

**PRIMARY FAILURE OF ERUPTION:  
FURTHER CHARACTERIZATION OF A RARE ERUPTION DISORDER**

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## **ABSTRACT**

**KAREN E. KOEHLER: Primary Failure of Eruption: Further Characterization of a Rare  
Eruption Disorder**

(Under the direction of Dr. Sylvia A. Frazier-Bowers)

Primary failure of eruption (PFE) is a rare condition that leads to spectacular posterior open bites and does not respond to orthodontic treatment. Records from 97 patients with posterior open bite were analyzed. Based on key characteristics, subjects were classified as having PFE, indeterminate failure of eruption (IFE), and mechanical failure of eruption (MFE). Results showed that PFE affects mostly posterior teeth, affects all teeth distal to the first affected tooth, often presents with a cleared eruption path that the tooth fails to follow, and appears to have two forms. Type I exhibits a similar lack of eruption potential of affected teeth, and Type II has a varied eruption potential. This study also supports the genetic etiology of PFE which is likely due to a defect in a tooth-specific gene product. Differentiation between PFE and ankylosis is key to determining prognosis for orthodontic treatment and requires adequate longitudinal data.

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## LIST OF ABBREVIATIONS

Description	Abbreviation
Indeterminate Failure of Eruption.....	IFE
Mechanical Failure of Eruption.....	MFE
Posterior Open Bite.....	POB
Primary Failure of Eruption.....	PFE

## **SECTION I**

### **LITERATURE REVIEW**

Primary failure of eruption is a rare condition that can lead to spectacular posterior open bites. It is difficult to diagnose and even more difficult to treat due to the lack of response to orthodontic forces. Adding to the complexity of diagnosis is the myriad of confusing and sometimes conflicting terms used in the literature to describe eruption problems. Proper diagnosis is paramount and can save the patient and the orthodontist years of frustration and disappointment. The role of heredity as an etiology has been questioned and evidence of familial occurrence warrants further study. Understanding the genetic component of failure of eruption can aid in differential diagnosis of PFE, help in the early identification of affected family members and may eventually lead to new treatment modalities.

The scientific literature presented will discuss failure to erupt and the terminology used in the description of eruption problems. Possible causes will be identified with emphasis on impaction, ankylosis and PFE. Current literature on PFE and potentially related conditions will be reviewed, and case studies on the familial component of this condition will be presented. Limitations of previous studies will also be discussed.

#### **Spectrum of Eruption Disturbances**

Tooth eruption has been defined as the movement of a tooth in an axial and occlusal direction from its developmental position within the jaw to its final functional position in the



occlusal plane.<sup>1</sup> In spite of concentrated research, the precise mechanisms that control eruption are still not well-understood, thus compounding the difficulty in studying the pathogenesis of abnormal eruption. Although eruption proceeds without incident in most individuals, sometimes eruption failures can occur because of a variety of environmental and genetic factors.

When a tooth with normal development and adequate root length fails to erupt significantly behind its appropriate schedule many options must be considered before an adequate differential diagnosis can be made. Possible etiologies fall into two broad categories: systemic and local factors. Some of the systemic conditions that can lead to delayed or failed eruption are genetic disorders like cleidocranial dysplasia, Gardner syndrome and osteopetrosis.<sup>2,3</sup> Endocrine derangements like hypothyroidism can also cause generalized underdevelopment and delayed eruption of the dentition.<sup>4,5</sup> In general, systemic causes lead to widespread impact on most of the dentition, as opposed to local factors that tend to affect a smaller number of teeth. Local causes are varied and range from physical barriers to local metabolic disturbances, trauma and infection.<sup>6,7</sup> Probably the most common local factor is mechanical obstruction either integral or peripheral to the tooth, as in ankylosis or impaction. Barriers can also be of soft tissue origin, as in tumors and cysts.<sup>8</sup> Events that shift the equilibrium environment of the tooth can affect the tooth's ability to erupt, such as an unfavorable tongue posture or digit habit.<sup>5,9,10</sup> Failure of the eruption mechanism itself is another possibility, as in primary failure of eruption.

The study of eruption, like the process itself, is complicated. Many conflicting terms have been used in the literature to describe eruption problems. Although unerupted permanent teeth are rare "in reviewing the scant literature, the terminology alone can be

confusing.”<sup>5</sup> Different authors define and apply the same terms to describe distinctly different problems, thus adding uncertainty to an already difficult topic. For instance, the terms submerged, depressed, reimpaction, reinclusion and ankylosis may be used to describe secondary retention.<sup>11,12</sup> Rasmussen uses the term “primary failure of eruption” to describe any tooth which fails to erupt regardless of whether the failure is due to a mechanical obstacle in the eruption path or a failure of the eruption mechanism itself. He includes local barriers such as supernumerary teeth and cysts, as well as, impaction due to lack of space and cleidocranial dysplasia as examples of primary failure of eruption. Rasmussen also makes a distinction between the terms “late” and “retarded.” The term late applies when the coordination between tooth development and eruption is normal although delayed by more than 2 SD. He uses the term retarded to describe an eruption pattern that has an interruption in the coordination between tooth development and eruption.<sup>13</sup> Other authors use do not apply the same criteria and use the term late in the general sense of simply behind schedule, regardless of the developmental stage.<sup>14</sup>

#### *Prevalence of Eruption Failures in Permanent Teeth*

Failure of permanent teeth to erupt, with the exception of third molars, is very rare, particularly when looking at first and second permanent molars.<sup>15</sup> Only two studies could be found evaluating the prevalence of delayed or unerupted permanent teeth, and local factors were the predominant cause. In Grover’s study of 5000 Army recruits, only 8 out of over 10,000 unerupted teeth were first or second molars. The etiology of at least two of these cases could be attributed to impaction or an odontoma.<sup>15</sup> In Johnsen’s study only 5 out of 1000 cases involved first or second molars. In all five cases, the delayed eruption was

attributed to impactions, cysts or ankyloses.<sup>16</sup> Failure of permanent molars to erupt without known cause is extremely uncommon.<sup>17</sup>

### *Impaction*

Impacted teeth are those prevented from erupting by some physical barrier in their path.<sup>6,11</sup> Impactions can occur as the result of malpositioning of the tooth bud, inadequate space in the dental arch, or obstruction in the path of eruption.<sup>12,15</sup> According to Kokich, impacted teeth are diverted from their normal eruption path or angulated aberrantly and eventually lose their potential to erupt. However, these teeth are not hopeless because orthodontics alone or in combination with surgery to remove the barrier can be employed to move these teeth into the arch.<sup>18</sup> The most commonly impacted teeth are the third molars and maxillary canines. Impaction of first and second molars is rare.<sup>15,16</sup> Raghoobar suggests that impaction may be diagnosed by examining the angulation of the tooth relative to its neighbors. If the long axis is not parallel to the normal eruption path, the tooth is diagnosed as impacted.<sup>12</sup>

### *Ankylosis*

Ankylosis is defined as a fusion of dentin or cementum with the alveolar bone.<sup>19</sup> The affected teeth are fixed in position and cannot continue to erupt or be moved orthodontically. Ankylosis can occur at any time during the lifespan of a tooth and is often a major contributing factor in dental malocclusion.<sup>11</sup> The cause is essentially unknown but is often attributed to local disturbances in metabolism or trauma. Given that certain teeth such as primary molars are frequently involved and that a familial tendency has been demonstrated by Kurol,<sup>20</sup> evidence points to the idea of genetic predisposition, at least in the case of primary molars.<sup>11,19</sup>

Diagnosis of ankylosis can be difficult. Andersson, et al, demonstrated in their study of reimplanted incisor teeth in monkeys that more than 20% of the root surface must be affixed to bone before an accurate clinical diagnosis can be made. Percussion and mobility tests were more sensitive and accurate than radiographic examination of the periodontal ligament space. In one case, 79% of the root surface was involved yet the radiograph was not indicative of ankylosis. In three cases, radiographic examination yielded a diagnosis of ankylosis, yet histologic examination proved normal.<sup>19</sup> Therefore, the diagnosis of ankylosis may not be supported by radiographic analysis alone.<sup>11</sup>

Incidence of ankylosis in primary teeth is fairly common and ranges from about 1.5% to 10%, depending on the study.<sup>11</sup> Occurrence of ankylosis in permanent teeth is largely unexamined, but frequency is estimated at only 10% of that of primary teeth.<sup>21</sup> The maxillary canine is believed to be most frequently affected.<sup>11</sup>

#### *Primary and Secondary Retention*

Primary retention has been described by Raghoobar and others as the cessation of eruption of a normally placed and developed tooth germ before emergence for which no physical barrier can be identified.<sup>7,22,23</sup> The term “primary retention” is synonymous with embedded and unerupted. When a tooth is at least two years behind its scheduled eruption primary retention should be suspected.<sup>12</sup> The etiology is unknown; however, a disturbance in the resorption of overlying bone similar to that found in cleidocranial dysplasia has been proposed. Primary retention is not believed to be related to an abnormality of the periodontal ligament but may be due to a disturbance of the dental follicle which fails to initiate the metabolic events necessary for resorption.<sup>12</sup>

Secondary retention refers to the cessation of eruption of a tooth after emergence without the evidence of a physical barrier in its path or as a result of an abnormal position.<sup>7</sup> Causative factors may be ankylosis, trauma, infection, disturbed local metabolism and genetic factors.<sup>7</sup> Illuminating studies by Raghoobar et al have provided histologic evidence of ankylosis as a primary etiologic agent. In their studies of secondarily retained molars, all retained teeth showed focal areas of ankylosis, mostly in the bifurcation and interradicular surfaces.<sup>7,24,25</sup> The proposed mechanism was the replacement of cementoblasts by osteoblasts due to a local disturbance in the periodontal ligament during the repair process of local physiologic resorption. In addition to histologic studies, focal ankylosis of secondarily retained molars has been shown using scanning electron and light microscopy. In the examination of 12 secondarily retained molars, the ankylosis involved 10-60% of the root surfaces.<sup>26</sup> Some of these were well below the clinically detectable level of 20%.<sup>19</sup>

Due to reports of a definite familial tendency, the cause of the developmental disturbance of the PDL may be inheritable.<sup>7,27</sup> Raghoobar demonstrated that this condition has a familial component in about 10% of the cases with the suggestion of an autosomal dominant inheritance pattern.<sup>25</sup> During one of his studies, six new cases of secondarily retained permanent molars occurred in the same sample population over four years.<sup>24</sup>

Many of the characteristics of secondary retention and the radiographs of index cases seem similar to primary failure of eruption. The fact that ankylosis was put forth as the causative factor of secondary retention does not preclude a failed eruption mechanism. Whether the mechanism of eruption is disturbed before or after ankylosis occurs is a question that remains unanswered, even by Raghoobars' studies. "It is apparent that some defect,

failure, or alteration of the periodontal ligament must precede ankylosis, because no ankylosis will occur in case of a normal periodontal membrane.”<sup>7</sup>

### **Primary Failure of Eruption**

When teeth do not erupt normally another possible etiology that must be considered is primary failure of eruption, or PFE. The term “primary failure of eruption” was first used by Proffit in a paper discussing equilibrium theory and the factors that affect the position of teeth.<sup>28</sup> The condition was further defined in the landmark paper published by Proffit and Vig in which PFE was described as a condition in which “nonankylosed teeth fail to erupt fully or partially because of malfunction of the eruption mechanism.” In their study of 16 cases, several key characteristics were identified:<sup>9</sup>

1. Posterior teeth were more frequently involved, and the teeth distal to the first affected tooth were also affected to some degree.
2. Capacity for eruption of affected teeth varied.
  - a. Involved teeth may have erupted partially and then ceased to erupt, relatively submerging although not ankylosed.
  - b. Involved teeth may have completely failed to erupt, with an uncoupling of the eruption and resorption mechanisms. In these cases the resorption appeared to be normal, but the tooth failed to follow the path created.
3. Deciduous molars were likely to be involved.
4. The condition was rarely symmetric, frequently unilateral, but could be bilateral.
5. Involved permanent teeth tended to become ankylosed at some point.
6. Orthodontic forces led to ankylosis rather than normal tooth movement.
7. Patients did not seem to have similarly affected close relatives.

Proffit and Vig also noted that involved teeth may erupt slightly but at rates that are far below the normal eruption rate. A cleared eruption pathway or enlarged follicle is sometimes seen radiographically lending evidence to the idea of aberrant eruption due to a failed eruptive force. Affected teeth that have been surgically exposed are generally reported to be easily movable within the crypt and not ankylosed. Although these teeth may have some response to orthodontic forces (at best 1-2mm), the response is abnormal and the teeth invariably become ankylosed before reaching occlusion.

The point is made that the permanent molars develop from a distal extension of the dental lamina. A gradient of eruption could explain why posterior teeth are affected more often than anterior teeth. The best evidence of a failure in the eruption mechanism is the lack of eruption in spite of the absence of any obstruction. Bone resorption without tooth movement is another indication. When posterior teeth erupt partially into the oral cavity and then stop, an asymmetrical pattern may indicate a problem with the eruption mechanism, as opposed to a bilaterally symmetric pattern which may indicate lip or tongue interference. Failure of these teeth to respond to orthodontic treatment such as vertical elastics is a strong indication that the eruption mechanism may be impaired.<sup>9</sup> Case studies illustrate that not only do affected teeth fail to respond to treatment, but also adjacent normal teeth are adversely affected by intrusion to the level of the affected teeth.<sup>9</sup>

Although an abnormal periodontal ligament seems to be the cause of PFE, “a precise definition of the problem in these patients will have to await elucidation of the eruption mechanism in normal persons.” Proffit and Vig concluded that “the problem in primary failure of eruption not only differs from the problem when there is mechanical obstruction to postemergent eruption but also is significantly different from the eruption failure owing to

lack of bone resorption which is observed in patients with cleidocranial dysplasia and related syndromes.”<sup>9</sup> Distinguishing between failure due to obstruction and failure due to an absent or abnormal eruption mechanism is key to determining the prognosis for the affected teeth because those that are mechanically blocked can presumably be treated orthodontically with some hope for success.

Prior to the Proffit and Vig paper, very few studies had been published on the subject and essentially all of the literature was in the form of case reports<sup>27,29,30</sup> describing either a failure of vertical adaptation<sup>31</sup> or reinclusion of molars. The same is true today.

#### *Case Studies of Eruption Failure*

Case studies offer powerful testimony to support the beliefs held and observations made concerning failure of eruption. Nashed’s case report on a patient with a severe posterior open bite suspected of PFE or mechanical obstruction illustrates the value of therapeutic diagnosis in some cases. The case involved one 13 year old boy with a Class III skeletal relationship and bilateral posterior open bites extending from the lateral incisors. The patient reported that his first molars had been extracted at age 8 (no reason given). After taking the patient’s history and completing the clinical and radiographic examinations, the differential diagnosis of PFE or mechanical obstruction was concluded. Nashed decided mechanical obstruction was the preferred diagnosis because of the bilateral, symmetrical pattern of the open bite. Mechanical obstruction was confirmed by successful orthodontic correction.<sup>10</sup>

Spieker reports a male patient with a maxillary right first molar which initially erupted into occlusion before age 9 and subsequently began to submerge. Although retrospective examination of radiographs revealed signs of submergence by the age of 10, the problem did not become clinically evident until one year later. Further observation at six months revealed



that the condition had worsened and the tooth was extracted. Although histologic examination was not performed, the oral surgeon who extracted the tooth noted no macroscopic ankylosis. As of nine months following the extraction, the adjacent second molar showed normal signs of eruption. Spieker comments that general dentists are in the best position to report on this phenomenon since they have the longitudinal radiographic data as well as access to family histories.<sup>5</sup>

Patients are not always aware of their malocclusions. Nagpal et al write about a 21 year old patient who reported to their clinic for a routine dental check up. The patient had no chief complaint related to difficulty in chewing and his medical history was unremarkable. On clinic examination, a significant bilateral posterior open bite was discovered involving all posterior teeth. All affected teeth showed radiographic signs of ankylosis. Since the patient had no functional problems, he declined treatment.<sup>17</sup>

### **Familial Aspect of Eruption Failures**

Although none of the cases examined by Proffit and Vig had similarly affected relatives, they did suppose that a genetic disturbance of varying penetrance and expressivity was the likely etiology, possibly leading to a local disturbance in metabolic activity or altered blood flow. They recommended further study of the families of affected individuals to examine the idea of autosomal dominant inheritance put forth by Bosker et al.<sup>27</sup>

### *Case Studies of Familial Occurrence*

Familial reinclusion of permanent molars was described by Bosker et al in their 1978 study of 55 individuals from 9 families affected by this condition. In a substantial number of cases, histologic autopsy of extracted teeth showed no evidence of ankylosis. Examination of pedigrees showed an autosomal dominant inheritance pattern with vertical transmission,

instances of male-to-male inheritance and no skipping of generations. Linkage studies were also done in which the possibility of close linkage between the “reinclusion gene” and blood group P could not be eliminated. They also proposed that the incidence of this failure of eruption may be more prevalent than previously reported due to the frequent overlooking of familial occurrence.<sup>27</sup>

Cases presented by Brady, Ireland and DiBiase highlight the difficulties in both diagnosis and treatment of affected patients as well as familial occurrence of PFE. Brady described a mother and son affected by primary failure of eruption. The son was followed for six years during which eruption was examined; teeth were exposed to no avail and finally extracted. Ultimately, prosthetic reconstruction was determined to be the best treatment. The mother also presented with symptoms suggestive of PFE. At an early age, her delayed eruption of permanent teeth led to a provisional diagnosis of cleidocranial dysplasia although the abnormalities were confined only to the dentition. Ireland reported on two sisters affected by abnormal eruption of posterior teeth. With the first sister he attempted to orthodontically extrude her posterior teeth using various techniques and eventually abandoned treatment after three years. The only occlusal contact attained was on the central incisors. When the younger sister presented with a similar although seemingly milder form of the problem, the decision was made to forego attempts for orthodontic extrusion. DiBiase also described PFE involving two sisters in which exposure of unerupted molars and extrusive mechanics failed to correct the open bites. The first sister presented with an asymmetrical bilateral posterior open bite that did not respond to orthodontic treatment of 4 ½ years. The younger sister also presented with an asymmetrical bilateral posterior open bite. Orthodontic correction was attempted, but again treatment was abandoned after 3 years leaving the patient with a posterior open bite.

Teeth were extracted atraumatically and were not thought to be ankylosed. In both cases, however, third molars erupted into occlusion.<sup>30,32,33</sup>

Winter et al determined their own definition of primary failure of eruption to be any tooth buried deep in the jaw bone covered by an intact mucosa. They studied severe infraocclusion of deciduous molars associated with eruptive disturbances of the permanent dentition. Their sample consisted of 28 children from 26 families with a mean observation time of 3 years and 7 months. In this sample 12 of the children had eruption disturbances of their permanent teeth, of which half were thought to be due to impaction and two of those confirmed. Winter also reported hypodontia in 17% along with a high incidence of taurodontism in his sample (68%). In the four families affected inheritance patterns were inconsistent. Three of the families showed an autosomal dominance pattern with complete penetrance and variable expressivity while the fourth showed an autosomal recessive pattern. Winter questions the role of ankylosis in the failed eruptive process as a possible secondary rather than initiating process and reiterates that orthodontic procedures designed to improve eruption are doomed to failure.<sup>34</sup>

Autosomal dominant inheritance has also been implicated in the etiology of a rare condition similar to PFE but involving all the permanent teeth. Inherited retarded eruption, so named by Rasmussen and Kotsaki, is a condition in which all permanent teeth fail to erupt well beyond the normal schedule. The eruption is called “retarded” because tooth formation and tooth eruption are uncoordinated. The typical presentation is severe retardation in eruption of the entire permanent dentition (most often considerably beyond 3 SD) with possible involvement of some primary teeth, eventual eruption of the teeth unless prevented by impaction, no other recognized somatic abnormalities, and familial inheritance following

an autosomal dominant pattern. Because the teeth eventually erupted, Rasmussen proposed that the “gene for tooth eruption” was present but demonstrated a “delayed onset.” This phenomenon is known to occur in human genetics as seen in Huntington’s disease.<sup>13,35</sup>

Rasmussen and Kotsaki studied 14 cases from 10 families over 15 years. The only etiological factor that could be identified was inheritance. The entire permanent dentition was affected; however, eruption of permanent teeth eventually occurred in the normal sequence although severely delayed (8 SD or more in some cases).<sup>35</sup>

Shokeir described a family with inherited retarded eruption in three individuals. Not only were the permanent teeth completely unerupted, but the primary teeth were considerably delayed with the first tooth emerging between 1-2 years of age. The father was 46 years old with no permanent teeth clinically present. Two of his five children displayed the same disorder. One had a history of dentigerous cysts.<sup>36</sup>

### **Limitations of Previous Studies**

Distinguishing between the many causes of delayed or failed eruption is challenging and the wide variety of terminology used in literature today is complicated. Thorough family histories and information from patient interviews were often missing or incomplete. The most critical step in the differential diagnosis of abnormal eruption is a thorough history.<sup>14</sup> Many of the systemic and local causes can only be eliminated as potential etiologies through the patient interview. The problem-oriented approach to diagnosis advocated by Proffit was not always in evidence.

“Unfortunately, the low prevalence of impaction of the first and second permanent molars and the difficulty of distinguishing between primary and secondary retention and impaction have been major factors underlying the lack of uniformity in the management of

these eruption disturbances.”<sup>22</sup> Since PFE is so rare, finding a sample size large enough to study the characteristics of the condition has been a difficult problem. Practically all of the current literature is in the form of isolated case studies.

### **Purpose of Present Study**

In spite of many years of research, the precise mechanisms that govern eruption are still not well-defined, although advances have been made in the field of molecular biology. Because of the gaps in knowledge, treatment decisions are often made via therapeutic diagnosis based on the practitioner’s judgment and clinical experience. Misdiagnosis can lead to years of unsuccessful treatment, deleterious effects on adjacent teeth, and frustrated patients and practitioners.

The purpose of this research is to provide critical information to the scientific and orthodontic communities that will aid in the diagnosis and characterization of primary failure of eruption. The specific aims are to define PFE in light of the new cases that have been collected, distinguish PFE from other causes of posterior open bite such as ankylosis and examine the hereditary nature of this condition. This is an observational, retrospective study of a series of cases sent between 1985 and 2005 by practicing orthodontists to the University of North Carolina for consultation regarding patients with suspected PFE.

## REFERENCES

1. Daskalogiannakis J. Glossary of Orthodontic Terms. First ed. van der Linden, F., Miethke RR, McNamara Jr. JA, editors. Berlin: Quintessence Publishing Co, Inc; 2000.
2. Wise GE, Frazier-Bowers S, D'Souza RN. Cellular, molecular, and genetic determinants of tooth eruption. *Crit Rev Oral Biol Med*. 2002;13(4):323-34.
3. O'Connell AC, Torske KR. Primary failure of tooth eruption: a unique case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999 Jun;87(6):714-20.
4. Loevy HT, Aduss H, Rosenthal IM. Tooth eruption and craniofacial development in congenital hypothyroidism: report of case. *J Am Dent Assoc*. 1987 Sep;115(3):429-31.
5. Spieker RD. Submerged permanent teeth: literature review and case report. *Gen Dent*. 2001 Jan-Feb;49(1):64,8; quiz 69-70.
6. Suri L, Gagari E, Vastardis H. Delayed tooth eruption: pathogenesis, diagnosis, and treatment. A literature review. *Am J Orthod Dentofacial Orthop*. 2004 Oct;126(4):432-45.
7. Raghoobar GM, Boering G, Jansen HW, Vissink A. Secondary retention of permanent molars: a histologic study. *J Oral Pathol Med*. 1989 Sep;18(8):427-31.
8. Baccetti T. Tooth anomalies associated with failure of eruption of first and second permanent molars. *Am J Orthod Dentofacial Orthop*. 2000 Dec;118(6):608-10.
9. Proffit WR, Vig KW. Primary failure of eruption: a possible cause of posterior open-bite. *Am J Orthod*. 1981 Aug;80(2):173-90.
10. Nashed RR, Holmes A. A posterior open bite. *Br J Orthod*. 1990 Feb;17(1):47-53.
11. Albers DD. Ankylosis of teeth in the developing dentition. *Quintessence Int*. 1986 May;17(5):303-8.
12. Raghoobar GM, Boering G, Vissink A, Stegenga B. Eruption disturbances of permanent molars: a review. *J Oral Pathol Med*. 1991 Apr;20(4):159-66.
13. Rasmussen P, Kotsaki A. Inherited retarded eruption in the permanent dentition. *J Clin Pediatr Dent*. 1997 Spring;21(3):205-11.
14. Kracke RR. Delayed tooth eruption versus impaction. *ASDC J Dent Child*. 1975 Sep-Oct;42(5):371-4.
15. Grover PS, Lorton L. The incidence of unerupted permanent teeth and related clinical cases. *Oral Surg Oral Med Oral Pathol*. 1985 Apr;59(4):420-5.

16. Johnsen DC. Prevalence of delayed emergence of permanent teeth as a result of local factors. *J Am Dent Assoc.* 1977 Jan;94(1):100-6.
17. Nagpal A, Sharma G, Sarkar A, Pai KM. Eruption disturbances: an aetiological-cum-management perspective. *Dentomaxillofac Radiol.* 2005 Jan;34(1):59-63.
18. Kokich VG, Mathews DP. Surgical and orthodontic management of impacted teeth. *Dent Clin North Am.* 1993 Apr;37(2):181-204.
19. Andersson L, Blomlof L, Lindskog S, Feiglin B, Hammarstrom L. Tooth ankylosis. Clinical, radiographic and histological assessments. *Int J Oral Surg.* 1984 Oct;13(5):423-31.
20. Kurol J. Infraocclusion of primary molars: an epidemiologic and familial study. *Community Dent Oral Epidemiol.* 1981 Apr;9(2):94-102.
21. Biederman W. The incidence and etiology of tooth ankylosis. *Am J Orthod.* 1956(42):921-6.
22. Valmaseda-Castellon E, De-la-Rosa-Gay C, Gay-Escoda C. Eruption disturbances of the first and second permanent molars: results of treatment in 43 cases. *Am J Orthod Dentofacial Orthop.* 1999 Dec;116(6):651-8.
23. Verma DK, Nair PN, Luder HU. Quantitative histological and ultrastructural features of opercula of normally erupting human teeth. *Microsc Res Tech.* 2005 Aug 15;67(6):279-85.
24. Raghoobar GM, Boering G, Vissink A. Clinical, radiographic and histological characteristics of secondary retention of permanent molars. *J Dent.* 1991 Jun;19(3):164-70.
25. Raghoobar GM, Ten Kate LP, Hazenberg CA, Boering G, Vissink A. Secondary retention of permanent molars: a report of five families. *J Dent.* 1992 Oct;20(5):277-82.
26. Raghoobar GM, Jansen HW, Jongebloed WL, Boering G, Vissink A. Secondary retention of permanent molars: an assessment of ankylosis by scanning electron and light microscopy. *Br J Oral Maxillofac Surg.* 1992 Feb;30(1):50-5.
27. Bosker H, ten Kate LP, Nijenhuis LE. Familial reinclusion of permanent molars. *Clin Genet.* 1978 Mar;13(3):314-20.
28. Proffit WR. Equilibrium theory revisited: factors influencing position of the teeth. *Angle Orthod.* 1978 Jul;48(3):175-86.
29. Kaban LB, Needleman HL, Hertzberg J. Idiopathic failure of eruption of permanent molar teeth. *Oral Surg Oral Med Oral Pathol.* 1976 Aug;42(2):155-63.

30. Brady J. Familial primary failure of eruption of permanent teeth. *Br J Orthod.* 1990 May;17(2):109-13.
31. Ballard CF. The adaptive alveolar processes. *Ann R Coll Surg Engl.* 1966 Nov;39(5):299-311.
32. Ireland AJ. Familial posterior open bite: a primary failure of eruption. *Br J Orthod.* 1991 Aug;18(3):233-7.
33. Dibiase AT, Leggat TG. Primary failure of eruption in the permanent dentition of siblings. *Int J Paediatr Dent.* 2000 Jun;10(2):153-7.
34. Winter GB, Gelbier MJ, Goodman JR. Severe Infra-occlusion and failed eruption of deciduous molars associated with eruptive and developmental disturbances in the permanent dentition: a report of 28 selected cases. *Br J Orthod.* 1997 May;24(2):149-57.
35. Rasmussen P, Kotsaki A. Inherited primary failure of eruption in the primary dentition: report of five cases. *ASDC J Dent Child.* 1997 Jan-Feb;64(1):43-7.
36. Shokeir MH. Complete failure of eruption of all permanent teeth: an autosomal dominant disorder. *Clin Genet.* 1974;5(4):322-6.



## **SECTION II**

### **MANUSCRIPT**

Normal eruption of teeth is of fundamental importance to dentists and orthodontists. The normal eruptive process involves navigation through bone and oral epithelium in a precise, bilaterally-timed sequence that must be coordinated with the growth of the jaws in all three planes of space. It is incorrect to think that an erupting tooth forces its way through the overlying tissues. Instead, the controlling element is resorption of overlying bone, tooth roots and the alveolar mucosa. Experiments in dogs, and inadvertent experiments in humans, have shown clearly that an eruption path is cleared, and then the tooth moves along the path that has been created for it.<sup>1,2</sup>

Eruption failure can be attributed to a variety of environmental and/or genetic factors, of which mechanical obstruction is the most common.<sup>3</sup> Obstacles can be any of a great variety of objects peripheral to the tooth, including cysts, other teeth, bone, unfavorable tongue posture, or digit habit. The obstruction can also be integral to the tooth in the form of fusion of cementum to bone. The resulting ankylosis prevents further eruption. Eruption failure due to mechanical obstruction may be thought of as a “secondary” failure, because the eruption mechanism is normal. If the obstruction is removed, eruption usually resumes; if not, the previously-obstructed tooth or teeth can be moved orthodontically. Because an area of the periodontal ligament is abnormal or even absent when ankylosis occurs, permanently removing this type of obstruction is impossible. If a small area of ankylosis is broken by

manipulating the tooth, it may be possible to move it for a short time, but re-ankylosis is inevitable.

The term “primary failure of eruption” (PFE) was coined by Proffit and Vig<sup>4</sup> to describe a condition in which nonankylosed teeth fail to erupt along an eruption path that has been cleared by normal resorption, because of a malfunction of the eruption mechanism. Only posterior teeth are affected, so the result is a posterior open bite. A key characteristic is an abnormal or complete lack of response to orthodontic force, except that a tooth that was not ankylosed when force was applied eventually became ankylosed. Although the cause of PFE remains unknown, it has been presumed that a genetic disturbance with varying penetrance and expressivity is the most likely explanation,<sup>5</sup> and subsequent reports of PFE have described a familial component.<sup>6-10</sup>

Since the original publication, orthodontists from around the country have been sending patient records with unusual eruption problems to Dr. Proffit for evaluation and consultation. Using this collection of clinical records, we seek to define PFE more clearly in light of the new cases that have been collected, distinguish it from other causes of posterior open bite (especially molar ankylosis with which it easily can be confused), and examine its hereditary nature.

## **MATERIALS AND METHODS**

### *Subjects*

The initial sample consisted of records of 112 individuals with posterior open bite, almost all of which were provided by orthodontists who sought consultation about diagnosis and treatment possibilities. In most cases, individual clinical examinations and patient interviews were not possible. The minimum record was a clear panoramic radiograph, but

additional photographs and cephalometric radiographs were available for many of the patients. Any information provided by the referring orthodontist such as patient demographics, significant medical and dental history, family history, treatment approaches and responses to treatment was recorded. From the initial sample, fifteen subjects were excluded due to a missing panoramic radiograph, suspected syndrome, successful orthodontic correction, or surgery in a location which may have interfered with eruption. The small sample of excluded patients who had successful orthodontic correction (n=2) may be explained by a tendency to refer only those patients who did not respond to orthodontics. Of the 97 subjects who were entered into the study, there were 50 males, 46 females and 1 gender unknown (data not provided). The sample population represented 24 states and Ireland, with ages ranging from 7 to 29 years. Dental age was established according to the method devised by Demirjian.<sup>11</sup> Dental age could not be compared with chronologic age because this information was not consistently available. Observation periods ranged from a single point in time to 9 years, with an average of 3 years. In 15 of these cases (9 families) there was a reported family history of eruption disturbance.

#### *Differentiation of Types of Eruption Problems*

Panoramic radiographs, and intraoral photos when available, were analyzed to confirm the presence and extent of a posterior open bite. In each case the posterior open bite was classified as unilateral or bilateral, and the location of the open bite and teeth involved was noted. In addition, any dental anomalies or unusual characteristics were recorded. In cases where a lateral cephalogram was provided, the skeletal relationship was determined using the ANB angle. This angular measurement was used because most radiographs were taken on different cephalostats with unknown magnification factors. Finally, each subject was

classified into one of four categories: mechanical obstruction of eruption (MFE), primary failure (PFE), indeterminate failure (IFE), or “other”. The parameters used to distinguish these groups were the number of affected teeth, impact on neighboring teeth, visible obstruction to eruption, teeth visible intraorally, and type of treatment response. The typology shown in Table I summarizes this information.

<i>Classification</i>	<i>Number of affected teeth</i>	<i>Impact on neighboring teeth</i>	<i>Observable obstruction to eruption</i>	<i>Affected teeth visible intraorally</i>	<i>Typical treatment response</i>	<i>Proposed cause of failure</i>
MFE	A few at most	Adjacent teeth normal	Yes	Maybe	Positive-may require luxation	Obstruction, impaction, ankylosis
PFE	Unilateral or bilateral, may involve whole quadrants	Distal teeth also affected	No	Usually some portion of at least one tooth	Negative	Failed eruption mechanism
IFE	Too early to determine	Unknown at this stage	No	Maybe	N/A	Unknown
Other	Any	Unknown	No	Yes	May respond but tends to relapse	Possible tongue or soft tissue interference
<p><b>Table I.</b> Typology of sample classification. Subjects were classified as MFE when the eruption problem was due to an apparent mechanical interference; as PFE when the posterior open bite involved all teeth distal to the first affected tooth, and no mechanical obstruction was identified; and as IFE when there was insufficient evidence for classification. Subjects who did not fit into the above categories were classified as “other” to be evaluated separately.</p>						

### *Pedigree Analysis*

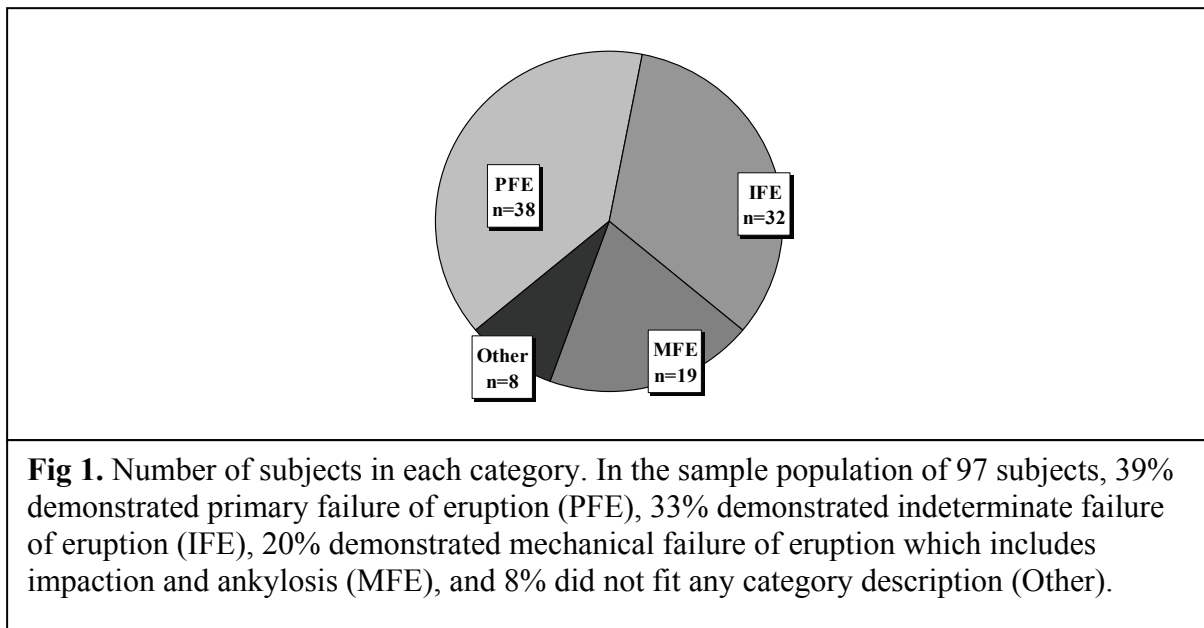
Subjects who indicated a family history of eruption problems were interviewed when accessible, and their families were recruited to participate in this study. This study was

reviewed and approved by the University of North Carolina Institutional Review Board. Consent was obtained for each individual who participated in the study and by parents in the case of a minor. When possible, family members were also interviewed and dental records obtained. Participants were categorized as affected or unaffected. Based on these diagnoses, pedigrees were constructed and analyzed by inspection to determine the pattern of inheritance.

## RESULTS

### *Quantification of the Sample by Category*

The number of subjects in each category (refer to Table 1) is summarized in Figure 1. Note that in 32 of the 97 subjects a diagnosis could not be made without additional longitudinal data (representative case shown in Fig 2) and 19 subjects showed MFE (representative case shown in Fig 3). Eight individuals did not fit the description of any category but were similar in presentation to each other (mild-to-moderate lateral open bites with the terminal molar in or nearly in occlusion) (Fig 4).





**Fig 2.** Representative example of IFE. 8 year old with ankylosis of primary molars and unerupted 16. This may in fact be PFE but at this point the second molars bilaterally are developed to the same extent and in the same position. Eruption progress should be monitored.



**Fig 3.** Subject exhibiting ankylosis. Adjacent teeth have erupted and drifted into the space.

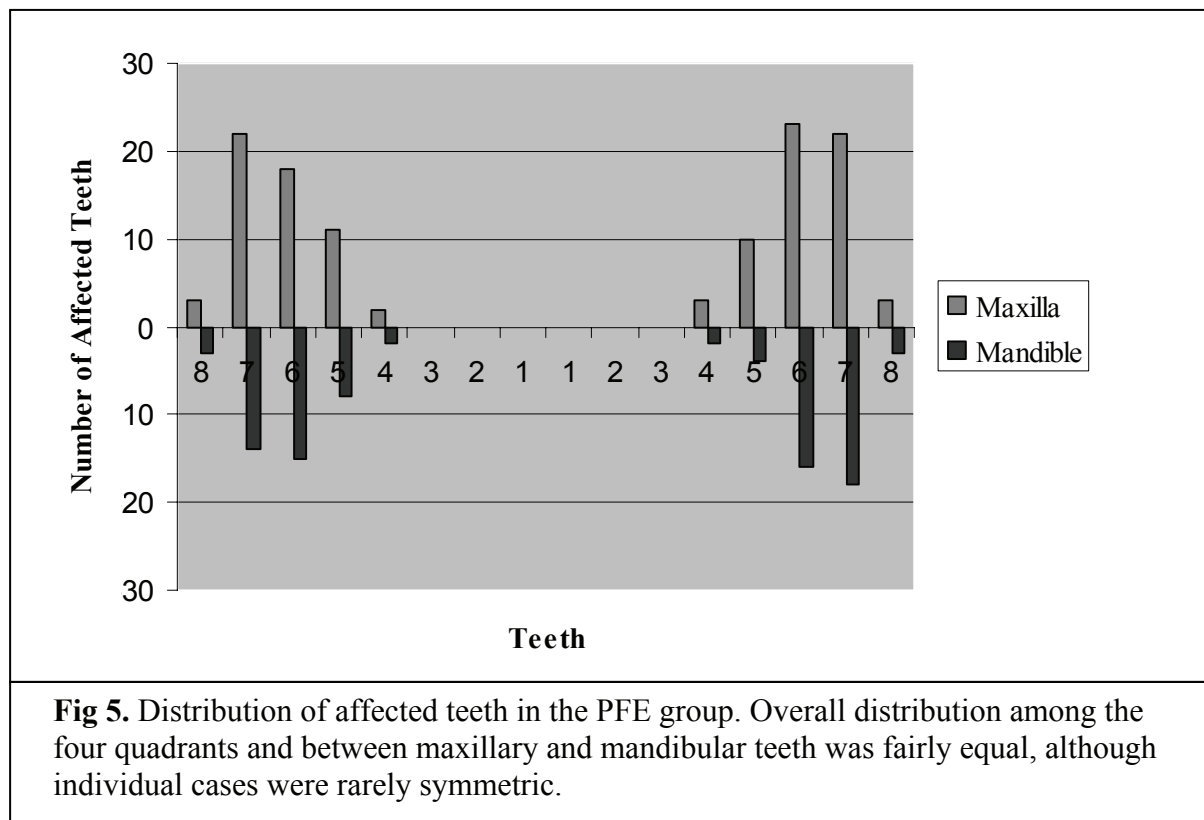




**Fig 4.** Subject demonstrating mild lateral open bite on the right side and moderate lateral open bite on the left. There is no indication of a failed eruption mechanism.

### Characterization of PFE

The location of affected teeth in the PFE group is shown in Figure 5. Subjects had affected teeth as far forward as the first premolars with increasing frequency toward the first and second molars. In most cases subjects were too young to evaluate the third molars, and only those third molars that were obviously affected were counted in the distribution.



The PFE group showed two distinguishable forms. One group (17 of 38) had a similar lack of eruption potential of all affected teeth with a progressive open bite from anterior to posterior (Fig 6). The second group (11 of 38) had a distal tooth with greater although inadequate eruption; therefore, the eruption potential varied among the affected teeth (Fig 7). Finally, ten of the cases showed a coexistence of the two types in different quadrants within the same patient. Sometimes MFE was also present in yet another quadrant.





**Fig 6.** PFE Type I in all four quadrants and showing cleared eruption path.



**Fig 7.** PFE type II with a Class III skeletal relationship. Affected teeth were easily surgically luxated and not ankylosed. Treatment with vertical elastics was rendered with no success.

Further characterization of PFE was carried out for the 29 subjects who had cephalometric records available. The Angle classifications for the sample population, the PFE group and the familial group are shown in Table II. Note the relative high percentage of Class III skeletal pattern. On further examination of the subgroups of PFE, there appears to be no difference, other than the varied eruption potential of affected teeth, between subjects with PFE Types I and II and those in the familial group.

	<i>Overall</i>	<i>PFE</i>	<i>Familial</i>
Class I	62%	55%	38%
Class II	10%	10%	38%
Class III	28%	35%	25%
<b>Table II.</b> Angle classification of sample.			

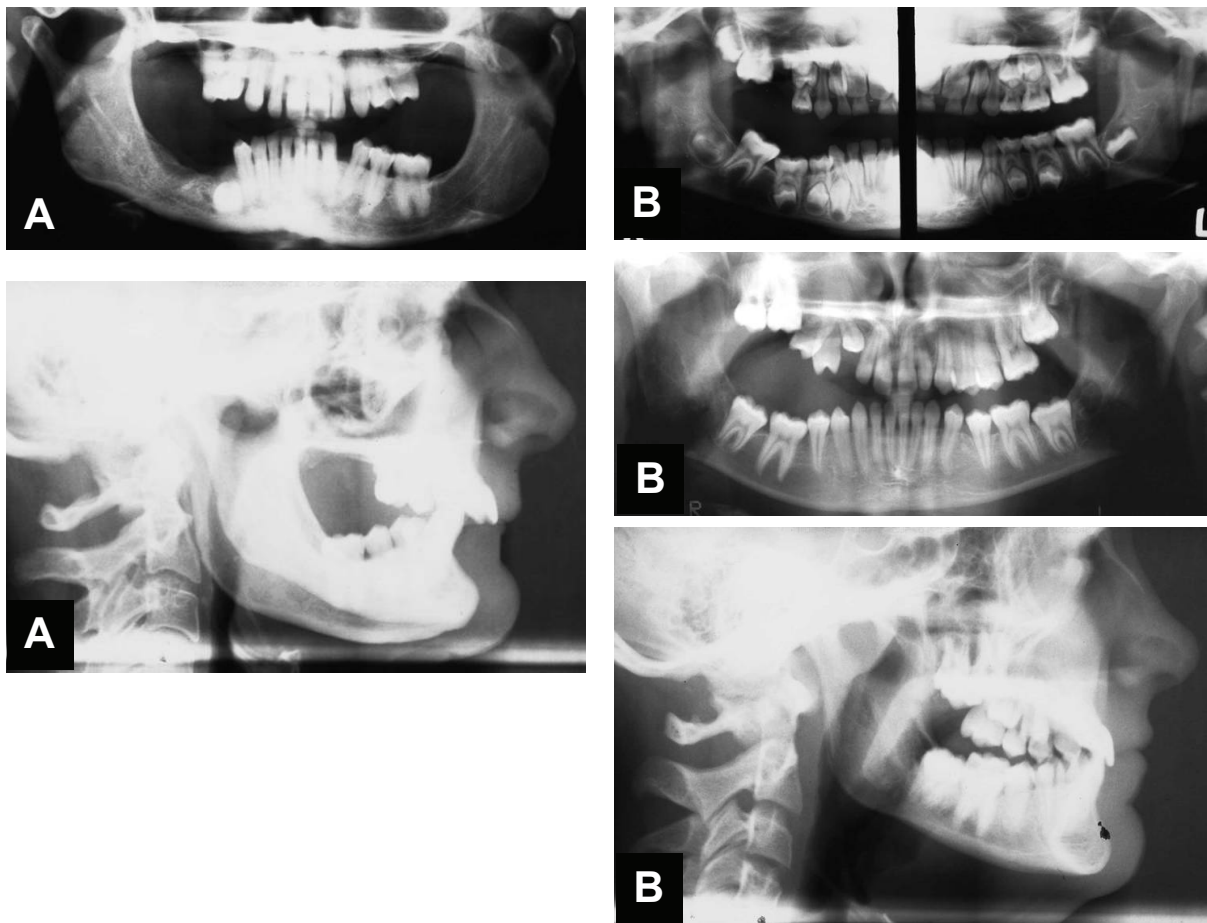
#### *Other Radiographic Findings*

At least one ankylosed primary tooth was noted in 24 of the 97 subjects (PFE = 8, IFE = 12, MFE = 2, other = 2). Dental anomalies were fairly rare and did not appear to be associated with PFE. In the entire sample of 97, four subjects showed hypodontia (IFE = 3, MFE = 1), five subjects showed hyperdontia (PFE = 2, IFE = 2, MFE = 1) and three subjects showed taurodontism (IFE = 3).

#### *Description of the Familial Subjects*

Twenty-six percent of the PFE cases in this sample were familial (10 out of 38). There was no obvious difference in the types of PFE expressed by family members versus the isolated cases. Figure 8 shows PFE in a mother and daughter. Five other subjects within the sample population of 97 reported familial eruption problems. Two subjects who were

brothers were classified as IFE because they were too young for diagnosis, and the other three (classified as either IFE or MFE) were related to PFE subjects. Other than a high prevalence of ankylosed primary molars (5 out 15 or 33%), no other dental anomalies were found in the familial group.

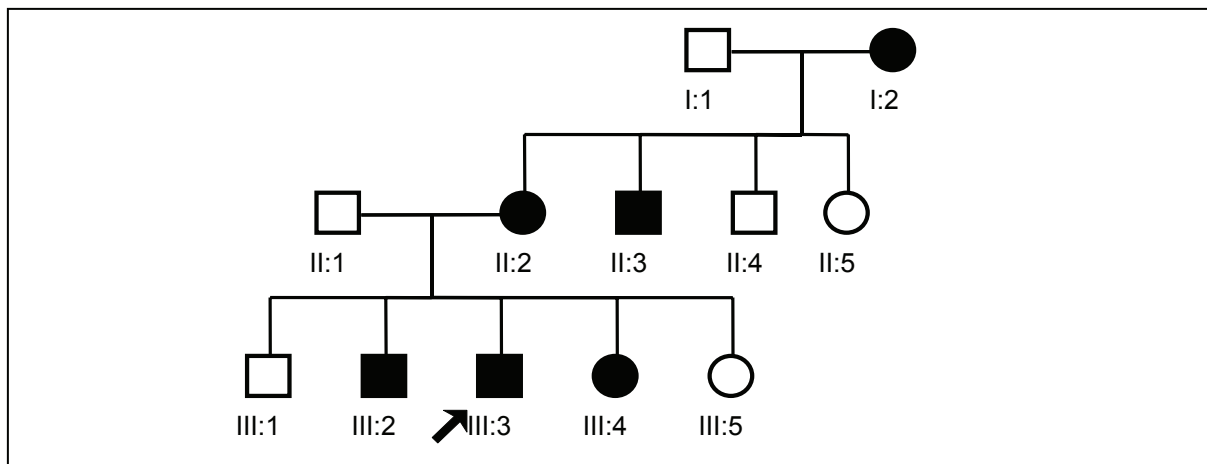


**Fig 8.** PFE in a mother (A) and daughter (B). Mother is affected in all four quadrants and has been treated with multiple extractions. Daughter has ankylosed primary teeth and is bilaterally affected although more severe on the right.

#### *Pattern of Inheritance*

Of the nine families who had a reported familial history of eruption problems four pedigrees were constructed. One of these pedigrees is shown in Figure 9. Pedigree analysis by inspection strongly suggests an autosomal dominant inheritance pattern in that both sexes

were affected without preference, about half the members in the kindred were affected, and the trait did not skip generations. The possibility of an X-linked autosomal dominant inheritance pattern cannot be excluded; however, this mode of inheritance is extremely rare and therefore a less likely candidate.



**Fig 9.** Pedigree of PFE-001. Analysis by inspection shows autosomal dominance with complete penetrance.

## DISCUSSION

### *Characteristics of PFE*

The original characteristics of PFE identified by Proffit and Vig in 1981 are still valid today. (1) Posterior teeth are more frequently involved; (2) the teeth distal to the first affected tooth are also affected to some degree; (3) involved teeth may erupt partially and then cease to erupt, relatively submerging although not ankylosed; (4) deciduous molars are likely to be involved; (5) the condition is rarely symmetric, frequently unilateral, but could be bilateral; (6) involved permanent teeth tend to become ankylosed at some point; (7) orthodontic forces lead to ankylosis rather than normal tooth movement.<sup>5</sup>

Because permanent molars develop from a distal extension of the same dental lamina from which the primary teeth are formed, a gradient of eruption could explain why posterior teeth are affected more often than anterior teeth.<sup>5</sup> The condition can affect any quadrant, may be unilateral or bilateral and is rarely symmetric. Involved teeth do not respond normally to orthodontic forces.

New findings from this study indicate two distinguishable types of PFE which may be related to the timing of onset. In Type I, which is the classic form described initially, loss of eruption potential appears to strike at a certain chronologic time leading to a similar lack of eruption potential of all the affected teeth. In Type II, the timing of onset may be related to the stage of root development, leading to a varied eruption potential among affected teeth. In a significant number of cases a combination of the two types was found, and a few cases showed PFE in one quadrant coupled with a single ankylosed tooth in a different quadrant. Therefore, PFE and ankylosis may be closely related, as the studies by Raghoobar seem to show.<sup>12,13</sup> Perhaps an abnormal periodontal ligament can lead to either condition.

#### *Association between Eruption Failure and Skeletal Relationship*

Within the small subset of this sample population for which a lateral cephalogram was available, a high percentage of subjects demonstrated a skeletal Class III relationship.<sup>2</sup> This finding is previously unreported. Of the other publications on PFE, only a few account for the skeletal relationships of some of their subjects. Proffit and Vig reported on one subject in eight who had a Class III relationship.<sup>5</sup> Ireland had two Class I subjects.<sup>8</sup> Brady reported one out of two with a Class II pattern.<sup>7</sup> Dibiase and Leggat reported that both of their subjects were Class II.<sup>10</sup> Since failure of permanent molars to erupt is so rare,<sup>14-16</sup> finding a sample size large enough to study the characteristics of the condition has been a difficult problem.

### *Role of Heredity in PFE*

Reports of a definite familial tendency associated with PFE indicate the cause of the developmental disturbance in the periodontal ligament may be inheritable.<sup>6,12</sup> In this study 26% of the PFE cases were familial. Raghoobar reported a heritable component to eruption failure in 10% of his cases, while other individual case reports provide studies of a few single families.<sup>7-10,17</sup>

Pedigree analysis by inspection of the familial cases in this study is highly suggestive of an autosomal dominant inheritance pattern with complete penetrance and variable expressivity. Most of the familial studies in the literature also report an autosomal dominant inheritance pattern,<sup>6,7,17</sup> however, Winter reported one family as autosomal recessive.<sup>17</sup>

### *Etiology of PFE*

Although none of the cases examined by Proffit and Vig in the original study had similarly affected relatives, they did suppose that a genetic disturbance of varying penetrance and expressivity was the likely etiology. The current reports of affected families support this hypothesis,<sup>6-10</sup> and suggest that spontaneous mutation(s) may account for the cases with no previous family history. Perhaps this leads to a local disturbance in metabolic activity or altered blood flow which then hinders the eruption mechanism. Raghoobar et al, based on histologic examination of 26 molars from 20 patients, suggest that the mechanism is replacement of cementoblasts by osteoblasts due to a local disturbance in the PDL during the repair process of local physiologic resorption.<sup>12</sup>

The best evidence of a failure in the eruption mechanism is bone resorption without tooth movement. Affected teeth that have been surgically exposed are generally reported to be easily movable within the crypt and not ankylosed. Although these teeth may have some

slight response to orthodontic forces, the response is abnormal and the teeth invariably become ankylosed before reaching occlusion. Case studies illustrate that not only do affected teeth fail to respond to treatment, but also adjacent normal teeth are adversely affected by intrusion to the level of the affected teeth (Fig 10). Winter and Raghoobar also concluded that ankylosis in the failed eruptive process may be a secondary rather than initiating process and reiterate that orthodontic procedures designed to improve eruption are doomed to failure in individuals with PFE.<sup>12,17</sup>



**Fig 10.** Orthodontic intrusion of normal teeth. Attempt at orthodontic treatment led to intrusion of normal teeth mesial to the affected teeth.

### *Differential Diagnosis*

In the diagnosis of eruption failures, the first step is to rule out local, systemic and endocrine factors. Endocrine abnormalities have not been identified in PFE or ankylosis



patients to our knowledge. Ultimately, the principal differential diagnosis is mechanical obstruction versus a failed eruption mechanism. Distinguishing between the two is key to determining the prognosis for the affected teeth. Unfortunately, MFE and PFE have very similar presentations in the early stages and definitive diagnosis cannot be made without sufficient longitudinal data and therapeutic diagnosis (an attempt at orthodontically erupting the tooth or teeth that may or may not be affected).

The first encounter with these patients often occurs around age 8 or 9 when an asymmetry in the eruption pattern of the first permanent molars is noticed. The conservative approach is to take a panoramic radiograph with the patient's teeth together and recall in 6-12 months to determine eruption progress. Evaluation at recall will show progress, no change, or relative submergence. If there is eruption progress, PFE and ankylosis can be ruled out. Ultimately assessing the eruption capacity of the neighboring teeth is the only way to distinguish PFE from ankylosis. The number of teeth affected, a positive family history and a skeletal Class III relationship may provide valuable clues. Differentiation between the two types of PFE cannot be done until at least age 14 or 15 when the second molar either completely fails to erupt or erupts partially and then stops.

#### *Clinical Application: Current View on Patient Management*

Once PFE has been diagnosed, treatment options are disappointing and limited. Patients and orthodontists must often either accept premolar occlusion or opt for more invasive techniques. In the mildest of cases, teeth may be restored with onlays and crowns;<sup>18</sup> however, definitive restorations should not be placed prior to completion of vertical growth. For moderate cases, extraction of teeth with placement of implants may be an option. Another option may be a small segmental osteotomy to surgically reposition teeth into occlusion.<sup>5</sup> In



the severest of cases, a significant deficit in alveolar bone height precludes implant restorations as well as subapical osteotomy. One report of distraction osteogenesis to correct an extreme posterior open bite provides an interesting potential treatment alternative.<sup>19</sup> Sometimes the only feasible option is a removable prosthesis.<sup>20</sup>

## CONCLUSIONS

Primary failure of eruption is a rare condition that can lead to spectacular posterior open bites. It is difficult to diagnose and even more difficult to treat due to the lack of response to orthodontic forces. Proper diagnosis can save the patient and the orthodontist years of frustration and disappointment. The developmental disturbance that leads to PFE may be inheritable. Future studies to determine the genetic etiology of PFE can aid in differential diagnosis, allow early identification of affected family members and may eventually lead to new treatment modalities.

### *Findings*

The original characteristics of PFE identified 1981 are still valid today

Two distinguishable forms of PFE were identified. Type I had a similar lack of eruption potential of all affected teeth, and Type II had a varied eruption potential.

About a third of the cases showed a coexistence of the two types in different quadrants.

Sometimes a mechanical failure was also present in yet another quadrant.

26% of the PFE cases were familial; analysis by inspection revealed an autosomal dominant inheritance pattern of complete penetrance and variable expressivity.

No difference other than eruption capacity of affected teeth was identified between subjects with PFE Types I and II and those with familial PFE.

Differential diagnosis requires adequate longitudinal data and sometimes therapeutic diagnosis (orthodontic traction); family history and skeletal pattern may provide valuable information.

Although there are many reasons why a tooth may fail to erupt, determining the origin is difficult yet vital to the success of orthodontic treatment. Eruption failure cases are among the most challenging that an orthodontist will encounter. Not only does proper eruption critically affect the success of the occlusal outcome, but it also greatly affects the efficiency of treatment.

## REFERENCES

1. Cahill DR. Eruption pathway formation in the presence of experimental tooth impaction in puppies. *Anat Rec*. 1969 May;164(1):67-77.
2. Proffit WR, Fields HW. *Contemporary Orthodontics*. 3rd ed. St. Louis: Mosby; c2000.
3. O'Connell AC, Torske KR. Primary failure of tooth eruption: a unique case. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1999 Jun;87(6):714-20.
4. Proffit WR. Equilibrium theory revisited: factors influencing position of the teeth. *Angle Orthod*. 1978 Jul;48(3):175-86.
5. Proffit WR, Vig KW. Primary failure of eruption: a possible cause of posterior open-bite. *Am J Orthod*. 1981 Aug;80(2):173-90.
6. Bosker H, ten Kate LP, Nijenhuis LE. Familial reinclusion of permanent molars. *Clin Genet*. 1978 Mar;13(3):314-20.
7. Brady J. Familial primary failure of eruption of permanent teeth. *Br J Orthod*. 1990 May;17(2):109-13.
8. Ireland AJ. Familial posterior open bite: a primary failure of eruption. *Br J Orthod*. 1991 Aug;18(3):233-7.
9. Raghoobar GM, Ten Kate LP, Hazenberg CA, Boering G, Vissink A. Secondary retention of permanent molars: a report of five families. *J Dent*. 1992 Oct;20(5):277-82.
10. Dibiasi AT, Leggat TG. Primary failure of eruption in the permanent dentition of siblings. *Int J Paediatr Dent*. 2000 Jun;10(2):153-7.
11. Demirjian A, Goldstein H, Tanner JM. A new system of dental age assessment. *Hum Biol*. 1973 May;45(2):211-27.
12. Raghoobar GM, Boering G, Jansen HW, Vissink A. Secondary retention of permanent molars: a histologic study. *J Oral Pathol Med*. 1989 Sep;18(8):427-31.
13. Raghoobar GM, Boering G, Vissink A, Stegenga B. Eruption disturbances of permanent molars: a review. *J Oral Pathol Med*. 1991 Apr;20(4):159-66.
14. Grover PS, Lorton L. The incidence of unerupted permanent teeth and related clinical cases. *Oral Surg Oral Med Oral Pathol*. 1985 Apr;59(4):420-5.
15. Johnsen DC. Prevalence of delayed emergence of permanent teeth as a result of local factors. *J Am Dent Assoc*. 1977 Jan;94(1):100-6.
16. Nagpal A, Sharma G, Sarkar A, Pai KM. Eruption disturbances: an aetiological-cum-management perspective. *Dentomaxillofac Radiol*. 2005 Jan;34(1):59-63.

17. Winter GB, Gelbier MJ, Goodman JR. Severe Infra-occlusion and failed eruption of deciduous molars associated with eruptive and developmental disturbances in the permanent dentition: a report of 28 selected cases. *Br J Orthod.* 1997 May;24(2):149-57.
18. Yatani H, Watanabe EK, Kaneshima T, Yamashita A, Suzuki K. Etched-porcelain resin-bonded onlay technique for posterior teeth. *J Esthet Dent.* 1998;10(6):325-32.
19. Kater WM, Kawa D, Schafer D, Toll D. Treatment of posterior open bite using distraction osteogenesis. *J Clin Orthod.* 2004 Sep;38(9):501,4; quiz 487-8.
20. Siegel SC, O'Connell A. Oral rehabilitation of a child with primary failure of tooth eruption. *J Prosthodont.* 1999 Sep;8(3):201-7.