar region.

Microscopically, stippling is produced by alternate rounded protuberances and depressions in the gingival surface. The papillary layer of the connective tissue projects into the elevations, and the elevated and depressed areas are covered by stratified squamous epithelium (Figure 2-29). The degree of keratinization and the prominence of stippling appear to be related.

Scanning electron microscopy has shown considerable variation in shape, but a relatively constant depth of stippling. At low magnification, a rippled surface is seen, interrupted by irregular depressions 50 μm in diameter. At higher magnification, cell micropits are seen.⁶²

Stippling is a form of adaptive specialization or reinforcement for function. It is a feature of healthy gingiva, and reduction or loss of stippling is a common sign of gingival disease. When the gingiva is restored to health after treatment, the stippled appearance returns.

The surface texture of the gingiva is also related to the presence and degree of epithelial keratinization. Keratinization is considered a protective adaptation to function. It increases when the gingiva is stimulated by toothbrushing. However, research on free gingival grafts (see Chapter 63) has shown that when connective tissue is transplanted from a keratinized area to a nonkeratinized area, it becomes covered by a keratinized epithelium.¹⁴² This finding suggests a connective tissue-based genetic determination of the type of epithelial surface.

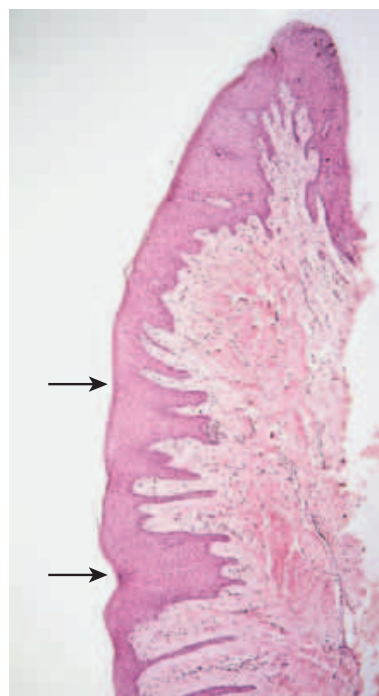


Figure 2-29 Gingival biopsy of patient shown in Figure 2-7, demonstrating alternate elevations and depressions (*arrows*) in the attached gingiva responsible for stippled appearance.

When the tooth erupts into the oral cavity, the margin and sulcus are at the tip of the crown; as eruption progresses, they are seen closer to the root. During this eruption process, as described earlier, the junctional epithelium, oral epithelium, and reduced enamel epithelium undergo extensive alterations and remodeling while maintaining the shallow physiologic depth of the sulcus. Without this remodeling of the epithelia, an abnormal anatomic relationship between the gingiva and the tooth would result.

Gottlieb and Orban¹⁰⁷ believed that active and passive eruption proceed together. Active eruption is coordinated with attrition; the teeth erupt to compensate for tooth substance worn away by attrition. Attrition reduces the clinical crown and prevents it from becoming disproportionately long in relation to the clinical root, thus avoiding excessive leverage on the periodontal tissues. Ideally, the rate of active eruption keeps pace with tooth wear, preserving the vertical dimension of the dentition.

As teeth erupt, cementum is deposited at the apices and furcations of the roots, and bone is formed along the fundus of the alveolus and at the crest of the alveolar bone. In this way, part of the tooth substance lost by attrition is replaced by lengthening of the root, and socket depth is maintained to support the root.

Although originally thought to be a normal physiologic process, passive eruption is now considered a pathologic process. Passive eruption is divided into the following four stages (Figure 2-30):

Stage 1: The teeth reach the line of occlusion. The junctional epithelium and base of the gingival sulcus are on the enamel.

Stage 2: The junctional epithelium proliferates so that part is on the cementum and part is on the enamel. The base of the sulcus is still on the enamel.

Stage 3: The entire junctional epithelium is on the cementum, and the base of the sulcus is at the cementoenamel junction. As the junctional epithelium proliferates from the crown onto the root, it does not remain at the cementoenamel junction any longer than at any other area of the tooth.

Stage 4: The junctional epithelium has proliferated farther on the cementum. The base of the sulcus is on the cementum, a portion of which is exposed. Proliferation of the junctional epithelium onto the root is accompanied by degeneration of gingival and periodontal ligament fibers and their detachment from the tooth. The cause of this degeneration is not understood. At present, it is believed to be the result of chronic inflammation and therefore a pathologic process.

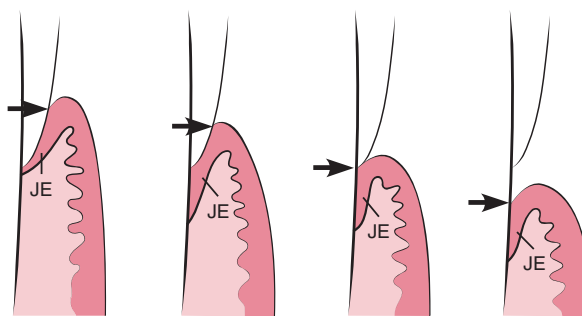


Figure 2-30 Diagrammatic representation of the four steps in passive eruption according to Gottlieb and Orban.¹⁰⁷ 1, Base of the gingival sulcus (arrow) and the junctional epithelium (JE) are on the enamel. 2, Base of the gingival sulcus (arrow) is on the enamel, and part of the junctional epithelium is on the root. 3, Base of the gingival sulcus (arrow) is at the cementoenamel line, and the entire junctional epithelium is on the root. 4, Base of the gingival sulcus (arrow) and the junctional epithelium are on the root.

As noted, apposition of bone accompanies active eruption. The distance between the apical end of the junctional epithelium and the crest of the alveolus remains constant throughout continuous tooth eruption (1.07 mm).⁹⁵

Exposure of the tooth by the apical migration of the gingiva is called *gingival recession*, or *atrophy*. According to the concept of continuous eruption, the gingival sulcus may be located on the crown, cementoenamel junction, or root, depending on the age of the patient and stage of eruption. Therefore some root exposure with age would be considered normal and referred to as *physiologic recession*. Again, this concept is not accepted at present. Excessive exposure is termed *pathologic recession* (see Chapter 13).

Collagen is a protein composed of different amino acids, the most important of which are glycine, proline, hydroxylysine, and hydroxyproline.⁵² The amount of collagen in a tissue can be determined by its hydroxyproline content. Collagen is responsible for maintenance of the framework and tone of tissue, and it exhibits a wide range of diversity.⁸³ There are at least 19 recognized collagen species encoded by at least 25 separate genes, dispersed among 12 chromosomes.⁸³

Collagen biosynthesis occurs inside the fibroblasts to form tropocollagen molecules. These aggregate into microfibrils that are packed together to form fibrils. Collagen fibrils have a transverse striation with a characteristic periodicity of 64 nm; this striation is caused by the overlapping arrangement of the tropocollagen molecules. In collagen types I and III these fibrils associate to form fibers, and in collagen type I the fibers associate to form bundles (Figure 2-33).

Collagen is synthesized by fibroblasts, chondroblasts, osteoblasts, odontoblasts, and other cells. The several types of collagen are all distinguishable by their chemical composition, distribution, function, and morphology.¹⁴⁰ The principal fibers are composed mainly of collagen type I,²¹⁶ whereas reticular fibers are composed of collagen type III. Collagen type IV is found in the basal lamina.^{217,219} The expression of type XII collagen during the tooth development is timed with the alignment and organization of periodontal fibers and is limited in tooth development to cells within

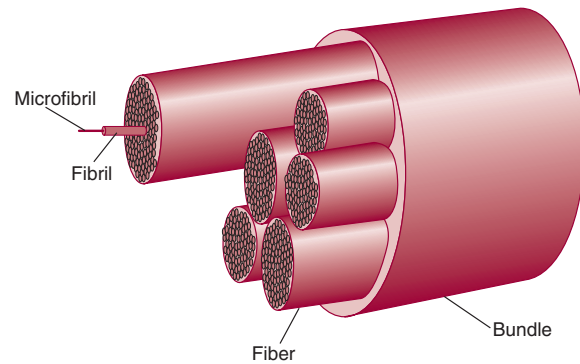


Figure 2-33 Collagen microfibrils, fibrils, fibers, and bundles.

the periodontal ligament.¹⁶⁶ Type VI collagen also has been immunolocalized in periodontal ligament and gingiva.⁸⁶

The molecular configuration of collagen fibers provides them with a tensile strength greater than that of steel. Consequently, collagen imparts a unique combination of flexibility and strength to the tissues.¹⁴⁰

Other well-formed fiber bundles interdigitate at right angles or splay around and between regularly arranged fiber bundles. Less regularly arranged collagen fibers are found in the interstitial connective tissue between the principal fiber groups; this tissue contains the blood vessels, lymphatics, and nerves.

Although the periodontal ligament does not contain mature elastin, two immature forms are found: oxytalan and elaunin. The so-called oxytalan fibers^{92,105} run parallel to the root surface in a vertical direction and bend to attach to the cementum⁹² in the cervical third of the root. They are thought to regulate vascular flow.⁹¹ An elastic meshwork has been described in the periodontal ligament¹³⁵ as being composed of many elastin lamellae with peripheral oxytalan fibers and elaunin fibers. Oxytalan fibers have been shown to develop *de novo* in the regenerated periodontal ligament.²²⁴

The principal fibers are remodeled by the periodontal ligament cells to adapt to physiologic needs^{270,300} and in response to different stimuli.²⁸²

In addition to these fiber types, small collagen fibers associated with the larger principal collagen fibers have been described. These fibers run in all directions, forming a plexus called the *indifferent fiber plexus*.²⁴⁹

Phenotypically distinct and functionally different subpopulations of fibroblasts exist in the adult periodontal ligament. They appear identical at both light and electron microscopic levels¹¹⁷ but may have different functions such as secretion of different collagen types and production of collagenase.

Osteoblasts and cementoblasts, as well as osteoclasts and odontoclasts, also are seen in the cemental and osseous surfaces of the periodontal ligament.

Epithelial rests are distributed close to the cementum throughout the periodontal ligament of most teeth and are most numerous in the apical area²¹² and cervical area.^{284,285} They diminish in number with age²⁵⁴ by degenerating and disappearing or by undergoing calcification to become cementicles. The cells are surrounded by a distinct basal lamina, are interconnected by hemidesmosomes, and contain tonofilaments.²⁴

Even though their functional properties are still considered to be unclear,²⁶⁵ the epithelial rests are reported to contain keratinocyte growth factors and have been shown to be positive for tyrosine kinase A neurotrophin receptor.^{94,286,296} Also, epithelial rests proliferate when stimulated^{266,271,280} and participate in the formation of periapical cysts and lateral root cysts.

The cell surface proteoglycans participate in several biologic functions, including cell adhesion, cell-cell and cell-matrix interactions, binding to various growth factors as co-receptors, and cell repair.²⁹⁷ For example, *fibromodulin*, a small proteoglycan rich in keratan sulfate and leucine, has recently been identified in bovine periodontal ligament.²⁸⁸ The most comprehensive study of the proteoglycans in periodontal ligament was performed using fibroblast cultures of human ligament.¹⁵¹

Cementicles may develop from calcified epithelial rests; around small spicules of cementum or alveolar bone traumatically displaced into the periodontal ligament; from calcified Sharpey's fibers; and from calcified, thrombosed vessels within the periodontal ligament.¹⁸²

Resistance to Impact of Occlusal Forces (Shock Absorption). Two theories pertaining to the mechanism of tooth support have been considered: the tensional and viscoelastic system theories.

The *tensional theory* of tooth support states that the principal fibers of the periodontal ligament are the major factor in supporting the tooth and transmitting forces to the bone. When a force is applied to the crown, the principal fibers first unfold and straighten and then transmit forces to the alveolar bone, causing an elastic deformation of the bony socket. Finally, when the alveolar bone has reached its limit, the load is transmitted to the basal bone. Many investigators find this theory insufficient to explain available experimental evidence.

The *viscoelastic system theory* states that the displacement of the tooth is largely controlled by fluid movements, with fibers having only a secondary role.^{31,44} When forces are transmitted to the tooth, the extracellular fluid passes from the periodontal ligament into the marrow spaces of bone through foramina in the cribriform plate. These perforations of the cribriform plate link the periodontal ligament with the cancellous portion of the alveolar bone and are more abundant in the cervical third than in the middle and apical thirds (Figure 2-39).

After depletion of tissue fluids, the fiber bundles absorb the slack and tighten. This leads to a blood vessel stenosis. Arterial back pressure causes ballooning of the vessels and passage of the blood ultrafiltrates into the tissues, thereby replenishing the tissue fluids.³¹

Transmission of Occlusal Forces to Bone. The arrangement of the principal fibers is similar to a suspension bridge or a hammock. When an axial force is applied to a tooth, a tendency toward displacement of the root into the alveolus occurs. The oblique fibers alter their wavy, untensed pattern; assume their full length; and sustain the major part of the axial force. When a horizontal or tipping force is applied, two phases of tooth movement occur. The first is within the confines of the periodontal ligament, and the second produces a displacement of the facial and lingual bony plates.⁷¹ The tooth rotates about an axis that may change as the force is increased.

The apical portion of the root moves in a direction opposite to the coronal portion. In areas of tension, the principal fiber bundles are taut rather than wavy. In areas of pressure, the fibers are compressed, the tooth is displaced, and a corresponding distortion of bone exists in the direction of root movement.²⁰⁷

In single-rooted teeth the axis of rotation is located in the area between the apical third and the middle third of the root (Figure 2-40). The root apex¹⁸⁷ and the coronal half of the clinical root have been suggested as other locations of the axis of rotation. The periodontal ligament, which has an hourglass shape, is narrowest in the

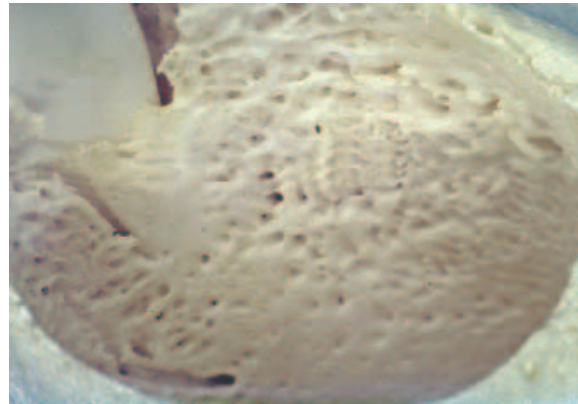


Figure 2-39 Foramina perforating the lamina dura (dog jaw).

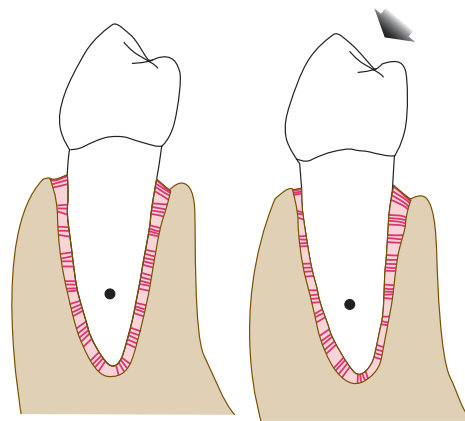


Figure 2-40 *Left*, Diagram of tooth (mandibular premolar) in a resting state. *Right*, When a force is exerted on the tooth, in this case in faciolingual direction (arrow) the tooth rotates around the fulcrum or axis of rotation (black circle on root). The periodontal ligament is compressed in areas of pressure and distended in areas of tension.

region of the axis of rotation^{67,147} (Table 2-1). In multirooted teeth the axis of rotation is located in the bone between the roots (Figure 2-41). In compliance with the physiologic mesial migration of the teeth, the periodontal ligament is thinner on the mesial root surface than on the distal surface.

TABLE 2-1 Thickness of Periodontal Ligament of 172 Teeth from 15 Human Subjects

	Average of Alveolar Crest (mm)	Average of Midroot (mm)	Average of Apex (mm)	Average of Tooth (mm)
Ages 11–16	0.23	0.17	0.24	0.21
83 teeth from 4 jaws				
Ages 32–50	0.20	0.14	0.19	0.18
36 teeth from 5 jaws				
Ages 51–67	0.17	0.12	0.16	0.15
35 teeth from 5 jaws				
Age 24 (1 case)	0.16	0.09	0.15	0.13
18 teeth from 1 jaw				

Modified from Coolidge ED: *J Am Dent Assoc* 24:1260, 1937.

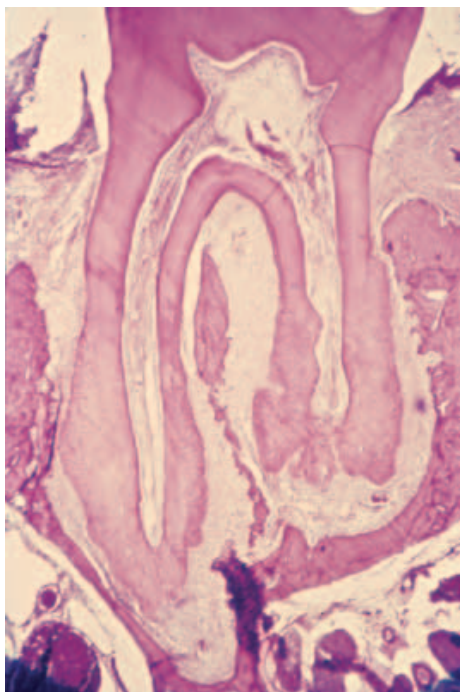


Figure 2-41 Microscopic view of rat molar subjected to occlusohorizontal forces. Note the alternating widened and narrowed areas of the periodontal ligament as the tooth rotates around its axis of rotation. The axis of rotation is in the interradicular space.

Variations in cellular enzyme activity are correlated with the remodeling process.⁹⁶⁻⁹⁸ Although applied loads may induce vascular and inflammatory reactive changes in periodontal ligament cells, current evidence suggests that these cells have a mechanism to respond directly to mechanical forces by activation of various mechanosensory signaling systems, including adenylate cyclase, stretch-activated ion channels, and by changes in cytoskeletal organization.¹⁷⁵

Cartilage formation in the periodontal ligament, although unusual, may represent a metaplastic phenomenon in the repair of this ligament after injury.²⁰

The periodontal ligament is constantly undergoing remodeling. Old cells and fibers are broken down and replaced by new ones, and mitotic activity can be observed in the fibroblasts and endothelial cells.¹⁸⁸ Fibroblasts form the collagen fibers, and the residual mesenchymal cells develop into osteoblasts and cementoblasts. Therefore the rate of formation and the differentiation of osteoblasts, cementoblasts, and fibroblasts affect the rate of formation of collagen, cementum, and bone.

Radioautographic studies with radioactive thymidine, proline, and glycine indicate a high turnover rate of collagen in the periodontal ligament. The rate of collagen synthesis is twice as fast as that in the gingiva and four times as fast as that in the skin, as established in the rat molar.²⁵⁶ A rapid turnover of sulfated glycosaminoglycans in the cells and amorphous ground substance of the periodontal ligament also occurs.²¹

It should be noted that most of these studies have been performed in rodents, and information on primates and humans is scarce.²³⁸

In relation to other ligaments and tendons, the periodontal ligament is highly vascularized tissue, and almost 10% of its volume in the rodent molar is blood vessels.^{35,176} This relatively high blood vessel content may provide hydrodynamic damping to applied forces, as well as high perfusion rates to the periodontal ligament.¹⁷⁵

The periodontal ligament is abundantly supplied with sensory nerve fibers capable of transmitting tactile, pressure, and pain sensations by the trigeminal pathways.^{14,30} Nerve bundles pass into the periodontal ligament from the periapical area and through channels from the alveolar bone that follow the course of the blood vessels. The bundles divide into single myelinated fibers, which ultimately lose their myelin sheaths and end in one of four types of neural termination: (1) free endings, which have a treelike configuration and carry pain sensation; (2) Ruffini-like mechanoreceptors, located primarily in the apical area; (3) coiled Meissner's corpuscles, also mechanoreceptors, found mainly in the midroot region; and (4) spindlelike pressure and vibration endings, which are surrounded by a fibrous capsule and located mainly in the apex.^{91,168}

The major proportion of the organic matrix of a cementum is composed of type I (90%) and type III (about 5%) collagens. Sharpey's fibers, which constitute a considerable proportion of the bulk of cementum, are composed of mainly collagen type I.²¹¹ Type III collagen appears to coat the type I collagen of Sharpey's fibers.¹⁶

Acellular cementum is the first cementum formed, covers approximately the cervical third or half of the root, and does not contain cells (Figure 2-42). This cementum is formed before the tooth reaches the occlusal plane, and its thickness ranges from 30 to 230 μm .²⁵⁴ Sharpey's fibers make up most of the structure of acellular cementum, which has a principal role in supporting the tooth. Most fibers are inserted at approximately right angles into the root surface and penetrate deep into the cementum, but others enter from several different directions. Their size, number, and distribution increase with function.¹²⁵ Sharpey's fibers are completely calcified, with the mineral crystals oriented parallel to the fibrils, as in dentin and bone, except in a 10- to 50- μm -wide zone near the cementodentinal junction, where they are only partially calcified. The peripheral portions of Sharpey's fibers in actively mineralizing cementum tend to be more calcified than the interior regions, according to evidence obtained by scanning electron microscopy.¹³⁹ Acellular cementum also contains intrinsic collagen fibrils that are calcified and irregularly arranged or parallel to the surface.²³⁸

Cellular cementum, formed after the tooth reaches the occlusal plane, is more irregular and contains cells (cementocytes) in individual spaces (lacunae) that communicate with each other through a system of anastomosing canaliculi (Figure 2-43). Cellular cementum is less calcified than the acellular type.¹²⁶ Sharpey's fibers occupy a smaller portion of cellular cementum and are separated by other fibers that are arranged either parallel to the root surface or at random. Sharpey's fibers may be completely or partially calcified or may have a central, uncalcified core surrounded by a calcified border.^{137,246}

Both acellular cementum and cellular cementum are arranged in lamellae separated by incremental lines parallel to the long axis of the root (see Figures 2-42 and 2-43). These lines represent "rest periods" in cementum formation and are more mineralized than the adjacent cementum.²²⁰ In addition, loss of the cervical part of the reduced enamel epithelium at the time of tooth eruption may place portions of mature enamel in contact with the connective tissue, which then will deposit an acellular, afibrillar type of cementum over the enamel.¹⁵⁹

Based on these findings, Schroeder^{135,136} has classified cementum as follows:

Acellular afibrillar cementum (AAC) contains neither cells nor extrinsic or intrinsic collagen fibers, except for a mineralized ground substance. AAC is a product of cementoblasts and is found as coronal cementum in humans, with a thickness of 1 to 15 μm .

Acellular extrinsic fiber cementum (AEFC) is composed almost entirely of densely packed bundles of Sharpey's fibers and lacks cells. AEFC is a product of fibroblasts and cementoblasts and is found in the cervical third of roots in humans but may extend farther apically. Its thickness is between 30 and 230 μm .

Cellular mixed stratified cementum (CMSC) is composed of extrinsic (Sharpey's) and intrinsic fibers and may contain cells. CMSC is a co-product of fibroblasts and cementoblasts, and in humans it appears primarily in the apical third of the roots and apices and in furcation areas. Its thickness ranges from 100 to 1000 μm .

Cellular intrinsic fiber cementum (CIFIC) contains cells, but no extrinsic collagen fibers. CIFIC is formed by cementoblasts, and in humans it fills resorption lacunae.

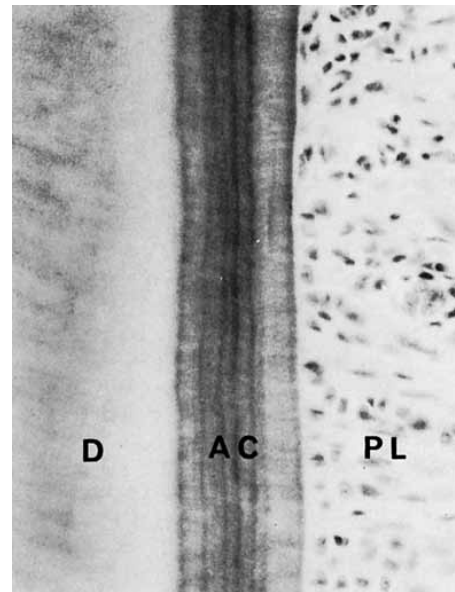


Figure 2-42 Acellular cementum (AC) showing incremental lines running parallel to the long axis of the tooth. These lines represent the appositional growth of cementum. Note the thin, light lines running into the cementum perpendicular to the surface; these represent Sharpey's fibers of the periodontal ligament (PL). D, Dentin. ($\times 300$.)

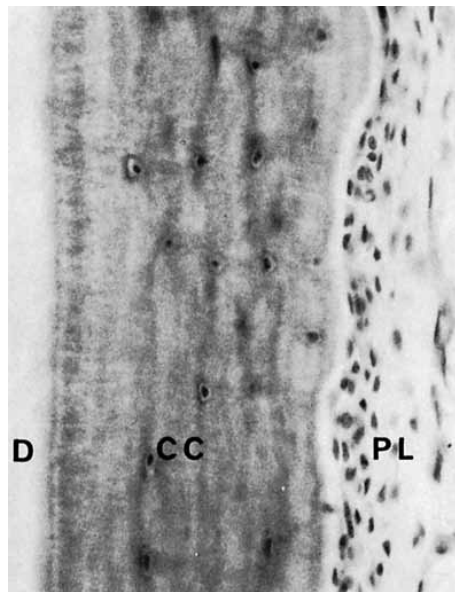


Figure 2-43 Cellular cementum (CC) showing cementocytes lying within lacunae. Cellular cementum is thicker than acellular cementum (see Figure 2-42). Evidence of incremental lines also exists, but they are less distinct than in acellular cementum. The cells adjacent to the surface of the cementum in the periodontal ligament (PL) space are cementoblasts. D, Dentin. ($\times 300$.)

Intermediate cementum is a poorly defined zone near the cementodental junction of certain teeth that appears to contain cellular remnants of Hertwig's sheath embedded in calcified ground substance.^{80,155}

The inorganic content of cementum (hydroxyapatite; $\text{Ca}_{10}[\text{PO}_4]_6[\text{OH}]_2$) is 45% to 50%, which is less than that of bone (65%), enamel (97%), or dentin (70%).³⁰⁴ Opinions differ about whether the microhardness increases¹⁹² or decreases with age,²⁸⁷ and no relationship has been established between aging and the mineral content of cementum.

It is well known that the protein extracts of mature cementum promote cell attachment and cell migration and stimulate protein synthesis of gingival fibroblasts and periodontal ligament cells.²³⁰ Studies on cementum have identified adhesion proteins with RGD motifs (Arg-Gly-Asp sequences): bone sialoprotein, osteopontin, and osteonectin.^{40,177} Bone sialoprotein and osteopontin are expressed during early tooth root development by cells along the root surface, and they are believed to play a major role in the differentiation of the cementoblast progenitor cells to the cementoblasts.^{111,230}

Some of the molecules unique to the cementum have been described. Recent work has investigated the role of *cementum attachment protein* (CAP), a collagenous cementum-derived protein. CAP has been shown to promote the adhesion and spreading of mesenchymal cell types, with osteoblasts and periodontal ligament fibroblasts showing better adhesion than gingival fibroblasts and keratinocytes.²²⁵ In addition, Ikezawa et al¹²⁴ reported the characterization of *cementum-derived growth factor* (CGF), which is an insulin-like, growth factor I-like molecule. CGF has been shown to enhance proliferation of gingival fibroblasts and periodontal ligament cells.



Figure 2-45 Cemental resorption associated with excessive occlusal forces. **A**, Low-power histologic section of mandibular anterior teeth. **B**, High-power micrograph of apex of left central incisor shortened by resorption of cementum and dentin. Note partial repair of the eroded areas (*arrows*) and cementicle at upper right.

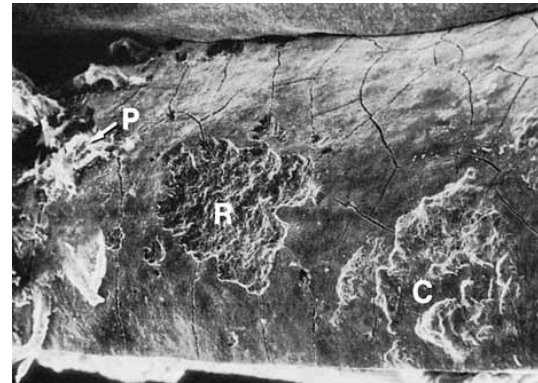


Figure 2-46 Scanning electron micrograph of root exposed by periodontal disease showing large resorption bay (*R*). Remnants of the periodontal ligament (*P*) and calculus (*C*) are visible. Cracking of the tooth surface occurs as a result of the preparation technique. ($\times 160$.) (Courtesy Dr. John Sottosanti, La Jolla, CA.)

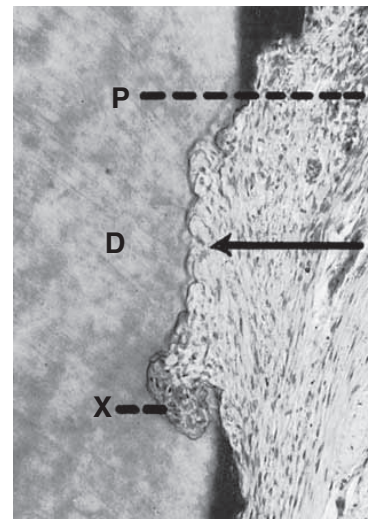


Figure 2-47 Resorption of cementum and dentin. A multinuclear osteoclast is seen at *X*. The direction of resorption is indicated by the arrow. Note the scalloped resorption front in the dentin (*D*). The cementum is the darkly stained band at the upper and lower right. *P*, Periodontal ligament.

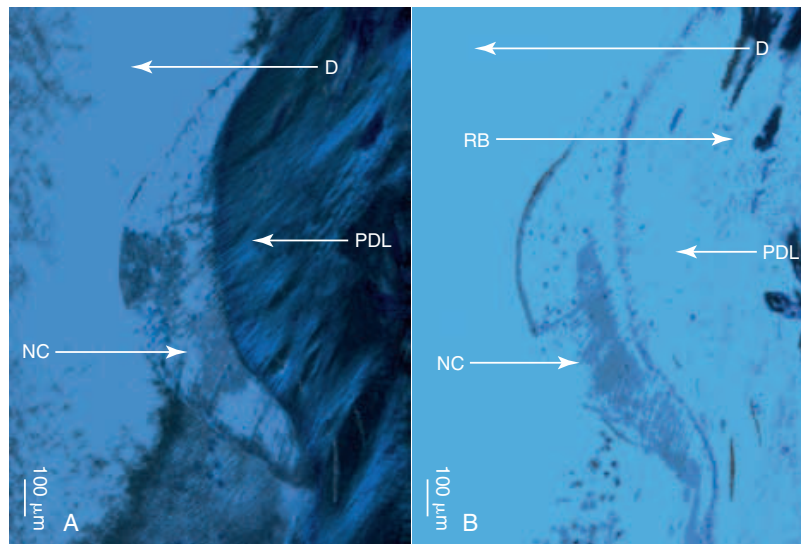


Figure 2-48 A clinical human histology shown that new cementum and new PDL fiber formed at previous periodontal defect treated with recombinant human Platelet Derived Growth Factor-BB with β -tricalcium phosphate. (Courtesy Dr. Daniel WK Kao, Philadelphia.)

The thickness of cementum on the coronal half of the root varies from 16 to 60 μm , or about the thickness of a hair. It attains its greatest thickness (up to 150–200 μm) in the apical third and in the furcation areas. It is thicker in distal surfaces than in mesial surfaces, probably because of functional stimulation from mesial drift over time.⁷⁰ Between 11 and 70 years of age, the average thickness of the cementum increases threefold, with the greatest increase in the apical region. Average thicknesses of 95 μm at age 20 and 215 μm at age 60 have been reported.³⁰³

Abnormalities in the thickness of cementum may range from an absence or paucity of cellular cementum (*cemental aplasia or hypoplasia*) to an excessive deposition of cementum (*cemental hyperplasia or hypercementosis*).¹⁵⁴

The term *hypercementosis* refers to a prominent thickening of the cementum. It is largely an age-related phenomenon, and it may be localized to one tooth or affect the entire dentition. Because of considerable physiologic variation in the thickness of cementum among different teeth in the same person and also among different persons, distinguishing between hypercementosis and physiologic thickening of cementum is sometimes difficult. Nevertheless, excessive proliferation of cementum may occur in a broad spectrum of neoplastic and nonneoplastic conditions, including benign cementoblastoma, cementifying fibroma, periapical cemental dysplasia, florid cemento-osseous dysplasia, and other benign fibro-osseous lesions.¹⁵⁴

Hypercementosis occurs as a generalized thickening of the cementum, with nodular enlargement of the apical third of the root. It also appears in the form of spikelike excrescences (cemental spikes) created by either the coalescence of cementsicles that adhere

to the root or the calcification of periodontal fibers at the sites of insertion into the cementum.¹⁵⁵

Radiographically, the radiolucent shadow of the periodontal ligament and the radiopaque lamina dura are always seen on the outer border of an area of hypercementosis, enveloping it as it would in normal cementum.¹⁵⁴ On the other hand, from a diagnostic standpoint, periapical cemental dysplasia, condensing osteitis, and focal periapical osteopetrosis may be differentiated from hypercementosis because all these entities are located outside the shadow of the periodontal ligament and lamina dura.²⁹⁵

The etiology of hypercementosis varies and is not completely understood. The spikelike type of hypercementosis generally results from excessive tension from orthodontic appliances or occlusal forces. The generalized type occurs in a variety of circumstances. In teeth without antagonists, hypercementosis is interpreted as an effort to keep pace with excessive tooth eruption. In teeth subject to low-grade periapical irritation arising from pulp disease, it is considered compensation for the destroyed fibrous attachment to the tooth. The cementum is deposited adjacent to the inflamed periapical tissue. Hypercementosis of the entire dentition may occur in patients with Paget's disease.²²³ Other systemic disturbances that may lead to or may be associated with hypercementosis include acromegaly, arthritis, calcinosis, rheumatic fever, and thyroid goiter.¹⁵⁴

Hypercementosis itself does not require treatment. It could pose a problem if an affected tooth requires extraction. In multirrooted tooth, sectioning of the tooth may be required before extraction.¹⁹

Microscopic cementum resorption is extremely common; in one study it occurred in 236 of 261 teeth (90.5%).¹²⁰ The average number of resorption areas per tooth was 3.5. Of the 922 areas of resorption, 708 (76.8%) were located in the apical third of the root, 177 (19.2%) in the middle third, and 37 (4.0%) in the gingival third. Approximately 70% of all resorption areas were confined to the cementum without involving the dentin.

Cementum resorption may be caused by local or systemic factors or may occur without apparent etiology (i.e., idiopathic). Local conditions causing cementum resorption include trauma from occlusion¹⁹⁸ (Figure 2-45); orthodontic movement^{119,197,222}; pressure from malaligned erupting teeth, cysts, and tumors¹⁴⁶; teeth without functional antagonists; embedded teeth; replanted and transplanted teeth^{3,137}; periapical disease; and periodontal disease. Systemic conditions cited as predisposing to or inducing cemental resorption include calcium deficiency,¹³⁸ hypothyroidism,²³ hereditary fibrous osteodystrophy,²⁷⁴ and Paget's disease.²²³

Cementum resorption appears microscopically as baylike concavities in the root surface. (Figure 2-46) Multinucleated giant cells and large mononuclear macrophages are generally found adjacent to cementum undergoing active resorption (Figure 2-47). Several sites of resorption may coalesce to form a large area of destruction. The resorptive process may extend into the underlying dentin and even into the pulp, but it is usually painless. Cementum resorption is not necessarily continuous and may alternate with periods of repair and the deposition of new cementum. The newly formed cementum is demarcated from the root by a deeply staining irregular line, termed a *reversal line*, which delineates the border of the previous resorption. A recent study showed that the reversal lines of human teeth contain a few collagen fibrils and highly accumulated proteoglycans with mucopolysaccharides (glycosaminogly-

cans) and that fibril intermingling occurs only in some places between reparative cementum and resorbed dentin or cementum.^{298,299} Embedded fibers of the periodontal ligament reestablish a functional relationship in the new cementum.

Cementum repair requires the presence of viable connective tissue. If epithelium proliferates into an area of resorption, repair will not take place. Cementum repair can occur in devitalized as well as vital teeth.

Histologic evidence demonstrates that cementum formation is critical for appropriate maturation of the periodontium, both in development and in regeneration of lost periodontal tissues.²³⁰ That is, a variety of macromolecules present in the extracellular matrix of the periodontium are likely to play a regulatory role in cementogenesis.¹⁷¹

Regeneration of cementum requires cementoblasts, but the origin of the cementoblasts and the molecular factors regulating their recruitment and differentiation are not fully understood. Recent research, however, provides a better understanding; for example, the epithelial cell rests of Malassez are the only odontogenic epithelial cells that remain in the periodontium after the eruption of teeth, and they may have some function in cementum repair and regeneration under specific conditions.¹¹⁶ The rests of Malassez may be related to cementum repair by activating their potential to secrete matrix proteins that have been expressed in tooth development, such as amelogenins, enamelin, and sheath proteins. Several growth factors have been shown to be effective in cementum regeneration, including members of the transforming growth factor superfamily (bone morphogenetic proteins), platelet-derived growth factor, insulin-like growth factor, and enamel matrix derivatives^{141,230} (Figure 2-48).

This condition is relatively uncommon and occurs most frequently in the primary dentition.¹⁷⁸

Ankylosis results in resorption of the root and its gradual replacement by bone tissue. For this reason, reimplanted teeth that ankylose will lose their roots after 4 to 5 years and will be exfoliated. Clinically, ankylosed teeth lack the physiologic mobility of normal teeth, which is one diagnostic sign for ankylotic resorption. In addition, these teeth usually have a special metallic percussion sound, and if the ankylotic process continues, they will be in infra-occlusion.⁹³ However, clinical diagnosis of ankylosis by mobility and percussion tests alone is only reliable when at least 20% of the root surface is affected.¹⁰

As the periodontal ligament is replaced with bone in ankylosis, proprioception is lost because pressure receptors in the periodontal ligament are deleted or do not function correctly. Furthermore, the physiologic drifting and eruption of teeth can no longer occur, and thus the ability of the teeth and periodontium to adapt to altered force levels or directions of force is greatly reduced.¹⁷⁵ Radiographically, resorption lacunae are filled with bone, and the periodontal ligament space is missing.

Because no definitive causes can be found in ankylotic root resorption, no predictable treatment can be suggested. Treatment modalities range from a conservative approach, such as restorative intervention, to surgical extraction of the affected tooth.¹⁸⁹

When titanium implants are placed in the jaw, healing results in bone that is formed in direct apposition to the implant without intervening connective tissue. This may be interpreted as a form of ankylosis. Because resorption of the metallic implant cannot occur, the implant remains indefinitely “ankylosed” to the bone. Also, a true periodontal pocket will not form because apical proliferation of the epithelium along the root, a key element of pocket formation, is not possible because of the ankylosis.

Exposure of Cementum to Oral Environment

Cementum becomes exposed to the oral environment in cases of gingival recession and as a result of loss of attachment in pocket formation. The cementum is sufficiently permeable to be penetrated in these cases by organic substances, inorganic ions, and bacteria. Bacterial invasion of the cementum occurs frequently in periodontal disease (see Chapter 13). Cementum caries can develop (see Chapter 13).

In addition, the bones of the jaw include the basal bone, which is the portion of the jaw located apically but unrelated to the teeth (Figure 2-50).

The alveolar process is divisible into separate areas on an anatomic basis, but it functions as a unit, with all parts interrelated in the support of the teeth. Figures 2-51 and 2-52 show the relative proportions of cancellous bone and compact bone that form the alveolar process. Most of the facial and lingual portions of the sockets are formed by compact bone alone; cancellous bone surrounds the lamina dura in apical, apicolingual, and interradicular areas.

Cells and Intercellular Matrix

Osteoblasts, the cells that produce the organic matrix of bone, are differentiated from pluripotent follicle cells. Alveolar bone is formed during fetal growth by intramembranous ossification and consists of a calcified matrix with osteocytes enclosed within spaces called *lacunae*. The osteocytes extend processes into *canaliculi* that radiate from the lacunae. The canaliculi form an anastomosing system through the intercellular matrix of the bone, which brings oxygen and nutrients to the osteocytes through the blood and removes metabolic waste products. Blood vessels branch extensively and travel through the periosteum. The endosteum lies adjacent to the marrow vasculature. Bone growth occurs by apposition of an organic matrix that is deposited by osteoblasts. Haversian systems (*osteons*) are the internal mechanisms that bring a vascular supply to bones too thick to be supplied only by surface vessels. These are found primarily in the outer cortical plates and the alveolar bone proper.

Bone consists of two-thirds inorganic matter and one-third organic matrix. The inorganic matter is composed principally of the minerals calcium and phosphate, along with hydroxyl, carbonate, citrate, and trace amounts of other ions^{103,104} such as sodium, magnesium, and fluorine. The mineral salts are in the form of hydroxyapatite crystals of ultramicroscopic size and constitute approximately two-thirds of the bone structure.

The organic matrix⁷⁷ consists mainly of collagen type I (90%),¹⁸⁸ with small amounts of noncollagenous proteins such as osteocalcin, osteonectin, bone morphogenetic protein, phosphoproteins, and proteoglycans.²¹⁴ Osteopontin and bone sialoprotein are cell adhesion proteins that appear to be important for adhesion of both osteoclasts and osteoblasts.¹⁶⁵ In addition, paracrine factors, including cytokines, chemokines, and growth factors, have been implicated in the local control of mesenchymal condensations that occur at the onset of organogenesis. These factors probably play a prominent role in the development of the alveolar processes.²⁵⁷

Although the alveolar bone tissue is constantly changing in its internal organization, it retains approximately the same form from childhood through adult life. Bone deposition by osteoblasts is balanced by resorption by osteoclasts during tissue remodeling and renewal. It is well known that the number of osteoblasts decreases with aging; however, no remarkable change in the number of osteoclasts has ever been reported.¹⁹⁵

Remodeling is the major pathway of bony changes in shape, resistance to forces, repair of wounds, and calcium and phosphate homeostasis in the body. Indeed, the coupling of bone resorption with bone formation constitutes one of the fundamental principles by which bone is necessarily remodeled throughout its life. Bone remodeling involves the coordination of activities of cells from two distinct lineages, the osteoblasts and the osteoclasts, which form and resorb the mineralized connective tissues of bone.²⁵⁷

Regulation of bone remodeling is a complex process involving hormones and local factors acting in an autocrine and a paracrine

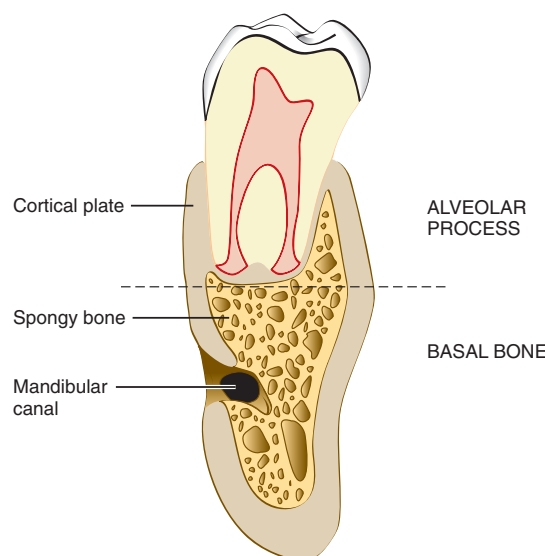


Figure 2-50 Section through human jaw with tooth in situ. The dotted line indicates the separation between basal bone and alveolar bone. (Redrawn from Ten Cate AR: Oral histology: development, structure, and function, ed 4, St Louis, 1994, Mosby.)

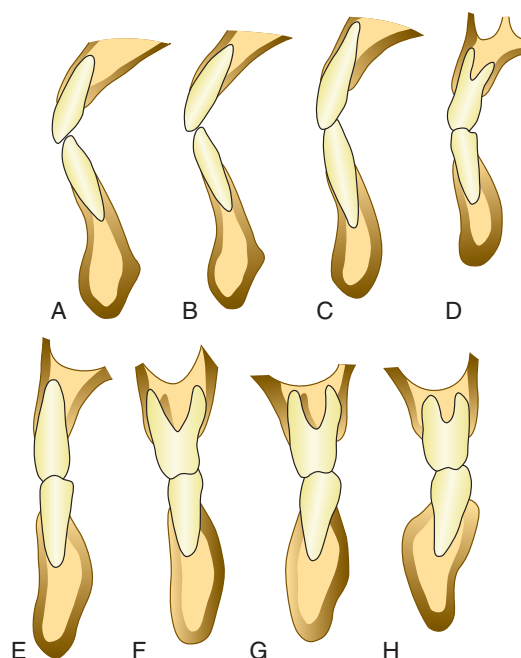


Figure 2-51 Relative proportions of cancellous bone and compact bone in a longitudinal faciolingual section of **A**, mandibular molars; **B**, lateral incisors; **C**, canines; **D**, first premolars; **E**, second premolars; **F**, first molars; **G**, second molars; and **H**, third molars.

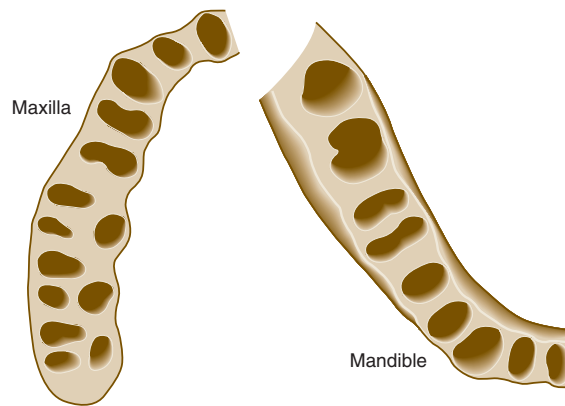


Figure 2-52 Shape of roots and surrounding bone distribution in a transverse section of maxilla and mandible at midroot level.

manner on the generation and activity of differentiated bone cells.²⁵⁷ Bone contains 99% of the body's calcium ions and therefore is the major source for calcium release when the calcium blood levels decrease; this is monitored by the parathyroid gland. A decrease in blood calcium is mediated by receptors on the chief cells of the parathyroid glands, which then release parathyroid hormone (PTH). PTH stimulates osteoblasts to release interleukin-1 and interleukin-6, which stimulate monocytes to migrate into the bone area. Leukemia-inhibiting factor (LIF), secreted by osteoblasts, coalesces monocytes into multinucleated osteoclasts, which then resorb bone, releasing calcium ions from hydroxyapatite into the blood. This release normalizes the blood level of calcium. A feedback mechanism of normal blood levels of calcium turns off the secretion of PTH. Meanwhile, osteoclasts have resorbed organic matrix along with hydroxyapatite. The breakdown of collagen from the organic matrix releases various osteogenic substrates, which are covalently bound to collagen, and this in turn stimulates the differentiation of osteoblasts, which ultimately deposit bone. This interdependency of osteoblasts and osteoclasts in remodeling is called *coupling*.

The bone matrix that is laid down by osteoblasts is nonmineralized *osteoid*. While new osteoid is being deposited, the older osteoid located below the surface becomes mineralized as the mineralization front advances.

Bone resorption is a complex process morphologically related to the appearance of eroded bone surfaces (Howship's lacunae) and large, multinucleated cells (osteoclasts) (Figure 2-53). Osteoclasts originate from hematopoietic tissue^{56,112,201} and are formed by the fusion of mononuclear cells of asynchronous populations.^{27,143,205,269} When osteoclasts are active rather than resting, they possess an elaborately developed ruffled border from which hydrolytic enzymes are believed to be secreted.²⁸³ These enzymes digest the organic portion of bone. The activity of osteoclasts and morphology of the ruffled border can be modified and regulated by hormones such as PTH (indirectly) and calcitonin, which has receptors on the osteoclast membrane.

Another mechanism of bone resorption involves the creation of an acidic environment on the bone surface, leading to the dissolution of the mineral component of bone. This event can be produced by different conditions, including a proton pump through the cell membrane of the osteoclast,³⁴ bone tumors, and local pressure,²⁰¹ translated through the secretory activity of the osteoclast.

Ten Cate²⁶⁹ described the sequence of events in the resorptive process as follows:



Figure 2-53 Rat alveolar bone. Histologic view of two multinucleated osteoclasts in Howship's lacuna.

1. Attachment of osteoclasts to the mineralized surface of bone.
2. Creation of a sealed acidic environment through action of the proton pump, which demineralizes bone and exposes the organic matrix.
3. Degradation of the exposed organic matrix to its constituent amino acids by the action of released enzymes, such as acid phosphatase and cathepsin.
4. Sequestering of mineral ions and amino acids within the osteoclast.

Notably, the cellular and molecular events involved in bone remodeling have a strong similarity to many aspects of inflammation and repair. The relationship between matrix molecules, such as osteopontin, bone sialoprotein, SPARC (secreted protein, acidic, rich in cysteine), and osteocalcin, and blood clotting and wound healing are clearly evident.²⁵⁷

Socket Wall

The socket wall consists of dense, lamellated bone, some of which is arranged in haversian systems and bundle bone. *Bundle bone* is the term given to bone adjacent to the periodontal ligament that contains a great number of Sharpey's fibers²⁹¹ (Figure 2-54). It is characterized by thin lamellae arranged in layers parallel to the root, with intervening appositional lines (Figure 2-55). Bundle bone is localized within the alveolar bone proper. Some Sharpey's fibers are completely calcified, but most contain an uncalcified central core within a calcified outer layer.²⁴⁶ Bundle bone is not unique to the jaws; it occurs throughout the skeletal system wherever ligaments and muscles are attached.

The cancellous portion of the alveolar bone consists of trabeculae that enclose irregularly shaped marrow spaces lined with a layer of thin, flattened endosteal cells. Wide variation occurs in the trabecular pattern of cancellous bone,²⁰⁴ which is affected by occlusal forces. The matrix of the cancellous trabeculae consists of irregularly arranged lamellae separated by deeply staining incremental and resorption lines indicative of previous bone activity, with an occasional haversian system.

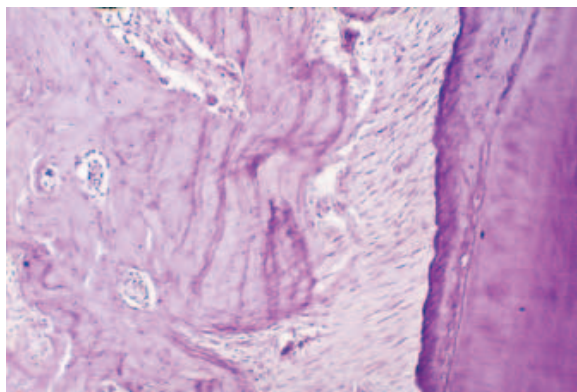


Figure 2-54 Deep penetration of Sharpey's fibers into bundle bone (rat molar).

Cancellous bone is found predominantly in the interradicular and interdental spaces and in limited amounts facially or lingually, except in the palate. In the adult human, more cancellous bone exists in the maxilla than in the mandible.

Bone Marrow

In the embryo and newborn the cavities of all bones are occupied by red hematopoietic marrow. The red marrow gradually undergoes a physiologic change to the fatty or yellow inactive type of marrow. In the adult the marrow of the jaw is normally of the latter type, and red marrow is found only in the ribs, sternum, vertebrae, skull, and humerus. However, foci of red bone marrow are occasionally seen in the jaws, often accompanied by resorption of bony trabeculae.⁴² Common locations are the maxillary tuberosity, the maxillary and mandibular molar and premolar areas, and the mandibular symphysis and ramus angle, which may be visible radiographically as zones of radiolucency.

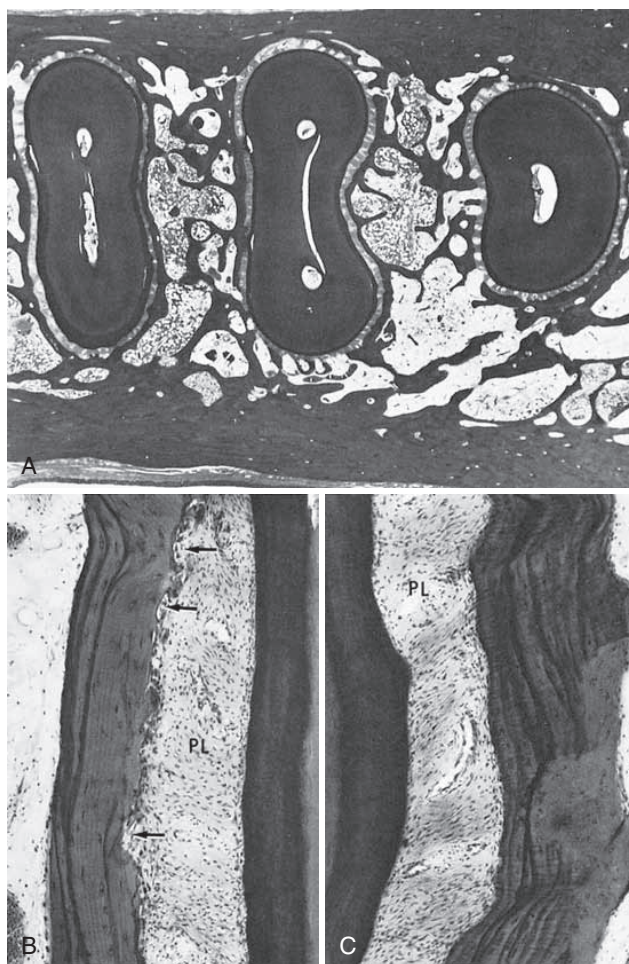


Figure 2-55 Bundle bone associated with physiologic mesial migration of the teeth. **A**, Horizontal section through molar roots in the process of mesial migration (*left*, mesial; *right*, distal). **B**, Mesial root surface showing osteoclas of bone (*arrows*). **C**, Distal root surface showing bundle bone that has been partially replaced with dense bone on the marrow side. *PL*, Periodontal ligament.

Cellular events at the periosteum modulate bone size throughout an individual's life span, and change in bone size is probably the result of the balance between periosteal osteoblastic and osteoclastic activities. Currently, little is known about the control of periosteal osteoblastic activity or the clinical importance of variations in periosteal bone formation.²⁰⁰ Moreover, the nature and impact of periosteal bone resorption are virtually unexplored.

Between maxillary molars, the septum consisted of cribriform plate and cancellous bone in 66.6% of cases, was composed of only cribriform plate in 20.8%, and had a fenestration in 12.5%.¹¹⁸

Determining root proximity radiographically is important (see Chapters 31 and 33). The mesiodistal angulation of the crest of the interdental septum usually parallels a line drawn between the cementoenamel junctions of the approximating teeth.²¹⁴ The distance between the crest of the alveolar bone and the cementoenamel junction in young adults varies between 0.75 and 1.49 mm (average, 1.08 mm). This distance increases with age to an average of 2.81 mm.⁹⁵ However, this phenomenon may not be as much a function of age as of periodontal disease.

The mesiodistal and faciolingual dimensions and shape of the interdental septum are governed by the size and convexity of the crowns of the two approximating teeth, as well as by the position of the teeth in the jaw and their degree of eruption.²¹⁴

On teeth in labial version, the margin of the labial bone is located farther apically than on teeth in proper alignment. The bone margin is thinned to a knife-edge and presents an accentuated arc in the direction of the apex. On teeth in lingual version, the facial bony plate is thicker than normal. The margin is blunt, rounded, and horizontal rather than arcuate. The effect of the root-to-bone

angulation on the height of alveolar bone is most noticeable on the palatal roots of maxillary molars. The bone margin is located farther apically on the roots, which forms relatively acute angles with the palatal bone.¹²² The cervical portion of the alveolar plate is sometimes considerably thickened on the facial surface, apparently as reinforcement against occlusal forces (Figure 2-59).

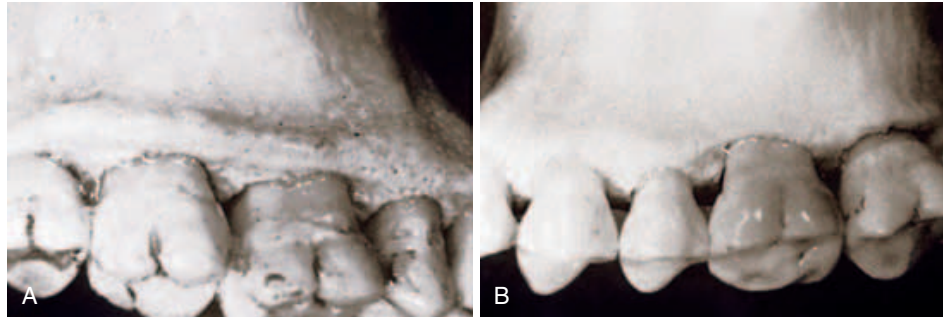


Figure 2-59 Variation in the cervical portion of the buccal alveolar plate. **A**, Shelflike conformation. **B**, Comparatively thin buccal plate.

Such defects occur on approximately 20% of the teeth; they occur more often on the facial bone than on the lingual bone, are more common on anterior teeth than on posterior teeth, and are frequently bilateral. Microscopic evidence of lacunar resorption may be present at the margins. The cause of these defects is not clear. Prominent root contours, malposition, and labial protrusion of the root combined with a thin bony plate are predisposing factors.⁸¹ Fenestration and dehiscence are important because they may complicate the outcome of periodontal surgery.

Remodeling of Alveolar Bone

In contrast to its apparent rigidity, alveolar bone is the least stable of the periodontal tissues because its structure is in a constant state of flux. A considerable amount of internal remodeling takes place by means of resorption and formation, which is regulated by local and systemic influences. Local influences include functional requirements on the tooth and age-related changes in bone cells. Systemic influences are probably hormonal (e.g., PTH, calcitonin, or vitamin D3).

The remodeling of the alveolar bone affects its height, contour, and density and is manifested in the following three areas: adjacent to the periodontal ligament, in relation to the periosteum of the facial and lingual plates, and along the endosteal surface of the marrow spaces.

After the crown has formed, the stratum intermedium and the stellate reticulum of the enamel organ disappear. The outer and inner epithelia of the enamel organ remain and form REE. The apical portion of this constitutes *Hertwig's epithelial root sheath*, which will continue to grow apically and determines the shape of the root. Before the beginning of root formation, the root sheath bends horizontally at the future CEJ, narrowing the cervical opening and forming the *epithelial diaphragm*. The epithelial diaphragm separates the dental follicle from the dental papilla.

After root dentin formation starts, Hertwig's root sheath breaks up and partially disappears; the remaining cells form the epithelial clusters or strands known as *epithelial rests of Malassez* (see Figure 2-37, A). In multirooted teeth, the epithelial diaphragm grows in such a way that tongue-like extensions develop horizontally, leaving spaces for each of the future roots to form.

The role of Hertwig's epithelial root sheath in root development, especially as it relates to the initiation of cementogenesis, has become a focus of research.²⁷⁶ Based on various studies, it is now generally accepted that there is a transient period of secretion of proteins, including bone sialoprotein, osteopontin, and amelogenin, by the cells of Hertwig's epithelial root sheath.^{38,88} In addition, research shows that growth and differentiation factors may play roles in the development of the attachment apparatus of periodontal tissues. Pluripotent dental follicle cells have been shown to differentiate into osteoblasts, cementoblasts, or periodontal fibroblasts.²⁴⁷

Cementum

The rupture of Hertwig's root sheath allows the mesenchymal cells of the dental follicle to contact the dentin, where they start forming a continuous layer of cementoblasts. Based on immunohistochemical and ultrastructural studies, Thomas²⁷⁵ and others^{35,167} have speculated that cementoblasts also can be of epithelial origin (Hertwig's root sheath), which would undergo an epithelial mesenchymal transformation.

Cementum formation begins by deposition of a meshwork of irregularly arranged collagen fibrils sparsely distributed in a ground substance or matrix called *precementum* or *cementoid*. This is followed by a phase of matrix maturation, which subsequently mineralizes to form cementum. Cementoblasts, which are initially separated from the cementum by uncalcified cementoid, sometimes become enclosed within the matrix and are trapped. Once they are enclosed, they are referred to as *cementocytes* and will remain viable in a manner similar to that of osteocytes.

A layer of connective tissue known as the *dental sac* surrounds the enamel organ, including the epithelial root sheath as it develops. The zone immediately in contact with the dental organ and continuous with the ectomesenchyme of the dental papilla is called the *dental follicle*^{267,268,271} and consists of undifferentiated fibroblasts.

Periodontal Ligament

As the crown approaches the oral mucosa during tooth eruption, these fibroblasts become active and start producing collagen fibrils. They initially lack orientation, but they soon acquire an orientation oblique to the tooth. The first collagen bundles then appear in the region immediately apical to the cemento-enamel junction and give rise to the gingivodental fiber groups. As tooth eruption progresses, additional oblique fibers appear and become attached to the newly formed cementum and bone. The transseptal and alveolar crest fibers develop when the tooth merges into the oral cavity. Alveolar bone deposition occurs simultaneously with periodontal ligament organization.²⁵⁶

Studies of the squirrel monkey have shown that during eruption, cemental Sharpey's fibers appear first, followed by Sharpey's

fibers emerging from bone.¹⁰⁹ Sharpey's fibers are fewer in number and more widely spaced than those emerging from the cementum. At a later stage, alveolar fibers extend into the middle zone to join the lengthening cemental fibers and attain their classic orientation, thickness, and strength when occlusal function is established.

Early investigators had suggested that the individual fibers, rather than being continuous, consisted of two separate parts spliced together midway between the cementum and the bone in a zone that is called the intermediate plexus. The plexus has been reported in the periodontal ligament of continuously growing incisors but not in the posterior teeth of rodents^{121,179,305} or in actively erupting human and monkey teeth¹⁰⁹ and not after teeth reach occlusal contact. Rearrangement of the fiber ends in the plexus is supposed to accommodate tooth eruption without necessitating the embedding of new fibers into the tooth and the bone.¹⁷⁹ The existence of such a plexus, however, has not been confirmed by radioautographic data and other studies, and it is considered a microscopic artifact.²³⁸

The developing periodontal ligament, as well as the mature periodontal ligament, contains undifferentiated stem cells that retain the potential to differentiate into osteoblasts, cementoblasts, and fibroblasts.¹⁷⁴

Alveolar Bone

Just before mineralization, osteoblasts start producing matrix vesicles. These vesicles contain enzymes, such as alkaline phosphatase, that help jump-start the nucleation of hydroxyapatite crystals. As these crystals grow and develop, they form coalescing bone nodules, which, with fast-growing nonoriented collagen fibers, are the substructure of woven bone and the first bone formed in the alveolus. Later, through bone deposition, remodeling, and secretion of oriented collagen fibers in sheets, mature lamellar bone is formed.^{28,29}

The hydroxyapatite crystals are generally aligned with their long axes parallel to the collagen fibers and appear to be deposited on and within the collagen fibers in mature lamellar bone. In this way, bone matrix is able to withstand the heavy mechanical stresses applied to it during function.

The alveolar bone develops around each tooth follicle during odontogenesis. When a deciduous tooth is shed, its alveolar bone is resorbed. The succedaneous permanent tooth moves into place, developing its own alveolar bone from its own dental follicle. As the tooth root forms and the surrounding tissues develop and mature, alveolar bone merges with the separately developing basal bone, and the two become one continuous structure. Although alveolar bone and basal bone have different intermediate origins, both are ultimately derived from neural crest ectomesenchyme.

Mandibular basal bone begins mineralization at the exit of the mental nerve from the mental foramen, whereas the maxillary basal bone begins at the exit of the infraorbital nerve from the infraorbital foramen.

Physiologic Migration of the Teeth

Tooth movement does not end when active eruption is completed and the tooth is in functional occlusion. With time and wear, the proximal contact areas of the teeth are flattened, and the teeth tend to move mesially. This is referred to as *physiologic mesial migration*. By age 40, it results in a reduction of about 0.5 cm in the length of the dental arch from the midline to the third molars. Alveolar bone is reconstructed in compliance with the physiologic mesial migration of the teeth. Bone resorption is increased in areas of pressure along the mesial surfaces of the teeth, and new layers of bundle bone are formed in areas of tension on the distal surfaces (see Figure 2-55).

The socket wall reflects the responsiveness of alveolar bone to external forces. Osteoblasts and newly formed osteoid line the socket in areas of tension; osteoclasts and bone resorption occur in areas of pressure. Forces exerted on the tooth also influence the number, density, and alignment of cancellous trabeculae. The bony trabeculae are aligned in the path of the tensile and compressive stresses to provide maximal resistance to the occlusal force with a minimum of bone substance^{102,253} (Figure 2-61). When forces are increased, the cancellous bony trabeculae increase in number and thickness, and bone may be added to the external surface of the labial and lingual plates.

A study has shown that the presence of antagonist of occlusal force and the severity of periodontal disease increase the extension of periodontal tissue resorption.⁶⁸

The periodontal ligament also depends on stimulation provided by function to preserve its structure. Within physiologic limits, the periodontal ligament can accommodate increased function with an increase in width (Table 2-2), a thickening of its fiber bundles, and an increase in diameter and number of Sharpey's fibers. Forces that exceed the adaptive capacity of the periodontium produce injury called *trauma from occlusion*. Since trauma from occlusion can only be confirmed histologically, the clinician is challenged to use clinical and radiographic surrogate indicators in an attempt to facilitate and assist in its diagnosis¹¹³ (see Chapter 20).

When occlusal forces are reduced, the number and thickness of the trabeculae are reduced.⁶⁶ The periodontal ligament also atrophies, appearing thinned, and the fibers are reduced in number and density, disoriented,^{11,213} and ultimately arranged parallel to the root surface (Figure 2-62). This phenomenon is termed *disuse atrophy* or *afunctional atrophy*. In this condition the cementum is either unaffected⁶⁶ or thickened, and the distance from the CEJ to the alveolar crest is increased.²⁰⁸

Decreased occlusal function causes changes in the periodontal microvasculature, such as occlusion of blood vessels and a decrease in the number of blood vessels.¹²³ For example, Murrell et al¹⁹⁰ reported that the application and removal of orthodontic force produced significant changes in blood vessel number and density; however, no evidence-based explanation exists for why the force stimulated such changes in blood vessel number.

Orthodontic tooth movement is believed to result from site-specific bone remodeling in the absence of inflammation. It is well recognized that tensional forces will stimulate the formation and activity of osteoblastic cells, whereas compressive forces promote osteoclastic activity.²⁵⁷



Figure 2-61 Bony trabeculae realigned perpendicular to the mesial root of tilted molar.

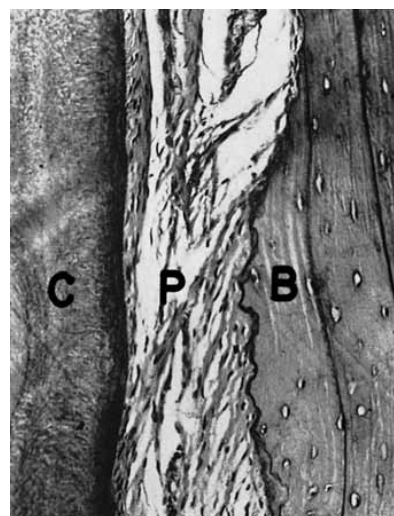


Figure 2-62 Atrophic periodontal ligament (P) of a tooth devoid of function. Note the scalloped edge of the alveolar bone (B), indicating that resorption has occurred. C, Cementum.

TABLE 2-2 Comparison of Periodontal Width of Functioning and Functionless Teeth in a 38-Year-Old Man

	AVERAGE WIDTH OF PERIODONTAL SPACE (mm)		
	Entrance of Alveolus	Middle of Alveolus	Fundus of Alveolus
<i>Heavy function:</i>	0.35	0.28	0.30
Left upper second bicuspid			
<i>Light function:</i>	0.14	0.10	0.12
Left lower first bicuspid			
<i>Functionless:</i>	0.10	0.06	0.06
Left upper third molar			

Modified from Kronfeld R: *J Am Dent Assoc* 18:1242, 1931.

The branches of the apical vessels supply the apical region of the periodontal ligament before the vessels enter the dental pulp. The transalveolar vessels are branches of the intraseptal vessels that perforate the lamina dura and enter the ligament. The intraseptal vessels continue to vascularize the gingiva; these gingival vessels in turn anastomose with the periodontal ligament vessels of the cervical region.⁸⁷

The vessels within the periodontal ligament are contained in interstitial spaces of loose connective tissue between the principal fibers and are connected in a netlike plexus that runs longitudinally and closer to the bone than the cementum⁵⁵ (Figures 2-63 and 2-64). The blood supply increases from the incisors to the molars; is greatest in the gingival third of single-rooted teeth, less in the apical third, and least in the middle; is equal in the apical and middle thirds of multirooted teeth; is slightly greater on the mesial and distal surfaces than on the facial and lingual surfaces; and is greater on the mesial surfaces of mandibular molars than on the distal surfaces.³³

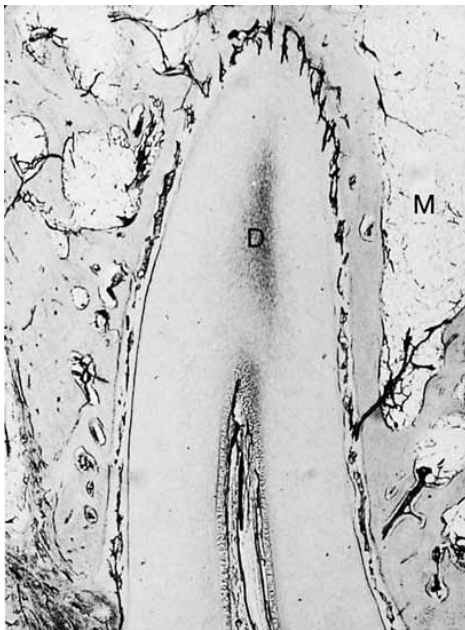


Figure 2-63 Vascular supply of monkey periodontium (perfused with India ink). Note the longitudinal vessels in the periodontal ligament and alveolar arteries passing through channels between the bone marrow (M) and periodontal ligament. D, Dentin. (Courtesy Dr. Sol Bernick, Los Angeles.)

The vascular supply to the bone enters the interdental septa through nutrient canals together with veins, nerves, and lymphatics. Dental arterioles, which also branch off the alveolar arteries, send tributaries through the periodontal ligament, and some small branches enter the marrow spaces of the bone through the perforations in the cribriform plate. Small vessels emanating from the facial and lingual compact bone also enter the marrow and spongy bone.

The **venous drainage** of the periodontal ligament accompanies the arterial supply. Venules receive the blood through the abundant capillary network. Also, arteriovenous anastomoses bypass the capillaries and are seen more frequently in apical and interracular regions; their significance is unknown.

Lymphatics supplement the venous drainage system. Lymphatic channels draining the region just beneath the junctional epithelium pass into the periodontal ligament and accompany the blood vessels into the periapical region.⁴³ From there, they pass through the alveolar bone to the inferior dental canal in the mandible or the infraorbital canal in the maxilla, then to the submaxillary lymph nodes.



Figure 2-64 Vascular supply to the periodontal ligament in rat molar, as viewed by scanning electron microscopy after perfusion with plastic and tissue corrosion. Middle and apical areas of the periodontal ligament are shown with longitudinal blood vessels from apex (below) to gingiva (above), perforating vessels entering the bone (b), and many transverse connections (arrowheads). Apical vessels (a) form a cap that connects with the pulp vessels. (Courtesy NJ Selliseth and K Selvig, University of Bergen, Norway.)

REFERENCES

1. Ababneh KT, Hall RC, Embery G: Immunolocalization of glycosaminoglycans in ageing, healthy and periodontally diseased human cementum, *Arch Oral Biol* 43:235, 1998.
2. Ababneh KT, Hall RC, Embery G: The proteoglycans of human cementum: immunohistochemical localization in healthy, periodontally involved and ageing teeth, *J Periodontol Res* 34:87, 1999.
3. Agnew RG, Fong CC: Histologic studies on experimental transplantation of teeth, *J Oral Surg* 9:18, 1956.
4. Ainamo A: Influence of age on the location of the maxillary mucogingival junction, *J Periodontol Res* 13:189, 1978.
5. Ainamo A, Ainamo J: The width of attached gingiva on supraerupted teeth, *J Periodontol Res* 13:194, 1978.
6. Ainamo J, Löe H: Anatomical characteristics of gingiva: a clinical and microscopic study of the free and attached gingiva, *J Periodontol* 37:5, 1966.
7. Ainamo J, Talari A: The increase with age of the width of attached gingiva, *J Periodontol Res* 11:182, 1976.
8. Ambrosini P, Cherene S, Miller N, et al: A laser Doppler study of gingiva blood flow variations following periosteal stimulation, *J Clin Periodontol* 29:103, 2002.
9. Anderson GS, Stern IB: The proliferation and migration of the attachment epithelium on the cemental surface of the rat incisor, *Periodontics* 4:15, 1966.
10. Andersson L, Blomlof L, Lindskog S, et al: Tooth ankylosis: clinical, radiographic and histological assessments, *Int J Oral Surg* 13:423, 1984.
11. Anneroth G, Ericsson SG: An experimental histological study of monkey teeth without antagonist, *Odontol Rev* 18:345, 1967.
12. Armitt KL: Identification of T cell subsets in gingivitis in children, *Periodontology* 7:3, 1986.
13. Attstrom R, Graf-de Beer M, Schroeder HE: Clinical and histologic characteristics of normal gingiva in dogs, *J Periodontol Res* 10:115, 1975.
14. Avery JK, Rapp R: Pain conduction in human dental tissues, *Dent Clin North Am* 489, July 1959.
15. Barakat NJ, Toto PD, Choukas NC: Aging and cell renewal of oral epithelium, *J Periodontol* 40:599, 1969.
16. Bartold PM: Turnover in periodontal connective tissues: dynamic homeostasis of cells, collagen and ground substances, *Oral Dis* 1:238, 1995.
17. Bartold PM, Narayanan AS: *Biology of the periodontal connective tissues*, Chicago, 1998, Quintessence.
18. Bartold PM, Walsh LJ, Narayanan AS: Molecular and cell biology of the gingiva, *Periodontol* 2000 24:28, 2000.
19. Basdra EK, Stellzig A, Komposch G: Generalized hypercementosis in a young female patient, *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 83:418, 1997.
20. Bauer WH: Effect of a faultily constructed partial denture on a tooth and its supporting tissue, with special reference to formation of fibrocartilage in the periodontal membrane as a result of disturbed healing caused by abnormal stresses, *Am J Orthod Oral Surg* 27:640, 1941.
21. Baumhammers A, Stallard RE: S35-sulfate utilization and turnover by connective tissues of the periodontium, *J Periodontol Res* 3:187, 1968.
22. Beagrie GS, Skougard MR: Observations on the life cycle of the gingival epithelial cells of mice as revealed by autoradiography, *Acta Odontol Scand* 20:15, 1962.
23. Becks H: Root resorptions and their relation to pathologic bone formation, *Int J Orthod Oral Surg* 22:445, 1936.
24. Beertsen W, McCullough CAG, Sodek J: The periodontal ligament: a unique, multifunctional connective tissue, *Periodontol* 2000 13:20, 1997.
25. Berkovitz BK: The structure of the periodontal ligament: an update, *Eur J Orthod* 12:51, 1990.
26. Berkovitz BK, Shore RC: Cells of the periodontal ligament. In Berkovitz BK, Moxham BJ, Newman HE, editors: *The periodontal ligament in health and disease*, London, 1982, Pergamon.
27. Bernard GW, Ko JS: Osteoclast formation in vitro from bone marrow mononuclear cells in osteoclast-free bone, *Am J Anat* 161:415, 1981.
28. Bernard GW, Marvaso V: Matrix vesicles as an assay for primary tissue calcification in vivo and in vitro. In Ascenzi A, Bonucci B, DeBernard B, editors: *Matrix vesicles: Proceedings of the 3rd International Conference on Matrix Vesicles*, Milano, 1981, Wichtig.
29. Bernard GW, Pease DC: An electron microscopic study of initial intramembranous osteogenesis, *Am J Anat* 125:271, 1969.
30. Bernick S: Innervation of the teeth and periodontium, *Dent Clin North Am*, 503, July 1959.
31. Bien SM: Hydrodynamic damping of tooth movement, *J Dent Res* 45:907, 1966.
32. Biolcati EL, Carranza FA Jr, Cabrini RL: Variaciones y alteraciones de la queratinizacion en encias humanas clinicamente sanas, *Rev Asoc Odontol Argent* 41:446, 1953.
33. Birn H: The vascular supply of the periodontal membrane: an investigation of the number and size of perforations in the alveolar wall, *J Periodontol Res* 1:51, 1966.
34. Blair HC, Teitelbaum SL, Ghiselli R, et al: Osteoclastic bone resorption by a polarized vacuolar proton pump, *Science* 245:855, 1989.
35. Blaushild N, Michaeli Y, Steigman S: Histomorphometric study of the periodontal vasculature of the rat incisor, *J Dent Res* 71:1908, 1992.
36. Blayney JR, Wassermann F, Groetzinger G, et al: Further studies in mineral metabolism of human teeth by the use of radioactive phosphorus, *J Dent Res* 29:559, 1941.
37. Bosch FX, Ouhayoun JP, Bader BL, et al: Extensive changes in cytokeratin expression patterns in pathologically affected human gingiva, *Virchows Arch B Cell Pathol* 58:59, 1989.
38. Bosshardt DD, Nanci A: Immunolocalization of epithelial and mesenchymal matrix constituents in association with inner enamel epithelial cells, *J Histochem Cytochem* 46:135, 1998.
39. Bosshardt DD, Schroeder HE: Cementogenesis reviewed: a comparison between human premolars and rodent molars, *Anat Rec* 245:267, 1996.
40. Bosshardt DD, Zalzal S, McKee MD, et al: Developmental appearance and distribution of bone sialoprotein and osteopontin in human and rat cementum, *Anat Rec* 250:13, 1998.
41. Bowers GM: A study of the width of the attached gingiva, *J Periodontol* 34:210, 1963.
42. Box HK: Bone resorption in red marrow hyperplasia in human jaws, *Can Dent Res Found, Bulletin* 21, 1936.
43. Box KF: Evidence of lymphatics in the periodontium, *J Can Dent Assoc* 15:8, 1949.
44. Boyle PE: Tooth suspension: a comparative study of the parodontal tissues of man and of the guinea pig, *J Dent Res* 17:37, 1938.

45. Bral MM, Stahl SS: Keratinizing potential of human crevicular epithelium, *J Periodontol* 48:381, 1977.
46. Cabrini R, Cabrini RL, Carranza FA Jr: Estudio histológico de la queratinización del epitelio gingival y de la adherencia epitelial, *Rev Asoc Odontol Argent* 41:212, 1953.
47. Cabrini RL, Carranza FA Jr: Histochemical study on alkaline phosphatase in gingivae, varying the pH and the substrate, *J Dent Res* 30:28, 1951.
48. Cabrini RL, Carranza FA Jr: Histochemistry of periodontal tissues: a review of the literature, *Int Dent J* 16:466, 1966.
49. Caffesse RG, Karring T, Nasjleti CE: Keratinizing potential of sulcular epithelium, *J Periodontol* 48:140, 1977.
50. Caffesse RG, Kornman KS, Nasjleti CE: The effect of intensive antibacterial therapy on the sulcular environment in monkeys. Part II. Inflammation, mitotic activity and keratinization of the sulcular epithelium, *J Periodontol* 5:155, 1980.
51. Caffesse RG, Nasjleti CE, Castelli WA: The role of sulcular environment in controlling epithelial keratinization, *J Periodontol* 50:1, 1979.
52. Carneiro J, Fava de Moraes F: Radioautographic visualization of collagen metabolism in the periodontal tissues of the mouse, *Arch Oral Biol* 10:833, 1955.
53. Carranza FA Jr, Cabrini RL: Mast cells in human gingiva, *J Oral Surg* 8:1093, 1955.
54. Carranza FA, Carranza FA Jr: The management of the alveolar bone in the treatment of the periodontal pocket, *J Periodontol* 27:29, 1956.
55. Carranza FA Jr, Itoiz ME, Cabrini RL, et al: A study of periodontal vascularization in different laboratory animals, *J Periodontol Res* 1:120, 1966.
56. Chambers TJ: The cellular basis of bone resorption, *Clin Orthop*, 283, September 1980.
57. Chavrier C: Elastic fibers of healthy human gingiva, *J Periodontol* 9:29, 1990.
58. Cho MI, Garant PR: Development and general structure of the periodontium, *Periodontol* 2000 24:9, 2000.
59. Ciancio SC, Neiders ME, Hazen SP: The principal fibers of the periodontal ligament, *Periodontics* 5:76, 1967.
60. Cimasoni G: Crevicular fluid updated, *Monogr Oral Sci* 12:1, 1983.
61. Clausen H, Moe D, Buschard K, et al: Keratin proteins in human oral mucosa, *J Oral Pathol* 15:36, 1986.
62. Cleaton-Jones P, Buskin SA, Volchansky A: Surface ultrastructure of human gingiva, *J Periodontol Res* 13:367, 1978.
63. Cohen B: Morphological factors in the pathogenesis of periodontal disease, *Br Dent J* 107:31, 1959.
64. Cohen L: Further studies into the vascular architecture of the mandible, *J Dent Res* 39:936, 1960.
65. Cohen L: ATPase and DOPA oxidase activity in human gingival epithelium, *Arch Oral Biol* 12:1241, 1967.
66. Cohn SA: Disuse atrophy of the periodontium in mice, *Arch Oral Biol* 10:909, 1965.
67. Coolidge ED: The thickness of the human periodontal membrane, *J Am Dent Assoc* 24:1260, 1937.
68. Crespo vázquez E, Crespo Abelleira A, Suárez Quintanilla JM, Rodríguez Cobos MA: Correlation between occlusal contact and root resorption in teeth with periodontal disease, *Journal of Periodontal Research* 46:82-88, 2011.
69. Dale BA: Periodontal epithelium: a newly recognized role in health and disease, *Periodontol* 2000 30:70, 2002.
70. Dastmalchi R, Polson A, Bouwsma O, et al: Cementum thickness and mesial drift, *J Clin Periodontol* 17:709, 1990.
71. Davies WR, Picton DC: Dimensional changes in the periodontal membrane of monkeys' teeth with horizontal thrusts, *J Dent Res* 46:114, 1967.
72. De Rouck T, Eghbali R, Collays K, De Bruyn H, Cosyn J: The gingival biotype revisited: transparency of the periodontal probe through the gingival margin as a method to discriminate thin from thick gingiva *J Clin Periodontol* 36(5):428-433, 2009 May.
73. Dewar MR: Observations on the composition and metabolism of normal and inflamed gingivae, *J Periodontol* 26:29, 1955.
74. DiFranco CF, Toto PD, Rowden G, et al: Identification of Langerhans cells in human gingival epithelium, *J Periodontol* 56:48, 1985.
75. Dummett CO: Physiologic pigmentation of the oral and cutaneous tissues in the Negro, *J Dent Res* 25:421, 1946.
76. Dummett CO et al: Oral pigmentation: physiologic and pathologic, *NY State Dent J* 25:407, 1959.
77. Eastoe JE: The organic matrix of bone. In Bourne GH, editor: *The biochemistry and physiology of bone*, New York, 1956, Academic Press.
78. Egelberg J: The topography and permeability of blood vessels at the dento-gingival junction in dogs, *J Periodontol Res* 1:1, 1967.
79. Eichel B, Shahrik HA, Lisanti VF: Cytochemical demonstration and metabolic significance of reduced diphosphopyridinenucleotide and triphospho-pyridinenucleotide reductases in human gingiva, *J Dent Res* 43:92, 1964.
80. El Mostehy MR, Stallard RE: Intermediate cementum, *J Periodontol Res* 3:24, 1968.
81. Elliot JR, Bowers GM: Alveolar dehiscence and fenestration, *Periodontics* 1:245, 1963.
82. Embery G, Waddington R: Gingival crevicular fluid: biomarkers of periodontal tissue activity, *Adv Dent Res* 8:329, 1994.
83. Embery G, Waddington RJ, Hall RC, et al: Connective tissue elements as diagnostic aids in periodontology, *Periodontol* 2000 24:193, 2000.
84. Embery G, Waddington RJ, Hall RC, et al: Connective tissue elements as diagnostic aids in periodontology, *Periodontol* 2000 24:193, 2000.
85. Engel MB: Water-soluble mucoproteins of the gingiva, *J Dent Res* 32:779, 1953.
86. Everts V, Niehof A, Jansen D, et al: Type VI collagen is associated with microfibrils and oxytalan fibers in the extracellular matrix of periodontium, mesenterium and periosteum, *J Periodontol Res* 33:118, 1998.
87. Folke LE, Stallard RE: Periodontal microcirculation as revealed by plastic microspheres, *J Periodontol Res* 2:53, 1967.
88. Fong CD, Slaby I, Hammarström L, et al: Amelin: an enamel-related protein, transcribed in the cells of epithelial root sheath, *J Bone Miner Res* 11:892, 1996.
89. Forsslund G: Structure and function of capillary system in the gingiva in man: development of stereophotogrammetric method and its application for study of the subepithelial blood vessels in vivo, *Acta Odontol Scand* 17:9, 1959.
90. Frank RM, Cimasoni G: On the ultrastructure of the normal human gingivo-dental junction, *Z Zellforsch Mikrosk Anat* 109:356, 1970.
91. Freeman E: The periodontium. In Ten Cate R, editor: *Oral histology*, ed 4, St Louis, 1994, Mosby.
92. Fullmer HM, Sheetz JH, Narkates AJ: Oxytalan connective tissue fibers: a review, *J Oral Pathol* 3:291, 1974.

93. Fuss Z, Tsesis I, Lin S: Root resorption: diagnosis, classification and treatment choices based on stimulation factors, *Dent Trauma* 19:175, 2003.
94. Gao Z, Flaitz CM, Mackenzie IC: Expression of keratinocyte growth factor in periapical lesions, *J Dent Res* 75:1658, 1996.
95. Gargiulo AW, Wentz FM, Orban B: Dimensions and relations of the dentogingival junction in humans, *J Periodontol* 32:261, 1961.
96. Gibson WA, Fullmer HM: Histochemistry of the periodontal ligament. I. The dehydrogenases, *Periodontics* 4:63, 1966.
97. Gibson WA, Fullmer HM: Histochemistry of the periodontal ligament. 2. The phosphatases, *Periodontics* 5:226, 1967.
98. Gibson WA, Fullmer HM: Histochemistry of the periodontal ligament. 3. The esterases, *Periodontics* 6:71, 1968.
99. Gillespie BR, Chasens AI, Brownstein CN, et al: The relationship between the mobility of human teeth and their supracrestal fiber support, *J Periodontol* 50:120, 1979.
100. Gillett R, Cruchley A, Johnson NW: The nature of the inflammatory infiltrates in childhood gingivitis, juvenile periodontitis and adult periodontitis: immunohistochemical studies using monoclonal antibody to HLADR, *J Clin Periodontol* 13:281, 1986.
101. Glickman I, Johannessen LB: Biomicroscopic (slit-lamp) evaluation of the normal gingiva of the albino rat, *J Am Dent Assoc* 41:521, 1950.
102. Glickman I, Roeber FW, Brion M, et al: Photoelastic analysis of internal stresses in the periodontium created by occlusal forces, *J Periodontol* 41:30, 1970.
103. Glimcher MJ: The nature of the mineral component of bone and the mechanism of calcification. In Avioli LV, Krane SM, editors: *Metabolic bone disease and clinical related disorders*, Philadelphia, 1990, Saunders.
104. Glimcher MJ, Friberg UA, Levine PT: The identification and characterization of a calcified layer of coronal cementum in erupted bovine teeth, *J Ultrastruct Res* 10:76, 1964.
105. Goggins JF: The distribution of oxytalan connective tissue fibers in periodontal ligaments of deciduous teeth, *Periodontics* 4:182, 1966.
106. Gottlieb B: Biology of the cementum, *J Periodontol* 13:13, 1942.
107. Gottlieb B, Orban B: Active and passive continuous eruption of teeth, *J Dent Res* 13:214, 1933.
108. Grant D, Bernick S: A possible continuity between epithelial rests and epithelial attachment in miniature swine, *J Periodontol* 40:87, 1969.
109. Grant D, Bernick S: Formation of the periodontal ligament, *J Periodontol* 43:17, 1972.
110. Greene AH: A study of the characteristics of stippling and its relation to gingival health, *J Periodontol* 33:176, 1962.
111. Grzesik WJ, Narayanan AS: Cementum and periodontal wound healing and regeneration, *Crit Rev Oral Biol Med* 13:474, 2002.
112. Hagel-Bradway S, Dziak R: Regulation of bone cell metabolism, *J Oral Pathol Med* 18:344, 1989.
113. Hallmon WW, Harrel SK: Occlusal analysis, diagnosis and management in the practice of periodontics, *Periodontol* 2000 34:151, 2004.
114. Hansen ER: Mitotic activity of the gingival epithelium in colchicized rats, *Odontol Tidskr* 74:229, 1966.
115. Hansson BO, Lindhe J, Branemark PI: Microvascular topography and function in clinically healthy and chronically inflamed dento-gingival tissues: a vital microscopic study in dogs, *Periodontics* 6:264, 1968.
116. Hasegawa N, Kawaguchi H, Ogawa T, et al: Immunohistochemical characteristics of epithelial cell rests of Malassez during cementum repair, *J Periodontol Res* 38:51, 2003.
117. Hassell TM, Stanek EJ 3rd: Evidence that healthy human gingiva contains functionally heterogeneous fibroblast subpopulations, *Arch Oral Biol* 28:617, 1983.
118. Heins PJ, Wieder SM: A histologic study of the width and nature of inter-radicular spaces in human adult premolars and molars, *J Dent Res* 65:948, 1986.
119. Hemley S: The incidence of root resorption of vital permanent teeth, *J Dent Res* 20:133, 1941.
120. Henry JL, Weinmann JP: The pattern of resorption and repair of human cementum, *J Am Dent Assoc* 42:270, 1951.
121. Hindle MC: Quantitative differences in periodontal membrane fibers, *J Dent Res* 43:953, 1964.
122. Hirschfeld I: A study of skulls in the American Museum of Natural History in relation to periodontal disease, *J Dent Res* 5:241, 1923.
123. Howard PS, Kucich U, Taliwal R, et al: Mechanical forces alter extracellular matrix synthesis by human periodontal ligament fibroblasts, *J Periodontol Res* 33:500, 1998.
124. Ikezawa K, Hart CE, Williams DC, et al: Characterization of cementum derived growth factor as an insulin-like growth factor-I like molecule, *Connect Tissue Res* 36:309, 1997.
125. Inoue M, Akiyoshi M: Histological investigation on Sharpey's fibers in cementum of teeth in abnormal function, *J Dent Res* 41:503, 1962.
126. Ishikawa G, Yamamoto H, Ito K, et al: Microradiographic study of cementum and alveolar bone, *J Dent Res* 43:936, 1964.
127. Itoiz ME, Carranza FA Jr, Cabrini RL: Histotopographic distribution of alkaline and acid phosphatase in periodontal tissues of laboratory animals, *J Periodontol* 35:470, 1964.
128. Itoiz ME, Carranza FA Jr, Cabrini RL: Histotopographic study of esterase and 5-nucleotidase in periodontal tissues of laboratory animals, *J Periodontol* 38:130, 1967.
129. Itoiz ME, Carranza FA Jr, Gimenez IB, et al: Microspectrophotometric analysis of succinic dehydrogenase and glucose-6-phosphate dehydrogenase in human oral epithelium, *J Periodontol Res* 7:14, 1972.
130. Itoiz ME, Conti CJ, Gimenez IB, et al: Immunodetection of involucrin in lesions of the oral mucosa, *J Oral Pathol* 15:205, 1986.
131. Itoiz ME, Conti CJ, Lanfranchi HE, et al: Immunohistochemical detection of filaggrin in preneoplastic and neoplastic lesions of the human oral mucosa, *Am J Pathol* 119:456, 1985.
132. Itoiz ME, Lanfranchi HE, Gimenez-Conti IB, et al: Immunohistochemical demonstration of keratins in oral mucosa lesions, *Acta Odontol Latinoam* 1:47, 1984.
133. Iusem R: A cytology study of the cornification of the oral mucosa in women: a preliminary report, *J Oral Surg* 3:1516, 1950.
134. Johnson RB: A new look at the mineralized and unmineralized components of intraosseous fibers of the interdental bone of the mouse, *Anat Rec* 206:1, 1983.
135. Johnson RB, Pylypas SP: A re-evaluation of the distribution of the elastic meshwork within the periodontal ligament of the mouse, *J Periodontol Res* 27:239, 1992.
136. Jones JC, Hopkinson SB, Goldfinger LE: Structure and assembly of hemidesmosomes, *Bioessays* 20:488, 1998.
137. Jones ML, Aldred MJ, Hardy P: Tooth resorption in the two-stage transplantation technique: a case report, *Br J Orthod* 10:157, 1983.

138. Jones MR, Simonton FV: Mineral metabolism in relation to alveolar atrophy in dogs, *J Am Dent Assoc* 15:881, 1928.
139. Jones SJ, Boyde A: A study of human root cementum surfaces as prepared for and examined in the scanning electron microscope, *Z Zellforsch Mikrosk Anat* 130:318, 1972.
140. Junqueira LC, Carneiro J, Kelley RO: *Basic histology*, ed 6, Norwalk, Conn, 1989, Appleton & Lange.
141. Kao D: Correlating of Clinical, Radiographic and Histological results in Periodontal Regeneration by Using Recombinant Human Platelet Derived Growth Factor-BB
- 4 306. Philadelphia (PA): University of Pennsylvania School of Dental Medicine; 2008.
307. Dissertation for MS degree, Philadelphia (PA): University of Pennsylvania School of Dental Medicine 208.
142. Karring T, Lang NP, Løe H: The role of gingival connective tissue in determining epithelial differentiation, *J Periodontol Res* 10:1, 1975.
143. Ko JS, Bernard GW: Osteoclast formation in vitro from bone marrow mononuclear cells in osteoclast-free bone, *Am J Anat* 161:415, 1981.
144. Kobayashi K, Rose GG: Ultrastructural histochemistry of the dento-epithelial junction. II. Colloidal thorium and ruthenium red, *J Periodontol Res* 13:164, 1978.
145. Kobayashi K, Rose GG: Ultrastructural histochemistry of the dento-epithelial junction. III. Chloramine T-silver methenamine, *J Periodontol Res* 14:123, 1979.
146. Kronfeld R: Histologic study of the influence of function on the human periodontal membrane, *J Am Dent Assoc* 18:1242, 1931.
147. Kronfeld R: The biology of cementum, *J Am Dent Assoc* 25:1451, 1938.
148. Kronfeld R: *Histopathology of the teeth and their surrounding structures*, Philadelphia, 1939, Lea & Febiger.
149. Kurahashi Y, Takuma S: Electron microscopy of human gingival epithelium, *Bull Tokyo Dent Coll* 3:29, 1962.
150. Lange D, Camelleri GE: Cytochemical demonstration of lysosomes in exfoliated epithelial cells of the gingival cuff, *J Dent Res* 46:625, 1967.
151. Larjava H, Häkkinen L, Rahemtulla F: A biochemical analysis of human periodontal tissue proteoglycans, *Biochem J* 284:267, 1992.
152. Laurell L, Rylander H, Sundin Y: Histologic characteristics of clinically healthy gingiva in adolescents, *Scand J Dent Res* 95:456, 1987.
153. Lavelle CLB: Mucosal seal around endosseous dental implants, *J Oral Implantol* 9:357, 1981.
154. Leider AS, Garbarino VE: Generalized hypercementosis, *Oral Surg Oral Med Oral Pathol* 63:375, 1987.
155. Lester KS: The incorporation of epithelial cells by cementum, *J Ultrastruct Res* 27:63, 1969.
156. Listgarten MA: The ultrastructure of human gingival epithelium, *Am J Anat* 114:49, 1964.
157. Listgarten MA: Electron microscopic study of the gingivodental junction of man, *Am J Anat* 119:147, 1966.
158. Listgarten MA: Phase-contrast and electron microscopic study of the junction between reduced enamel epithelium and enamel in unerupted human teeth, *Arch Oral Biol* 11:999, 1966.
159. Listgarten MA: A light and electron microscopic study of coronal cementogenesis, *Arch Oral Biol* 13:93, 1968.
160. Listgarten MA: Changing concepts about the dento-gingival junction, *J Can Dent Assoc* 36:70, 1970.
161. Listgarten MA: Structure of surface coatings on teeth: a review, *J Periodontol* 47:139, 1976.
162. Løe H, Karring T: Mitotic activity and renewal time of the gingival epithelium of young and old rats, *J Periodontol Res* 4:18, 1969.
163. Løe H, Karring T: A quantitative analysis of the epithelium-connective tissue interface in relation to assessments of the mitotic index, *J Dent Res* 48:634, 1969.
164. Luthman J, Johansson O, Ahlström U, et al: Immunohistochemical studies of the neurochemical markers CGRP, enkephalin, galanin, gamma-MSH, NPY, PHI, proctolin, PTH, somatostatin, SP, VIP, tyrosine hydroxylase and neurofilament in nerves and cells of the human attached gingiva, *Arch Oral Biol* 33:149, 1988.
165. Mackie EJ: Osteoblasts: novel roles in orchestration of skeletal architecture, *Int J Biochem Cell Biol* 35:1301, 2003.
166. MacNeil RL, Berry JE, Strayhorn CL, et al: Expression of type I and XII collagen during development of the periodontal ligament in the mouse, *Arch Oral Biol* 43:779, 1998.
167. MacNeil RL, Thomas HF: Development of the murine periodontium. II. Role of the epithelial root sheath in formation of the periodontal attachment, *J Periodontol* 64:285, 1993.
168. Maeda T, Kannari K, Sato O, et al: Nerve terminals in human periodontal ligament as demonstrated by immunohistochemistry for neurofilament protein (NFP) and S-100 protein, *Arch Histol Cytol* 53:259, 1990.
169. Magnusson B: Mucosal changes in erupting molars in germ-free rats, *J Periodontol Res* 4:181, 1969.
170. Marchetti C, Poggi P: Lymphatic vessels in the oral cavity: different structures for the same function, *Microsc Res Tech* 56:42, 2002.
171. Matias MA, Li H, Young WG, et al: Immunohistochemical localization of fibromodulin in the periodontium during cementogenesis and root formation in the rat molar, *J Periodontol Res* 38:502, 2003.
172. Matsuo M, Takahashi K: Scanning electron microscopic observation of microvasculature in periodontium, *Microsc Res Tech* 56:3, 2002.
173. Mattos CM, Santana RB: A quantitative evaluation of the spatial maxillary anterior dentition, *J Periodontol* 79(10):1880-1885, 2008 Oct.
174. McCulloch CA: Basic considerations in periodontal wound healing to achieve regeneration, *Periodontol* 2000 1:16, 1993.
175. McCulloch CA, Lekic P, McKee MD: Role of physical forces in regulating the form and function of the periodontal ligament, *Periodontol* 2000 24:56, 2000.
176. McCulloch CA, Melcher AH: Cell density and cell generation in the periodontal ligament of mice, *Am J Anat* 167:43, 1983.
177. McKee MD, Zalzal S, Nanci A: Extracellular matrix in tooth cementum and mantle dentin: localization of osteopontin and other noncollagenous proteins, plasma proteins, and glycoconjugates by electron microscopy, *Anat Rec* 245:293, 1996.
178. McNamara TG, O'Shea D, McNamara CM, et al: The management of traumatic ankylosis during orthodontics: a case report, *J Clin Pediatr Dent* 24:265, 2000.
179. Melcher AH: Remodeling of the periodontal ligament during eruption of the rat incisor, *Arch Oral Biol* 12:1649, 1967.
180. Melcher AH: On the repair potential of periodontal tissues, *J Periodontol* 47:256, 1976.
181. Meyer J, Marwah AS, Weinmann JP: Mitotic rate of gingival epithelium in two age groups, *J Invest Dermatol* 27:237, 1956.

182. Mikola OJ, Bauer WH: "Cementicles" and fragments of cementum in the periodontal membrane, *Oral Surg Oral Med Oral Pathol* 2:1063, 1949.
183. Miller EJ: A review of biochemical studies on the genetically distinct collagens of the skeletal system, *Clin Orthop* 92:260, 1973.
- 5 184. Miller SC, Soberman A, Stahl SS: A study of the cornification of the oral mucosa of young male adults, *J Dent Res* 30:4, 1951.
185. Morgan PR, Leigh IM, Purkis PE, et al: Site variation in keratin expression in human oral epithelia: an immunocytochemical study of individual keratins, *Epithelia* 1:31, 1987.
186. Moss ML: Phylogeny and comparative anatomy of oral ectodermal-ectomesenchymal inductive interactions, *J Dent Res* 48:732, 1969.
187. Mühlemann HR: The determination of tooth rotation centers, *Oral Surg* 7:392, 1954.
188. Mühlemann HR, Zander HA, Halberg F: Mitotic activity in the periodontal tissues of the rat molar, *J Dent Res* 33:459, 1954.
189. Mullally BH, Blakely D, Burden DJ: Ankylosis: an orthodontic problem with a restorative solution, *Br Dent J* 179:426, 1995.
190. Murrell EF, Yen EH, Johnson RB: Vascular changes in the periodontal ligament after removal of orthodontic forces, *Am J Orthod Dentofac Orthop* 110:280, 1996.
191. Ness KH, Morton TH, Dale BA: Identification of Merkel cells in oral epithelium using antikeratin and antineuroendocrine monoclonal antibodies, *J Dent Res* 66:1154, 1987.
192. Nihei I: A study on the hardness of human teeth, *J Osaka Univ Dent Soc* 4:1, 1959.
193. Noyes FB, Schour I, Noyes HJ: *A textbook of dental histology and embryology*, ed 5, Philadelphia, 1938, Lea & Febiger.
194. Nuki K, Hock J: The organisation of the gingival vasculature, *J Periodontol Res* 9:305, 1974.
- 6 195. Ogasawara T, Yoshimine Y, Kiyoshima T, et al: In situ expression of RANKL, RANK, osteoprotegerin and cytokines in osteoclasts of rat periodontal tissue, *J Periodontol Res* 39:42, 2004.
196. Oliver RC, Holm-Pederen P, Loe H: The correlation between clinical scoring, exudate measurements and microscopic evaluation of inflammation in the gingiva, *J Periodontol* 40:201, 1969.
197. Oppenheim A: Human tissue response to orthodontic intervention of short and long duration, *Am J Orthodont Oral Surg* 28:263, 1942.
198. Orban B: Tissue changes in traumatic occlusion, *J Am Dent Assoc* 15:2090, 1928.
199. Orban B, Kohler J: Die physiologische Zahn-fleischtasche, Epithelansatz und Epitheltiefenwucherung, *Z Stomatol* 22:353, 1924.
200. Orwoll ES: Toward an expanded understanding of the role of the periosteum in skeletal health, *J Bone Miner Res* 18:949, 2003.
201. Otero RL, Parodi RJ, Ubios AM, et al: Histologic and histometric study of bone resorption after tooth movement in rats, *J Periodontol Res* 8:327, 1973.
202. Page RC, Ammons WF, Schectman LR, et al: Collagen fibre bundles of the normal marginal gingiva in the marmoset, *Arch Oral Biol* 19:1039, 1972.
203. Papic M, Glickman I: Keratinization of the human gingiva in the menstrual cycle and menopause, *Oral Surg Oral Med Oral Pathol* 3:504, 1950.
204. Parfitt GJ: An investigation of the normal variations in alveolar bone trabeculation, *Oral Surg Oral Med Oral Pathol* 15:1453, 1962.
205. Parodi RJ, Ubios AM, Mayo J, et al: Total body irradiation effects on the bone resorption mechanism in rats subjected to orthodontic movement, *J Oral Pathol* 2:1, 1973.
206. Person P, Felton J, Fine A: Biochemical and histochemical studies of aerobic oxidative metabolism of oral tissues. 3. Specific metabolic activities of enzymatically separated gingival epithelium and connective tissue components, *J Dent Res* 44:91, 1965.
207. Picton DC, Davies WI: Dimensional changes in the periodontal membrane of monkeys (*Macaca irus*) due to horizontal thrusts applied to the teeth, *Arch Oral Biol* 12:1635, 1967.
208. Pihlstrom BL, Ramfjord SP: Periodontal effect of nonfunction in monkeys, *J Periodontol* 42:748, 1971.
209. Pöllänen MT, Salonen JL, Uitto VJ: Structure and function of the tooth-epithelial interface in health and disease, *Periodontol* 2000 31:12, 2003.
210. Raisz LG, Rodan GA: Cellular basis for bone turnover. In Avioli LV, Krane SM, editors: *Metabolic bone disease and clinical related disorders*, Philadelphia, 1990, Saunders.
211. Rao LG, Wang HM, Kalliecharan R, et al: Specific immunohistochemical localization of type I collagen in porcine periodontal tissues using the peroxidase-labelled antibody technique, *Histochem J* 11:73, 1979.
212. Reeve CM, Wentz FM: The prevalence, morphology and distribution of epithelial rests in the human periodontal ligament, *Oral Surg Oral Med Oral Pathol* 15:785, 1962.
213. Rippin JW: Collagen turnover in the periodontal ligament under normal and altered functional forces. II. Adult rat molars, *J Periodontol Res* 13:149, 1978.
214. Ritchey B, Orban B: The crests of the interdental alveolar septa, *J Periodontol* 24:75, 1953.
215. Roberts WE, Chamberlain JG: Scanning electron microscopy of the cellular elements of rat periodontal ligament, *Arch Oral Biol* 23:587, 1978.
216. Romaniuk K: Some observations of the fine structure of human cementum, *J Dent Res* 46:152, 1967.
217. Romanos G, Schroter-Kermani C, Hinz N, et al: Immunohistochemical distribution of the collagen types IV, V and VI and glycoprotein laminin in the healthy rat, marmoset (*Callithrix jacchus*) and human gingivae, *Matrix* 11:125, 1991.
218. Romanos GE, Bernimoulin JP: Collagen as a basic element of the periodontium: immunohistochemical aspects in the human and animal. 1. Gingiva and alveolar bone, *Parodontologie* 4:363, 1990.
219. Romanos GE, Schroter-Kermani C, Bernimoulin J-P: Das Kollagen als Basis-element des Parodonts: Immunohistochemische Aspekte beim Menschen und bei Tieren, *Parodontologie* 1:47, 1991.
220. Romanos GE, Schroter-Kermani C, Hinz N, et al: Immunohistochemical localization of collagenous components in healthy periodontal tissues of the rat and marmoset (*Callithrix jacchus*). I. Distribution of collagens type I and III, *J Periodontol Res* 27:101, 1992.
221. Rosenberg HM, Massler M: Gingival stippling in young adult males, *J Periodontol* 38:473, 1967.
222. Rudolph CE: An evaluation of root resorption occurring during orthodontic treatment, *J Dent Res* 19:367, 1940.
223. Rushton MA: The dental tissues in osteitis deformans, *Guy's Hosp Rep* 88:163, 1938.

224. Saffar JL, Lasfargues JJ, Cherruau M: Alveolar bone and the alveolar process: the socket that is never stable, *Periodontol* 2000 13:76, 1997.
225. Saito M, Narayana AS: Signaling reactions induced in human fibroblasts during adhesion to cementum-derived attachment protein, *J Bone Miner Res* 14:65, 1999.
226. Salonen JI: Proliferative potential of the attached cells of human junctional epithelium, *J Periodontol Res* 29:41, 1994.
227. Salonen JI, Pöllänen MT: Junctional epithelial cells directly attached to the tooth, *Acta Med Dent Helv* 2:137, 1997.
228. Sawada T, Yamamoto T, Yanagisawa T, et al: Electron-immunocytochemistry of laminin and type-IV collagen in the junctional epithelium of rat molar gingiva, *J Periodontol Res* 25:372, 1990.
229. Sawaf MH, Ouhayoun JP, Forest N: Cytokeratin profiles in oral epithelial: a review and a new classification, *J Biol Buccale* 19:187, 1991.
230. Saygin NE, Giannobile WV, Somerman MJ: Molecular and cell biology of cementum, *Periodontol* 2000 24:73, 2000.
231. Schor SL, Ellis I, Irwin CR, et al: Subpopulations of fetal-like gingival fibroblasts: characterisation and potential significance for wound healing and the progression of periodontal disease, *Oral Dis* 2:155, 1996.
232. Schroeder H: *Oral structural biology*, New York, 1991, Time Medical Publishers.
233. Schroeder HE: Melanin containing organelles in cells of the human gingiva, *J Periodontol Res* 4:1, 1969.
234. Schroeder HE: Ultrastructure of the junctional epithelium of the human gingiva, *Helv Odontol Acta* 13:65, 1969.
235. Schroeder HE: Transmigration and infiltration of leucocytes in human junctional epithelium, *Helv Odontol Acta* 17:6, 1973.
236. Schroeder HE: *Differentiation of human oral stratified epithelia*, New York, 1981, Karger.
237. Schroeder HE: Gingiva. In Oksche A, Vollrath L, editors: *The periodontium handbook of microscopic anatomy*, vol. 5, Berlin, 1986, Springer-Verlag.
238. Schroeder HE: *The periodontium*, Berlin, 1986, Springer-Verlag.
239. Schroeder HE, Listgarten MA: Fine structure of the developing epithelial attachment of human teeth. In *Monographs in developmental biology*, vol 2, Basel, 1971, Karger.
240. Schroeder HE, Listgarten MA: The gingival tissues: the architecture of periodontal protection, *Periodontol* 2000 13:91, 1997.
241. Schroeder HE, Theilade J: Electron microscopy of normal human gingival epithelium, *J Periodontol Res* 1:95, 1966.
242. Schultz-Hautt SD, From S: Dynamics of periodontal tissues. I. The epithelium, *Odont T* 69:431, 1961.
243. Schultz-Hautt SD, Paus S, Assev S: Periodic acid-Schiff reactive components of human gingiva, *J Dent Res* 40:141, 1961.
244. Schweitzer G: Lymph vessels of the gingiva and teeth, *Arch Mik Anat Ent* 69:807, 1907.
245. Schwint AE, Itoiz ME, Cabrini RL: A quantitative histochemical technique for the study of vascularization in tissue sections using horseradish peroxidase, *Histochem J* 16:907, 1984.
246. Selvig KA: The fine structure of human cementum, *Acta Odontol Scand* 23:423, 1965.
247. Sena K, Morotome Y, Baba O, et al: Gene expression of growth differentiation factors in the developing periodontium of rat molars, *J Dent Res* 82:166, 2003.
248. Seymour GJ, Crouch MS, Powell RN, et al: The identification of lymphoid cell subpopulations in sections of human lymphoid tissue and gingivitis in children using monoclonal antibodies, *J Periodontol Res* 17:247, 1982.
249. Shackelford JM: The indifferent fiber plexus and its relationship to principal fibers of the periodontium, *Am J Anat* 131:427, 1971.
250. Shapiro S, Ulmansky M, Scheuer M: Mast cell population in gingiva affected by chronic destructive periodontal disease, *J Periodontol* 40:276, 1969.
251. Shelton LE, Hall WB: Human gingival mast cells, *J Periodontol Res* 3:214, 1968.
252. Shimada Y, Tai H, Tanaka A, Ikezawa-Suzuki I, Takagi K, Yoshida Y, Yoshie H: Effects of ascorbic acid on gingival melanin pigmentation in vitro and in vivo, *J Periodontol* 80(2):317-323, 2009 Feb.
253. Sicher H, DuBrul EL: *Oral anatomy*, ed 6, St Louis, 1975, Mosby.
254. Simpson HE: The degeneration of the rest of malassez with age as observed by the apoxestic technique, *J Periodontol* 36:288, 1965.
255. Skougard MR, Beagrie GS: The renewal of gingival epithelium in marmosets (*Callithrix jacchus*) as determined through autoradiography with thymidine-H3, *Acta Odontol Scand* 20:467, 1962.
256. Sodek J: A comparison of the rates of synthesis and turnover of collagen and non-collagen proteins in adult rat periodontal tissues and skin using a microassay, *Arch Oral Biol* 22:655, 1977.
257. Sodek J, McKee MD: Molecular and cellular biology of alveolar bone, *Periodontol* 2000 24:99, 2000.
258. Squier CA, Waterhouse JP: The ultrastructure of the melanocyte in human gingival epithelium, *J Dent Res* 46:113, 1967.
259. Stein TJ, Corcoran JF: Anatomy of the root apex and its histologic changes with age, *Oral Surg, Oral Med Oral Pathol* 69:238, 1990.
260. Stern IB: Electron microscopic observations of oral epithelium. I. Basal cells and the basement membrane, *Periodontics* 3:224, 1965.
261. Stern IB: The fine structure of the ameloblast-enamel junction in rat incisors, epithelial attachment and cuticular membrane. Presented at 5th International Congress for Electron Microscopy, 1966, p 6.
262. Stern IB: Further electron microscopic observations of the epithelial attachment, International Association for Dental Research Abstracts, 45th general meeting, 1967, p 118.
263. Susi F: Histochemical, autoradiographic and electron microscopic studies of keratinization in oral mucosa, Tufts University, 1967 (PhD thesis).
264. Swift JA, Saxton CA: The ultrastructural location of the periodate-Schiff reactive basement membrane of the dermo-epidermal junctions of human scalp and monkey gingiva, *J Ultrastruct Res* 17:23, 1967.
265. Tadokoro O, Maeda T, Heyeraas KJ, et al: Merkel-like cells in Malassez epithelium in the periodontal ligament of cats: an immunohistochemical, confocal-laser scanning and immuno electron-microscopic investigation, *J Periodontol Res* 37:456, 2002.
266. Ten Cate AR: The histochemical demonstration of specific oxidative enzymes and glycogen in the epithelial cell rests of Malassez, *Arch Oral Biol* 10:207, 1965.

267. Ten Cate AR: The development of the periodontium. In Melcher AH, Bowen WH, editors: *Biology of the periodontium*, New York, 1969, Academic Press.
268. Ten Cate AR: Formation of supporting bone in association with periodontal ligament organization in the mouse, *Arch Oral Biol* 20:137, 1975.
269. Ten Cate AR: Hard tissue formation and destruction. In Ten Cate AR, editor: *Oral histology: development, structure, and function*, ed 4, St Louis, 1994, Mosby.
270. Ten Cate AR, Deporter DA: The degradative role of the fibroblast in the remodeling and turnover of collagen in soft connective tissue, *Anat Rec* 182:1, 1975.
271. Ten Cate AR, Mills C, Solomon G: The development of the periodontium: a transplantation and autoradiographic study, *Anat Rec* 170:365, 1971.
272. Thilander H: Permeability of the gingival pocket epithelium, *Int Dent J* 14:416, 1964.
273. Thilander H, Bloom GD: Cell contacts in oral epithelia, *J Periodontol Res* 3:96, 1968.
274. Thoma KH, Sosman MC, Bennett GA: An unusual case of hereditary fibrous osteodystrophy (fragilitas ossium) with replacement of dentine by osteocementum, *Am J Orthodont Oral Surg* 29:1, 1943.
275. Thomas HF: Root formation, *Int J Dev Biol* 39:231, 1995.
276. Thomas HF, Kollar EJ: Tissue interactions in normal murine root development. In Davidovitch Z, editor: *The biological mechanisms of tooth eruption and root resorption*, Birmingham, 1988, EBSCO Media.
277. Thonard JC, Scherp HW: Histochemical demonstration of acid mucopolysaccharides in human gingival epithelial intercellular spaces, *Arch Oral Biol* 7:125, 1962.
278. Trott JR: An investigation into the glycogen content of the gingivae, *Dent Pract* 7:234, 1957.
279. Trott JR, Gorenstein SL: Mitotic rates in the oral and gingival epithelium of the rat, *Arch Oral Biol* 8:425, 1963.
280. Trowbridge HO, Shibata F: Mitotic activity in epithelial rests of Malassez, *Periodontics* 5:109, 1967.
281. Turesky S, Glickman I, Litwin T: A histochemical evaluation of normal and inflamed human gingivae, *J Dent Res* 30:792, 1951.
282. Ubios AM, Cabrini RL: Tritiated thymidine uptake in periodontal tissue subject to orthodontic movement, *J Dent Res* 50:1160, 1971.
283. Vaes G: Cellular biology and biochemical mechanism of bone resorption: a review of recent developments on the formation, activation, and mode of action of osteoclasts, *Clin Orthop* 231:239, 1988.
284. Valderhaug JP, Nylen MU: Function of epithelial rests as suggested by their ultrastructure, *J Periodontol Res* 1:69, 1966.
285. Valderhaug JP, Zander H: Relationship of "epithelial rests of Malassez" to other periodontal structures, *Periodontics* 5:254, 1967.
286. Vandevska-Radunovic V, Kvinnsland IH, Kvinnsland S, et al: Immunocompetent cells in rat periodontal ligament and their recruitment incident to experimental orthodontic tooth movement, *Eur J Oral Sci* 105:36, 1997.
287. Warren EB, Hansen NM, Swartz ML, et al: Effects of periodontal disease and of calculus solvents on microhardness of cementum, *J Periodontol* 35:505, 1964.
288. Watanabe T, Kubota T: Characterization of fibromodulin isolated from bovine periodontal ligament, *J Periodontol Res* 33:1, 1998.
289. Waterhouse JP: The gingival part of the human periodontium, its ultrastructure and the distribution in it of acid phosphatase in relation to cell attachment and the lysosome concept, *Dent Pract Dent Rec* 15:409, 1965.
290. Weinmann JP, Meyer J: Types of keratinization in the human gingiva, *J Invest Dermatol* 32:87, 1959.
291. Weinmann JP, Sicher H: *Bone and bones: fundamentals of bone biology*, ed 2, St Louis, 1955, Mosby.
292. Weinstock A, Albright JT: Electron microscopic observations on specialized structures in the epithelium of the normal human palate, *J Dent Res* 45:79, 1966.
293. Weinstock A, Albright JT: The fine structure of mast cells in normal human gingiva, *J Ultrastruct Res* 17:245, 1967.
294. Weski O: Die chronische marginale Entzündungen des Alveolarfortsatzes mit besonderer Berücksichtigung der Alveolarpyorrhoe, *Vierteljahrsschr Zahnheilk* 38:1, 1922.
295. Wood NK, Goaz PW: *Differential diagnosis of oral lesions*, ed 2, St Louis, 1984, Mosby.
296. Woodnutt DA, Wager-Miller J, O'Neill PC, et al: Neurotrophin receptors and nerve growth factor are differentially expressed in adjacent nonneuronal cells of normal and injured tooth pulp, *Cell Tissue Res* 299:225, 2000.
297. Worapamorn W, Li H, Pujic Z, et al: Expression and distribution of cell-surface proteoglycans in the normal Lewis rat molar periodontium, *J Periodontol Res* 35:214, 2000.
298. Yamamoto T, Domon T, Takahashi S, et al: The fibrillar structure of cement lines on resorbed root surfaces of human teeth, *J Periodontol Res* 35:208, 2000.
299. Yamamoto T, Domon T, Takahashi S, et al: The fibrous structure of the cemento-dentinal junction in human molars shown by scanning electron microscopy combined with NaOH-maceration, *J Periodontol Res* 35:59, 2000.
300. Yamamoto T, Wakita M: Bundle formation of principal fibers in rat molars, *J Periodontol Res* 27:20, 1992.
301. Yamasaki A, Nikai H, Niitani K, et al: Ultrastructure of the junctional epithelium of germ-free rat gingiva, *J Periodontol* 50:641, 1979.
302. Zander HA: The distribution of phosphatase in gingival tissue, *J Dent Res* 20:347, 1941.
303. Zander HA, Hurzeler B: Continuous cementum apposition, *J Dent Res* 37:1035, 1958.
304. Zipkin J: The inorganic composition of bones and teeth. In Schraer H, editor: *Biological calcification*, New York, 1970, Appleton-Century-Crofts.
305. Zwarych PD, Quigley MB: The international plexus of the periodontal ligament history and further observations, *J Dent Res* 44:383, 1965.

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