Enamel Defects in the Permanent Dentition: Prevalence and Etiology

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Abstract

The prevalence of developmental defects of enamel (DDE) in the permanent dentition in developed countries has been reported to be in the range of 9–68 % and with no gender predilection. Several etiological factors have been implicated as being responsible for DDE in the permanent teeth. Although local, systemic, genetic or environmental factors have been attributed to DDE frequently they are likely to be multifactorial in nature. These factors are discussed in relation to the timing of enamel development with consideration of the evidence, or lack thereof, for the association between the putative etiological factors and the nature of the subsequent abnormalities.

Introduction

The first permanent tooth to begin calcification is the first molar. This occurs around the time of birth, while the anterior teeth commence calcification between 4 and 6 months of age in a sequential order from the central incisor to the canine. The maxillary lateral incisor is the exception as calcification of this tooth occurs around 10–12 months of age [1]. At around 6 years of age, the first permanent molar tooth begins to erupt into the oral cavity and by the age of 14 years, most children have all of their permanent teeth erupted except for their third molars (Table 2.1). Many factors have been implicated in the etiology of developmental defects of enamel (DDE) in permanent teeth. This chapter discusses these factors in relation to the timing of

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Table 2.1 The calcification and eruption dates of permanent teeth

Permanent tooth type	Calcification begins at	Crown formation completes at	Eruption[a]	
			Maxillary	Mandibular
Central incisor	3–4 mo	4–5 y	7–8 y	6–7 y
Lateral incisor	Maxilla: 10–12 mo	4–5 y	8–9 y	7–8 y
	Mandible: 3–4 mo	4–5 y		
Canine	4–5 mo	6–7 y	11–12 y	9–11 y
First premolar	18–24 mo	5–6 y	10–11 y	10–12 y
Second premolar	24–30 mo	6–7 y	10–12 y	11–13 y
First molar	Birth	30–36 mo	5.5–7 y	5.5–7 y
Second molar	30–36 mo	7–8 y	12–14 y	12–14 y
Third molar	Maxilla: 7–9 y		>16 y	>16 y
	Mandible: 8–10 y			

mo months, *y* year
[a]It is noteworthy that the sequence is not simply in rank order

enamel development and considers the evidence, or lack thereof, for the association between the etiological factors and the nature of the subsequent abnormalities.

Prevalence of DDE in the Permanent Dentition

Mouth and tooth prevalence are the most commonly used systems to report the prevalence data for DDE. Mouth prevalence is determined by the inclusion of any individual who has been found to have at least one tooth affected by the condition, while tooth prevalence illustrates the percentage of teeth affected per person. Mouth prevalence figures reflect the extent of the distribution of enamel defects in a population group because individuals who are mildly and severely affected are grouped together. Tooth prevalence indicates the proportion of teeth affected and hence reflects the severity of the condition [2].

Table 2.2 summarizes the prevalence of DDE in the permanent dentition as reported in the literature. Wide variations exist in the literature because of the use of various terminologies and the different diagnostic criteria employed to describe the enamel defects in the permanent dentition [21, 22, 24, 26]. Nevertheless, the majority of reports have failed to demonstrate any difference in the prevalence of enamel defects between girls and boys [12, 27]. Furthermore, for all types of enamel defects, the published mouth prevalence in the permanent dentition ranges from 9.8 % to 93 % [8, 26], while tooth prevalence figures range from 2.2 % to 21.6 % [26, 28].

Etiology of DDE in the Permanent Dentition

Enamel morphogenesis is a continuous, complex process that starts with the secretion of enamel matrix proteins followed by mineralization and finally maturation. This process has been shown to start at the cusps on the molars and the incisal part

Table 2.2 The prevalence figures, reported in the literature, for any type developmental defects of enamel in the permanent dentition of healthy children

Author	Year	Country	F level (ppm)	Age (years)	Prevalence %	
					Mouth	Tooth
Suckling et al. [3]	1985	New Zealand	1.0	12	56.6	18.8
Dooland and Wylie [4]	1989	Australia	1.0	8–9	–	25.5
			0			15.6
Dummer et al. [5]	1990	UK	<0.1	15–16	50.1	5.71
					26.2	11.8
Nunn et al. [6]	1992	UK	<0.2	15	64.1	38.7
					–	57.5
			1.0		78.9	59
					–	83.9
			1.0–1.3		83.9	66.2
					–	81.5
Fyffe et al. [7]	1996	UK	–	13–14	48.7	–
Rugg-Gunn et al. [8]	1997	Saudi Arabia	0.25	14	75	–
			0.80		82	–
			2.71		93	–
Hiller et al. [9]	1998	Germany	<0.02	8–10	39.9	
Dini et al. [10]	2000	Brazil	0.7	9–10	26.1	–
Jalevik et al. [11]	2001	Sweden	Low	7–8	33.3	–
Zagdwon et al. [12]	2002	UK	<0.1	7	14.5	7.2
Ekanayake and van der Hoek [13]	2003	Sri Lanka	<0.3	14	29	–
			0.3–0.5		35	
			0.5–0.7		43	–
			>0.7		57	–
Cochran et al. [14]	2004	Finland	<0.01	8	59	–
		Greece	<0.01		43	–
		Iceland	0.05		54	–
		Portugal	0.08		49	–
		UK	<0.1		48	–
		The Netherlands	0.13		70	–
		Ireland	1.0		69	–
Mackay and Thomson [15]	2005	New Zealand	–	9–10	51.6	–
Balmer et al. [16]	2005	UK	<0.1	8–16	–	27.3
		Australia	0.9–1.1			51.6
Wong et al. [17]	2006	Hong Kong	1.0 (1983)	12	92.1	–
			0.7 (1991)		55.8	–
			0.5 (2001)		35.2	–
Hoffmann et al. [18]	2007	Brazil	–	12	46.4	–
Muratbegovic et al. [19]	2008	Bosnia and Herzegovina	<0.1	12	32.8	–
Arrow [20]	2008	Australia	0.8	7	22	–
Kanagaratnam et al. [21]	2009	New Zealand	–	9	35[a]	–

(continued)

Table 2.2 (continued)

Author	Year	Country	F level (ppm)	Age (years)	Prevalence %	
					Mouth	Tooth
Seow et al. [22]	2011	Australia	0.1	13.5[b]	58	–
Casanova-Rosado et al. [23]	2011	Mexico	–	6–12	7.5	–
Robles et al. [24]	2013	Spain	0.07	3–12	52	8.3
Vargas-Ferreira et al. [25]	2014	Brazil	–	8–12	64	–

[a]Both fluoridated and non-fluoridated areas
[b]Mean age

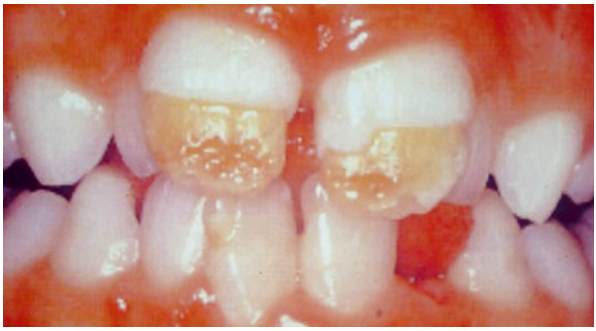

Fig. 2.1 Hypoplasia of the maxillary central incisors

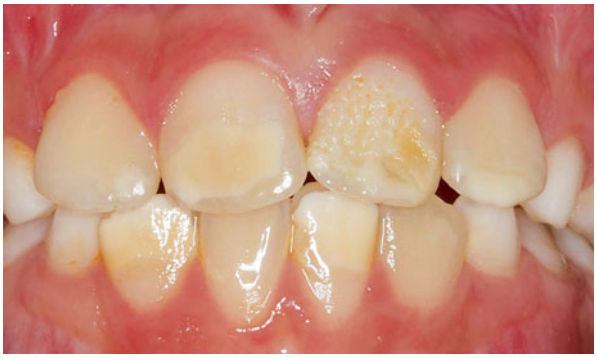

Fig. 2.2 Hypomineralization and hypoplasia of the maxillary and mandibular incisor teeth

of the incisors, progressing to the cervical areas of the teeth [29]. However, there is still limited understanding of how mineralization progresses across the crowns of the teeth. This could be important in determining the timing of defects to relate to specific disturbances caused by systemic disorders. Disturbances in the different stages of enamel formation may result in a range of enamel defects with quite different clinical appearances and structural changes. Defective formation of the enamel matrix results in hypoplasia, a *quantitative* defect, depicted by generalized thinning or pitting types of defects (Fig. 2.1). Defective calcification of an otherwise normal fully developed organic enamel matrix results in hypomineralization, a *qualitative* defect (Fig. 2.2). This is seen clinically as changes in color and

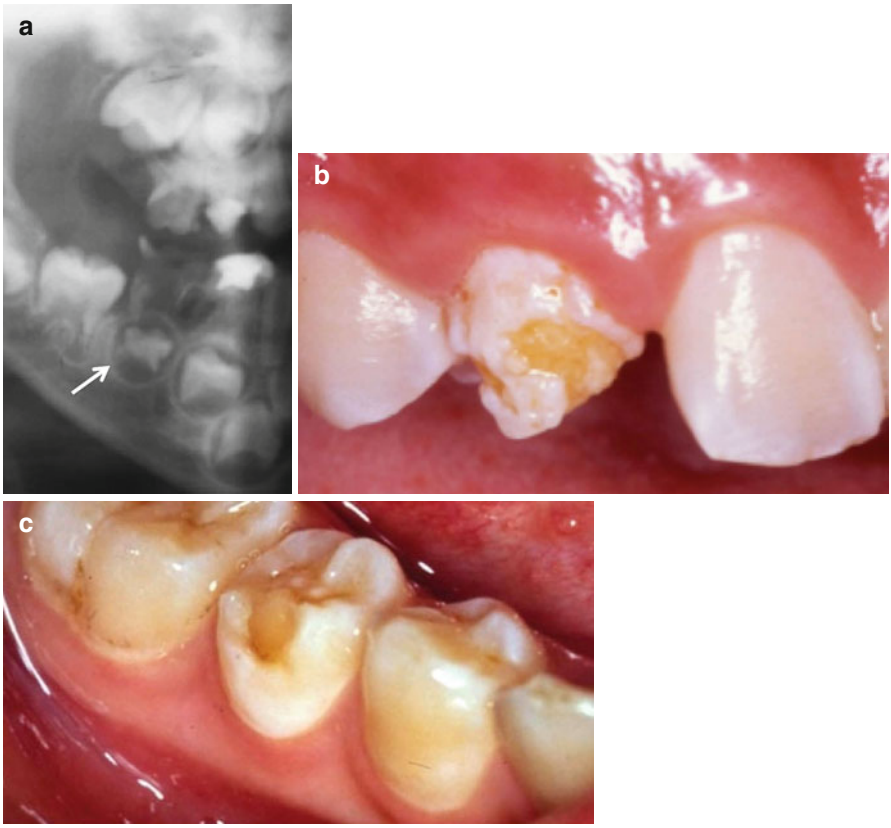

Fig. 2.3 (**a**) Caries in the mandibular second primary molar has led to the intra-radicular infection which has resulted in hypoplasia of the developing second premolar. (**b**) Hypoplasia of the maxillary permanent canine as a consequence of infection of the primary predecessor. (**c**) Hypoplasia in the form of missing enamel is exhibited by this mandibular second premolar following infection of the primary second molar

translucency of the enamel and presents as enamel opacities which can be either demarcated or diffuse [2, 30].

Although the etiology of enamel defects may be attributed to local, systemic, genetic, or environmental factors, most are likely to be multifactorial in nature. This makes it difficult to identify a single cause for many cases of DDE. The time frame of exposure and the mechanism underpinning the causative factors determine the presentation of these defects. Defects on a single tooth or only a few teeth suggest a local etiological factor e.g. a defect in a permanent tooth due to damage (trauma or infection) to its primary predecessor (Fig. 2.3a–c). Alternatively, a systemic factor (both short and longer term) may affect all the teeth that are developing during the time of the insult and lead to what is described as a chronological defect. Genetic factors can be considered separately. Defects caused by genetic factors are most often (although not always) generalized in distribution, affecting both the primary and permanent dentitions. They may present as either enamel defects alone as seen

in amelogenesis imperfecta (see Chap. 5) or as enamel defects associated with other general genetic disorders/syndromes (see Chap. 4).

Enamel defects can be classified clinically as demarcated and diffuse opacities and hypoplasia. The location of isolated defects depends on the stage of amelogenesis at the time of the insult or injury [31]. The general consensus regarding the etiology of isolated opacities, which may be demarcated or diffuse and present as white, creamy, or yellow in color, is that amelogenesis is affected by a disturbance during the mineralization phase. It remains unclear why this would involve only an isolated patch of enamel on the crown and not the whole surface. Conversely, hypoplasia occurs when there is a disturbance during the secretory stage of amelogenesis while the enamel is only partly mineralized. Thus, enamel defects with similar presentations may have been caused by a variety of etiological factors. Furthermore, the same etiological factor can produce enamel defects with different presentations depending on the timing of the insult. Examples of this are commonly seen following primary tooth trauma. When a maxillary anterior primary tooth is intruded in infancy (during the first year of life), the crown of the permanent successor may suffer severe structural damage with missing enamel and even dilaceration of the root or the crown, while an intrusion in the later preschool years may only cause an isolated labial hypomineralized enamel opacity on the permanent successor (Fig. 2.4a, b).

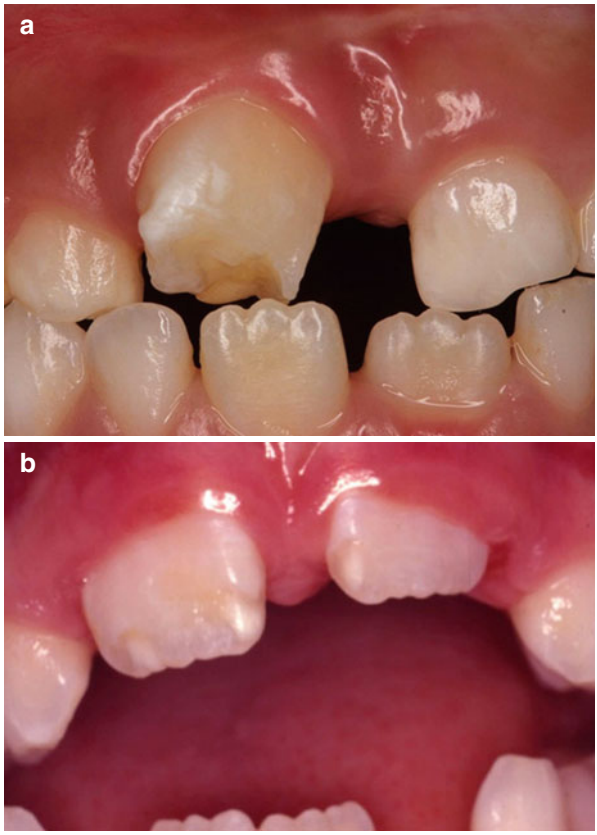

Fig. 2.4 (**a**) Hypoplasia of the maxillary permanent incisor tooth as a consequence of trauma to the predecessor. (**b**) Hypomineralization and hypoplasia of the maxillary central incisor teeth as a consequence of trauma to the predecessor

Determining the Etiology

Based on the number of teeth affected, the possible etiological factors for DDE in permanent teeth can be categorized as being local or general. However the evidence is equivocal, with the majority of published reports being animal studies or case reports of children with specific systemic disorders. The putative etiological factors reported in the literature are summarized in Table 2.3. Only a few of these factors have good evidence supporting a direct causal effect, e.g., trauma to a primary predecessor or high levels of ingested fluoride during early childhood.

Localized Enamel Defects

When only one or few adjacent teeth exhibit an enamel defect, it is usually considered to be caused by a very localized or isolated factor rather than a more generalized systemic or genetic factor [32]. The most common causes of localized enamel defects are trauma, chronic radicular infection resulting from pulpal necrosis in a primary predecessor tooth, surgery in the adjacent area or radiation therapy. Other isolated defects with incompletely formed enamel such as those associated with dens invaginatus and dens evaginatus may be due to a genetic influence in certain teeth.

Intrusive and lateral luxation injuries to the primary teeth often result in enamel defects in the succedaneous permanent teeth [33, 34]. This occurs most often in the anterior teeth as they are more likely to suffer the direct impact of trauma from falling or being struck by an object than the posterior teeth. The severe consequences arise because of the direct or nearly direct impact of the apex of the root of a primary incisor on the crown or follicle of the developing permanent successor or may occur as a consequence of post-traumatic complications of inflammation and infection. Furthermore, if the trauma to the primary tooth leads to pulpal necrosis, then there is a greater likelihood of enamel defects occurring in the succedaneous permanent tooth. This can also occur following severe dental caries with pulp exposure leading to untreated chronic infection [35]. Surgical procedures such as extraction of primary teeth, removal of supernumerary teeth, cleft palate repair or distraction osteogenesis have all been reported to cause localized enamel defects in the succedaneous or adjacent permanent teeth [36–39]. Untreated carious lesions extending into the pulp of primary teeth may result in pulpal necrosis and infection which may result in DDE in the succedaneous permanent teeth (Fig. 2.3) [40–42]. The reported defects have ranged from demarcated opacities to hypoplastic defects [43].

Generalized Enamel Defects

Generalized enamel defects are those defects that are seen either on the crowns of groups of teeth or in all the teeth. As mentioned previously, the stage of amelogenesis in the particular tooth germ at the time of the insult or injury is often critical to the resulting location and type of enamel defect. The timing of the disturbances

Table 2.3 List of etiological factors, reported in the literature, responsible for the formation of enamel defects in the permanent dentition

	Systemic		
Local	Perinatal and neonatal	Postnatal	Hereditary conditions
Trauma	Neonatal hypocalcemia	Nutritional and gastrointestinal disturbances resulting in hypocalcemia and vitamin D deficiency	22q11 deletion syndrome
Primary tooth			
Surgery			
Distraction osteogenesis			
Tooth forceps			
Chronic periapical infection in a primary tooth	Severe perinatal and neonatal hypoxic injury	Bacterial and viral infections associated with high fever	Autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy
Cleft lip and palate	Prolonged delivery	Exanthematous diseases	Candidiasis endocrinopathy syndrome
Radiation	Prematurity	Juvenile hypothyroidism	Cleidocranial dysostosis
Burns	Low birth weight	Hypothyroidism	Celiac disease
Osteomyelitis	Twins	Hypogonadism	Congenital adrenal hyperplasia
Jaw fracture	Cerebral injury	Phenylketonuria	Congenital contractual arachnodactyly
	Neurological disorders	Alkaptonuria	Congenital unilateral facial hypoplasia
	Hyperbilirubinemia	Renal disorders	Ectodermal dysplasias
	Prolonged neonatal diarrhea and vomiting	Congenital heart disease	Ehlers-Danlos syndrome
	Severe neonatal infections	Congenital allergy	Epidermolysis bullosa
	High fever	Oxalosis	Focal dermal hypoplasia
		Mercury poisoning (acrodynia)	Heimler's syndrome
		Fluoride	Hypoparathyroidism
		Prolonged use of medicines	Ichthyosis vulgaris
		Prolonged diarrhea and vomiting	Lacrimo-auriculo-dento-digital syndrome
		Radiation and cytotoxic therapy	Morquio syndrome
			Mucopolysaccharidosis
			Oculodentodigital dysplasia
			Orodigitofacial dysostosis
			Prader-Willi syndrome
			Pseudohypoparathyroidism
			Seckel syndrome
			Tricho-dento-osseous syndrome
			Tuberous sclerosis
			Vitamin D-resistant rickets
			William's syndrome

during tooth morphogenesis will determine the location and type of defects and the number of teeth that will be affected. Homologous pairs of teeth will usually have enamel defects in similar locations although the severity of the defects may not always be the same suggesting that even homologous teeth do not always mineralize at exactly the same rate. As the process of enamel development occurs in the different tooth types over different developmental times, the locations of enamel defects will differ between different homologous pairs of teeth [44]. Developmental defects with this type of distribution are referred to as generalized defects of enamel and may be caused by environmental factors or systemic conditions that have either a defined time of influence or an ongoing influence throughout childhood, or they may be caused by genetic factors. These conditions and their association with DDE are discussed more fully in Chaps. 4 and 5.

Environmental Factors

Several environmental factors have been associated with DDE. These are believed to cause systemic disturbances that affect enamel development rather than the environmental agent affecting the ameloblasts directly. Environmental agents such as lead, mercury, bisphenol A (an endocrine-disrupting chemical), some drugs such as anticancer agents and tetracycline and some trace elements including fluoride and strontium have been implicated in DDE. The systemic ingestion of these chemical substances may exert an adverse effect on enamel formation during and after fetal development [45, 46]. Exposure to such substances during amelogenesis may result in the formation of defective enamel depending on the stage of enamel development, the timing of exposure, the length of exposure and the underlying health of the individual [47]. It should be remembered that some of the substances also have a very positive effect, such as the ingestion of low levels of fluoride to improve enamel maturation and decrease dental caries risk.

DDE arising from excess fluoride ingestion have been found in areas with high natural levels of fluoride in the drinking water. Ingestion of excess fluoride during tooth development can result in dental fluorosis, a form of enamel hypomineralization where the white striations contain less mineral and retain more developmental enamel proteins. The hypomineralization can vary from minor white striations to small or more extensive opacities [48, 49]. The first 3 years of life is generally understood to be the window of maximum susceptibility for the development of fluorosis in the permanent maxillary central incisor teeth [50]. Nevertheless, for the whole permanent dentition, excluding the third molars, the first 6–8 years of life is an important period when exposure to appropriate levels of fluoride as defined in local guidelines should be followed [51]. Fluorotic hypomineralization defects do have specific characteristics which allow them to be differentiated from defects caused by other factors [52], and this can be useful for the clinician to consider when diagnosing DDE. The characteristic lesions in fluorosis are dull and chalky in appearance; they may vary in color from chalky white, yellow, or brown, and in some cases there are small pits which accumulate organic matter producing yellow to brown spots (Fig. 2.5). When diagnosing DDE that

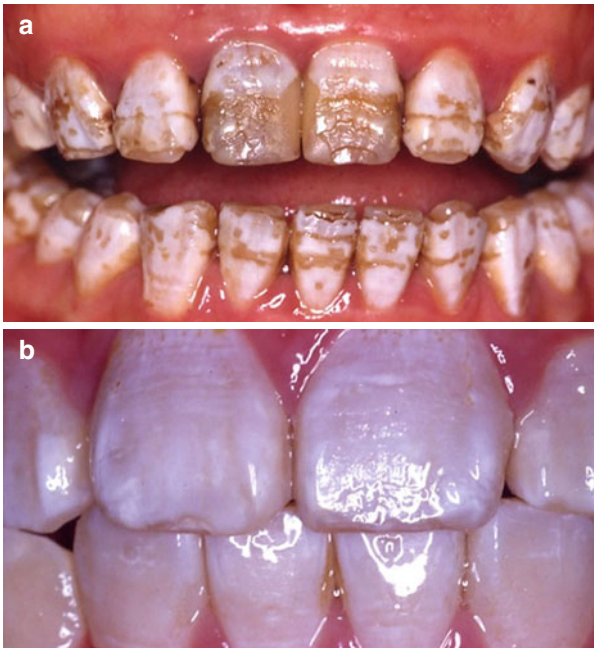

Fig. 2.5 (**a**) Fluorosis is evident in this permanent dentition of a child who was brought up in an area with 9 ppm of fluoride in the drinking water. (**b**) An example of less severe fluorosis

may be related to fluoride, a careful history of total fluoride ingestion as well as medical and developmental histories should be taken for the appropriate developmental period of the affected teeth. Another trace element that can have an influence on the development of hypomineralization in enamel is strontium which has been shown to be associated with enamel hypomineralization similar to that caused by excess fluoride [53].

Several animal experiments have shown that teeth are very sensitive to the effects of dioxins [54]. The most toxic dioxin, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD), arrests degradation and/or removal of enamel matrix proteins which is a pre-requisite for the completion of enamel mineralization [55]. It has been hypothesized that prolonged breast-feeding might increase the risk of DDE due to the environmental contamination of breast milk with dioxins or dioxin-like compounds [56, 57]. A dose-response relationship between high levels of dioxins or polychlorinated biphenyls (PCBs) exposure (serum concentration) and DDE in permanent teeth has been reported [58, 59]. However the evidence remains mixed with other studies reporting contradictory findings [11] and more recent studies failing to identify any correlation between DDE in children living in areas polluted by dioxins and in those living in areas with low pollution [60, 61]. It has also been reported that there is an increase in incidence of diffuse white/creamy mottling of enamel with elevated levels of chemicals such as fluorine, ammonia and sulfur in the atmosphere [62]; hypervitaminosis D [63]; chronic lead poisoning [64]; diphosphonate poisoning [65]; and polychlorinated biphenyl poisoning [66]. Antineoplastic therapy in the form of radiation treatment and/or chemotherapy can affect any cells including ameloblasts and

consequently lead to DDE [67]. It has been reported that central nervous system irradiation with scattered irradiation of 0.72–1.44 Gy to the dental arches can result in a range of enamel defects in developing permanent teeth [68, 69].

Genetic Disorders

Amelogenesis imperfecta (AI) is a heterogeneous group of genetic disorders that affects the development of dental enamel resulting in varying degrees of hypoplasia, hypomineralization and/or hypomaturation [70]. A single-gene defect can occur as X-linked, autosomal dominant, or autosomal recessive inheritance. There is evidence that AI may present as part of a hereditary syndrome, examples of which are epidermolysis bullosa [71, 72], pseudohypoparathyroidism [73], and tricho-dento-osseous syndrome [74]. See Chaps. 4 and 5.

Systemic Conditions

It has been suggested that perinatal and postnatal problems, hypoxia and malnutrition may be related to the occurrence of DDE in permanent teeth. However, the mechanisms are not clearly understood and it is difficult to link any of the conditions directly to the defects. Children with low birth weights have been shown to be more at risk for developing DDE in their primary teeth. However the evidence is weaker in relation to the permanent dentition [75]. Similarly, problems at the time of delivery such as caesarean section and labor in excess of 20 h and poor respiratory response in the postnatal period (hypoxia and respiratory diseases in early childhood) have all been linked with the occurrence of DDE, but currently there is insufficient evidence to be confident about any of these as direct causes of DDE [76].

There are numerous reports of DDE in the permanent dentition being associated with diseases and infectious conditions occurring in early childhood. Infectious diseases occurring during early childhood that may be related to DDE include chickenpox, asthma, measles, mumps, scarlet fever, exanthematous fevers, pneumonia and urinary tract infections. Other conditions such as convulsions, tuberculosis, diphtheria, whooping cough, otitis media, bulbar polio with encephalitis, gastrointestinal disturbances, cyanotic congenital heart disease, neurological disorders and renal disorders have also all been mentioned in association with DDE.

Vitamin D deficiency, hypocalcemia, hypophosphatemia and hyperparathyroidism have also all be implicated in DDE in the permanent dentition. Vitamin D-dependent rickets (VDDR) is a condition which appears to be increasing in prevalence either due to vitamin D deficiency in the mother during pregnancy or vitamin D deficiency in the young child [77]. Vitamin D deficiency contributes to the development of hypocalcemia and hypophosphatemia which is then compounded by secondary hyperparathyroidism which in turn increases renal inorganic phosphate (P_i) clearance, effectively worsening the hypophosphatemia. Consequently the low

concentrations of Ca^{2+} and P_i prevent proper mineralization of the organic bone matrix and this also leads to defects in enamel mineralization [78].

There is a growing body of literature reporting associations between DDE and systemic conditions such as celiac disease, cystic fibrosis and tuberous sclerosis though the mechanisms involved are often not fully understood [79–82]. Hypocalcemia has also associated with the occurrence of enamel hypoplasia in the permanent dentition in hereditary vitamin D-resistant rickets, X-linked hypophosphatemia, and hypoparathyroidism [83].

Despite the numerous reports of DDE in association with all of these conditions, there is little strong evidence to support any condition as being a primary etiological agent responsible for the formation of the enamel defects in the permanent dentition.

Summary

The prevalence of DDE in the permanent dentition (in developed countries) is reported to be between 9 and 68 %. This wide variation can be attributed to the use of different criteria and terminologies to describe enamel defects. The etiology of enamel defects may be local or systemic, genetic, or acquired in origin. The clinical presentation of DDE varies greatly depending on the etiology and severity. Single-tooth defects can be attributed to a local factor, whereas in those of systemic etiology many or all of the teeth that are developing during the time of influence of the etiological factor are affected (chronological defects). Defects with a genetic etiology form a separate entity, usually affecting both the primary and permanent teeth. Identifying the presence of DDE and establishing a diagnosis are essential to inform appropriate treatment planning in both the short and longer term (see Chap. 8).

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