

# The clinical features and aetiological basis of primary eruption failure

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**SUMMARY** Primary failure of eruption (PFE) is a poorly understood condition associated with tooth eruption failure. This investigation systematically reviews the literature, evaluates clinical features and associations with PFE, and describes five further cases.

Publications were selected and identified as describing PFE when there was no identifiable aetiological factor contributing to eruption failure and no evidence of successful orthodontic extrusion of the affected tooth or teeth. A data abstraction form recorded the following additional information; subject age, gender, general health status, and teeth present. Eighteen publications were sourced that detailed at least one case of PFE in a manner conforming to the selection criteria; these papers included a total of 35 individual cases, to which five previously unreported subjects were added. Within the whole sample of 40 cases, a total of 24 (60 per cent) were females and 16 (40 per cent) males.

First and second molar teeth were most commonly affected; incisors, canines, and premolars were also involved, but with a reduced individual frequency. There was no significant difference in incidence between the maxilla and mandible, or between left and right sides. A family history of eruption failure was found in almost 50 per cent of the sample, with eruption failure or ankylosis affecting at least one primary tooth, also a common finding. Within the 40 cases, hypodontia was present at levels higher than population norms.

PFE appears to be a condition that predominantly affects the molar dentition. The increased frequency of hypodontia in affected individuals and common findings of a family history regarding tooth eruption problems suggests a significant genetic component to the aetiology of this rare condition.

## Introduction

Teeth of the permanent dentition may fail to erupt either as a result of mechanical obstruction, be it idiopathic or pathological in origin, or because of disruption to the eruptive mechanism itself (Raghoobar *et al.*, 1991a). Eruption failure may affect one or a number of teeth, in either the primary or the permanent dentition, and can be partial or complete, depending upon the underlying aetiology. In some cases, a clear genetic origin can be ascribed, with a number of known human syndromes demonstrating an eruption defect as part of their spectrum of clinical presentation (Online Mendelian Inheritance In Man; <http://www.ncbi.nlm.nih.gov/omim>). A small number of syndromes are specifically associated with eruption failure in the permanent dentition, the causative gene having in some instances been identified (Table 1).

Primary retention of permanent teeth is an isolated condition associated with a localized failure of eruption but no other identifiable local or systemic involvement (Raghoobar *et al.*, 1991a). Secondary retention involves the unexplained cessation of further eruption after a tooth has penetrated the oral mucosa (Raghoobar *et al.*, 1991a,b). The term primary failure of eruption (PFE) is also used in reference to tooth eruption failure (Proffit and Vig, 1981; Brady, 1990; Piattelli and Eleuterio, 1991; Wise *et al.*,

2002), with the most comprehensive analysis of PFE suggesting that this condition demonstrates most, if not all, of the following characteristics: (1) posterior teeth are more commonly involved than anterior; (2) involved teeth may erupt into initial occlusion and then cease to erupt further, or may fail to erupt entirely; (3) both primary and permanent molars may be affected; (4) involvement may be unilateral or bilateral; (5) involved permanent teeth tend to become ankylosed; (6) application of orthodontic force in an attempt to bring the affected teeth into the arch leads to ankylosis rather than normal tooth movement; and (7) the condition tends to occur in isolation, with an absence of affected family members (Proffit and Vig, 1981). Thus, a definitive diagnosis of PFE is not straightforward, with this clinical entity incorporating features of both primary and secondary retention. Indeed, these findings, that in some cases teeth may erupt into initial occlusion before further dentoalveolar development ceases, while in others a total failure of eruption occurs, suggest the possibility of PFE having two separate mechanisms (Oliver *et al.*, 1986) or two separate manifestations of the same mechanism.

All these factors present something of a diagnostic challenge to the clinician. In the absence of any clear genetic, pathological, or environmental factor being responsible for preventing the eruption of a permanent tooth, a definitive

**Table 1** Genetic disorders associated with tooth eruption failure.

Syndrome	Causative gene	Encoded protein
Cleidocranial dysplasia (OMIM 119600)	<i>CBFA1 (RUNX2)</i>	Transcription factor
Osteopetrosis (OMIM 166600/259700)	<i>TRAF6</i>	Transcription factor
Rutherford syndrome (OMIM 180900)	Unknown	
GAPO syndrome (OMIM 230740)	Unknown	
Osteoglophonic dysplasia (OMIM 166250)	<i>FGFR1-3</i>	Receptors
Dental non-eruption (OMIM 125350)	Unknown	

OMIM, Online Mendelian Inheritance In Man.

diagnosis of PFE might only be made retrospectively, following the failure of orthodontic extrusion to alter the position of an affected tooth or teeth. The aims of this study were to identify all previously reported cases of PFE in the scientific literature, systematically collect sufficient data for those described to allow an objective analysis of clinical factors associated with this condition, and evaluate the likelihood of a genetic contribution. In addition, five further previously unpublished examples of eruption failure are described and incorporated into the data set.

### Materials and methods

The appropriate English language case reports and case series were selected using an electronic search of the following databases: PubMed and Medline (from 1966 to week 50 of 2004), Embase (from 1988 to week 50 of 2004), and Web of Science (from 1975 to week 50 of 2004). Articles were selected using combinations of the terms 'tooth', 'eruption', 'failure', 'orthodontics', and 'PFE'. This was supplemented by a manual search of reference lists taken from identified publications in relevant articles from refereed journals.

#### Selection criteria

Eligibility of selected articles was determined by screening the titles, keywords, and abstracts of potential studies identified from the literature searches. Articles that appeared to contain cases of relevance were sourced and examined independently by two of the authors (SA, MTC). Any inclusion disputes were referred to the third author (DB) whose decision was final. Reference lists of articles were also screened to supplement the electronic literature search. The identified cases were grouped together and descriptive statistics applied.

The principle criterion for inclusion in this study was the ability to make a diagnosis of PFE affecting teeth in the permanent dentition (excluding third molars) for a reported

case or members of a case series. This diagnosis was made in the presence of the following information:

1. No evidence of a mechanical, pathological, or systemic cause of obstruction contributing to eruption failure of the affected tooth or teeth (involved teeth may have erupted initially and then ceased to erupt prior to establishing occlusal contact or may have failed to erupt entirely);
2. No evidence of successful orthodontic extrusion of the affected tooth or teeth.

Having made a diagnosis of PFE for a reported case, the following information was recorded using a data abstraction form: age of the affected subject at the time of diagnosis, recording of all teeth present at the time of diagnosis (third molars were excluded from the analysis), and no evidence of systemic disease in the affected individuals. The following information was also included if reported, but an absence did not exclude the case from inclusion: any family history of eruption failure, any evidence of initial eruption of the tooth or affected teeth, any evidence of ankylosis, infraocclusion, or eruption failure affecting the primary dentition, and any other reported dental anomalies.

### Results

A total of 18 publications were identified which described at least one case of PFE with sufficient accuracy to conform to the inclusion criteria (Table 2). From these publications, a total of 35 individual cases were obtained, to which an additional five previously unreported cases were added (Table 3; Figure 1). In this total sample, 24 (60 per cent) were females and 16 (40 per cent) males. The mean age at diagnosis was 13.65 years of age, with a range of 38.5 years. In the permanent dentition as a whole, all teeth were described as being affected at least once (with the exception of third molars; Figure 2). The teeth most commonly involved were the first and second molars in all four quadrants of the mouth. A total of 269 teeth were included in the sample, of which 87 (32 per cent) were first and 47 (17 per cent) second molars. The remaining teeth (incisors, canines, and premolars) were also affected, but with a reduced frequency. The overall distribution of affected teeth showed no significant difference in incidence between the maxillary and mandibular dentitions. Twelve subjects (30 per cent) had teeth affected in all four quadrants of the oral cavity, while eight (25 per cent) demonstrated PFE in only one quadrant. There was no significant dominance of affected side. Eighteen of the affected subjects (45 per cent) demonstrated a complete absence of eruption of the affected teeth (primary retention), while the remaining 22 (55 per cent) experienced some occlusal development of affected teeth (secondary retention).

**Table 2** Publications selected on the reported inclusion criteria.

Authors	Year of Publication	Age in years		Teeth affected
		Male	Female	
Reid	1954	42		$\overline{6}$
		10.5		$\overline{6}$
Brenchley	1960	11		$\overline{6}$
				6/6
Shokeir	1974	46		$\frac{87654321}{87654321}/\frac{12345678}{12345678}$
		18		$\frac{87654321}{654321}/\frac{12345678}{123456}$
		12		$\frac{87654321}{87654321}/\frac{12345678}{12345678}$
Koskinen and Rahkamo	1975	13		$\overline{76}$
Bosker <i>et al.</i>	1978	13		$\frac{6}{6}$
			12	$\overline{6}$
				$\overline{6}$
Hall and Reade	1981	24		$\frac{876}{6}$ 8
				8 6/678
Proffit and Vig	1981	13		$\overline{76}$
		13		$\frac{54}{567}$
				6 / 6
Rasmussen <i>et al.</i>	1983	15.5		$\frac{754321}{76432}/\frac{123457}{3467}$
		7.5		$\frac{621}{126}$
				6 21/12 6
Oliver <i>et al.</i>	1986	9		$\overline{6}$
			10	$\overline{6}$
		8		$\overline{6}$
		7		$\overline{76}$
Brady	1990	9.5		$\frac{87}{8}$ $\frac{1678}{68}$
			10	$\frac{7}{1}$
				87/123 7
Ireland	1991	11		$\frac{6}{567}$
		7		86/ 78
				$\overline{6}$
Pytlik	1991	13		$\frac{65}{5}$
				6/ 6
Piattelli and Eleuterio	1991	14		$\frac{3}{6}$
				/ 567
Winter <i>et al.</i>	1997	15		$\frac{65}{56}$
		14		$\overline{76}$
		9		$\overline{6}$
		6		$\overline{6}$
		10		$\overline{6}$
		7		$\overline{6}$
Siegel and O'Connell	1999	10		$\frac{7654321}{754321}/\frac{1234567}{1234567}$
O'Connell and Torske	1999	6		$\frac{7654312}{754321}/\frac{123457}{1234567}$
DiBiase and Leggat	2000	14		$\frac{61}{6}$
		12		$\frac{7}{4567}$
				$\overline{76}$ / 67
Wise <i>et al.</i>	2002	15		$\overline{765}$
				$\overline{76}$ /

**Table 3** Previously unreported cases.

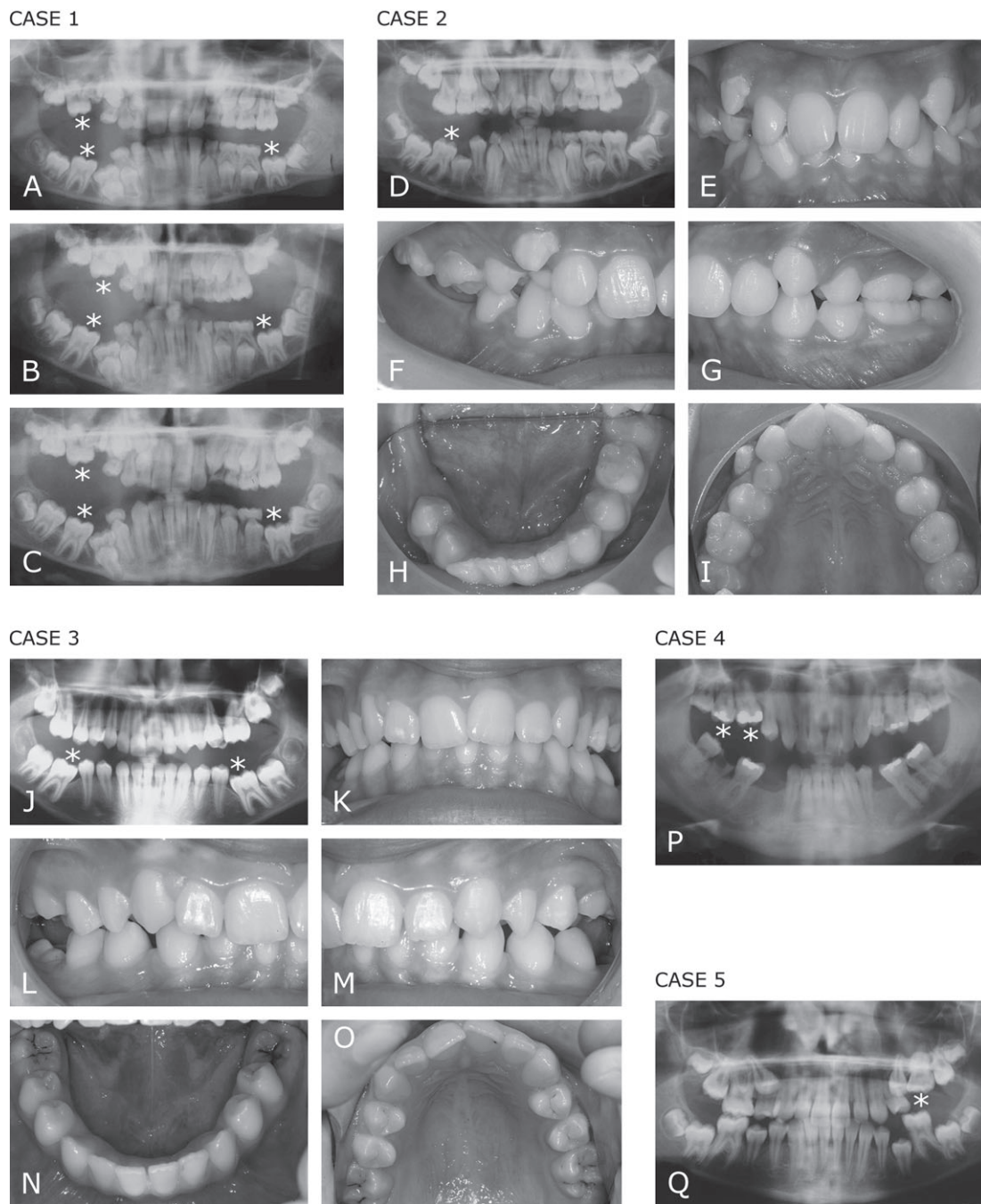
Case	Age in years		Teeth affected
	Male	Female	
1	10		$\overline{6}$
			$\overline{6}$ /6
2	12		$\overline{6}$
3		12	$\overline{6}$ /6
4	35		$\overline{76}$
5		11	$\overline{16}$

In 18 of the 40 cases (45 per cent) there was a reported family history of eruption failure, while in 17 (43 per cent) there was a reported history of eruption failure or ankylosis affecting at least one primary tooth. Five cases (13 per cent) had associated hypodontia, one described the presence of diminutive second premolars, and one had supernumerary teeth. Other described dental anomalies included impacted canines (2 cases) and second premolars (6 cases).

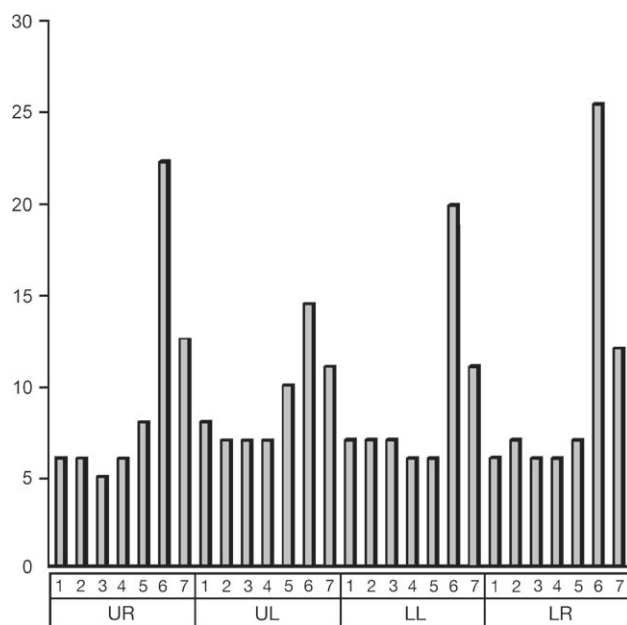
**Discussion**

This study investigated 35 cases of PFE reported in the literature over a period of 48 years and five previously unreported cases. This represents one of the largest and most detailed analyses of teeth affected by PFE. In a previous study, Proffit and Vig (1981) analysed 16 cases, describing only two in detail, and found that PFE can affect all teeth, with the posterior dentition being most commonly involved. This is in agreement with the present sample, where the first and second molars were found to be the most frequently affected teeth (Palma *et al.*, 2003). While other teeth in the dentition were involved, this occurred at significantly lower levels than in the molar dentition. There was no evidence that this condition occurred more frequently in one jaw or the other; teeth in both the maxillary and mandibular dentitions were equally affected. Furthermore, there were no differences in the side affected; PFE occurred both unilaterally and bilaterally.

Another feature of PFE is that teeth may erupt into initial occlusion and then cease to erupt, or may fail to erupt entirely (Proffit and Vig, 1981). These contrasting characteristics were found in the present sample with over half the cases described as having some initial eruption of the affected teeth. The term PFE may, therefore, incorporate two independent conditions; one with a localized complete failure of tooth eruption and one where there is some initial eruption of the affected tooth or teeth prior to the eruption failure, a condition also described as secondary retention (Hall and Reade, 1981; Raghoebar *et al.*, 1991b). Alternatively, PFE might represent a single disorder of tooth eruption with differing degrees of severity, a hypothesis



**Figure 1** A selection of cases demonstrating primary failure of eruption (PFE). Case 1: Serial panoramic radiographs of a male subject affected by severe PFE. At 10 years of age (A) LL6, LR6, and UR6 have failed to erupt and there is evidence of infraocclusion affecting the LRE, although the LR5 is present. From 11(B) to 13(C) years of age, there is a lack of occlusal development of the affected teeth, but evidence of limited eruption involving all the second molars, except LL7, which appears to be impacted. Case 2: Clinical records of a male subject affected by localized PFE (D–I). At 12 years of age, there is a lack of occlusal development associated with LR6, which has completely failed to erupt; development of the remaining dentition appears normal. Case 3: Clinical records of a female subject affected by PFE bilaterally in the mandibular arch (J–O). At 12 years of age, eruption of LL6 has only progressed to gingival level, while LR6 demonstrates more vertical development; however, neither tooth has reached occlusion. Case 4: Panoramic radiograph of a 35-year-old male subject who presented with PFE affecting the UR6 and UR7 (P). Clearly, there has been some occlusal development associated with these teeth, as both are heavily restored. Case 5: Panoramic radiograph of an 11-year-old female subject, UL6 has failed to erupt (Q). All the subjects were Caucasian and only one (case 1) described any family history of eruption failure. There was no evidence of hypodontia in the permanent dentition of any subject; however, in case 1 there was impaction of UR5, in case 2 the upper canines were labially placed, and in case 5 UL5 and UR5 were impacted. Teeth affected with PFE are identified (\*). UR, upper right; UL, upper left; LR, lower right; LL, lower left.



**Figure 2** Distribution of teeth affected by primary failure of eruption within the sample (UR, upper right; UL, upper left; LR, lower right; LL, lower left).

supported by the fact that these two manifestations can occur in the same subject (Figure 1).

PFE appears to be a condition that predominantly affects the posterior dentition, the eruption failure can be preceded by a period of normal eruption, but any attempt to extrude an affected tooth orthodontically is likely to result in ankylosis (Proffit and Vig, 1981). An important question, therefore, is what is the possible aetiological basis for this disorder? Evidence for a genetic component to a particular clinical condition can be provided by investigation of associated factors. It is interesting to note that a strong family history of eruption failure or eruption problems in the primary dentition was present in the sample, a finding at odds with the investigation of Proffit and Vig (1981). Thus, a comprehensive family history may provide some aid in early diagnosis of this condition. At 13 per cent, the level of hypodontia described in these subjects was considerably higher than that found in normal populations (Mattheeuws *et al.*, 2004). The evidence of a strong family history in many cases (Reid, 1954; Brady, 1990; Ireland, 1991; DiBiase and Leggat, 2000) and an association with a dental anomaly of known genetic origin would suggest that PFE may have a significant genetic component.

There is evidence for failure of molar tooth eruption being associated with other disturbances of tooth eruption and position, these conditions being under common genetic control (Baccetti, 2000). Indeed, eruption disturbance affecting the entire permanent dentition in isolation has been associated with a Mendelian pattern of inheritance (Shokeir, 1974) and tooth eruption can be affected in a

number of defined syndromes (Table 1). In many syndromic cases, the causative gene or genes have been identified, with the defect a direct result of the function of the encoded protein during normal tooth eruption. The process of tooth eruption itself involves complex interactions between osteoblast, osteoclast, and dental follicular cell lines associated with the tooth germ; a host of signalling molecules, receptors, transcription factors, and cell adhesion molecules achieve this (Wise *et al.*, 2002). The result of these cellular processes is co-ordinated alveolar bone resorption and emergence of the tooth within the oral cavity. To date, no such direct genetic association has been made with PFE, but the clinical manifestations suggest that the dental follicle might play an important role. While candidate genes do exist, many of the encoded proteins are also active during both embryonic and post-natal development; therefore, an isolated condition such as PFE may be the result of mutation in a novel gene or one that only has phenotypic consequences for tooth eruption. The identification of any candidate gene for PFE will require the collection of suitable family pedigrees and positional cloning of relevant loci.

The management of PFE is difficult, not least because diagnosis of this condition relies principally upon exclusion, where all possible causative factors have been considered and eliminated. Active orthodontic force will most likely result in localized ankylosis and failure to extrude an affected tooth into occlusion, a finding that is essentially diagnostic (Proffit and Vig, 1981). Where the condition is a localized problem affecting only one tooth, management may include extraction of the affected tooth, followed either by orthodontic space closure or by prosthetic replacement. Alternatively, a localized bony osteotomy and orthodontic extrusion of the whole segment would seem to be the only option if an occlusal position of the tooth or teeth is to be obtained. If some eruption of the tooth has occurred, a coronal build-up may be the treatment of choice, in this case accepting the vertical position of the affected tooth but achieving occlusion via the restoration. Cases where multiple teeth are involved are more difficult to manage; the only available method of bringing them into occlusion is a segmental osteotomy (Proffit and Vig, 1981; Piattelli and Eleuterio, 1991). Careful planning in these cases is essential to ensure that no damage is caused to adjacent teeth. While surgical repositioning may not move teeth into an entirely acceptable position, it will certainly aid prosthetic management.

## Conclusions

PFE can be regarded as an eruption defect, manifesting as a complete failure of eruption or cessation of initial eruption with no obvious local or systemic causative factor. Evidence from the current literature would suggest that this disorder has a substantial genetic component.

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