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Primary Failure Of Eruption – A Review Article

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Abstract:
Primary Failure of Eruption (PFE) is a rare, non-syndromic eruption disorder characterized by incomplete eruption of posterior teeth in the absence of any mechanical obstruction. Unlike ankylosis or mechanical eruption failure, teeth affected by PFE demonstrate minimal or no response to orthodontic traction, often resulting in posterior open bite, asymmetric dental arches, and complex therapeutic challenges. This review article provides a comprehensive overview of Primary Failure of Eruption (PFE), highlighting its etiology, genetic mechanisms, clinical manifestations, diagnostic challenges, and treatment considerations. It synthesizes evidence on the role of PTH1R mutations and the PTHrP–PTH1R signaling pathway in eruption failure, examines variable clinical patterns, it also explores evidence-based management strategies, emphasizing the importance of a coordinated interdisciplinary approach that integrates orthodontic assessment with restorative, prosthetic, and surgical interventions when necessary. This review aims to provide clinicians and researchers with a structured framework for understanding, diagnosing, and managing PFE effectively.

Key Word: *Primary Failure of Eruption (PFE); PTH1R Gene Mutations; Tooth Eruption Disorders; Posterior Open Bite; Orthodontic Management,*

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I. Introduction

Tooth eruption is a complex, biologically orchestrated process that enables the transition of a tooth from its developmental site within the alveolar bone to its functional position in the oral cavity. Massler and Schour (1941) defined eruption as "the movement of a tooth from its site of development within the alveolar process to its functional position in the oral cavity".[1] This pathway necessitates a coordinated interaction of bone resorption and formation, root development, and soft tissue remodeling. During eruption, bone and root development occur in one direction, while bone resorption—often involving the roots of primary teeth—takes place in the direction of movement.[2] Carlson (1944), in his radiographic study of permanent premolars, reported that eruption begins only after crown completion, is accompanied by root formation at the expense of basal bone, and is characterized by rapid pre-occlusal eruption, gradual occlusal adjustment, and lifelong compensatory eruption with alveolar growth.[3]

Although the precise biological triggers governing eruption initiation, rate modulation, and deceleration at the occlusal plane remain incompletely understood, studies across species suggest that eruption is largely dependent on the dental follicle. Following crown formation, the follicle initiates a cascade of cellular and molecular events that mediate bone resorption and establish the eruption pathway. Various mediators, including matrix metalloproteinases, interleukin-1, epidermal growth factor-1, and yet unidentified proteins from the follicle and enamel organ, have been implicated in this regulatory network.[2]

Failures in tooth eruption, although relatively rare, can have significant clinical consequences. For instance, the prevalence of non-eruption of first or second permanent molars is approximately 0.06%,[4] and such cases are frequently associated with posterior open bite malocclusion.[5] Proffit and Vig defined Primary Failure of Eruption (PFE) as incomplete eruption of teeth despite the presence of a clear eruption pathway, distinguishing it from eruption failure due to mechanical obstruction.[6] Frazier-Bowers and colleagues further classified PFE into three types: Type I, where all affected teeth lack eruptive potential leading to a progressive posterior open bite; Type II, where eruptive potential varies among teeth distal to the most mesially affected tooth; and Type III, which combines features of both Type I and Type II. Additionally, an alternative classification proposed by the same group differentiates between two chronologic patterns: Type I, with a consistent loss of eruption potential at a defined developmental stage, and Type II, where teeth show variable eruption potential depending on the timing of onset and stage of root development.[7]

Complementing these perspectives, Raghoebar et al. described localized eruption failures as either primary retention, where the eruption process ceases before penetration of the oral mucosa, or secondary retention, characterized by cessation of eruption after the tooth has emerged into the oral cavity.[8] Collectively,

these classifications underscore the heterogeneity of PFE and highlight the importance of accurate diagnosis, as management requires precise differentiation from other forms of eruption disturbance.

This review aims to synthesize current knowledge on the etiology, classification, diagnostic criteria, and management strategies of Primary Failure of Eruption, with a focus on bridging molecular insights with clinical implications.

II. Etiology

Eruption failure has been attributed to a wide range of systemic and local factors.[9] One of the key molecular mediators implicated in eruption biology is parathyroid-hormone-related protein (PTHrP). Although PTHrP is known to influence bone biology, its role in modulating human periodontal ligament (PDL) cells has been further clarified. Fukushima et al. demonstrated that PTHrP promotes osteoclastogenesis via PDL cells by upregulating RANKL expression while simultaneously downregulating osteoprotegerin (OPG), the decoy receptor for RANKL. This mechanism was shown to be independent of the classical cAMP/Protein Kinase A pathway, instead relying significantly on Protein Kinase C signaling. The findings suggest that locally produced PTHrP, such as that released by developing teeth, may influence PDL cells to facilitate osteoclast formation, thereby contributing to physiological processes like deciduous root resorption and alveolar bone remodeling.[10]

Genetic factors have also been strongly implicated in primary failure of eruption (PFE). Decker et al. suggested that PFE is associated with mutations in the *PTH1R* gene, although the precise molecular mechanisms remain unclear.[11] Frazier-Bowers et al. reported that these mutations often result in truncations of the receptor protein, impairing receptor activation, ligand binding, and downstream signaling. They further proposed a dose-dependent model of clinical manifestation: carriers with modest phenotypic expression or partial receptor function may not exhibit eruption failure, whereas more severe disruptions, particularly in tissues with high PTH1R dependence such as teeth and joint cartilage, may result in both dental phenotypes and osteoarthritis.[12]

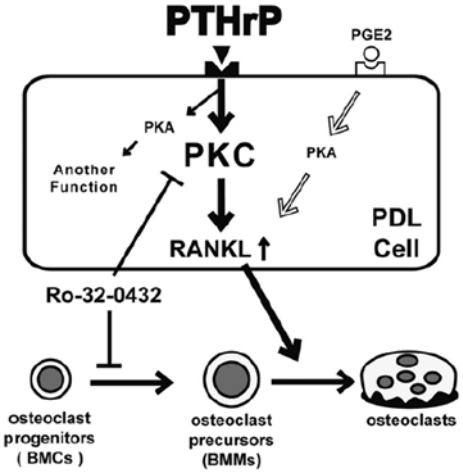

Figure 1: Etiology Of PFE

Further evidence for the centrality of the PTHrP–PTH1R pathway in eruption was provided by Nagata et al. (2020), who showed that this signaling axis directly regulates the growth and differentiation of dental mesenchymal progenitor cells into alveolar osteoblasts, cementoblasts, and PDL cells. Through the RANKL–RANK pathway, it also indirectly modulates osteoclast activity and bone resorption.[13] Importantly, this suggests that tooth eruption and root formation are not independent processes but rather closely coupled, with dental follicle–derived mesenchymal progenitors acting as a common source for osteoclastogenesis, root formation, and periodontal attachment apparatus development.

Autocrine signaling of PTHrP through its receptor (PPR) has been shown to be critical in maintaining mesenchymal progenitor cell populations and guiding their fate decisions. Disruption of this signaling cascade results in defective root development, impaired periodontal attachment apparatus formation, and ultimately molar eruption failure—phenotypes that closely parallel clinical presentations of PFE in humans.[13]

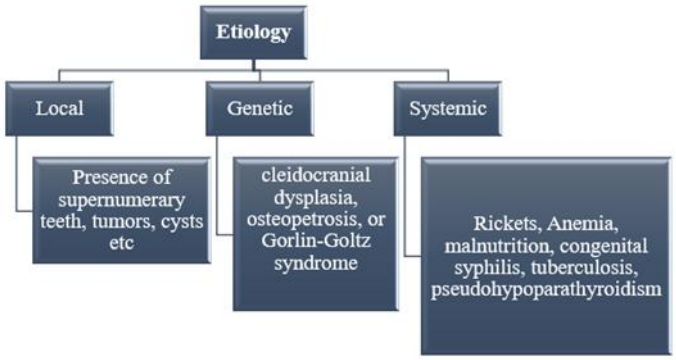

Fig 2: PTHrP–PTH1R pathway

III. Clinical Features

Proffit and Vig (1981) list seven characteristics that could point to an eruption's primary failure.[14]

a. Posterior teeth are more commonly affected, and the bite distal to the first affected tooth is usually completely open.
b. The affected teeth may or may not have initially erupted into occlusion before submerging.
c. Deciduous teeth, especially second deciduous molars, are commonly submerged.
d. Involvement may be unilateral or bilateral.
e. Involved permanent teeth may become ankylosed after failure of eruption has occurred.
f. Orthodontic extrusion is unsuccessful and usually leads to ankylosis.
g. Although other members of the family may be affected they are not usually close relatives.

Ahmad et al. (2006) further described the clinical presentation, noting that first and second permanent molars are the most commonly affected teeth across all four quadrants, with equal distribution between maxillary and mandibular arches as well as between the left and right sides.[15] The hallmark features of PFE include infraocclusion of the affected teeth, the presence of a significant posterior open bite despite otherwise normal vertical facial growth, and the inability to orthodontically move affected teeth.[15]

The etiology underlying the wide phenotypic variability of PFE remains incompletely understood. Even within families harboring identical *PTH1R* mutations, clinical expression may vary: some individuals exhibit unilateral involvement, whereas others present with bilateral involvement. This intra-familial variability suggests the potential contribution of additional genetic, epigenetic, or environmental modifiers.[16] Another unresolved question concerns the preferential susceptibility of posterior teeth, with anterior dentition typically spared.

Frazier-Bowers et al. proposed that this posterior predilection may be attributable to the spatially and temporally regulated function of *PTH1R*, whose activity may play a more critical role in the posterior alveolar regions.[16] This hypothesis parallels the expression patterns of other tooth-patterning genes such as *MSX1*, *DLX2*, and *PAX9*, which demonstrate region- and stage-specific influences on tooth development and eruption.[16]

IV. Management

The management of primary failure of eruption (PFE) requires careful consideration of the clinical presentation, as treatment strategies vary depending on the number of teeth involved, the severity of malocclusion, and the degree of alveolar deformity. Orthodontic treatment is generally contraindicated, as the application of extrusive forces to affected teeth often induces ankylosis, rendering tooth movement impossible.[6] Consequently, conventional orthodontic therapy alone is insufficient for correcting PFE-associated malocclusion.

In cases of limited involvement, where only a few teeth are affected and an acceptable occlusion can be achieved, prosthodontic restoration is considered the treatment of choice.[17] Prosthetic rehabilitation not only restores function but also improves the level of the occlusal plane, thereby alleviating malocclusion.[18] In more severe presentations, prosthetic buildups may be inadequate, and extraction of the affected teeth followed by implant placement—often in combination with alveolar ridge augmentation—may be necessary. For extensive cases characterized by multiple unerupted teeth and significant alveolar deformity, removable prosthetic rehabilitation provides an effective early solution to re-establish occlusion.[19]

Surgical interventions are indicated in select cases. Segmental osteotomy of the alveolar bone associated with PFE has been employed to reposition the affected segment and correct the occlusal plane. Stability may be enhanced through placement of a bone graft between the repositioned segment and the basal

alveolar bone.[17] Additionally, distraction osteogenesis of the alveolar bone has been reported as a viable approach in patients with severe lateral open bite secondary to PFE.[20,21] Overall, management strategies for PFE must be individualized, balancing restorative, surgical, and prosthetic approaches to achieve functional occlusion and long-term stability.

V. Conclusion

A clear understanding of abnormal tooth eruption can only be achieved by first establishing a thorough knowledge of the normal eruption process, including its timing, sequence, and underlying biological mechanisms.

Primary Failure of Eruption (PFE) is an uncommon but clinically important eruption disorder, most commonly linked to pathogenic variants in the PTH1R gene. The condition is characterized by its heterogeneous clinical presentation, with variable expressivity, a predilection for the posterior dentition, and a consistent lack of responsiveness to orthodontic traction. These features make both diagnosis and treatment uniquely challenging. Early and accurate identification is crucial, as inappropriate orthodontic intervention not only proves ineffective but may also worsen infraocclusion and increase the risk of ankylosis, thereby complicating long-term management.

Successful treatment planning relies on a multidisciplinary approach, incorporating careful clinical and radiographic evaluation, genetic testing where appropriate, genetic counseling for affected families, and individualized prosthetic or surgical rehabilitation strategies. Furthermore, as our understanding of the molecular mechanisms governing tooth eruption advances, novel diagnostic tools and targeted therapeutic approaches may emerge, offering the potential to improve prognosis and expand treatment options for patients with PFE. Continued research in this field is therefore essential, bridging the gap between molecular genetics and clinical practice, and ultimately enhancing patient care.

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