

Update on the Etiology of Tooth Resorption in Domestic Cats

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Feline odontoclastic resorptive lesions (FORL) were first recognized and histologically differentiated from caries in the 1920s [1,2]. Some anecdotal reports describing caries-like lesions at the cervical region of feline teeth followed in the 1950s and 1960s, until two microscopic studies in the 1970s again revealed that FORL were not caries but a type of tooth resorption [3,4]. A recent study showed that cats with FORL have a significantly lower urine specific gravity and significantly higher serum concentration of 25-hydroxyvitamin D (25OHD) compared with cats without FORL [5], indicating that multiple tooth resorption in domestic cats could be the manifestation of some systemic insult rather than a local cause. In this article, the histologic and radiographic appearance of FORL and certain other peculiarities of feline teeth are reviewed. An attempt is then made to compare these findings with changes of the periodontium induced by administration of excess vitamin D or vitamin D metabolites in experimental animals.

Histologic and radiographic features of feline odontoclastic resorptive lesions

Tooth resorption is caused by *odontoclasts*. Their precursors derive from hematopoietic stem cells of bone marrow or spleen and migrate from blood vessels of the alveolar bone or periodontal ligament toward the external root

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surface, where mononuclear cells fuse with other cells to become multinucleated mature odontoclasts [6,7]. One important fact to understand is that FORL develop anywhere on the root surface and not just close to the cementoenamel junction [8]. Resorption of enamel as the initial event is only rarely observed [9]. Resorption may also start on the same tooth at various root surfaces simultaneously, progressing from cementum coronally into crown dentin as well as apically into root dentin. As the resorption progresses into crown dentin, the enamel often becomes undermined and a pink discoloration may be observed at the crown surface [10].

FORL that emerge at the gingival margin were originally referred to as *neck lesions* (Fig. 1) [4]. Exposure to periodontal inflammation, which is caused and maintained by bacterial infection, results in the formation of highly vascular and inflamed granulation tissue [11–16]. These defects may be painful and bleed easily when probed with a dental instrument [10]. One characteristic feature of *inflammatory root resorption* is that the alveolar bone adjacent to the tooth defect is also resorbed [17]. Such root lesions have been categorized as *type I root lesions* if unaffected root areas are surrounded by a radiographically visible periodontal space (Fig. 2) [18]. Although pulp involvement may be seen in advanced stages of FORL [19,20], the cervical root resorption in human beings typically proceeds laterally and in an apical and coronal direction, surrounding a thin shell of dentin and predentin, and envelops the root canal, leaving an apple core appearance of the cervical area of the tooth [21].

It has been demonstrated in several studies in human beings that superficial external resorption is common and usually self-limiting [22]. Spontaneously repaired defects of cementum and superficial dentin are called *surface resorptions*, in which the anatomic contour of the root surface is restored [17]. Most clinically evident FORL appear histologically to be in resorptive and reparative phases simultaneously [14]. Although attempts at repair can be noted by production of bone, cellular cementum, and bone-cementum [12–14,19,20,23], tooth resorption in cats is usually progressive



Fig. 1. Classic “neck lesions” at the right lower third (*) and fourth premolar teeth (arrowheads).



Fig. 2. Radiograph of teeth in Fig. 1; note that inflammatory root resorption is associated with adjacent alveolar bone resorption (*dotted line* outlining the alveolar margin).

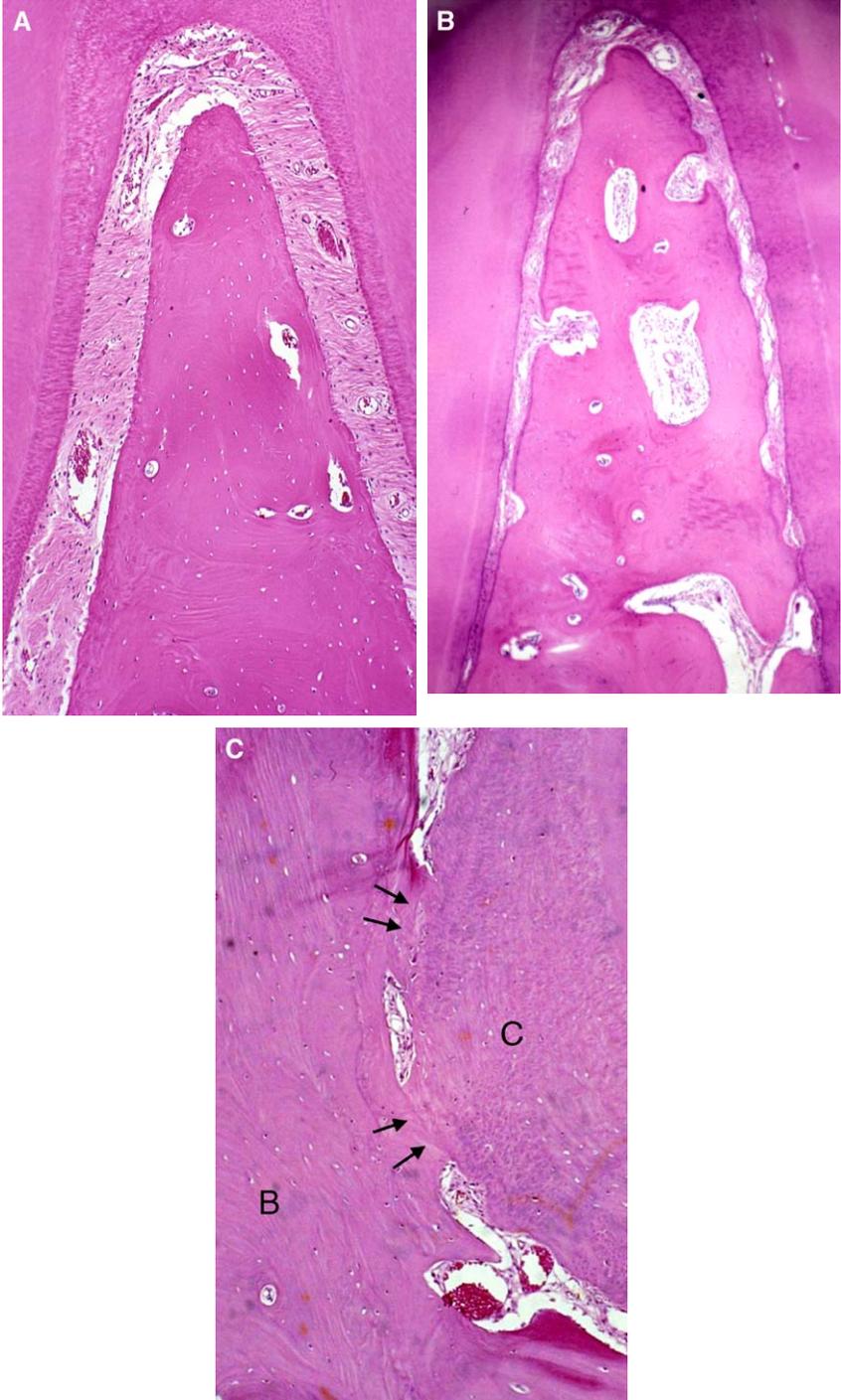
and continues until the roots are completely resorbed or the crown breaks off, leaving root remnants behind [10].

Most previous research focused on FORL emerging at the gingival margin. The commonly observed fusion of roots of feline teeth with alveolar bone (*dentoalveolar ankylosis*) has not received the same investigative attention. It has previously been reported that the periodontal space is quite narrow in mandibular premolars and molars of adult cats [24]. In a recent histologic study, clinically and radiographically healthy teeth from cats with FORL on other teeth were evaluated. These apparently “healthy” teeth showed hyperemia, edema, and degeneration of the periodontal ligament, with marked fiber disorientation, increased osteoid formation along alveolar bone surfaces (*hyperostoidosis*), gradual narrowing of the periodontal space, and areas of ankylotic fusion between the tooth and alveolar bone (Fig. 3) [25]. These findings demonstrate events that occur before resorption and suggest that the early FORL may be noninflammatory in nature [25]. Ankylosed roots are at risk of being incorporated into the normal process of bone remodeling, and the tooth substance is gradually resorbed and replaced by bone (*replacement resorption*) (Fig. 4) [10]. Ankylosed roots and those with replacement resorption have been categorized radiographically as *type II root lesions* [18].

Peculiarities of feline permanent teeth

It has previously been suggested that there is a need for further microscopic research to differentiate histopathologic findings of FORL from normal anatomy of feline teeth [26]. Several peculiarities can be noted in permanent teeth of cats that could represent separate pathologic entities or be associated with FORL.

Cementum is an avascular bone-like tissue covering the roots of mammalian teeth. It normally covers the cervical root surface as a thin



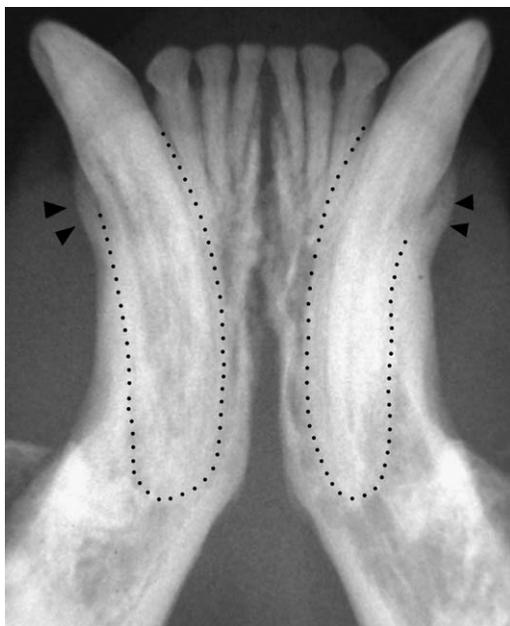


Fig. 4. Radiograph of dentoalveolar ankylosis and root replacement resorption of mandibular canine teeth (*dotted line* outlining original root contour); also note the bulbous enlargement of crestal alveolar bone (*arrowheads*).

layer that gradually becomes wider apically. Two types of cementum (acellular and cellular) are usually recognized, which can be further subdivided depending on the presence and origin of collagen fibers (afibrillar, intrinsic, or extrinsic). Cementum formation beyond physiologic deposition is called *hypercementosis* and can commonly be observed in teeth of cats with FORL [12]. In one study, hypercementosis was demonstrated in all investigated feline teeth [14]. Excessive amounts of cellular cementum are deposited particularly at apical and midroot surfaces, sometimes causing bulbous root apices (Fig. 5), whereas an abnormal thickening of acellular cementum can be found on cervical root surfaces (Fig. 6) [25]. In other species, hypercementosis has been observed in unerupted, hypofunctional, and extruding teeth without opposing antagonists [27–30] and in certain conditions, such as hyperthyroidism [31], hyperpituitarism [32–34], Paget's

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Fig. 3. Histopathologic pictures of a feline premolar tooth with a normal furcation area (*A*) and a premolar tooth of a cat with feline odontoclastic resorptive lesions on other teeth showing degeneration of the periodontal ligament, narrowing of the periodontal space, and dentoalveolar ankylosis (*B*). Close-up of apical area of tooth root showing periodontal ligament degeneration and two areas of ankylotic fusion (*arrows*) between cementum (*C*) and alveolar bone (*B*).



Fig. 5. Radiograph showing bulbous root apices of the right lower fourth premolar and first molar in a cat; note the missing third premolar tooth (*).

disease [35–37], and vitamin A deficiency [38,39]. It has also been demonstrated that occlusal trauma does *not* lead to hypercementosis [40,41].

Some cats seem to exhibit abnormal extrusion of teeth, referred to as *supereruption* [10]. Supereruption is most commonly observed in maxillary

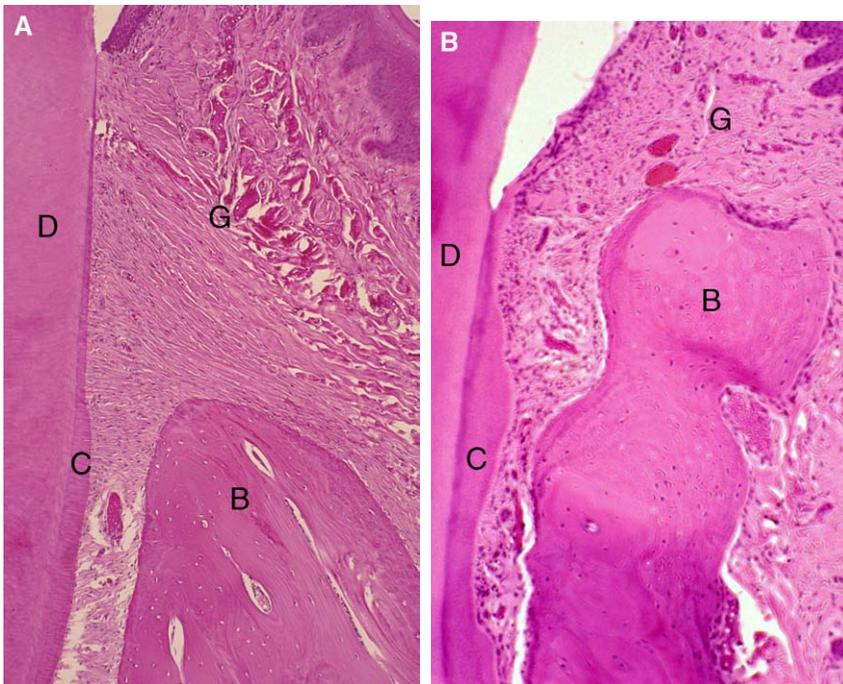


Fig. 6. Histopathologic pictures of a premolar in a cat with thin cervical cementum and normal biologic width (A) and a premolar of a cat with feline odontoclastic resorptive lesions on other teeth showing cervical hypercementosis, bulbous enlargement of crestal alveolar bone, and loss of biologic width (B). B, alveolar bone; C, cementum; D, dentin; G, gingival connective tissue.

canine teeth, leading to exposure of the root surface (Fig. 7). Normally, active eruption of brachyodont teeth does not cease when they meet their opposing teeth but continues throughout life; ideally, the rate of eruption keeps pace with tooth wear, preserving the vertical dimension of the dentition [42]. It has been speculated that supereruption in cats may be the result of hypercementosis [43] or increased osteoblastic activity of periapical alveolar bone [44]. Another peculiarity found in cats is a distinct thickening of bone along the alveolar margin or the surfaces of the alveolar plates, alone or in combination with supereruption. This *alveolar bone expansion* is commonly seen in maxillary canine teeth but occurs with less intensity around other teeth as well (Fig. 8) [10]. In human beings, a similar condition is called “peripheral buttressing” and is believed to be a result of the body’s attempt to compensate for lost bone during the reparative process associated with trauma from occlusion. The condition may present as shelf-like thickening of the alveolar margin, referred to as “lipping”, or as a pronounced bulge in the contour of the alveolar bone [45].

Unusual dentin formation has been described in feline teeth. In one study, *osteodentin* could be demonstrated in most feline premolars and molars, particularly in furcation areas of root dentin close to the root canal [13]. In osteodentin, cellular inclusions (remnants of odontoblasts) can be found between randomly running dentinal tubules. FORL were observed in areas of the tooth in which osteodentin was most typically found [13]. *Vasodentin* was found in 3 of 10 control teeth and in 6 of 49 teeth with FORL and was most often observed in the outer third of circumpulpal dentin [46]. In vasodentin, dentinal tubules run randomly, with penetration of canals that may contain vascular-like tissue. Another study found vasodentin almost equally in teeth with or without FORL, although the

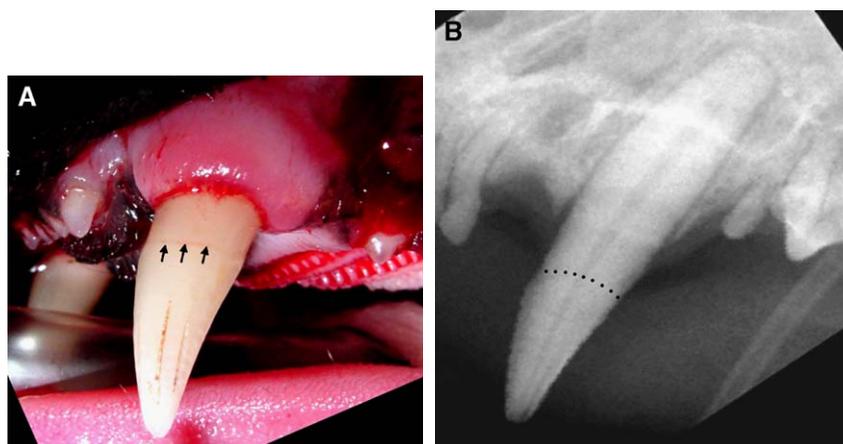


Fig. 7. Clinical picture (A) and radiograph (B) of the left upper canine tooth showing supereruption (arrows and dotted line outlining the cemento-enamel junction).

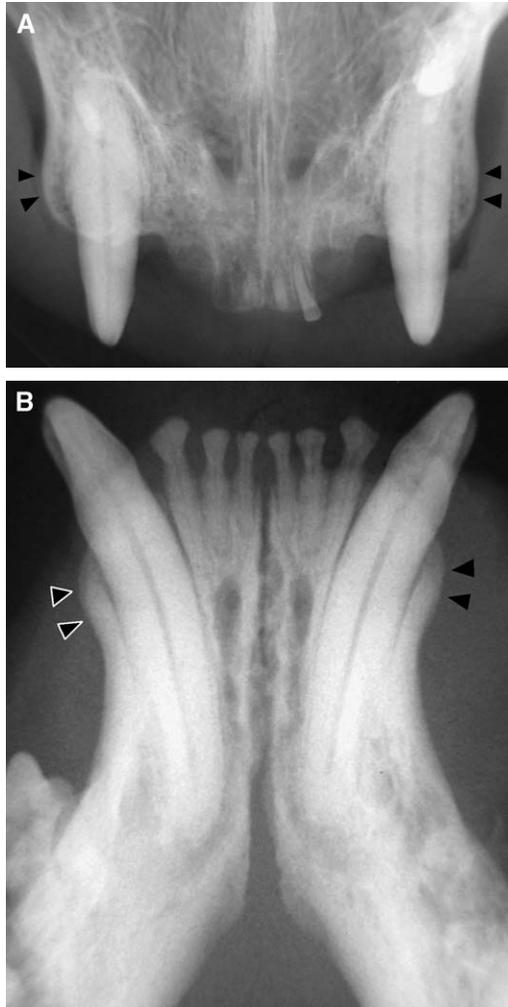


Fig. 8. Radiographs of alveolar bone expansion (*arrowheads*) of upper (*A*) and lower canine teeth (*B*) in cats with missing teeth and feline odontoclastic resorptive lesions on other teeth.

locations of vasodentin and FORL differed [13]. Furcation canals connecting the pulp chamber and the periodontal ligament were found in deciduous premolar teeth in kittens as well as in teeth of adult cats [47,48]. After experimental pulp injury, changes in the periodontal ligament at the opening of the furcation canal and resorption of dental tissues and alveolar bone in the furcation area took place [48]. In a more recent study, patent furcation canals were found in 27% of permanent carnassial teeth in adult cats [49].

Irregularities in dentin formation are generally considered to be evidence of deficient mineralization during dentinogenesis [50]. The inclusion of

odontoblasts or pulp tissue into dentin may also be attributable to times of rapid mineralization of newly formed dentin matrix, however. This view is supported by the observation that the layer of predentin appeared extremely thin or was not present in teeth of cats with FORL [51].

Increased vitamin D activity in cats with feline odontoclastic resorptive lesions

Although FORL may have occurred more than 800 years ago [52], retrospective studies of zoologic collections of feline skulls showed a low prevalence of FORL before the 1960s [53,54]. It was suggested that the increased prevalence of FORL might be associated with aspects of domestication, such as altered feeding practices, vaccination, and neutering programs [10].

Unlike bone that undergoes resorption and apposition as part of a continual remodeling process, the roots of permanent teeth are normally not resorbed because of resorption-inhibiting characteristics of unmineralized layers on external and internal root surfaces (eg, periodontal ligament, cementoblasts and cementoid, odontoblasts and predentin) [10,17]. Odontoclasts may be attracted only to, or can attach only to, mineralized tissue. It has been postulated that removal or mineralization of the organic matrix of the root covering would make it possible for odontoclasts to recognize the mineral component [10,17].

Measurement of biochemical markers of bone turnover, bone alkaline phosphatase (BAP) and deoxypyridinoline (DPD), did not show significant differences between cats with and without FORL [55]. It has recently been demonstrated that cats with FORL expressed a significantly higher mean serum concentration of 25OHD compared with cats without FORL, however [5]. Furthermore, the mean serum concentrations of blood urea nitrogen and phosphorus were significantly higher and the mean urine specific gravity and mean calcium-phosphorus ratio were significantly lower in cats with FORL compared with cats without FORL [5]. Although the mean values of renal parameters remained within physiologic range, the results suggest the possibility of gradual impairment of renal function in cats with FORL. Using a human radioimmunoassay not yet validated for use in cats, calcitonin was significantly more often detected in blood sera of cats with FORL, which may be an expression of protective secretion during times of transient mild hypercalcemia [5]. It was also demonstrated that cats with FORL vomited significantly more often than cats without FORL [5,56].

The diet represents the only source of vitamin D in cats because they are unable to produce vitamin D in the skin [57]. Based on feeding studies in the 1950s, the National Research Council proposed a minimum vitamin D requirement for growing kittens of 500 IU/kg of dietary dry matter [58]. Later studies demonstrated that kittens given a diet with vitamin D₃ per kilogram of dry matter at a rate of 250 or 125 IU did not show clinical signs

Table 1
Changes in dental and periodontal tissues of experimental animals receiving excess vitamin D or vitamin D metabolites

Reference no.	Species	Age/weight at start of experiment	Type of vitamin D	Dose	Route of administration	Additional methods	Diagnostic tools
[103]	Rats	127–182 g	Vit D (nfd)	307,000–1,860,000 IU (once); killed after 48 h	SC	n/a	H
[108]	Dogs	39 d	irrad D2 or D3	10,000 IU/kg BW × 9.5 mo	Food	Some dogs also given excess vit A	R + H
[109,119]	Dogs	29 or 34 d	irrad D2	450,000 IU (once); killed at 2.5, 4, or 9 mo of age	PO	n/a	R + H
[110,114]	Dogs	2 mo	D2 or D3	10,000 IU/kg BW/d × 6 mo (intermittently) (total 1,270,000 and 1,450,000 IU); killed after additional 5 mo of "recovery period"	Food	n/a	R + H
[105]	Rats	21 d (~100 g)	D2	500,000 IU (once); killed after 6 d	P	n/a	R + H (I + M)
[97]	Rats	40–50 g	D2	100,000 IU on 1st, 4th, 7th, 10th, and 14th d; killed on 15th d	IP	Some rats also given a collagen-damaging lathyrogen	H (M)
[121]	Rats	50–150 g	D2	50,000–200,000 IU × 2–4/wk; sacrifice after 1–12 wk	PO	n/a	H (LM + EM)
[111]	Rats	154 g	D2	1.25 mio IU/kg of diet × 6 wk	Food	n/a	H (M)
[112]	Hamsters	4 mo	D2	5,000 IU twice/wk × 8 wk	IP	n/a	H (M)
[102]	Pigs	5 d	D3	45,000–162,000 IU/d × 17–48 d	PO	n/a	H

Pulp/dentin	Cementum	Periodontal ligament	Gingival connective tissue	Alveolar bone	Comments
Calciotraumatic line on inner edge of dentin, followed by hypomineralized layer, wide hypermineralized zone, and ↓width of predentin	n/r	n/r	n/r	n/r	Formation of dentin proceeded at same rate as that of control rats but MIN was accelerated
DEG; pulp stones in permanent C + M	HC	MIN; ANK	MIN	Initial OP, followed by OS with ↓lumen of ES in younger dogs; less OS in older dogs	↓changes in dogs given vit D from tuna or halibut liver oil than irradi D2; ↓changes in dogs given excess vit A
DEG; MIN	HC; resorption	MIN	n/r	OP	n/a
Pulp stones	HC	Development of granulation tissue in furcation and interdental areas; MIN; ANK	MIN	Increased vascularity; granulation tissue formation; ↑periodontitis in dog given D3	OP was predominant
Hemorrhage, odontoblast DEG, accelerated dentin formation, MIN in M	n/r	n/r	n/r	n/r	n/a
n/r	n/r	MIN	MIN	n/r	↑changes in rats given the lathyrogen
n/r	Intracellular MIN of cementoblast-like cells; HC	DEG; MIN of fibers close to cemental surface ("sunburst" pattern)	MIN	OP followed, by HO and OS; alveolar crest raised to CEJ	n/a
n/r	HC	FD; ↓PS; MIN; ANK	MIN with 'sunburst' pattern near transeptal fibers	OP followed, by HO and OS; alveolar crest raised to CEJ; marrow spaces filled with young connective tissue	n/a
n/r	Cemental spurs	↓PS; MIN; ANK	n/r	Thinning of cortical bone and endosteal resorption, followed by HO	n/a
DEG and hyperemia; MIN; osteodentin formation	Resorption of cementum and dentin with pulp exposure	Hyperemia; MIN; ANK	n/r	OP, followed by HO	n/a

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Table 1 (continued)

Reference no.	Species	Age/weight at start of experiment	Type of vitamin D	Dose	Route of administration	Additional methods	Diagnostic tools
[101]	Rabbits	15 d (~150 g)	D3	600,000 IU/kg BW once/wk × 4 wk; killed 30, 45, or 60 d after initial injection	IM	n/a	R + H
[106]	Rats	n/r	D3	10,000 IU/d × 1–4 wk	TGT	n/a	H (I + M)
[107]	Rats	8 or 12 wk (35–271 g)	D3	200,000 IU/d (on 6 d/wk) × up to 2 mo	TGT	n/a	H (I + M)
[122]	Rats	100 g	DHT	50 µg/d × 17 d	TGT	n/a	H (M)
[123]	Rats	140–150 g	DHT	50 µg/d × 31 or 62 d	TGT	Some rats also given FD	H (M)
[120]	Rats	~220 g	DHT	50 µg/d × 50 d	TGT	n/a	H
[91]	Rats	215 g	DHT	50 µg/d × 50 d	PO	Some rats also given FD	H (M)
[98]	Rats	200 g	DHT	50 µg/d × 7–50 d	TGT	Some rats also given FD	H
[95]	Rats	~100 g	DHT	50 µg/d × 40 d	TGT	Some rats also given TS	H (M)

Pulp/dentin	Cementum	Periodontal ligament	Gingival connective tissue	Alveolar bone	Comments
n/r	n/r	FD; MIN	n/r	OP, followed by HO and OS	n/a
Pulp stones in I	HC	MIN; ANK in M	n/r	HO and OS	n/a
↓width of predentin; DEG of odontoblasts; pulp stones (primarily in I of young and older rats)	HC (most intense in apical areas of young rats); resorption of cementum and dentin in nearly all M of rat fed longest with D3	↓PS; MIN; ANK in M	n/r	OP, followed by HO and OS (predominantly in young rats); ↓lumen of ES; ↑crestal alveolar bone (predominantly in young rats)	n/a
Hyperemia, hemorrhage, and separation of odontoblasts	HC	DEG, edema, and hemorrhage; FD; MIN; ANK	n/r	HO; ↓lumen of ES; edema of bone marrow	n/a
Edema, hyperemia, hemorrhage, and reticular atrophy; pulp stones	HC; "club"-shaped root apices; resorption of cementum and dentin, particularly in furcation areas	DEG, edema, and hemorrhage; FD; ↓PS; MIN; ANK	n/r	HO; ↓lumen of ES; bulbous enlargement of alveolar plates; edematous marrow tissue	↓changes in rats given FD
n/r	HC; "club"-shaped root apices; resorption of cementum and dentin with ingrowth of connective tissue cells into resorptive defects	FD; ↓PS; MIN; ANK	MIN with 'sunburst' pattern near transeptal fibers	Rapid and progressive resorption, followed by HO and OS	n/a
n/r	HC	DEG; FD; ANK	MIN with 'sunburst' pattern near transeptal fibers	HO and OS; ↓lumen of ES; bulbous enlargement of alveolar plates	↓changes in rats given FD; most severe changes in furcation areas
n/r	HC ("club"-shaped root apices)	DEG, hyperemia, and edema; ↓PS; MIN; ANK	MIN with 'sunburst' pattern near transeptal fibers	HO and OS; bulbous enlargement of alveolar plates causing coronal displacement of transeptal fibers; hyperemia and progressive fibrosis of bone marrow	↓changes in rats given FD; most severe changes in furcation areas
Hemorrhage; pulp stones	HC	DEG, hyperemia, and edema; ↓PS; ANK	n/r	HO; ↓lumen of ES; fibrosis of bone marrow; enlargement of buccal and lingual bone at areas of muscle insertion	↓changes in rats given TS

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Table 1 (continued)

Reference no.	Species	Age/weight at start of experiment	Type of vitamin D	Dose	Route of administration	Additional methods	Diagnostic tools
[96]	Rats	~260 g	DHT	1 mg/100 g BW (once); killed after 10, 17 or 31 d	TGT	Gingival wound created 3 d after DHT was given	H (M)
[125]	Rats	40 d	DHT	50 µg/d × 50 d	TGT	n/a	H (M)
[99]	Rats	~100 g	DHT	50 mg/d × 1–7 wk	TGT	Some rats had all L max M extracted	H (M)
[117]	Rats	100 g	D2 or DHT	10,000 IU (D2)/d or 50 µg (DHT)/d × 50 d	SC (D2) or TGT (DHT)	Some rats also given TS or ED	H (M)
[116]	Rats	100 g	DHT	50 µg/d × 7–35 d	TGT	n/a	H (M)
[100]	Rats	180–220 g	DHT	50 µg/100 g BW/d × 28 d	TGT	Traumatic occlusion induced in some rats	H (M)
[118]	Rats	5 wk	DHT	50 µg/100 g BW/d × 28 d	TGT	Some rats also given SF	H (M)
[124]	Rats	140 g	DHT	50 µg/100 g BW/d × up to 20 d	TGT	n/a	
[115]	Rats	6 wk	DHT	25 or 50 µg/d × 1–4 wk	TGT	n/a	H (M)
[104]	Rats	4 wk	1,25(OH)2D3	0.075 µg/d × 5 wk	SC	n/a	H + R (I + M)

Abbreviations: ANK, ankylosis; BW, body weight; C, canine teeth; CEJ, cemento-enamel junction; d, days; D2, vitamin D₂; D3, vitamin D₃; DEG, degeneration; DHT, dihydrotachysterol; ED, estradiol; EM, electron microscopy; FD, ferric dextran; h, hours; H, histology; HC, hypercementosis; HO, hyperosteooidosis; I, incisor teeth; IM, intramuscular junction; IP, intraperitoneal injection; irradi, irradiation; L, left; LM, light microscopy; M, molar teeth; max, maxillary; MIN, mineralization; mio, million; mo, months; nfd, not further defined; n/a, not applicable; n/r, not reported; 1,25(OH)2D3, 1,25-dihydroxyvitamin D₃; OP, osteoporosis; OS, osteosclerosis; P, parenteral; PO, per os; PS, periodontal space; R, radiography; SC, subcutaneous; SF, sodium fluoride; TGT, transoral gastric tube; TS, testosterone; vit, vitamin; wk, weeks.

Pulp/dentin	Cementum	Periodontal ligament	Gingival connective tissue	Alveolar bone	Comments
n/r	HC	ANK	n/r	HO; new bone formation at alveolar crest below the injury	n/a
↓ number of pulp cells; MIN; ↓ lumen of pulp cavity	HC	DEG and FD; ↓PS; MIN	n/r	HO and OS; ↓ lumen of ES; bulbous enlargement of alveolar plates	n/a
n/r	HC	DEG and FD; ↓PS	n/r	HO and OS; ↓ lumen of ES; fibrosis of bone marrow; bulbous enlargement of alveolar plates	↓ changes in male rats and teeth without opposing antagonists
n/r	HC	DEG, hyperemia, and FD; ↓PS; MIN	n/r	HO; ↓ lumen of ES	↓ changes in rats given D2; when given DHT, ↑ changes in female rats; ↓ changes in rats given DHT when also given sexual hormones
n/r	HC	DEG and FD; MIN; ANK	n/r	HO	n/a
n/r	HC	FD; ↓PS	n/r	HO	↑ changes in rats with traumatic occlusion
n/r	HC	FD; ↓PS	n/r	HO	↓ changes in rats given FD
n/r	HC	DEG and FD; ↓PS; ANK	n/r	HO	n/a
n/r	HC	DEG; ↓PS; ANK	n/r	HO; ↓ lumen of ES; fibrosis of bone marrow	Progeria-like changes
↓ width of predentin; DEG of odontoblasts and fibroblasts; formation of irregular dentin and osteodentin	HC	ANK of M	n/r	HO	n/a

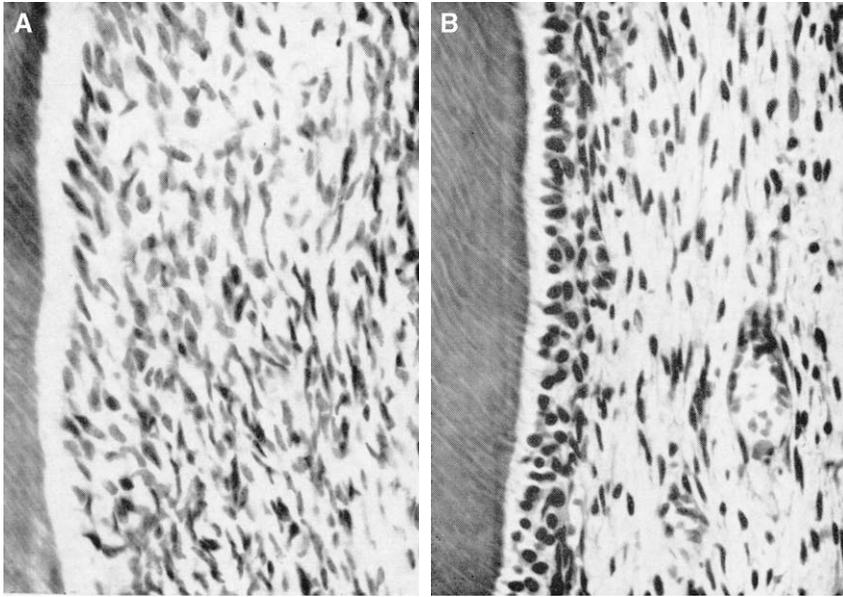


Fig. 9. Histopathologic pictures of pulp from molar teeth of a control rat (*A*) and pulp from a molar tooth of a rat given dihydrotachysterol showing increased activity of odontoblasts, fluid accumulation in the odontoblastic layer, and reticular atrophy with hyperemia and edema (*B*). (From Ratcliff PA, Itokazu H. The effect of dihydrotachysterol on the teeth and periodontium. *J Periodontol* 1964;35:324; with permission.)

of vitamin D deficiency [59,60]. Furthermore, it was found that one third of commercial cat foods contained vitamin D₃ in excess of current maximal allowances (>10,000 IU/kg of dietary dry matter), and a direct linear relation was demonstrated between 25OHD serum concentrations and dietary intake of vitamin D [61]. Therefore, higher 25OHD serum concentrations in cats with FORL suggest that they had ingested larger amounts of vitamin D or vitamin D metabolites compared with cats without FORL [5]. Three separate incidences of fatal hypervitaminosis D were reported in cats in Japan after consumption of commercial cat foods prepared from fish [62–64]. Clinical, laboratory, and histopathologic findings in these cats included vomiting, hypercalcemia, hyperphosphatemia, azotemia, proteinuria, calciuria, phosphaturia, decreased urine specific gravity, and mineralization of various body tissues, particularly the kidneys and walls of large blood vessels [62]. One may speculate as to whether there is indeed a predisposition to impairment of renal function in cats with FORL, because results of experimental studies on cats fed diets high in vitamin D₃ (15,000–33,840 IU/kg of dry matter) were contradictory, ranging from no evidence of detrimental effects on feline health to a high prevalence of renal dysfunction and mortality [65].

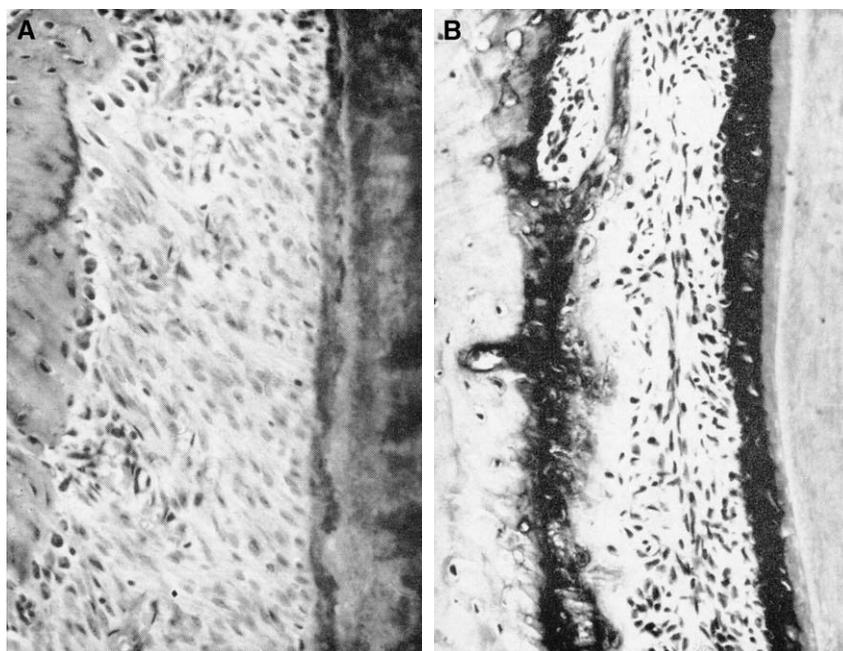


Fig. 10. Histopathologic picture showing periodontal space from molar teeth of a control rat (A) and a rat given dihydrotachysterol showing periodontal ligament fiber disorientation, edema, hyperemia, hypercementosis, hyperosteoïdosis with bone spur formation, and narrowing of the periodontal space (B). (From Ratcliff PA, Itokazu H. The effect of dihydrotachysterol on the teeth and periodontium. *J Periodontol* 1964;35:323; with permission.)

Vitamin D and vitamin D metabolites are important regulators of osteoclastic bone resorption [66]. Serum calcium concentration is maintained within a normal range through the primary action of 1,25-dihydroxy-vitamin D₃ [1,25(OH)₂D₃], which increases intestinal absorption of dietary calcium and recruits hematopoietic stem cells to become osteoclasts. Osteoclasts, in turn, mobilize calcium stores from bone into the circulation. Osteoclasts do not possess receptors for 1,25(OH)₂D₃, however [66]. Receptors for 1,25(OH)₂D₃ are located on osteoblasts that produce factors stimulating osteoclasts, such as receptor activator of nuclear factor- κ B ligand (RANKL), which plays an important role in osteoclastogenesis [67] and osteoclast activation [68].

Role of local trauma

The occlusal stress (tooth flexure) theory was created in an attempt to explain *noncarious cervical lesions*, an overall term for tooth wear (not resorption) at the cervical portion of human teeth [69–71]. Repeated compressive and tensile forces attributable to tooth flexure during

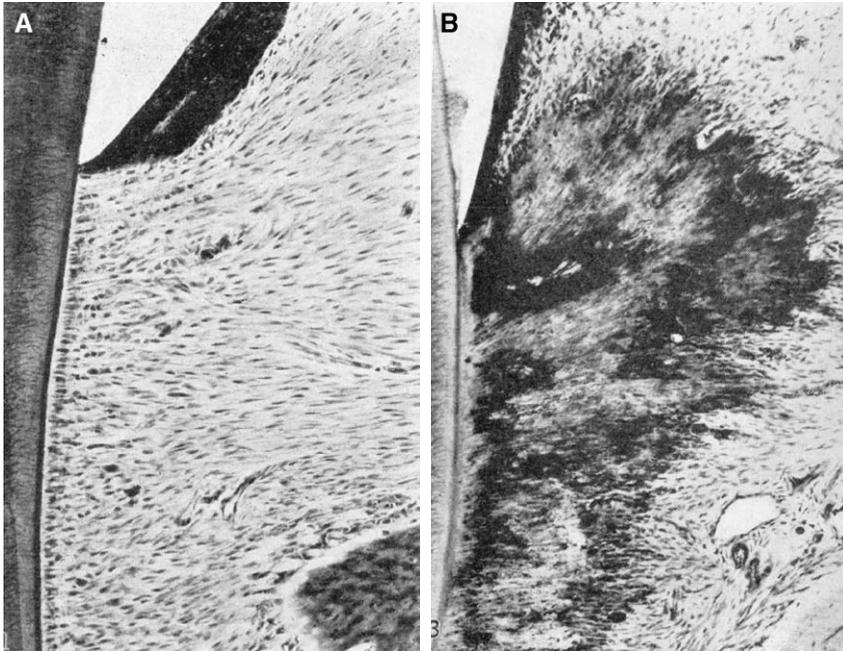


Fig. 11. Histopathologic pictures of cervical portion from teeth of a control dog (A) and a dog given excessive amounts of vitamin D showing abnormal thickening of cervical cementum (B). (From Becks H. Dangerous effects of vitamin D overdosage on dental and paradental structures. *J Am Dent Assoc* 1942;29:1960; with permission.)

mastication and malocclusion may disrupt the bonds between enamel rods and between enamel and dentin, resulting in abfraction of enamel, exposure of dentin, and cervical hypersensitivity [72,73]. Although FORL are clearly resorptive in nature and develop on any tooth and any root surface (not just on those exposed to occlusal or shearing forces), occlusal stress caused by eating large dry kibbles has been suggested to be associated with FORL [18,74,75]. A different approach for a possible role of occlusal stress in the development of FORL is presented in this article.

Surface resorption of cementum and superficial dentin may develop in response to normal masticatory stress [76] and excessive occlusal force [77–80]. Apical root resorption has been linked with bruxism in human beings, although the apical defect in that case report could also have resulted from endodontic disease [81]. Traumatic occlusion from maloccluding teeth may cause resorption of roots in rats and people, with the apical area being affected most often [22,82–86]. Root resorption has been demonstrated after experimental intrusion of teeth in people [87] and long-standing occlusal trauma in dogs and monkeys [88,89]. Subsequent repairs could eventually result in ankylosis [90].

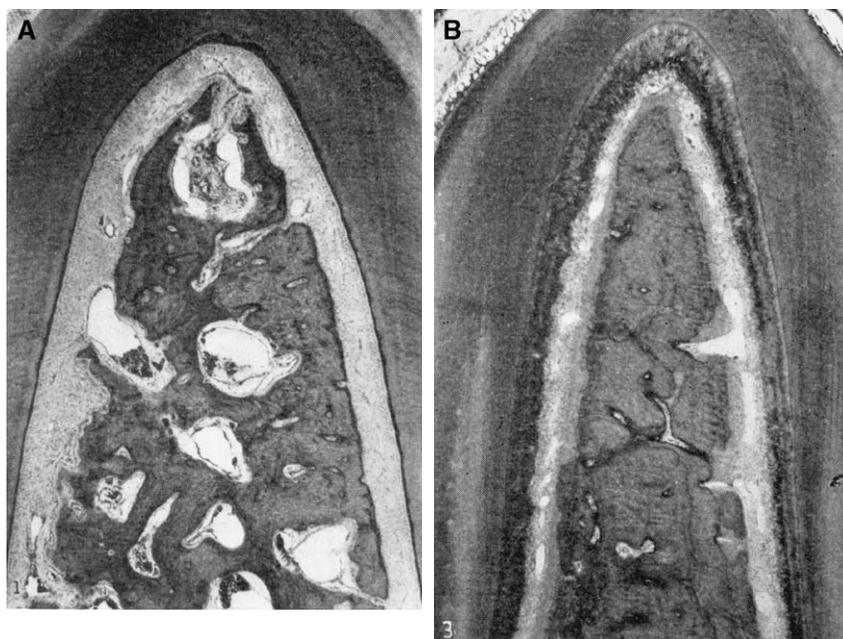


Fig. 12. Histopathologic pictures of furcation area from teeth of a control dog (A) and a dog given excessive amounts of vitamin D showing hypercementosis, hyperosteoidosis, and narrowing of the periodontal space (B). (From Becks H. Dangerous effects of vitamin D overdosage on dental and parodontal structures. J Am Dent Assoc 1942;29:1951; with permission.)

Calciophylaxis is a condition of induced local or systemic hypersensitivity in which tissues respond to appropriate challenging agents with precipitous, sometimes evanescent, local mineralization of various tissues and organs [91,92]. Substances that predispose the organism to calciophylaxis are known as *sensitizers*. Sensitizers are systemically administered agents that promote mineralization of tissues and include vitamin D and vitamin D metabolites, parathyroid hormone, and sodium acetylsulfathiazole among many other calcium salts and phosphates [91]. Agents that precipitate the calciophylaxis phenomenon are known as *challengers*. Challengers may be direct or indirect. Direct challengers include mechanical trauma and various chemical agents (eg, salts of iron, chromium, aluminum, zinc, manganese, cesium) that cause mineralization at the site of application and may elicit some form of systemic calciophylaxis when administered intravenously or intraperitoneally. Indirect challengers have little or no effect at the site of application and produce diverse systemic syndromes of mineralization and sclerosis [91].

Experiments in dihydrotachysterol (DHT)-sensitized rats indicated that functional stress and topical trauma can produce local calcium deposits in various parts of the body [91,93,94]. In rats given DHT, enlargement of

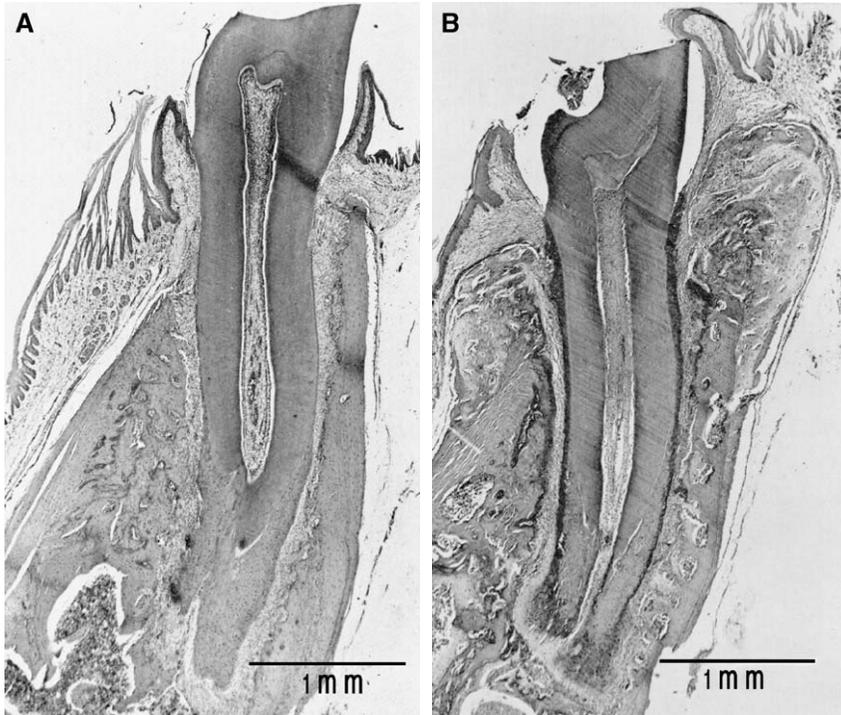


Fig. 13. Histopathologic pictures of molar teeth of a control rat (A) and a rat given dihydrotachysterol showing hypercementosis, hyperosteoidosis, narrowing of the periodontal space, and bulbous enlargement of crestal alveolar bone with loss of biologic width (B). (From Glickman I, Selye H, Smulow JB. Reduction by calciphylaxis of the effects of chronic dihydrotachysterol overdose upon the periodontium. *J Dent Res* 1965;44:735-6; with permission.)

buccal and lingual bone occurred most notably at muscle insertions [95]. Alveolar bone formation at the site of a gingival injury took place more rapidly and was more evident in experimentally injured than noninjured rats that also received DHT [96]. Similarly, mineralization of the periodontal ligament and gingival connective tissue was enhanced when a collagen-damaging agent was given to rats receiving intraperitoneal injections of vitamin D₂ [97]. In rats given DHT, degeneration of the periodontal ligament, hypercementosis, hyperosteoidosis, narrowing of the periodontal space, and ankylosis were markedly more pronounced in furcation areas [91,98] and teeth that were in occlusion [99] or subjected to traumatic occlusion [100]. Daily masticatory stress could be the reason why chronic increased vitamin D intake manifests sooner and is more pronounced in periodontal tissues compared with other soft tissues, and FORL may therefore occur before or without obvious signs of vitamin D-induced systemic disease.



Fig. 14. Histopathologic pictures of interdentary area from teeth of a control rat (A) and a rat given dihydrotachysterol showing hypercementosis, hyperosteoidosis, edematous degeneration of the periodontal ligament, narrowing of the periodontal space, bulbous enlargement of crestal alveolar bone, coronal displacement of transeptal fibers, and reduction of biologic width (B). (From Glickman I, Selye H, Smulow JB. Reduction by calciphylaxis of the effects of chronic dihydrotachysterol overdose upon the periodontium. *J Dent Res* 1965;44:738; with permission.)

Experimental studies with vitamin D and vitamin D metabolites

Numerous reports describe the effects of excess vitamin D and vitamin D metabolites on the pulp-dentin complex and periodontium in experimental animals (rodents, lagomorphs, pigs, and dogs) (Table 1).

In the pulp-dentin complex, pulpal hyperemia and degeneration, decreased width of the predentin layer, and formation of osteodentin and



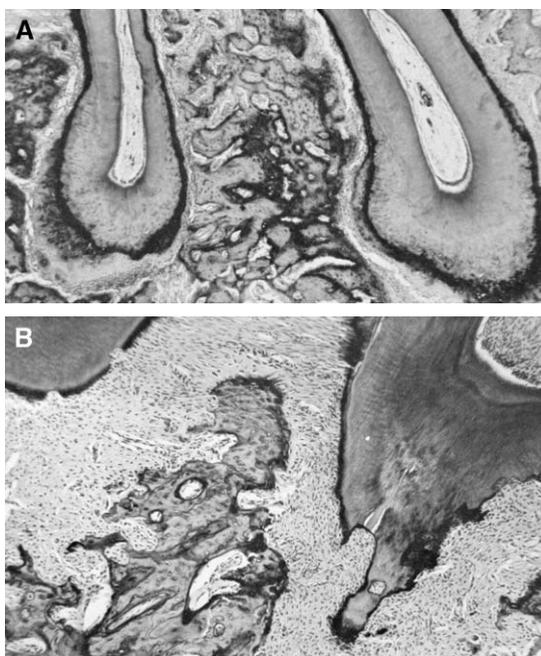


Fig. 16. Histopathologic pictures of rats given dihydrotachysterol showing bulbous enlargement of root apices (*A*) and resorption of cementum, dentin, and alveolar bone (*B*). (From Moskow BS, Baden E. The effect of chronic dihydrotachysterol overdosage on the tissues of the periodontium. *Periodontics* 1964;2:279–80; with permission.)

irregular dentin containing small vascular canals (Fig. 9) have been reported [101–107].

In the periodontium, periodontal ligament hyperemia, edema, and degeneration with fiber disorientation; mineralization of Sharpey's fibers; hypercementosis with abnormal thickening of cervical cementum and a bulbous appearance of root apices; hyperosteoidosis along periosteal and endosteal surfaces; reduced endosteal lumina; bone marrow fibrosis; bulbous enlargement of alveolar plates with coronal displacement of transeptal fibers at the alveolar margin; narrowing of the periodontal space; dentoalveolar ankylosis; granulation tissue formation; irregular resorptive lacunae in cementum and dentin; and a mixed pattern of osteoporosis and osteosclerosis (Fig. 10–16) have been reported [91,95–102,104,106–125].



Fig. 15. Histopathologic pictures of furcation area of molar teeth in a control rat (*A*) and a rat given dihydrotachysterol showing hypercementosis, hyperosteoidosis, degeneration of the periodontal ligament, and narrowing of the periodontal space (*B*). (From Glickman I, Selye H, Smulow JB. Reduction by calciphylaxis of the effects of chronic dihydrotachysterol overdosage upon the periodontium. *J Dent Res* 1965;44:743–4; with permission.)

Extrapolating these findings to the domestic cat should be done with caution, however, because the results of these experimental studies are not uniform. Furthermore, the ages, sizes, and species of animals; the character of their diets; the varying forms, quantities, and routes of administration of vitamin D and vitamin D metabolites; and the duration of the experiments differed. Nevertheless, there are distinct similarities between the changes in dental and periodontal tissues induced by administration of excess vitamin D and vitamin D metabolites in experimental animals and radiographic and microscopic features that can be found in teeth from cats with FORL (eg, thin predentin layer, irregular dentin formation, periodontal ligament degeneration and fiber disorientation, hypercementosis, hyperosteoidosis, thickening of crestal alveolar bone, narrowing of the periodontal space, dentoalveolar ankylosis, root resorption, mixed pattern of osteoporosis and osteosclerosis). Vitamin D-induced thickening of cervical cementum and abnormal apposition of osteoid at the alveolar crest and other periosteal surfaces causing bulbous enlargement of alveolar plates and coronal displacement of transeptal fibers could result in reduction of the biologic width (the dimension of space occupied by junctional epithelium and gingival connective tissue) and loss of gingival attachment. Supereruption of teeth in cats with increased vitamin D activity may actually be an attempt to maintain or re-establish normal biologic width.

Certain findings are worthy of additional discussion, including (a) differences in effects of vitamin D and vitamin D metabolites between continuously growing and continuously erupting teeth and between young and adult animals and (b) apparent alleviation of the detrimental effects of vitamin D and vitamin D metabolites by concurrent administration of other agents. In rats, pulpal mineralization and pulp stones occurred more commonly in incisors than in molars and more commonly in younger than in older animals [107], which may be an indication that vitamin D activity is more influential on "young" or continuously renewing tissue. Although pulpal mineralization has not been reported in permanent teeth of cats with FORL, pulp stones have been demonstrated in experimental vitamin D studies in puppies [108,110,114]. Young animals (dogs and rats) showed initial alveolar bone resorption and osteoporosis followed by hyperosteoidosis and osteosclerosis with a narrowing of endosteal spaces, whereas alveolar bone resorption and osteoporosis were predominant in adult or older animals [107,108]. Studies investigating the appearance of alveolar bone in younger and older FORL-affected cats have not yet been conducted. Effects of vitamin D or vitamin D metabolites were less severe or could be reduced in animals given various amounts of vitamin A [108,114], sexual hormones [95,117], ferric dextran [91,98,123], or sodium fluoride [118], in addition to excess administration of vitamin D or vitamin D metabolites. This may be of interest when considering future research that focuses on prevention of FORL.

Summary

The following conclusions can be drawn:

1. Cats depend on dietary vitamin D intake because they are not able to produce vitamin D in the skin.
2. Some commercial cat foods contain vitamin D concentrations in excess of current maximal allowances.
3. Cats with FORL have significantly higher serum concentrations of 25OHD compared with cats without FORL, indicating that cats with FORL must have ingested higher concentrations of dietary vitamin D.
4. Cats with FORL have significantly decreased urine specific gravity compared with cats without FORL.
5. Experimental studies on laboratory animals have shown that excess administration of vitamin D or vitamin D metabolites causes changes to dental and periodontal tissues that resemble many characteristics of teeth from cats with FORL.
6. Clinical and experimental studies have shown that excess administration of vitamin D or vitamin D metabolites can lead to soft tissue mineralization and various degrees of renal disease.

Dietary intake of excess vitamin D over several years may lead to periodontal ligament degeneration, narrowing of the periodontal space, dentoalveolar ankylosis, and root replacement resorption. If such a process occurs close to the gingival margin, an inflammatory component may join the disease. Further histologic and experimental studies are required to determine the role of daily masticatory stresses on the development of FORL and to verify relations between FORL, vitamin D, and renal insufficiency.

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