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Recent advances in understanding theories of eruption (evidence based review article)

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ABSTRACT

Eruption is; movement of the tooth from its developmental site in alveolar bone to its functional position in the oral cavity. Erupt has been a matter of long historical debate. Each of the eruption theories has a say in tooth eruption. So, the aim of this research is to explore the integration of eruption theories to understand the aetiology of the eruption process.

1. Introduction

Eruption is necessary for survival of diverse species [1]. Eruption is continuous process. It does not stop by reaching the occlusal plane, but continues throughout life [2].

2. Types of tooth eruption

2.1. Active eruption

Active eruption is; the movement of the tooth from its developmental site in alveolar bone to its functional position in the oral cavity [3]. Eruption can generally be divided into different phases [4].

2.2. Pre-eruptive movement

It is made by the teeth germs. It is best thought of as the mean by which the teeth are positioned within the jaw for eruptive movement. The Pre-eruptive phase starts from the end of early bell stage till the beginning of root formation [4].

2.3. Eruptive movement

Tooth movements during eruptive phase are subdivided into; intraosseous and supraosseous stages. The eruptive phase begins with the onset of root formation and terminates by tooth appearance in the oral cavity, just before function (pre-functional phase) [4].

2.4. Post-eruptive movement

This movement maintains the tooth position in occlusion by compensation for occlusal and proximal tooth wear. The post-eruptive phase starts when the teeth attain occlusion and continues for as long as each tooth remains in the oral cavity (functional phase) [4].

2.5. Passive eruption

Passive eruption is characterized by the apical shift of the dentogingival junction. As this occurs, the length of the clinical crown increases as the epithelial attachment migrates apically [5].

Although the movement of teeth into function has been the subject of extensive research, there is no consensus regarding the mechanism involved [1].

2.6. Normal eruption of human teeth

Tooth eruption in humans has numerous aspects [6]. The eruption process starts with onset of root formation [7]. From this time till tooth appearance in the oral cavity is called eruption time [6].

3. Theories of eruption

There is no consistent understanding of the cause behind tooth eruption. The aetiology behind eruption and explanation of the eruption mechanism seem to be essential to perform aetiology based treatment [6].

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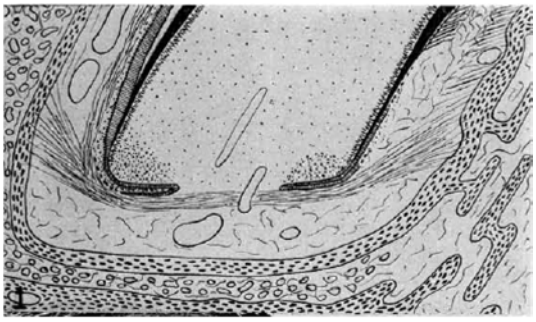

Fig. 1. Diagram of basal end of rat incisor showing cushioned hammock ligament [8].

3.1. Eruption theories with recent points of view

3.1.1. Cushioned hammock theory

It was proposed by *Harry Sicher* [8]. This theory assumed that ligament (cushioned hammock ligament) below a tooth is responsible for eruption (Fig. 1).

However the ligament described by *Sicher* [8] was an artifact in slide preparation [9].

3.1.2. Root formation theory

The root formation theory assumes that the proliferating root encounters a fixed structure; and the apically directed force is converted into a reactive occlusal force that causes coronal movement of the erupting tooth (Fig. 2) [4].

However, there are facts refuted this hypothesis such as; rootless teeth can erupt, some teeth erupt greater distance than the total root length; and the teeth erupt after completion of root formation or when the tissue forming the root is removed [4]. Also, the onset of root formation does not coincide with the eruptive movement [4]. Moreover, newly formed dentin at root apex is unmineralized and can be deformed by trauma [10].

Recently it is postulated that since tension results in bone deposition, the tensile responses that occur during teeth eruption are of great concern.

In the (intra-osseous stage of eruptive phase), root formation and jaw growth lead to compressive coronal hydrostatic stress. This induces the dental follicle and stellate reticulum cells to secrete mediators for bone resorption. Furthermore, the root formation would produce tensile apical hydrostatic stress in the teeth germs that leads to bone deposition [11,12]. Moreover, pre-occlusal eruption (supra-osseous stage of eruptive phase) is completed by root growth and bone formation at crypt base [3].

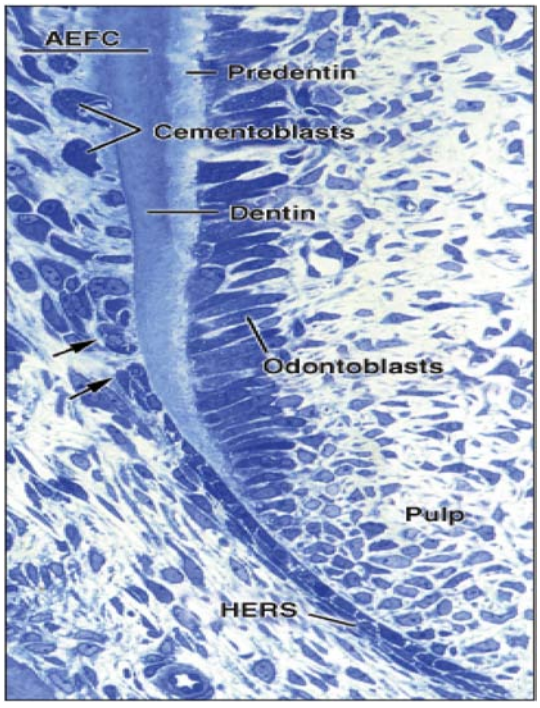

Fig. 2. Photomicrograph showing root formation [4].

3.1.3. Vascular pressure/blood vessel thrust or hydrostatic pressure theory

This theory suggests that a local increase in tissue fluid pressure in the periapical region is sufficient to move the tooth [13].

However, this is debatable because root and local vasculature excision, does not prevent tooth eruption [13].

Recently it is reported that the hydrostatic pressure theory occurs during postemergent eruption [12]. This is due to that dental follicle secrete mediators, such as vascular endothelial growth factor (VEGF), that cause angiogenesis and so increase in the apical tissue pressure that lead to tooth eruption [12]. Moreover, hydrostatic pressure theory was supported by several studies that confirm tooth eruption after a local injection of vasodilators [12]. Whereas injection of vasoconstrictors caused decrease in the rate of eruption [14].

3.1.4. Bone remodeling theory

This theory based on; bone resorption occurs coronally and bone apposition occurs apically. The dental follicle is the source for osteoblasts and osteoclasts [4,13].

Whether bone remodeling that occurs around teeth causes or is the effect of tooth movement is not known, and both circumstances may apply [13]. The strongest evidence in support of bone remodeling as a cause of tooth movement comes from a series of experiments in dogs. When the developing premolar is removed without disturbing the dental follicle, or if eruption is prevented by wiring the tooth germ down to the lower border of the mandible, an eruptive pathway still forms within the bone overlying the enucleated tooth as osteoclasts widen the gubernacular canal (Fig. 3). If the dental follicle is removed, however, no eruptive pathway forms. Furthermore, if a metal or silicone replica replaces tooth germ and so as long as the dental follicle is

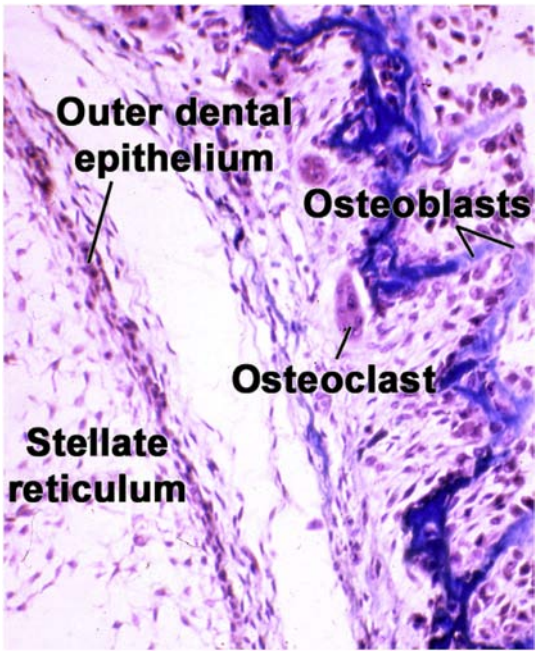

Fig. 3. Photomicrograph showing bone remodeling [4].

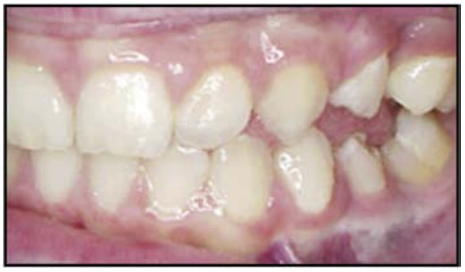

Fig. 4. Clinical photograph of patient with mutation in the PTH1R gene [12].

retained, the replica will erupt, with formation of an eruptive pathway. It is concluded that programmed bone remodeling can and does occur (i.e., an eruptive pathway forms in bone without a developing and growing tooth). Second, the dental follicle is involved. However, the conclusion cannot be drawn that the demonstration of an eruptive pathway forming within bone means that bone remodeling is responsible for tooth movement unless coincident bone deposition also can be demonstrated at the base of the crypt where its prevention can interfere with tooth eruption [4].

Recently the molecular basis of tooth eruption supports bone remodeling theory as it confirms that mutation of the parathyroid hormone receptor 1 (PTH1R) gene is correlated with disturbances in bone remodeling and leads to primary failure of eruption (PFE) [12]. PFE is nonsyndromic eruption disturbance that is not associated with defective osteoclasts [12]. The affected teeth had supracrestal presentation and progressive open bite which is hallmark criteria of PFE (Fig. 4) [12,15].

3.1.5. Dental follicle theory

The follicular theory postulates that the dental follicle is capable of inducing, bone resorption above the developing crown and bone apposition below it (Fig. 5). This enables the formation of an eruptive path to occur through which the tooth will be passively conducted [16]. In osteopetrotic animal, which lack a factor that stimulates differentiation of osteoclasts, eruption is prevented, because no mechanism for bone removal exists. However, local administration of this factor, colony-stimulating factor 1 (CSF-1), permits the differentiation of osteoclasts and eruption occurs [4].

Recently molecular studies have revealed that eruption is regulated by inductive signals between the dental follicle, reduced enamel epithelium (REE), stellate reticulum and alveolar bone [17]. Regional differences in the dental follicle were described [17]. It is suggested that the coronal aspect of the dental follicle regulates osteoclastogenesis (bone resorption) and the basal aspect of the dental follicle regulates osteogenesis (bone formation) [17]. This was assessed using laser capture microdissection (Fig. 6). Real time reverse transcription-

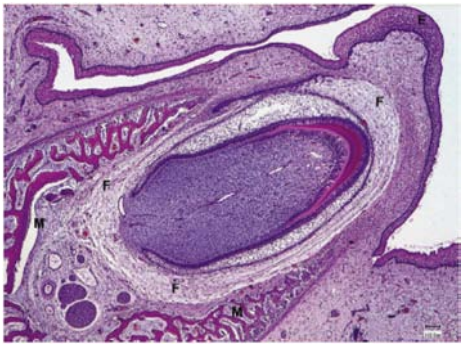

Fig. 5. Photomicrograph of a developing dog tooth indicating the position of the dental follicle (F) around the developing tooth, developing mandibular alveolar bone (M) and overlying oral epithelium (E) [17].

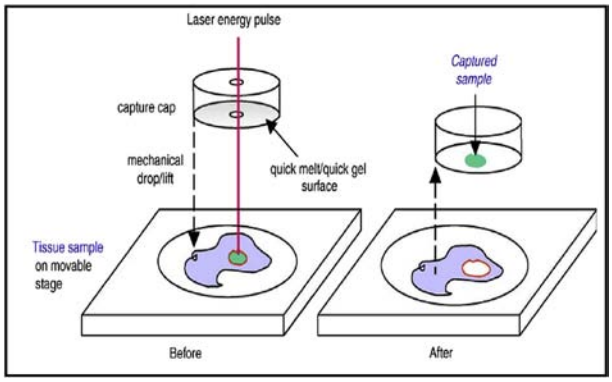

Fig. 6. A diagram showing: Laser capture microdissection (LCM) [18].

polymerase chain reaction (RT-PCR) was used to assess the expression of bone resorption and bone formation marker genes. The receptor activator of nuclear factor kappa B ligand (RANKL) gene is a marker gene for bone resorption. Bone morphogenetic protein-2 (BMP-2) gene is a marker for bone formation. The results showed a higher expression of RANKL genes in the coronal half of the dental follicle, and higher expression of BMP-2 genes in the basal half of the follicle [17].

3.1.5.1. Current concepts concerning the paracrine signaling function of the dental follicle in tooth eruption. Tooth development is regulated by a cascade of mutual interactions between the dental epithelium and the dental mesenchyme [19].

Correspondingly, the process of tooth eruption is regulated by cellular events leading to the recruitment of monocytes to the dental follicle followed by bone resorption [20]. This molecular events are initiated by interactions between the dental follicle, the REE and the stellate reticulum [21].

Apoptosis of epithelial cells during the advanced stages of enamel secretion have been reported [22]. This apoptotic process is has a direct influence on osteoclastogenesis through the release of interleukin-1α (IL-1α) by stellate reticulum cells, which its receptors are located in the dental follicle [20]. IL-1α consequently stimulates the expression of CSF-1 and monocyte chemotactic protein-1 (MCP-1) in the dental follicle, allowing the dental follicle to act as a chemoatractant for monocytes [20]. The stellate reticulum cells also participate in bone resorption by releasing parathyroid hormone-related protein (PTHrP) which further increases the expression of both MCP-1 and CSF-1 [23]. CSF-1 down-regulates the expression of osteoprotegerin (OPG), a well-known snare receptor for RANKL which inhibit osteoclast differentiation [24]. The cells of the REE and stellate reticulum therefore exert a paracrine effect on the dental follicle, enhancing the expression of chemoattractant molecules [25]. Additionally, the REE also secretes proteases that aid in creating an eruption pathway through enzymatic digestion of collagens [26]. Other molecules such as epidermal growth factor (EGF) and transforming growth factor β 1 (TGF-β1) released by the cells of the dental follicle enhance also the expression of CSF-1 in the dental follicle (Figs. 7 and 8) [27].

Bone resorption is however not sufficient for the displacement of the tooth. Thus, coronal bone resorption must be coupled with apical bone formation [28]. The expression of these BMPs is greatly enhanced by tumor necrosis factor–α (TNF-α) [28]. The cascade of signaling events at the apical aspect of the developing tooth, are not completely elucidated [29].

Matrix metalloproteinases (MMPs) are capable of degrading extracellular matrix (ECM) structural. They play important roles in tissue development [31].

Membrane-type 1 matrix metalloproteinase (MT1-MMP) is specific for collagens (I, II, and III), gelatin, fibronectin, and other matrix molecules [32]. MT1-MMP is essential during development and expressed

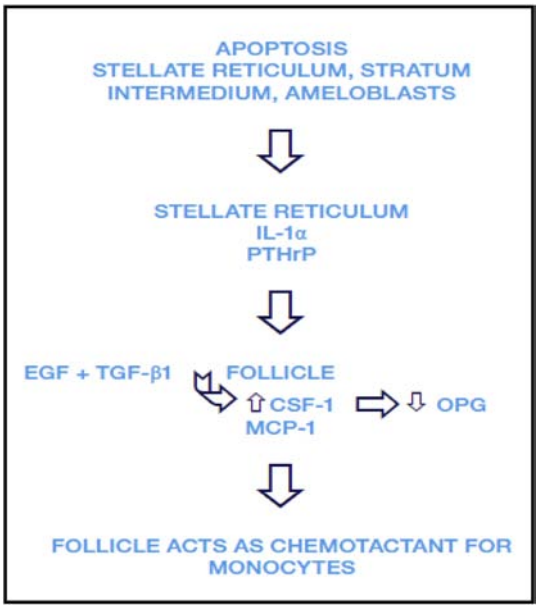

Fig. 7. Paracrine signaling at the coronal half of the erupting tooth [17].

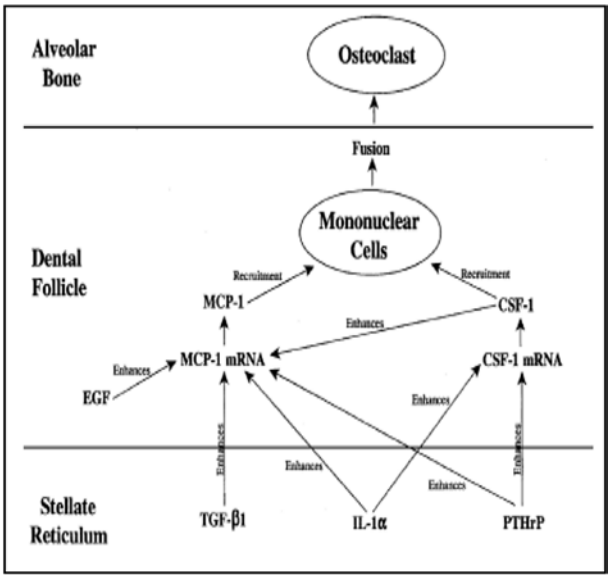

Fig. 8. Paracrine signaling between the stellate reticulum and dental follicle, as well as within the dental follicle only [30].

in the tooth and the surrounding connective tissue [33,34].

Migratory capabilities of follicle cells are disturbed in the absence of MT1-MMP, as collagen content increases in the dental follicle. Also MMPs have role in cell migration [35].

3.1.6. Periodontal ligament traction theory

This theory is based on the postulation that periodontal ligament (PDL)-dental follicle complex possesses eruptive force due to the traction power that fibroblasts have [4]. In continuously growing rodent and rabbit incisors teeth, surgical procedures performed and effectively eliminated dental pulpal pressure, dentin formation, and the cervical loop from contributing to incisor eruption, and PDL is the only tissue responsible for eruption of this tooth [36]. Moreover, fibroblasts move incisally along the erupting tooth, and their contraction generates significant force for tooth eruption [37].

However, experiments in a rat model using lathyrogens (amino acid derivatives that cause defective fibril formation when applied to the PDL) did not cause different rate of eruption when compared to untreated rats [38]. Moreover, the rate of collagen turnover is much higher than that of eruption [39]. Additionally, there is no difference in metabolic structures within fibroblasts in the PDL of rapidly erupting teeth and fully erupted teeth [40]. Also, periodontal fibroblasts exhibit characteristics of cells actively synthesizing and secreting [41]. Moreover, the ability of rootless teeth to erupt on schedule indicates that the PDL is not essential for eruption [42].

Recently it is hypothesized that functional stress results in greater strain in dental follicle and PDL than in bone, these soft tissues act as stress sensors [43]. Bone resorption and deposition involved with tooth movement, is critical surface phenomena at the interface between soft and bony tissues surrounding the developing tooth [44]. Moreover, teeth normally drift forward and upwards in the jaws, which is not the case in either osseo-integrated implants or when there is pathological fusion of the bone to teeth [45]. Furthermore, The PDL has mechanosensor activity during orthodontic treatment [46].

Lately, it is confirmed that PDL fibroblast orientation increased significantly during eruption (Fig. 9) [47]. It is proposed that PDL fibroblasts connect to collagen fibers inserting into the tooth's cementum so their occlusal migration pulls the tooth toward the oral cavity [47].

PDL fibroblasts are spindle-shaped with multiple processes that join with other cells during ligament development [48]. The fibroblasts long axis is aligned parallel with the orientation of collagen fibers [49]. They both create and are responsive to mechanical forces through focal adhesion complexes [50]. In PDL fibroblasts, changes in the strain environment induce changes in gene expression, such as the upregulation of collagen 1 [51]. Also, the importance of the CD44 receptor in cell–cell and cell–matrix interactions is demonstrated [52]. The proliferation and migration of PDL cells has been linked with CD44/HA interactions [53].

3.1.7. Molecular determinants in tooth eruption

Eruption molecules control the timing of the cellular events of eruption [54].

The RANKL needed for alveolar bone resorption come from the dental follicle. Also CSF-1, down-regulates the expression of OPG to enable osteoclastogenesis to occur. Also secreted frizzled-related protein-1 (SFRP-1) that inhibits osteoclastogenesis, also has its gene expression down-regulated in the dental follicle [55].

CSF-1 and MCP-1 were maximally expressed in the dental follicle. Endothelial monocyte-activating polypeptide (EMAP-II) has been shown to have a chemotactic effect on mononuclear cells. It up regulates the gene expression of both CSF-1 and MCP-1 [56].

The transcription factor gene c-fos and the transcription factor genes nuclear factor kappa-light-chain-enhancer of activated B cells (NFkB 1) and (NFkB 2) are needed for osteoclast differentiation [57]. Type I receptor of interleukin-1α (IL-1R), is present in the dental follicle, and its gene is enhanced by a ligand in the stellate reticulum [58].

Prior to eruption, CSF-1 expression is reduced and appears to be replaced by VEGF which is highly expressed in the dental sac. VEGF up regulates the expression of RANK [59].

BMP-2 is highly expressed in the basal half of the dental follicle. BMPs regulate the expression of Cbfa1 (core binding factor a1). It acts as a key transcriptional regulator of osteoblast differentiation during bone formation [60].

At the onset of eruption, the sialoprotein of 95,000 relative molecular weight (DF-95), is reduced by exactly the amount of three new sialoproteins with MW 20–25,000. Fragmentation of DF-95 is a biochemical marker of the beginning of tooth eruption. Immunolocalization of DF-95 in the REE is a biochemical evidence in initiation of eruption. Proteases of the enamel organ cause fragmentation of DF-95 and release metalloproteinase thus they initiate eruption [61].

Wnt/β-catenin signaling plays an important role in bone formation and regeneration [62].

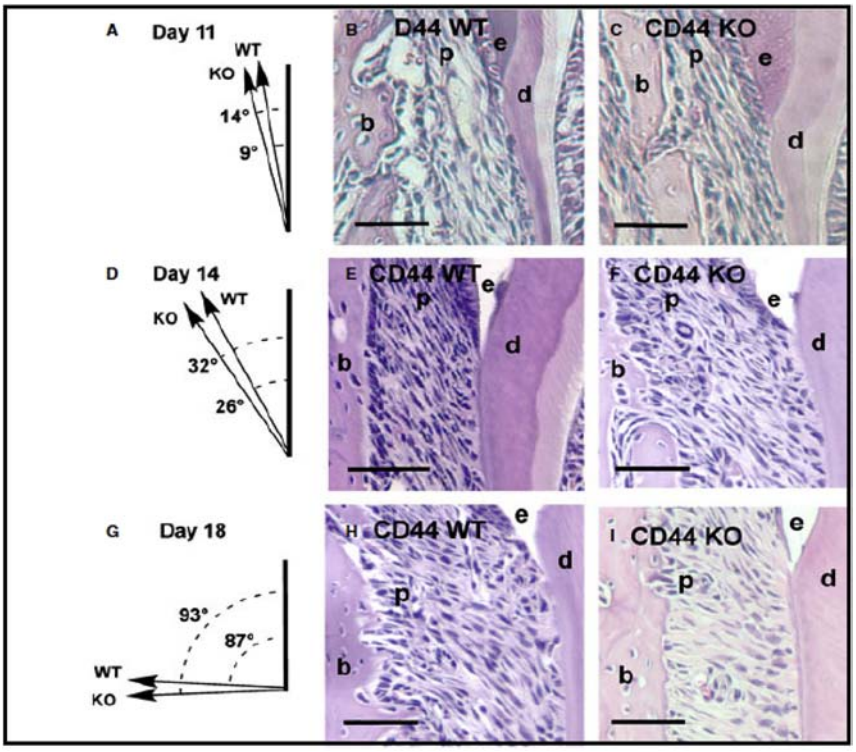

Fig. 9. Photomicrographs showing: PDL fibroblast orientation within the cervical region during mandibular first molar (M1) eruption and occlusion. Intraosseous eruption, (A–C), mucosal penetration, (D–F), and preocclusal eruption (G–I). Enamel (e), dentin (d), bone (b) and the PDL (p). KO, knockout; WT, wild type. Scale bar = 100 μm [47].

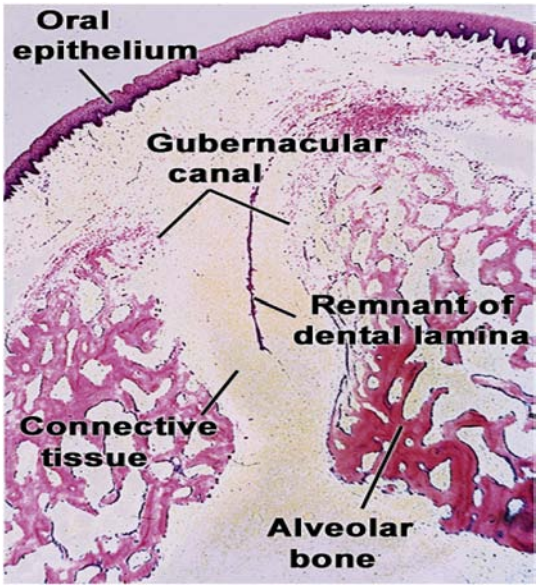

Fig. 10. Photomicrograph showing gubernacular canal and cord [4].

The gubernacular cord formation starts from the remnants of dental lamina cells [63]. This structure is located behind the deciduous tooth [64]. In this cord, there is EGF (epithelial growth factor), which has the capacity to induce bone resorption leaving a space surrounding this cord, so-called the gubernacular canal (Fig. 10) [65].

3.2. Recent theories of eruption

3.2.1. Bite forces sensed by soft tissue dental follicles theory

This theory postulates that follicular soft tissues detect bite-forces and so direct bone remodeling with the effect of enabling tooth eruption [11].

The authors reported the highest equivalent strains induced by bite forces in the dental follicle and PDL in both erupted and unerupted teeth irrespective of incisive or unilateral molar bite forces (Fig. 11). Examination of the soft tissue dental follicles, suggested broad areas of compression in overlying crowns, and wide zones of tension in follicle below root apices (Fig. 12) [11]. So, these soft act as relevant stress sensors [11].

3.2.2. Innervation-provoked pressure theory

This theory postulates that the root membrane acts as a glandular membrane. So, the innervation in this membrane causes pressure in the apical part of the tooth which results in tooth eruption [6].

It is hypothesized that tooth eruption depends on [6].
(1) Space in the pathway of eruption,
(2) Pressure from below,
(3) Adaptation of the periodontal membrane.

1. The crown follicle creates the necessary space in the eruption path [6].
2. The root membrane functions as a glandular membrane. So, the innervation causes overpressure that causes the tooth to elevate in the eruption direction [6,66,67].
3. The adaptability of the periodontal membrane is essential for eruption [6,68].

3.2.3. The equilibrium theory

After the functional plane is reached, the eruption of the tooth is balanced in response to the growth of the vertical growth of the mandible [69].

As the mandible grows vertically away from the maxilla, the teeth have more room to erupt occlusally in order to maintain occlusal contact with the opposing arch. This model of tooth eruption reinforces the idea that postemergent tooth eruption, after reaching functional occlusion, is controlled by forces impeding eruption, as opposed to encouraging forces. These balancing forces of masticatory function and the soft tissue pressures from the lips, cheeks, and tongue are the rate-limiting factors of postfunctional occlusal eruption [12,69]

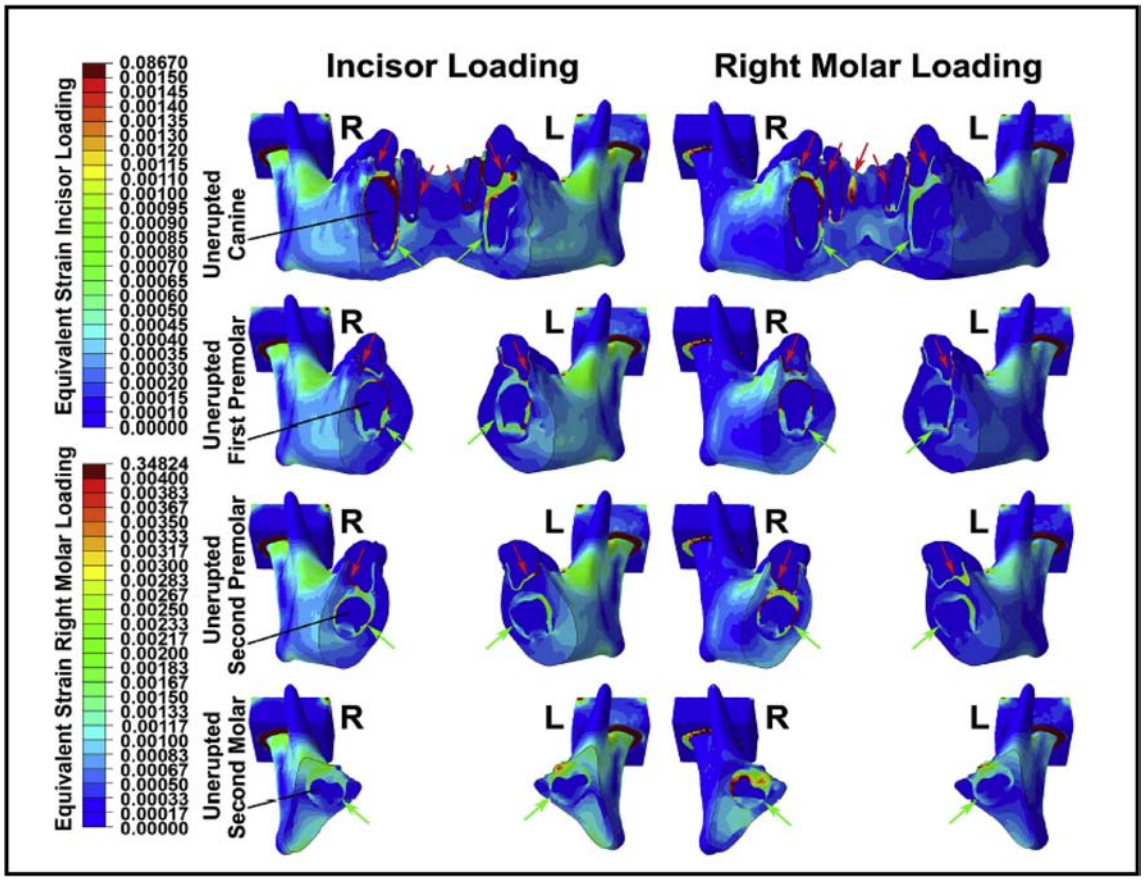

Fig. 11. Diagrams showing patterns of equivalent strain. Irrespective the loading applied, equivalent strain was high in soft tissues of the PDL (red arrows) and dental follicles (green arrows), and lower levels of strain in the hard tissues [11].

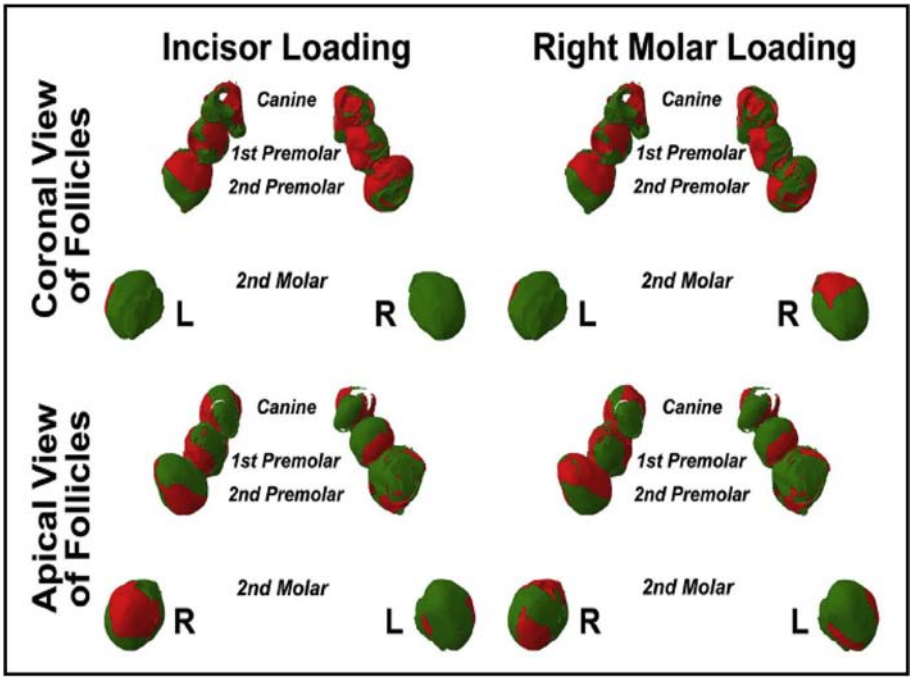

Fig. 12. Dental follicle compression (red) and tension (green) during bite forces. The upper surfaces of dental follicles are subject to greater compression, as compared with the lower surfaces which were subject to greater tension [11].

The lasting eruptive movement that occurs while the teeth are free of contact, supports the idea that eruptive control is based on the continuous force of the surrounding soft tissues [12].

3.2.4. Neuromuscular theory or unification theory

The neuromuscular theory or unification theory of tooth eruption states that the synchronized forces of the orofacial muscles, under the control of the central nervous system, are responsible for the active movements of a tooth and the molecular events prepared a pathway under the control of these forces [68,70−74].

The coordinated neuromuscular forces are converted into electrical, electrochemical and biomechanical energies for the stimulation of cellular and molecular activities within and around the dental follicle and enamel organ to prepare a pathway as well as other cellular functions for eruption of a developing tooth [55,70].

4. Evidence based on current systematic reviews

[1] A detailed analysis of the findings from scientific studies on mechanisms of tooth eruption was conducted [70].
[2] Systematic analysis of epidemiologic studies as well as many studies on animal tissues was carried out to understand the mechanisms behind tooth eruption [6].
[3] Other authors conducted a systematic review to outline the possible mechanism of tooth eruption right from its development in the bony crypt to its eruption till the occlusal level [3].

5. Conclusions and future considerations

- To sum up, tooth eruption must be considered as a stage of tooth development.
- Root follicle, periodontal membrane, and crown follicle are involved in the eruption process.
- Dental follicle and PDL play mechanosensor role in tooth eruption.
- The orientation of PDL fibroblasts determines the tooth directional movement.
- Root formation produces compressive coronal and tensile apical hydrostatic stress resulting in tooth eruption.
- The molecular and enzymic activities, are controlled by neuromuscular forces.
- Each of the eruption theories has a say to some portion of the eruption process.

The presence of stem cells in the dental follicle [75], raises around their potential role in tooth eruption. Identification of role of stem cells during tooth eruption still needs further research.

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