CLINICAL ORAL SCIENCE AND DENTISTRY

REVIEW ARTICLE ISSN 2688-7428 Open Access

Mechanisms Implicated in Tooth Eruption

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Received date: November 01, 2022 , **Accepted date:** November 12, 2022, **Published date:** November 21, 2022.

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Abstract

Tooth eruption is a complex multifactorial process. Association of alveolar bone remodeling, root elongation, cementum apposition, and periodontal ligament formation leads to include in eruption a series of events. After a pre-eruptive phase, following intra-osseous and extra-osseous movements, mucosal penetration, pre-occlusal and post-occlusal eruption. The tooth becomes functional (occlusion). Gubernacular cord and canal are involved in the eruption process, including vascular pressure, maturation of the periodontal ligament, changes at the alveolar bone level, collagen fibers maturation in the periodontal ligament, and cementum formation. Transcription factors and growth factors are integral parts of these multifactorial events. Hormones such as of IL-1 and PTHrP located in the Stratum Reticulum, enzymes, and metalloproteinases suggests that they are also implicated in these complex processes. Genesis of osteoclasts and osteoblasts, tooth eruption molecules, biological aspects of the periodontal ligament, molecules synthetized in the stratum reticulum, are all involved in tooth eruption, however, a single process for tooth eruption has not been identified, but multifactorial effects may combine together and shed lights on the different causes of tooth eruption.

Keywords: Alveolar Bone, Pre-eruptive, Intra-osseous, Extra-osseous, Pre-occlusal Eruption, Post-occlusal, Periodontal Ligament, Cementum Apposition, Stellated Stratum, Root Formation, Vascular Pressure, Gubernaculum, Transcription and Growth Factors, Osteoblasts, Osteoclasts, Mesial Drift, Metalloproteinases, Hormones, Enzymes.

Introduction

Tooth eruption is a continuous multifactorial process, associated with alveolar bone remodeling, root elongation, cementum apposition and periodontal ligament formation.

There is no consensus in the mechanisms involved, but include five successive stages:

Preeruptive movement

Intra-osseus eruption

Mucosal penetration

Preocclusal eruption

Postocclusal eruption (Marks & Schroeder 1996, Kjer 2014)

Other events may also be implicated: such as pulpal pressure, pulpal growth, root lengthening, traction by periodontal fibroblasts acellular and cellular cementum formation, and vascular pressure.

Developmental anomalies of tooth are recognized, including flexion, dilacerations, concrescence, fusion, dwarted roots, accessory roots, hypercementosis, and enamel pearl (Figure 1).

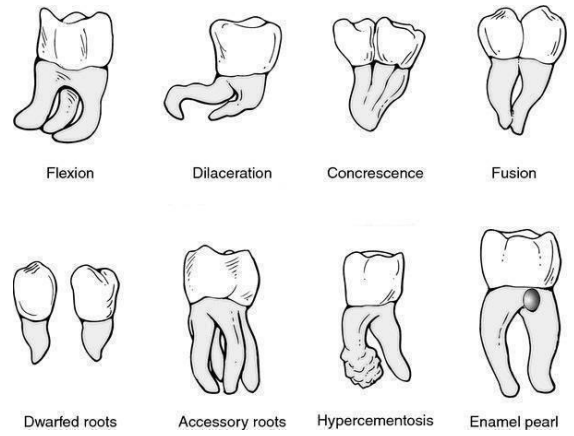

Figure 1: Developmental anomalies of the roots

First, the crown part of the tooth is formed. Then, from the cervical region (labial or lingual parts) starts the formation of a tongue of epithelial cells that contributes to the division of the cervical space into two (for mandibular molars - Figure 2) or three divisions of the cervical space - (Figure 3). These events are leading to the formation of furcation dentin and to the onset of root formation.

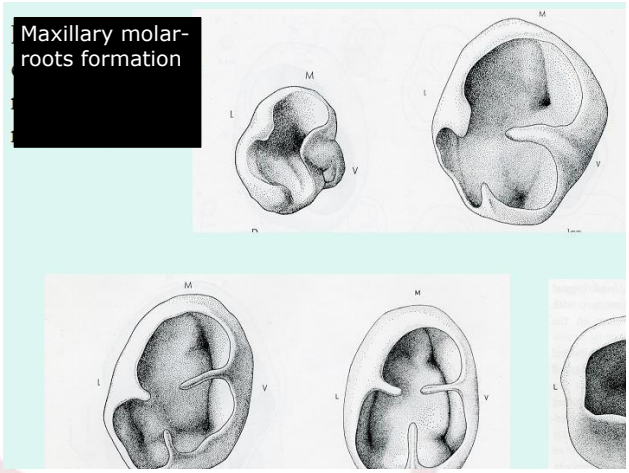

Figure 2

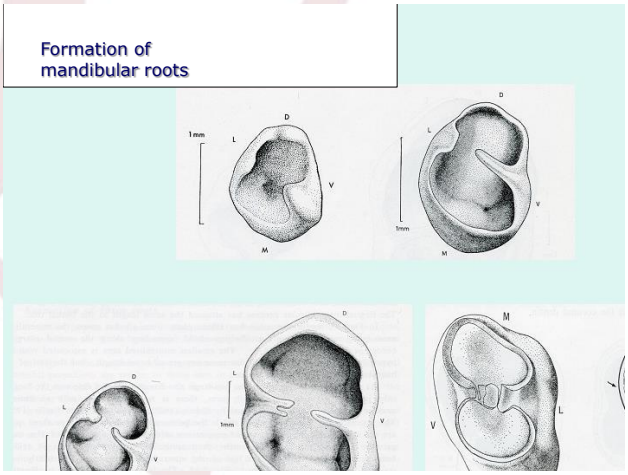

Figure 3

Tooth eruption implies 3 different phases (Figure 4):

1-Pre-eruptive Phase, also named primary eruption. Pre-eruptive tooth movement implies that second molar is moving backward, whereas anterior teeth are moving forward.

2-Eruptive Phase: the tooth moves from its position within bone to its functional position in occlusion. Two successive stages are reported:

- An intra-osseous stage, with a parallel formation of roots, together with alveolar bone and
- An extra-osseous compartment. These events include 4 stages: root formation, movement, penetration in the oral cavity ending by occlusal contact.

3- Post-eruptive Phase: That maintain the erupted tooth in occlusion while the jaws continue to grow, and compensate for occlusal and proximal wear. In addition, during these three stages, the progression from primary to permanent dentition involves the shedding (exfoliation) of primary teeth.

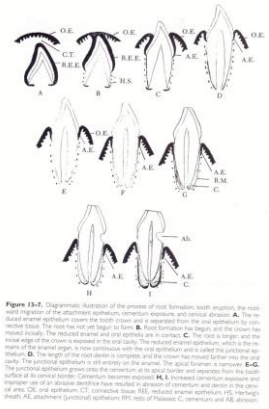

Figure 4: Two sets of dentition occur in human (diphiodont): (deciduous vs permanent dentition). At some moment: the two dentitions are present (occurrence of a mixed dentition

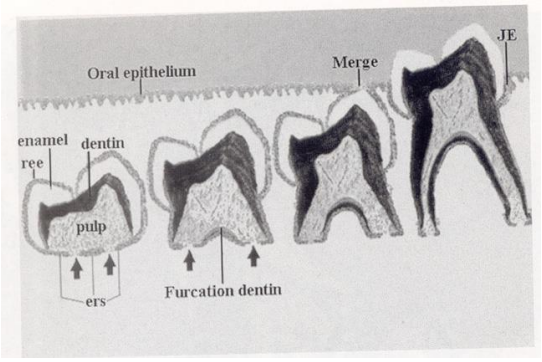

Figure 5: The formation of the furcation dentin is followed by the merge of the crown into the oral cavity. The occurrence of occlusal contact between lower and upper molars signify the end of the tooth eruption

Four erupting tooth movements are recognized. They are due to:

1- Root Formation

2- Incisally or occlusally movements. The reduced enamel epithelium fuses and contacts the oral epithelium

3- Penetration of the tooth crown into the fused epithelial layers, allowing entrance of the crown into the oral cavity.

4-Movement of the crown of the erupting tooth until clinical contact with the opposing crown occurs.

Gubernacular cord and canal are involved in tooth eruption: vascular pressure, periodontal ligament maturation, changes at the alveolar bone level. Widening of the gubernacular canal allows the tooth to erupt. The rate of tooth eruption depends on two different phases:

Intraosseous phase: Rate 1-10 μm/day
Extraosseous phase: 75 μm/day
Intraosseous phase: Rate 1-10 μm/day
Extraosseous phase: 75 μm/day

The mechanisms of eruptive tooth movement involve a multifactorial process due to:

1-Root Formation: Tongues formed from the internal and external border (the 4 layers of the enamel organ: outer enamel epithelium, stratum reticulum, stratum intermedium, inner enamel epithelium), are reduced from four to two layers forming the Nasmith's cuticule (inner and outer enamel epithelium) that are at the origin of alveolar bone, periodontal ligament and cementum. The formation of apical foramen, involved in growth and development toward the eruptive zone is an important step during these phenomenons (Figures 6 & 7).

2-Bone Remodeling.

3- Defects in Osteoclast Differentiation.

4-Periodontal ligament (PDL) is present, but the tooth is not erupting, however, it is obvious that rootless teeth are erupting, despite the lack of root formation (Figures 8 & 9).

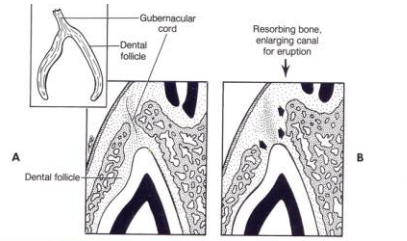

FIG. 6-10 Developing eruption pathway. **A,** Gubernaculum dentis. **B,** Bone resorption in eruption pathway.

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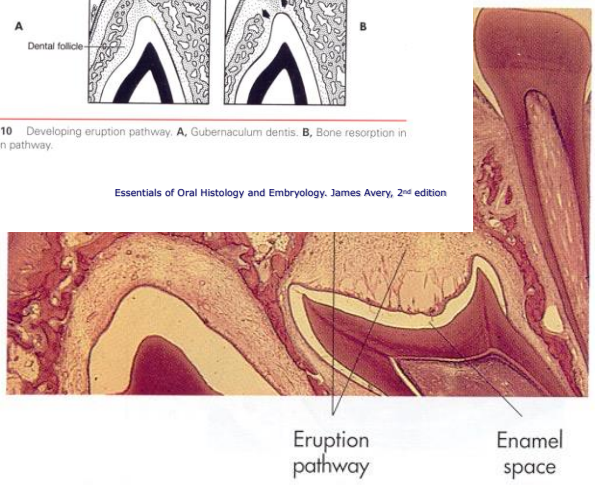

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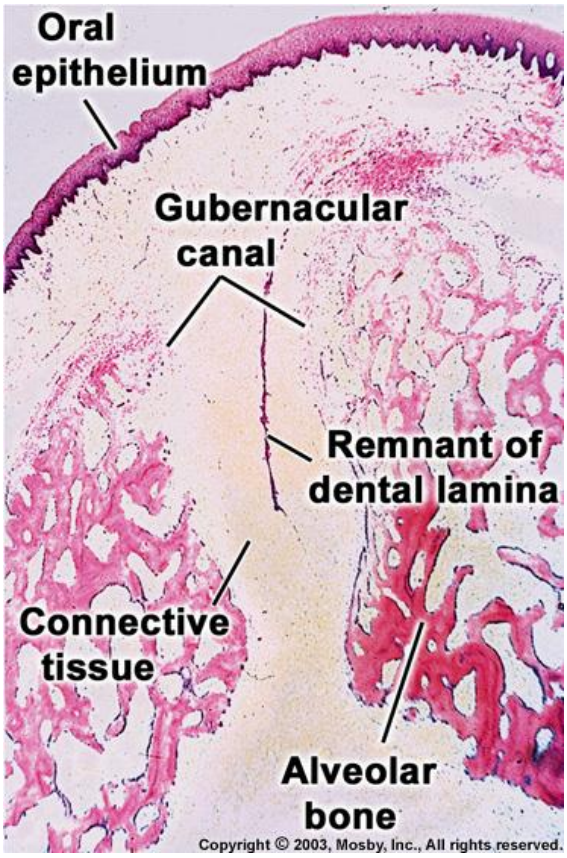

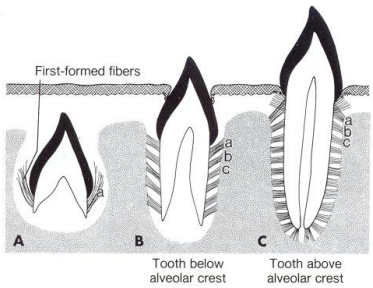

FIG. 6-20 Principal fiber development during tooth eruption. **A,** Origin of fibers at the cervical area. **B,** Fiber development with root growth. **C,** Change in orientation of the fibers with occlusal function. *a,* Initial fiber formation. *b,* Development of secondary fibers. *c,* Further fiber development. Initial fiber groups change direction. Observe the changes in direction of these initial fiber groups.

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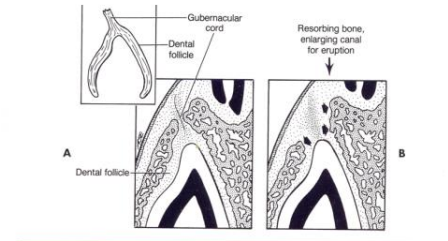

FIG. 6-10 Developing eruption pathway. **A,** Gubernaculum dentis. **B,** Bone resorption in eruption pathway.

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Figure 7

Periodontal ligament comprises five different groups of fibers

- **Alveolar crest**; just below the cemento-enamel junction, inserted at the crest of the alveolar bone socket.

- **Horizontal fibers**, below the alveolar crest group. This group originate from the cementum and is directed at right angle to the long axis of the tooth, inserted into the alveolar bone

- **Oblique fibers**, taking origin from the cementum in an oblique direction, ending into the alveolar bone lining the socket coronally.

- **Apical fibers** are present at the base of the socket. The take origin from the cementum around the apex of the root and they are inserted into the adjacent alveolar bone.

- Present only in multi-rooted teeth, interradicular fibers originate from the inter radicular septum of the alveolar bone.

- In single rooted teeth, groups of fibers are found forming the:

1) Dento-gingival group of fibers,

2) Alveolo-gingival group,

3) Circular group,

4) Dento-periosteal group.

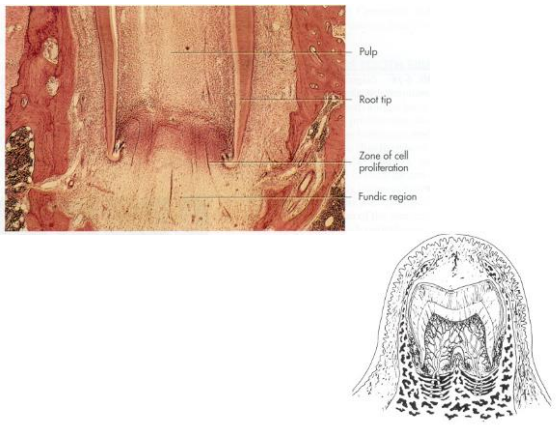

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Figure 8

Lately, the molars are sliding mesially.

Control factors of the mesial drift.

Mesial drift is due to:

- Contraction of the transseptal fibers
- Adaptability of bone tissue
- Occlusal forces: forward directed forces generated from intercuspal forces.
- Pressure from soft tissues buccal mucosa and tongue pushing teeth mesially

II-Mechanisms implicated in tooth eruption

Active eruption: compensates incisal and occlusal wear

Passive eruption: gradual recession of the gingiva and the underlying alveolar bone (lengthening of clinical crown)

4 events have been implicated in tooth eruption

Root formation: the crown migrates in the bone.

Collagen contraction; Hydrostatic pressure

1) The fibrous hammock

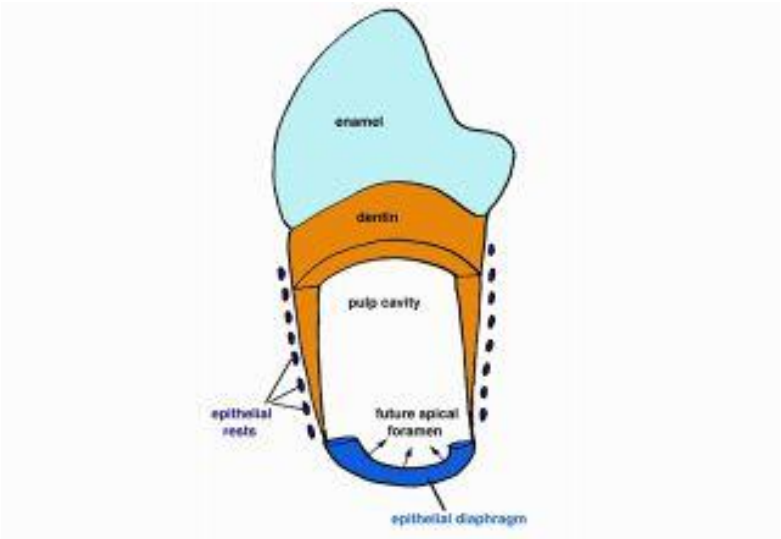

Figure 9

2) Vascular pressure

Formation and maturation of the periodontal ligament/ Migration of fibroblasts, contraction of collagen gels; Maturation of the ADL from the native collagen to mature collagen fibers (1000 ・m of the native collagen, to 670 ・m in length of the mature collagen, after ablation of the N- and C- termini). Increases in the lysosomal enzymes, acid phosphatase, tartrate-resistant acid phosphatase and cathepsin B are also localized at compression sites, suggesting that they may play pivotal roles during orthodontic tooth movement in the process of hard- and soft-tissue degradation by increased numbers of macrophage and dendritic-like cells

3) Increases in the lysosomal enzymes, acid phosphatase, tartrate-resistant acid phosphatase and cathepsin B are also localized at compression sites, suggesting that they may play pivotal roles during orthodontic tooth movement in the process of hard- and soft-tissue degradation by increased numbers of macrophage and dendritic-like cells

4) Changes in alveolar bone:

- First, compression sites clearly have a tissue injury component superimposed on physiological transduction, with the former producing inflammatory products that are primarily resorptive and stimulate cells to remove the injured tissue.
- Second, resorption at compression sites in tooth movement could be perceived as a result of lowering of the normal strain from the functioning periodontal ligament, while osteogenesis at tension sites could be a reflection of loading of the

principal fibers of the periodontal ligament

Many theories of tooth eruption mechanisms have been reported, such as root elongation, pulp cell proliferation, bone deposition, and tissue fluid pressure. It was also suggested that the force of eruption might come from the PDL (Wise et al., 2002). At the end of active treatment period (15 min), the samples are rinsed with distilled water and dried. Every group is then divided into two subgroups of 15 each.

The mechanisms involved in tooth eruption are numerous, including:

- **Dental Follicle** in also implicated in tooth eruption, at least for the intraosseous phase of eruption leading to tooth emergence. For the supra-osseous phase of eruption, the follicle plays a lesser role. According to Wise and Lin, (1995); Cahill & Marks (1980) ablation or removal of dental follicle may influence or coordinate the process of tooth eruption. There is evidence that dental follicles play an important role in this cascade because they produce several factors including tumour necrosis factor-a(TNF-a), transforming growth factor-b(TGF-b), interleukin-1(IL-1), colony-stimulating factor 1 (CSF-1) and receptor activator of nuclear factor kB ligand (RANKL). TNF-□, CSF-1 and RANKL are released by dental follicle cells and stimulate the migration and differentiation of bone-marrow precursors or mononuclear cells into multinucleated osteoclasts

- **Periodontal ligament**

  From a biomaterials perspective, the periodontal ligament is a complex, fiber-reinforced substance that responds to force in a viscoelastic and non-linear manner.

- **Adjacent alveolar bone**

  A bone remodeling cycle has four phases: activation, resorption, reversal, and formation Inhibition of the molecules that promote osteoclastogenesis can inhibit eruption. In knock-out mice devoid of receptor activator of nuclear factor kappa B (RANKL), the teeth do not erupt. In osteopetrotic rodents in which osteoclasts are either absent or non-functional, teeth do not erupt.

• All these modifications are influenced by genes that expressed molecules such as: Transcription factors: Runx2/Cbfa 1

Growth factors: insulin-like GF-1

Vascular endothelial GF (VEGF)

Tumor necrosis factor-alpha (TNF-alpha >>>stimulation of the monocyte 1 protein chemotactin and VEGF.

Hormones: Growth Factor receptors and parathyroïd related protein (PTHrP). Cells are regulated by autocrine signaling. Indeed, the parathyroid hormone–related protein (PTHrP) and its parathyroid hormone/PTHrP receptor PPR signaling appears to crosstalk with other signaling pathways. They regulate the proper cell fates of mesenchymal progenitor cell populations.

Enzymes (Protein-kinase C; PKA)

MetalloProteases: MMP-8 and MMP-13 and Disintegrins (PGs are cleaved: e.g. versican is cleaved by ADAMTS 1, ADAMTS 4, ADAMTS 5)(Kardos, 1996).

Potential role of MT1-MMP:

Data indicate that MT1-MMP activity in the dental mesenchyme, and not in epithelial-derived HERS, are essential for proper tooth root formation and eruption. These studies point to an indispensable role for MT1-MMP-mediated matrix remodeling in tooth eruption through effects on bone formation, soft tissue remodeling and organization of the follicle/PDL region.

The data obtained by analyzing MT1-MMP, a transmembrane zinc-endopeptidase that breaks down extracellular matrix components, including several collagens, indicate that MT1-MMP activity in the dental mesenchyme, and not in epithelial-derived HERS, is essential for proper tooth root formation and eruption. These studies point to an indispensable role for MT1-MMP-mediated matrix remodeling in tooth eruption through effects on bone formation, soft tissue remodeling and organization of the follicle/PDL region (Xu et al., 2016).

In addition, resorption of deciduous teeth (by dentinoclasts) is associated to the eruption of permanent teeth.

Bone growth: Marks and Cahill (1984) have interpreted their experiments, with the eruption of metal and silicone replica, as providing evidence for alveolar bone growth (apposition and resorption) passively 'carrying' the tooth through bone into function. It is evident that bone cells respond to mechanical forces. The first evidence of eruption is bone resorption beneath the calcified crown, in a direction opposite to the one in which the tooth is expected to move. Such cellular activity is not unexpected if a significant 'origin' of force within the follicle becomes displaced apically subsequent to calcification of the crown. The mechanics of tooth eruption lead to the conclusion that pulsatile forces from the apical vasculature are the likely source of the eruptive force. As tooth eruption can be explained

by the action of forces acting in a dynamic relationship with bone remodeling there will be many factors (e.g. age, nutritional, hormonal, cellular, molecular and physicochemical) that modify the rate and direction of the process.

Role of dental follicle: Cellular events – Molecules involved in tooth eruption:

Dental Follicle-95 is selectively degraded at the onset of tooth eruption (Wise & Lin, 1995). In fact, eruption molecules are implicated in tooth movements: EGF ,TGF-• and EGF utilize the same receptor. Indeed, the Colony-stimulating factor-1 (CSF-1) is also contributing to the tooth migration. The presence of IL-1 and PTHrP in the Stratum Reticulum suggests that the SR portion of the enamel organ may play such a role, DF-95 is present at the onset of eruption and then decline in amount. CSF-1 is expressed in the SR, and have a role in eruption. The cells are regulated by autocrine signaling by parathyroid hormone–related protein (PTHrP) and its parathyroid hormone/PTHrP receptor PPR. This PTHrP-PPR signaling appears to crosstalk with other signaling pathways and regulates proper cell fates of mesenchymal progenitor cell populations. Disruption of this autocrine PTHrP-PPR signaling in these cells leads to defective formation of the periodontal attachment apparatus, tooth root malformation, and failure of tooth eruption in molars, which essentially recapitulate primary failure of eruption in humans, a rare genetic disorder exclusively affecting tooth eruption.

Analyses at different stages of premolar eruption indicate that selective fragmentation of dental follicle protein DF-95 correlates with the presence of elevated levels of follicular collagenase and stromelysin (Gorski et al., 1992)

Mononuclear cells (osteoclast precursors) must be recruited into the dental follicle prior to the onset of eruption. These cells, in turn, fuse to form osteoclasts that resorb alveolar bone, forming an eruption pathway for the tooth to exit its bony crypt.

Recruitment of the mononuclear cells to the follicle may require colony-stimulating factor-one (CSF-1) and/or monocyte chemotactic protein-1 (MCP-1). Osteoclastogenesis is needed for the bone resorption and may involve inhibition of osteoprotegerin transcription and synthesis in the follicle, as well as enhancement of receptor activator of NFκB ligand (RANKL), in the adjacent alveolar bone and/or in the follicle. Paracrine signaling by parathyroid-hormone-related protein and interleukin -1α, produced in the stellate reticulum adjacent to the follicle, may also play a role in regulating eruption.

Osteoblasts might also influence the process of eruption, the most important physiologic role likely being at the eruptive site, in the formation of osteoclasts through signaling via the RANKL/OPG pathway. Evidence thus far supports a role for an osteoblast-specific transcription factor, Cbfa1 (Runx2), in molecular events that regulate tooth eruption. Cbfa1 is also expressed at high levels by the dental follicle cells (Wise et al., 2002).

Putative Tooth Eruption Molecules:

EGF, EGF-R CSF-1, CSF-R, IL -1 • , IL-1R, c-Fos, NFkB

MCP-1, TGF- • 1, PTHrP, Cbfa1, OPG/OCIF, RANKL

Fibroblasts may play a possible role in tooth eruption. Interstitial fluid pressure may also be related to tooth eruption

Role of osteoclasts in tooth eruption: Mononuclear CSF-1 and MCP-1 are candidates for recruiting osteoclast precursors. Osteoblasts differentiation Osf2 or Cbfa1 (Core-binding factor a1) is a key transcriptional regulator of osteoblast differentiation during bone formation.

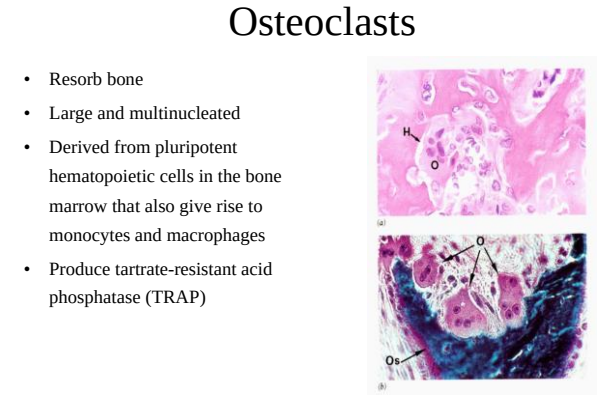

Figure 10

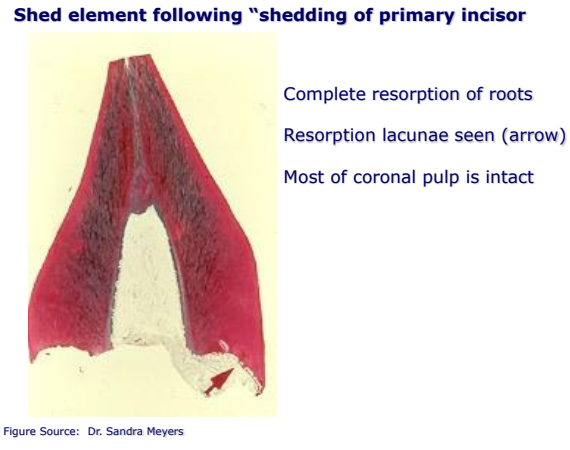

Figure -11

Human conditions affecting tooth eruption: Primary Failure of Eruption (PFE): Eruption results from interactions between cells of the dental enamel organ, the dental follicle, and bonny alveolus (involving osteoclasts and osteoblasts) (Figures 11 & 12)

Conclusions

Tooth eruption is a multifactorial event. Collagen maturation constitutes the basis for periodontal ligament maturation. Ablation of the collagen C and N termini leads to a reduced length of fibers firsty synthetized as pro-collagen (1000 ‣m) then reduced to a 670 Å periodicity (mature collagen). This shrinkage may contribute to the periodontal ligament maturation and consequently to tooth eruption. Changes were also identified in hormones (PTHrP), growth and transcription factors (TNF -a, -b, CSF-1, RANKL) metalloproteinases (MMP-8, 13, disintegrins, MT1-MMPs), enzymes expression of the surface of the bonny socket, all being expressed inside the ligament and in cementum (acellular and cellular enzymes expression at the surface of the bonny socket). There is also a possibility for the expression of proteases in the stellate reticulum (SR) of the enamel organ. The fact that these proteins work together and interact during epithelial morphogenesis is not well understood. Membrane localization of Baz, Par6-a PKC and Crb depend on Baz. Cdc-42 drives morphogenesis by conferring apical identity of Par6. (Nunes de Almeida et al., 2019). The apical STEM cells were also shown to contribute to tooth eruption (root lengthening).

References

1. Marks SCJr Schroeder HE Tooth eruption: theories and facts. Anat Rec .1996, 245(2): 374-393.

2. Kjer I. Mechanism of human tooth eruption; review article including a new theory for future studies on the eruption process. Hindawi Publ Comp 2014; Article ID 341 905.

3. Cahill DR, Marks Jr SC Tooth eruption: evidence for the central role of the dental follicle J Oral Pathology & Medicine 1980; 9(4): 189-200.

4. Wise GE, Frazier-Bowers S, D'Souza RN. Cellular, molecular and genetic determinants of tooth eruption. Crit Rev Oral Biol Med 2002; 13: 323–334.

5. Wise GE, Lin F. The Molecular Biology of Initiation of Tooth Eruption J Dent Res . 1995; 74(1): 303-306.

6. Kardos TB. The mechanism of tooth eruption. British Dental Journal 1996, 181(3), 91-95.

7. Xu H, Snider TN, Wimer SS, Yamada T, Yang K, Holmbeck B.L. Foster BL Multiple essential MT1-MMP functions in tooth root formation, dentinogenesis, and tooth eruption. Matrix Biology 2016; 52-54; 266-283.

8. Marks SC, Cahill DR. Experimental study in the dog of the non-active role of the tooth in the eruptive process. Arch Oral Biol. 1984; 29: 311-322.

9. Gorski JP, Marks Jr.SC. Current Concepts of the biology of tooth eruption. Crit. Rew. Oral Biol & Medicine 1992; 3(3): 185-206.

10. Nunes de Almeida F, Walther RF, Pressé MT, Vlassaks EV, Pichaud F. Cdc 42 defines apical identity and regulates epithelial morphogenesis by promoting apical recruitment of Par6-aPKC and Crumbs. Development 2019; 148(15): 175487