Molar Incisor Hypomineralization

A Clinical Guide to Diagnosis and Treatment

Katrin Bekes
Editor

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Preface

Molar incisor hypomineralization (MIH) is defined as "demarcated, qualitative developmental defects of systemic origin of the enamel of one or more first permanent molars with or without the involvement of incisors." Recent data indicates MIH is a frequently encountered dental condition worldwide. The condition could be associated with dental complications including hypersensitive teeth, rapid progression of caries, mastication impairment due to rapid attrition, and esthetic repercussions. These might affect patients' quality of life as well as create treatment challenges to dentists. Given this life-long burden, MIH clearly merits increased attention as a global concern for dental public health.

This book functions as a wide-ranging reference of current clinical and scientific knowledge of the various aspects of MIH. Background information including structural properties of hypomineralized enamel as well as prevalence data and potential etiological factors are presented first. The following chapters focus on clinical considerations in clinical practice by discussing diagnostic criteria, classifications and treatment strategies plus potential associations between MIH and caries, occurrence of hypomineralized primary teeth, and knowledge as well as experience of dentists regarding MIH. In the last part of the book, the various treatment options are then systematically presented and reviewed, covering pain control, prophylaxis, desensitizing, fissure sealing, restoration approaches, and extraction therapy. The final part of the book focuses on cost-effectiveness of different procedures.

The book is written by recognized experts in the field. It provides dental professionals as well as postgraduate students, seeking to extend their knowledge, with a clear understanding of current clinical and foundational knowledge on the various aspects of MIH.

Vienna, Austria
December 2019

Katrin Bekes

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Part I

Background

MIH: An Introduction

1

Göran Koch

1.1 "The Beginning"

During the last decades, extensive research has been devoted to the very specific enamel developmental disturbance denominated MIH. This introductory chapter will try to present reactions and thoughts in the very beginning of the MIH era.

Developmental disturbances in dental hard tissues have been recognized by the dental profession since the time of modern dentistry. They can be genetic or achieved. Basically, the enamel defects are classified as hypoplastic and/or hypomineralized. Besides amelogenesis imperfecta of the hypomineralized type and fluorosis, hypomineralizations, in the literature, are often referred to as non-fluoride enamel opacities, opaque spots or idiopathic enamel opacities [1].

In the FDI Technical Report No 15, 1982 [2] on developmental defects in dental enamel, opacity is defined as "a quality defect of enamel identified visually as an abnormally in the translucency of enamel. It is characterized by a white or discoloured (cream, brown, yellow) area but in all cases the enamel surface is smooth and the thickness of the enamel is normal". Solitary non-fluoride enamel opacities in permanent teeth can be found in 20–80% of the population [3].

In the late 70s, dentists working in the public dental service (PDS) in Sweden reported an unusual and increasing number of children with extensive, demarcated severe enamel hypomineralizations of unknown aetiology in their first permanent molars and incisors (Fig. 1.1). The enamel defects were difficult to treat and clean due to extreme sensitivity. The restorative material available at that time for stress-bearing dental restorations in children was silver amalgam. The common restorative treatment was placing improper extensive atypical restorations with restricted survival time, often due to fractures (Fig. 1.2).

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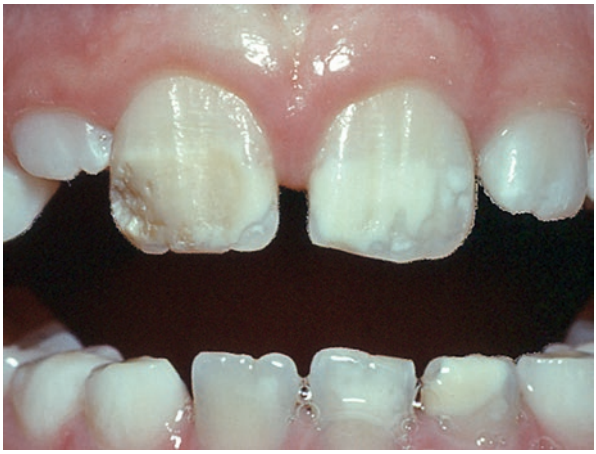

Fig. 1.1 Severe MIH in the maxillary incisors. Observe the strict boundary to normal enamel and also the post-eruptive breakdown of the hypomineralized enamel due to attrition

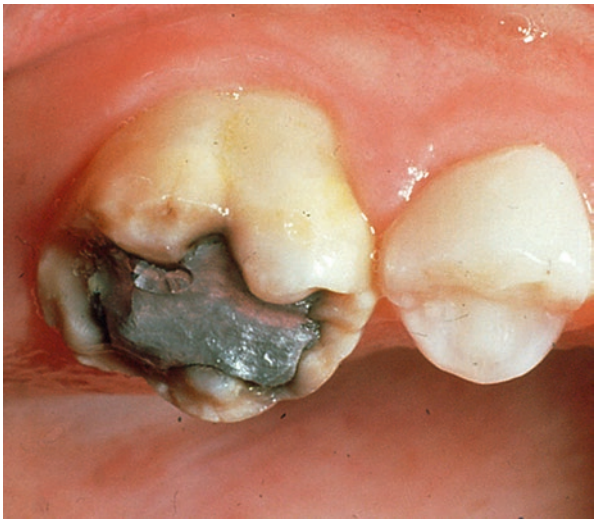

Fig. 1.2 Maxillary first permanent molar with atypical amalgam restoration due to severe MIH in the occlusal surface. Note the post-eruptive breakdown of the enamel and the fracture of the amalgam restoration

In 1978, the National Board of Health and Welfare in Sweden asked the PDS to report cases showing these unique and specific enamel disturbances to the board. These reports indicated that child populations with high prevalence of enamel disturbances were mostly born around 1970. However, the reported cases gave no information of the true prevalence.

1.2 Pioneer Work

In 1977, an epidemiologic study was initiated at the Institute for Postgraduate Dental Education in Jönköping, Sweden, to estimate the prevalence and character of this "new" type of idiopathic enamel hypomineralization in children born in the

year 1970 and the nearest years before and after. The results of this study [4] were published about 15 years ahead of most other studies on the same enamel disturbance. That might justify a short presentation of how this study was planned and performed as well as to comment on the results and also what we, at that time, speculated about tentative aetiologic factors.

All the children within three school districts in the municipality of Jönköping and born in 1966, 1969, 1970, 1971, 1972 and 1974 took part in the study. All 2252 children were included, and they were examined during the period 1979 to 1983. The clinical examination was a two-step procedure. First, all children were examined in the classroom by three trained specialists in paediatric dentistry using mirror, probe and portable light. Children showing any sign of enamel hypomineralization in their first permanent molars and incisors were referred to a fully equipped dental clinic where one and the same trained specialist in paediatric dentistry performed all the clinical examinations according to specially developed criteria. The enamel defects were also documented photographically.

At the start of the study, no established scoring system was established for idiopathically hypomineralized enamel that is why we had to develop such a system for the actual study. Basically, the hypomineralization should be clearly demarcated which means that a sharp and distinct border to normal enamel should be available. In severe cases, the hypomineralized enamel was soft and easily abraded by attrition-post-eruptive breakdown of the enamel (Fig. 1.3). First, permanent molars and incisors were examined. The term idiopathic hypomineralization used in the study proved to be congruent with the more than 20 years later internationally accepted denomination molar incisor hypomineralization (MIH) [5, 6]. Therefore, from now on, the term MIH will be used in this chapter.

The developed scoring system was used accordingly. Each tooth (first permanent molars and incisors) surface was divided into units as follows: The occlusal (incisal) surface formed one unit. All smooth tooth surfaces were horizontally divided into three units. Thus, a single tooth had 13 units. Each unit was scored according to colour changes (white, yellow, brown) and surface changes (rough, abraded, disintegrated, atypical restoration). To be recognized as a defect in colour or surface structure, the change had to involve at least one third of a unit. By using this scoring system, the extent and severity of MIH could be assessed.

The general findings of the study [4] were that irrespectively of year of birth, a certain percentage of children were suffering from MIH. However, a clear peak in frequencies of affected children born around 1970 was evident (Fig. 1.4). The percentages of children with MIH according to year of birth were 15.4% for born in 1970, 7.3% for born in 1969, 7.1% for born in 1971, 3.6% for born in 1966, 5.2% for born in 1972 and 4.4% for born in 1974, respectively. It could also be confirmed that the most affected teeth were the first permanent molars. In a low percentage of the children, both the first permanent molars and incisors showed MIH (Fig. 1.5). Most often, more than one first permanent molar was affected in the same child. Another experience was the great similarities regarding the extent of MIH in affected children irrespectively of year of birth.

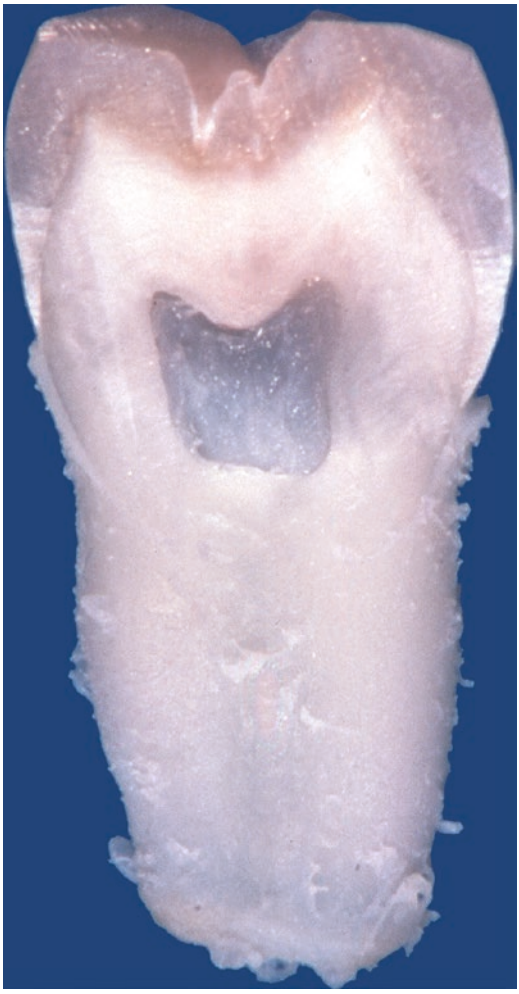

Fig. 1.3 Maxillary first permanent molar with severe and extended MIH. After extraction, the tooth has been divided. Note the abraded cusps and the distinct boundary between hypomineralized and normal enamel. Moreover, note that the defect goes all the way through the enamel thickness

The outcome of the epidemiologic study was an incitement to go further and see if we could find any tentative aetiological factors to MIH. The most plausible explanation was that MIH was caused by some interactive processes affecting the amelogenesis starting very early in life, maybe during the period from birth to 4–6 months of life. Such interaction may be caused by ingested substances (e.g. special baby food formulas, medication or infections/diseases). There are further two specific features that had to be involved in the analyses. Why is there a strict boundary between affected and normal enamel, and why does it seem the hypomineralization changes go all the way through the thickness of the enamel? Why is the coronal enamel more exposed to MIH than the cervical enamel-a time or growth factor? Why are not all molars in same individual affected to the same extent? Why was a

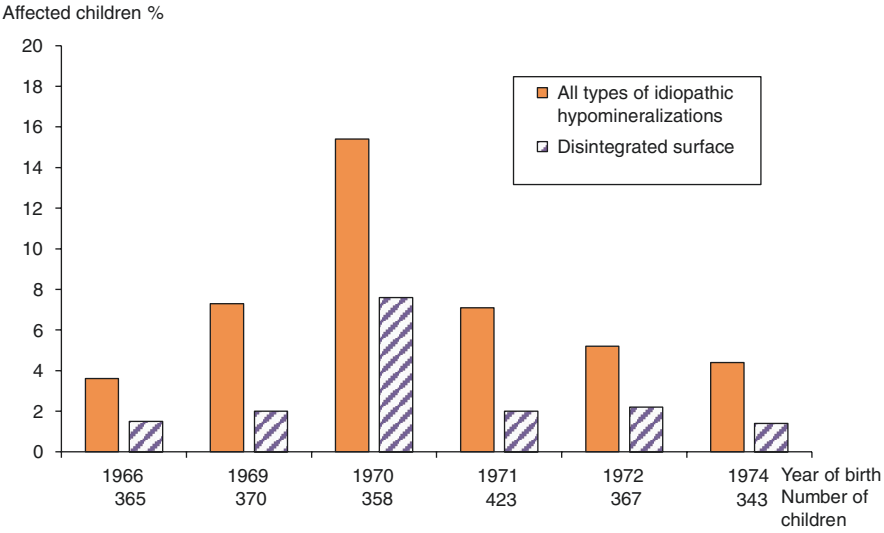

Fig. 1.4 Percentage of children born in 1966, 1969, 1970, 1971, 1972 and 1974, respectively, distributed according to type of hypomineralization in permanent first molars and/or incisors [4]

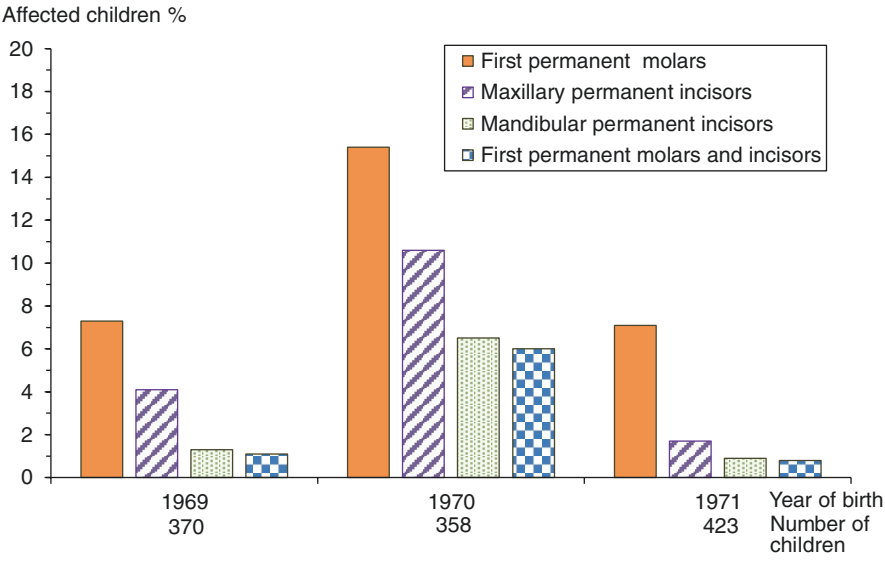

Fig. 1.5 Percentage of children born in 1969, 1970 and 1971 with hypomineralization according to groups of affected teeth [4]

higher percentage of children born in 1970 affected with MIH compared to children born before or after that year? Why do not all siblings in a family with one MIH child develop MIH? To try to find answers to some of the above question, a search for aetiological factors was initiated.

In the prevalence study, 150 children had MIH. Of these children, 55 with the most severe enamel changes formed the test group. About half of children were born in 1970 and the other half during the period 1966–1972. A control group served a randomly selected group of 55 children born in the same years as the test group and without any sign of MIH. The mothers to the children were individually interviewed concerning diseases, infections and medications as well as occupational exposures during the pregnancy and delivery. Information was collected of the child's health and breeding (breast feeding and type of additional infant formulas) during the peri-, neo- and natal period and up to 3 years of age. Also, information if any sibling had the same enamel disturbance was notified.

Two specialists in Paediatrics at the Regional Hospital in Jönköping collected information available in all medical records concerning the mother's health during pregnancy and timing for delivery and the child's condition at birth concerning weight and growth, diseases and medications during the first 3 years of life.

More than 100 issues were analyzed. However, there were no clear differences concerning the studied items between the MIH group and the control. Not even the much higher prevalence of MIH in children born in 1970 compared with children born the years around could be explained. The reasons that no differences were found could be that the material was limited, that the medical journals were incomplete for this type of study or that the mothers had problem to remember details around their child's situations 7 years later, especially if she had more children. Therefore, aetiologic studies on MIH should preferably be specially designed and prospective. These results were never published.

1.3 MIH and Fluoride Intake

When the increasing prevalence of the specific MIH changes was recognized in children born in the early 1970s, the anti-fluoride groups claimed that these changes were caused by fluoride intake. In Sweden, the Fluoride Commission, appointed by the Swedish Government, in their report in 1981 (SOU 1981:32) on fluoride in drinking water included a number of appendices. One of these appendices was from an epidemiological investigation on the prevalence of mineralization disturbances in dental enamel in a Swedish city (Uppsala) with natural fluoride (1–1.2 ppm F) in the tap water. Special attention was in this appendix given to fluorosis and MIH. The study sample consisted of 748 children born in Uppsala 1967–1970 and living in Uppsala. The control group was 486 children born in the same years as the test group, but they have moved into Uppsala after the mineralization of their first permanent molars and incisors had taken place. A group of MIH experienced examiners trained against a "golden standard" performed the clinical examinations [7].

In children born in Uppsala, 62% showed enamel disturbances diagnosed as fluorosis compared with 42% in children not born in Uppsala. However, the fluorosis changes were of low level, especially in the control group. Concerning the frequency of children showing mineralization disturbances diagnosed as MIH, the group born in Uppsala was affected in 5.5% and the controls in 6.7%. It could be concluded that MIH is a distinct and separate entity which easily can be clinically differentiated from fluorosis. The results of the study also confirmed that MIH cannot be connected to intake of fluoride.

1.4 The Future

To summarize: This introductory chapter is an attempt to describe how the interest in MIH started about 40 years ago. At that time, very few scientific papers concerning MIH were published. However, during the last decades, an extreme increase in number of reports has occurred. Elfrink et al. [8] published in 2015 a systematic review of studies dealing with prevalences of MIH. They started up with 1078 papers resulting in 52 eligible for detailed analyses. Concerning studies on the aetiology of MIH, a recent review [9] screened 2254 studies, but after thorough evaluation, only 28 were eligible for further analyses. This scenario reveals the enormous amount of research going on worldwide concerning MIH. Today, we have internationally standardized diagnostic criteria which also means that the prevalences of MIH are well documented and comparable. The demand for suitable methods and resources to clinically monitor the internationally high occurrence of MIH is a central issue. To help the clinicians in their decision-making and suggesting adequate and successful therapy, treatment need indices are welcome [10]. Concerning the aetiology of MIH, we still have not reached a clear consensus. However, in the years to come, research can be expected to give a definite explanation of how MIH is initiated and developed.

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2 Structural, Mechanical, and Chemical Evaluation of Molar Incisor Hypomineralization-Affected Enamel

Karim Elhennawy, Katrin Bekes, Anton Dobsak, Stefan Tangl, Hassan Shokoohi-Tabrizi, and Falk Schwendicke

2.1 Enamel Defects

Enamel hypoplasia is defined as *quantitative* defects, which are mainly caused by a disturbance to the amelogenesis during the matrix secretion phase [1–6]. Enamel hypomineralization is defined as *qualitative* defects that are caused by disturbances in either the calcification or maturation phase [5, 7–9]. To understand the different pathways towards enamel defects, we will now discuss enamel formation.

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2.2 Enamel Formation

Dental enamel is the hardest and most mineralized structure in the human body. The uniqueness of enamel compared with other mineralized tissues is due to its high mineral content. Around 87% of the enamel's volume and 95% of its weight are composed of tightly packed and organized crystallites. Compared with the crystal volume of other mineralized tissues such as bone, dentin, and cementum, the enamel crystallites' volume is a thousand times higher [10, 11].

Amelogenesis is the process of enamel formation, which takes place in different phases/stages, in parallel to dentin formation. Enamel is the product of the cells of the inner enamel epithelium. Enamel formation commences along the future dentino-enamel junction (DEJ) during the bell stage of tooth development. The formation of enamel begins at the cusp tips or in the middle of the incisal edge and is further deposited layer by layer towards the cervical area [10, 11]. The ameloblasts are the enamel-forming cells. The inner enamel epithelium shows different states of maturity of the ameloblasts [12, 13], which enables them to first produce a protein-rich enamel matrix, acting as crystal nuclei that elongate into long thin ribbons. Later on, these are formed into enamel rods [14, 15]. Once the cells of the inner enamel epithelium differentiate, they can no longer divide. The undifferentiated epithelial cells are first cuboid, but rapidly become slender and columnar in shape. Creating a favorable extracellular environment for mineral deposition and laying the organic matrix of proteins is the responsibility of the so-called secretory ameloblasts. The enamel matrix is produced in the endoplasmic reticulum, stored in the Golgi apparatus, and transported to the top of the ameloblast in the form of secretory granules. This procedure costs a lot of energy, which is why a variety of mitochondria are recognizable. Shortly before secretion, the cells become very long, up to 50 μm long but only about 7 μm in diameter [11]. The mature, secretive ameloblast is finally recognizable by its Tomes' process, which has a secretory surface where the enamel matrix emerges from the secretory granules.

The resulting structure of the enamel are the enamel prisms, shaped according to this secretory surface [11]. The term "enamel prism" stems from a time when research on tooth enamel was strongly mineralogical [16]. The stronger biologically oriented research has made it clear that the prisms are the products of living cells, with a shape that cannot be geometrically described [10]. In literature in addition to the name "prism", also "rod" is used. Every prism represents the fossilized image of the path the associated ameloblast has traveled from the dentino-enamel junction to the outer enamel surface.

The matrix is an important intermediate step in the arrangement of the crystals in the enamel. It forms a molecular framework into which the crystals are deposited. Thus, the crystal skeleton is provided, in which mainly phosphate and calcium ions are arranged to hydroxyapatite [$Ca_{10}(PO_4)_6(OH)_2$]. The crystals are oriented perpendicularly to the Tomes' process. The more matrix is reabsorbed by the ameloblasts, the more space is created for the crystals, which are arranged closer and closer [10]. This absorption and maturation of the enamel is controlled by then maturational ameloblasts. Taking up to two thirds of the enamel formation time, the maturational stage is considered the longest stage, during which enamel proteins and fluids are

Table 2.1 Main enamel proteins

Protein name	Prevalence	Location	Function
Amelogenin (18 to 25 kDa)	Most prevalent 80–90%	Found at the mineralization front	Regulates crystal formation and orientation and prevents lateral growth of the crystals [17]
Ameloblastin (65 kDa)	Less prevalent 5–10%	Localized to the secretory end of the ameloblast	Functions relating to crystal growth and the attachment of the ameloblast to the enamel matrix [17]
Enamelin (180 to 190 kDa)	Least prevalent 1–5%	Found at the mineralization front	A role in regulating crystal elongation with peptide fragments preventing volumetric crystal growth in the secretory phase [17]

incrementally removed from the enamel [14, 15]. Enamel proteins are essential to the formation of dental enamel, which explains their possible role in MIH.

Beginning just before the onset of dentin biomineralization and until the end of the secretory stage, ameloblasts secrete enamel proteins. Amelogenin, ameloblastin, and enamelin (Table 2.1) are the major proteins secreted at the mineralization front to incrementally increase the length of the existing crystallites (Table 2.1) [17].

A genetically programmed shift occurs at a certain time and results in the reduction of protein secretion and the increase in proteinases secretion [5, 18–21]. Enamelysin (MMP-20, 45, and 41 kDa) processes enamel proteins into a series of cleavage products. Kallikrein 4 (KLK4, 34, and 31 kDa) is the main glycosylated serine proteinase in the maturational stage of amelogenesis and is responsible for degradation and removal of enamel matrix proteins.

The result of this activity shift is a cease in crystal length elongation, and accelerated growth in width and thickness, as well as a degradation of the organic matrix and finally its near-complete disappearance [17]. The reabsorption of the enamel matrix and the simultaneous incorporation of the enamel crystals is a highly complex process, which until now has not yet been fully clarified. The astonishing fact is that the ameloblasts perform this function without a direct connection to blood vessels, because they seep away from the pulp through the enamel, which acts as a self-produced barrier.

Although tooth enamel is formed continuously, individual layers of deposits, which indicate a daily increase of 4 μm or which correspond to a longer period, can be seen microscopically. They are called the striae of Retzius. On the side surfaces of the teeth, these growth layers come to the surface and become visible as perikymata. Once enamel is complete, the ameloblasts convert to cuboid cells that can no longer form enamel [22].

Many enamel malformations are attributed due to the disruption of one of the relevant processes, such as matrix production, matrix secretion, matrix arrangement, crystal formation, and above all matrix resorption. Incomplete absorption of the matrix does not allow sufficient mineralization. Enamel that easily shears from the underlying dentin might be a result of disturbances during the development of the dentino-enamel junction. Defects during the secretory stage will result in inadequate crystal elongation and leave the enamel layer pathologically thin, or hypoplastic. Defects of the maturation stage will lead to enamel of normal thickness with

a pathologically soft consistency. Nonhereditary enamel defects are usually a result of a systemic disease, affecting only teeth that are actively developing at the time of the illness [17, 23, 24].

Molar incisor hypomineralization (MIH) is likely caused by disturbances in either the calcification or the maturation phase. The resulting structural and further changes in the enamel will be described now.

2.3 MIH-Affected Enamel

2.3.1 Microstructural Changes

Different methods such as light microscopy, polarized light microscopy, scanning electron microscopy, and transmission electron microscopy were used to study structural properties (the "microstructure") of MIH-affected enamel. Studies using light microscopy or polarized light microscopy [25–28] reported that MIH-affected teeth show increased porosity, ranging from 5% to 25% in comparison with sound enamel [25–27], creamy/white colored lesions, and those without post-eruptive enamel breakdown being the least porous lesions [25, 26]. The degree of porosity correlated to the degree of clinical opacity of the lesion [25, 26, 29]. The majority of studies reported that the MIH lesions do extend through the full thickness of enamel, starting at the dentino-enamel junction (DEJ) and ending at the enamel surface [26, 27, 29] (Fig. 2.1).

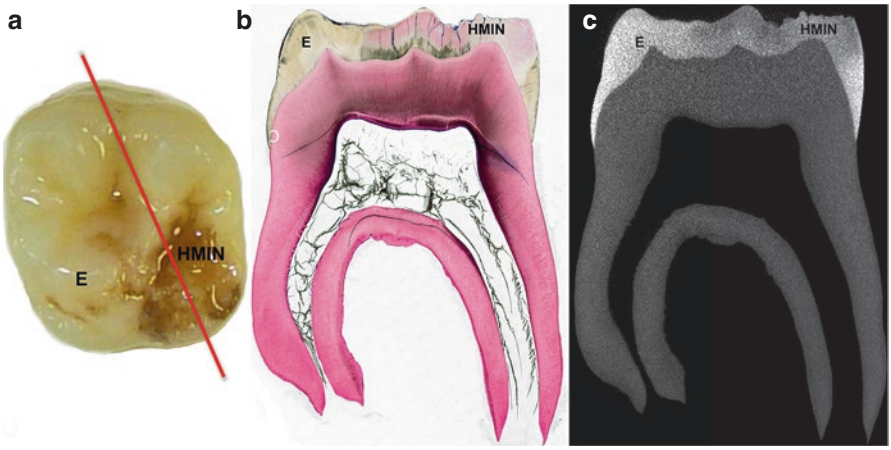

Fig. 2.1 Tooth 26 showing brown opacities as a result of post eruptive enamel breakdown in the disto-palatal area (*HMIN* hypomineralized enamel, *E* sound enamel). (**a**) Clinical picture (occlusal view) with red line indicating direction and position of the section for light microscopy and micro-CT scans. (**b**) Undecalcified thin ground section: Clear differences in staining ability can be seen between sound and hypomineralized enamel, with the latter staining pink similar to dentine. (**c**) Micro-CT image of the same region as depicted in (**b**)

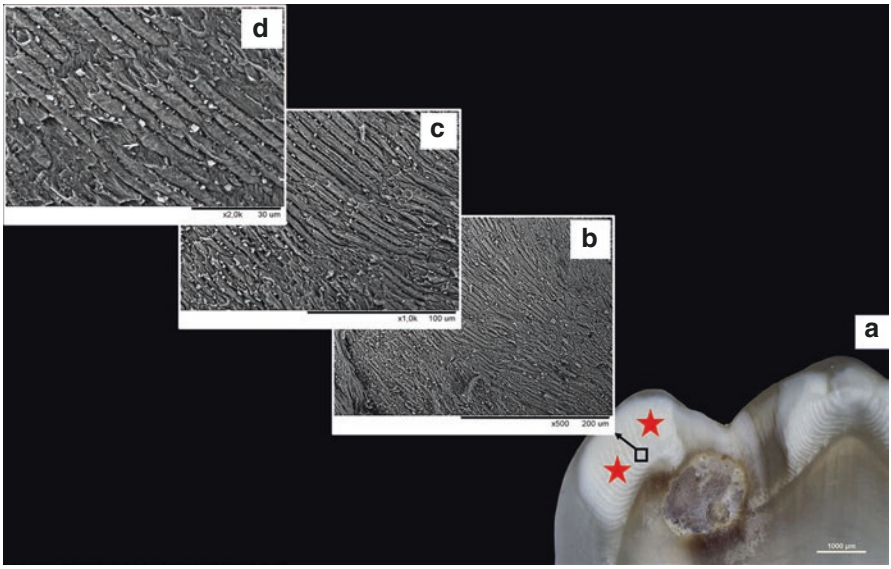

Fig. 2.2 (**a**) Light microscopic picture of a bucco-oral section of a permanent first molar seen with hypomineralization. Normally mineralized enamel appears as translucent, hypomineralized enamel as opaque with a whitish color. (**b**–**d**) Corresponding SEM radiographs of affected enamel showing less organized prism structure and a larger inter-prismatic space (**b**: 500×; **c**: 1000×; **d**: 2000×). The tooth was cut along the long axis through the region of interest with the help of a diamond saw. Afterwards, the tooth was polished and cleaned in an ultrasound bath for 5 min. A Toshiba Tabletop TM-1000 scanning electron microscope in ESEM mode was used for evaluating the surfaces and creating images

Studies using scanning electron microscopy and transmission electron microscopy [26, 30–35] showed less dense prism structures, partial loss of prismatic patterns, loosely packed crystals, less distinct prism borders, more marked inter-prismatic space, and wider sheath regions [26, 31–35] (Fig. 2.2). Scanning electron microscopy was also used to assess acid-etched MIH-affected enamel and found abnormal etching pattern compared with sound enamel [27, 31, 35]. The number of cracks and deep pores was increased in MIH-affected enamel when acid-etched [35].

2.3.2 Mechanical Properties

Studies investigating mechanical properties, usually measured as hardness and modulus of elasticity, of MIH-affected enamel, found significantly lower values compared with sound enamel [3, 26, 30, 33, 34, 36]. MIH enamel is unlikely to support restorations placed on top of it as good as sound enamel, which shows a high hardness.

2.3.3 Mineral Density

Mineral density of MIH-affected enamel was studied using different methods, such as radiography micro-tomography, radiographic micro-computed tomography, and transverse microradiography. All methods reported a significant decrease in the mineral density (around −20%) in MIH-affected teeth compared with that of sound enamel [15, 21, 27, 29, 37–39] (Fig. 2.3). Mineral density decreased from the cemento-enamel junction (CEJ) to the occlusal surface but increased again in the cusp tip region; the highest mineral density values were reported near the dentino-enamel junction (DEJ) [15].

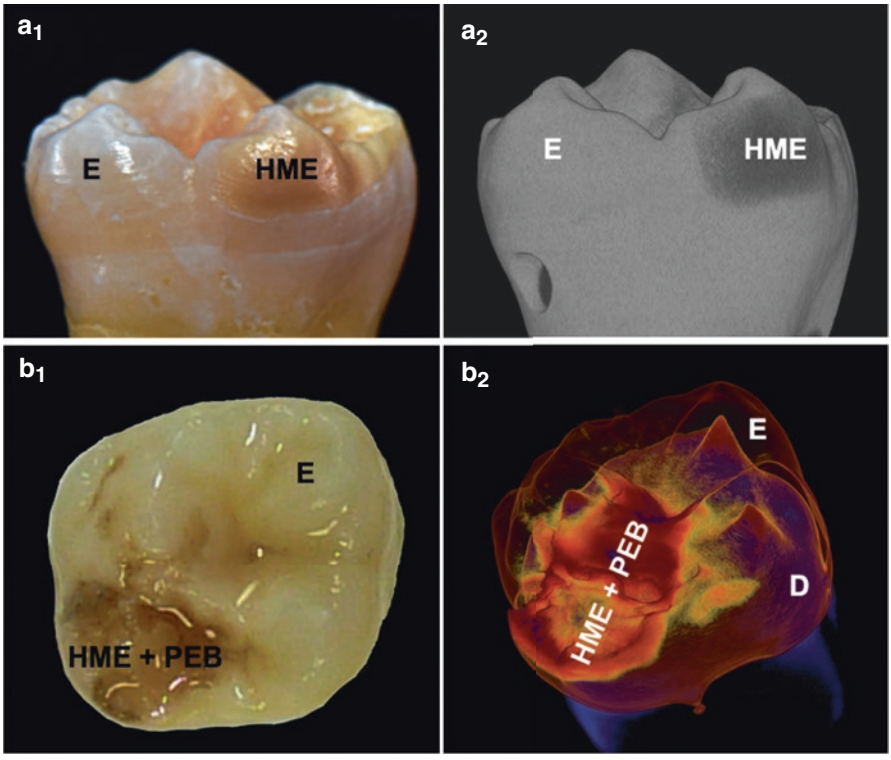

Fig. 2.3 Clinical photographs ($\mathbf{a_1}$, $\mathbf{b_1}$) and 3D visualizations of micro-CT images ($\mathbf{a_2}$, $\mathbf{b_2}$ in false colors) of two MIH-affected molars. In (**a**) the buccal cusp was affected by hypomineralization. In (**b**) the occlusal surface was affected in the disto-palatal area (*HME* hypomineralized enamel, *PEB* post-eruptive enamel breakdown, *E* sound enamel). ($\mathbf{a_1}$) Clinical photo of a molar with the buccal cusp being affected by hypomineralization. ($\mathbf{a_2}$) 3D visualization of micro-CT image. Hypomineralized area shows markedly lower values than sound enamel. ($\mathbf{b_1}$) Clinical photo of a molar with the occlusal surface being affected in the disto-palatal area. The tooth also shows PEB. ($\mathbf{b_2}$) 3D visualization of micro-CT image of same molar as in $\mathbf{b_1}$ in false colors. Sound enamel is rendered transparent, and hypomineralized enamel is displayed in yellow-reddish colors. Dark red is least mineralized

Another important finding was that a significant decrease in the mineral density and a notable structural and mechanical alteration were not only noted in the clinically MIH-affected enamel but also in the so-called transitional zone (i.e., the healthy-looking enamel right next to the MIH-defect). This scenario may have great clinical relevance, as dentists currently use the clinically detectable MIH lesion borders to, for example, plan cavity preparation [15, 30, 33, 35]. We will discuss this further below.

2.3.4 Chemical Properties

Most studies measured chemical properties as mineral composition, protein concentration, and carbon/carbonate concentration [14, 26, 28, 30, 34–36, 40–43]. Mineral composition, for example, was analyzed using methods such as x-ray microanalysis [34, 40, 43], x-ray diffraction [30], secondary ion mass spectroscopy [40], and energy dispersive x-ray spectrometry [30, 35]. All studies in this direction concluded that MIH-affected teeth showed a significant decrease in the mineral content compared with sound enamel, without a significant difference regarding the Ca/P ratio between MIH-affected and sound enamel [26, 28, 30, 34, 35, 43].

The protein content of MIH-affected enamel was evaluated using different methods such as SDS-polyacrylamide gel electrophoresis and mass spectrometry [14, 28, 41]. A significantly higher protein content of MIH-affected enamel in comparison with sound enamel was agreed on. Notably, there was a difference in the protein content and concentration of differently colored MIH-enamel defects. Yellow and brown lesions had the highest protein content, with ameloblastin (as a remnant of amelogenesis) only found in brown lesions. Higher concentrations of serum albumin, alpha-1-antitrypsin, and antithrombin III were present in yellow and brown lesions more than in white lesions [14, 41].

The carbon/carbonate concentration and the carbon content of MIH-affected enamel was also addressed [26, 28, 40, 42]. It was agreed upon that a significant increase in the carbon concentration and carbonate content existed in MIH-affected enamel compared with normal enamel.

2.4 Heterogeneity in Current Research Findings

A comparison between the different studies revealed numerous contradictory results. For example, the mineral composition of the Ca/P ratio was found both reported to be similar to sound enamel [26, 30, 34] and to be reduced by 5–20% [40, 42]. In addition, most studies reported that MIH lesions extend from the surface of the enamel to the DEJ, while a few studies found that creamy/white lesions were restricted to the inner layer of the enamel alone. This situation might be explained due to different sample preparations and sectioning angulations/directions.

Some studies associated the mineral density with the clinical appearance (especially color) of the lesion. A lower mineral density appeared to exist in darker

(brown) lesions, compared with the relatively high mineral density found in creamy/white lesions [26, 27, 29, 38]. However, this phenomenon has not been confirmed by all studies [15, 44]. It is possible that different measurement methods (2D vs. 3D) and different sample storage media are responsible for these contradictions [37].

2.5 Clinical Considerations

Based on the described findings, a number of clinical considerations could be carefully deduced as follows:

1. Because MIH-affected enamel shows reduced hardness and elasticity, the support for overlying restorations is reduced. Restorations, which are able to withstand the presumably higher flexural stress during mastication resulting from this lower support, may hence be preferable. Flexural-resistant restorative materials such as fiber-reinforced composites or indirect metal-based restorations should hence be considered when restoring MIH-affected defects; and materials with low flexural strength such as amalgams should be avoided (amalgam should also be avoided as it requires unnecessary macro-retentive preparation, removing sound enamel). Also, overhanging and unsupported/undermined MIH-affected enamel areas should be removed during cavity preparation.
2. An extension of the cavity preparation beyond the MIH-affected enamel into the transition zone could be useful in order to ensure that all cavity borders are in sound enamel before the restoration. Tools indicating where the different, clinically not discernable enamel zones start and end are needed.
3. Conditioning MIH-affected enamel prior to the placement of adhesive (composite) restorations should be modified in comparison with sound enamel. For example, the removal of proteins from the MIH-affected enamel may increase adhesive strength of dental adhesives. However, so far, any conditioning protocols (involving, e.g., sodium hypochlorite for deproteination) have not been found too useful.

2.6 Conclusions

MIH-affected enamel is characterized by a reduction in mineral quantity and quality (reduced Ca and P content) and a reduced hardness and modulus of elasticity (including the transition zone). In addition, MIH-affected enamel shows an increased porosity, increased carbon and carbonate concentrations, and higher protein contents than sound enamel [15, 25, 26, 29, 41, 45]. MIH-affected enamel crystals are less dense than those of healthy enamel, with thicker prismatic sheaths and higher inter- and intraprismatic concentrations of organic particles [3, 30–32]. Etched MIH-affected enamel also shows more cracks and deep pores than sound enamel; retentive etch patterns of MIH-affected enamel are

suboptimal for subsequent bonding [27, 31, 35]. A better understanding of the structural, mechanical, and chemical properties of MIH-affected enamel may help to guide future research and support the development of science-based clinical recommendations.

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Prevalence, Incidence, and Burden of Molar Incisor Hypomineralization

3

Falk Schwendicke, Karim Elhennawy, and Joachim Krois

3.1 The Need for Epidemiologic Estimates on MIH

Molar incisor hypomineralization (MIH) (i.e., "demarcated, qualitative developmental defects of systemic origin of the enamel of one or more first permanent molar with or without the affection of incisors" [1–3]) is hypothesized to follow a multifactorial pathogenesis, with a genetic component and also prenatal, perinatal, and postnatal exposures playing a role [4–9]. Clinically, patients complain about hypersensitivity or pain, and dentists are faced with posteruptive enamel breakdown and associated carious lesions [1, 2, 10, 11]. The resulting pulpitis hampers effective local anaesthesia [12]. Partially as a result of this case, children with MIH show significantly more dental anxiety and fear [13]. Generally, MIH negatively affects childrens' general health, quality of life, and sociopsychological status [2, 14]. Consequently and in line with the diversity in appearance and symptomatology, a large range of preventive and therapeutic strategies, including the management of pain and mineral loss, restorations, and extraction with or without orthodontic treatment, are available [1–3].

For dentists, and also policymakers, it is relevant to know how often a condition is present (prevalence) and how many new cases there are each year (incidence). This allows to tailor clinical decision-making, including tailored diagnostics, and

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also preventive approaches (while MIH itself cannot be prevented, breakdown, and development of hypersensitivity may well be if managed early enough). Also, health service planners may allocate resources accordingly, workforce planning may consider the condition appropriately, and dental schools may make room in their curricula appropriately.

The reported prevalence of MIH varies significantly between studies [15]. To allow to identify possible reasons underlying the heterogeneity between studies and possibly also between different geographic entities, methodologies have been established by the Global Burden of Disease (GBD) studies. These methodologies analyze prevalence and incidence and, more generally, burden of diseases within super-regions and regions which share certain socioeconomic and also geographic (environmental) similarities [16]. Making use of such similarities allows to build on common socioeconomic and environmental variables which are possibly associated with disease occurrence, to estimate the prevalence, incidence, and burden also for countries where no epidemiologic datapoints are available [17].

3.2 Estimating the Global Prevalence, Incidence, and Burden

A recent systematic review and meta-regression analysis has estimated the global prevalence and incidence of MIH [18, 19]. The studies used spatial definitions according to the GBD studies [20], as shown in Fig. 3.1. The study systematically compiled and then meta-regressed reported prevalence rates of MIH and applied them to super-regional, regional, and national population data.

A large range of databases (MEDLINE via PubMed, EMBASE via OVID, LILACS via BIREME, Web of Science, and Google Scholar) were searched for

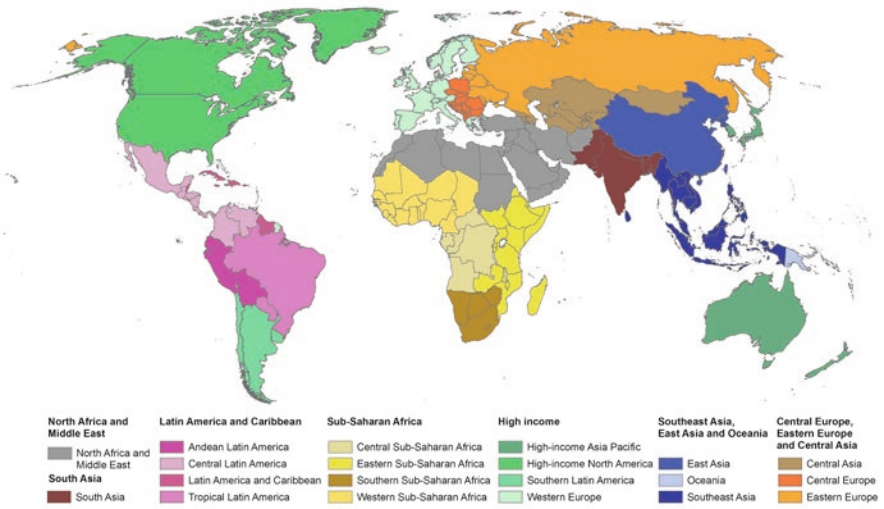

Fig. 3.1 Super-regions and regions, as used in the Global Burden of Disease (GBD) studies. (From [21])

observational studies reporting on the prevalence of MIH. MIH needed to be defined according to the European Academy of Paediatric Dentistry (EAPD) [2] or its modifications or as a component of other indices (e.g., DDE index) [22]. Studies on enamel defects not restricted to MIH (e.g., diffuse opacities) were excluded.

Prevalence was pooled on global, super-regional, regional, and national level using random effects meta-analysis. Meta-analysis was also used to assess differences according to sex (male vs. female) or MIH case definition (EAPD vs. other). The treatment need (i.e., with subjective symptoms and/or posteruptive breakdown vs. no need) was also estimated.

For symptomatic (painful, hypersensitive) MIH, there are no data allowing to compare the subjective impact of MIH with that from other diseases. Such data in the form of weights have been established for many other conditions, allowing to quantify the burden of a disease, for example, in form of disability-adjusted life years (DALYs). DALYs indicate the time of suffering from a disease multiplied with the weight (i.e., the subjective impact of the disease). For this book chapter, we assumed that MIH teeth with treatment need would have similar disability weight as untreated dental caries [23] to quantify the burden of MIH.

As with most diseases, not all countries show datapoints on the occurrence of MIH. To nevertheless allow estimating prevalence, incidence, and burden, a meta-regression approach was used. To do so, a large range of social, environmental, and demographic variables, such as health system access, climate, and food consumption from the GBD 1980–2015 covariates dataset (www.ghdx.healthdata.org), were used to associate them with MIH occurrence. A range of meta-regression analyses were tested; the best performing model was used to estimate prevalence in 195 countries globally. Building on the resulting prevalence dataset and the GBD 1970–2015 population estimate dataset [24], the number of prevalent cases in 2015 and incident cases in 2016 were calculated. The authors assumed all individuals aged 6 years or above to be possible prevalent cases and all individuals aged 5 years in 2015 to be possible incident cases in 2016. The global burden in 2015 was estimated by multiplying all symptomatic cases with the disability burden of dental caries.

3.3 The Global Prevalence, Incidence, and Burden of MIH

The systematic review identified 99 studies (113 reports) reporting on 113,144 participants from 43 countries. The mean (95% CI) global prevalence was 12.9% (11.7–14.3%), with significant differences between super-regions, regions, and countries (Fig. 3.1). The prevalence did not differ significantly between female and male individuals (OR: 0.92; 0.81–1.04), while studies using EAPD-case definition found significantly higher prevalence than those using other case definitions. It was estimated that the proportion of cases in need of care (i.e., with symptoms or posteruptive breakdown) was 27.4% (23.5–31.7%).

The prevalence of MIH on super-regional, regional, and national level is shown in Fig. 3.2a; detailed quantification can be found in Tables 3.1 and 3.2. The estimated number of prevalent cases of MIH in 2016 was 811 million people (Fig. 3.2b). The highest numbers of prevalent cases at a super-regional level were found in

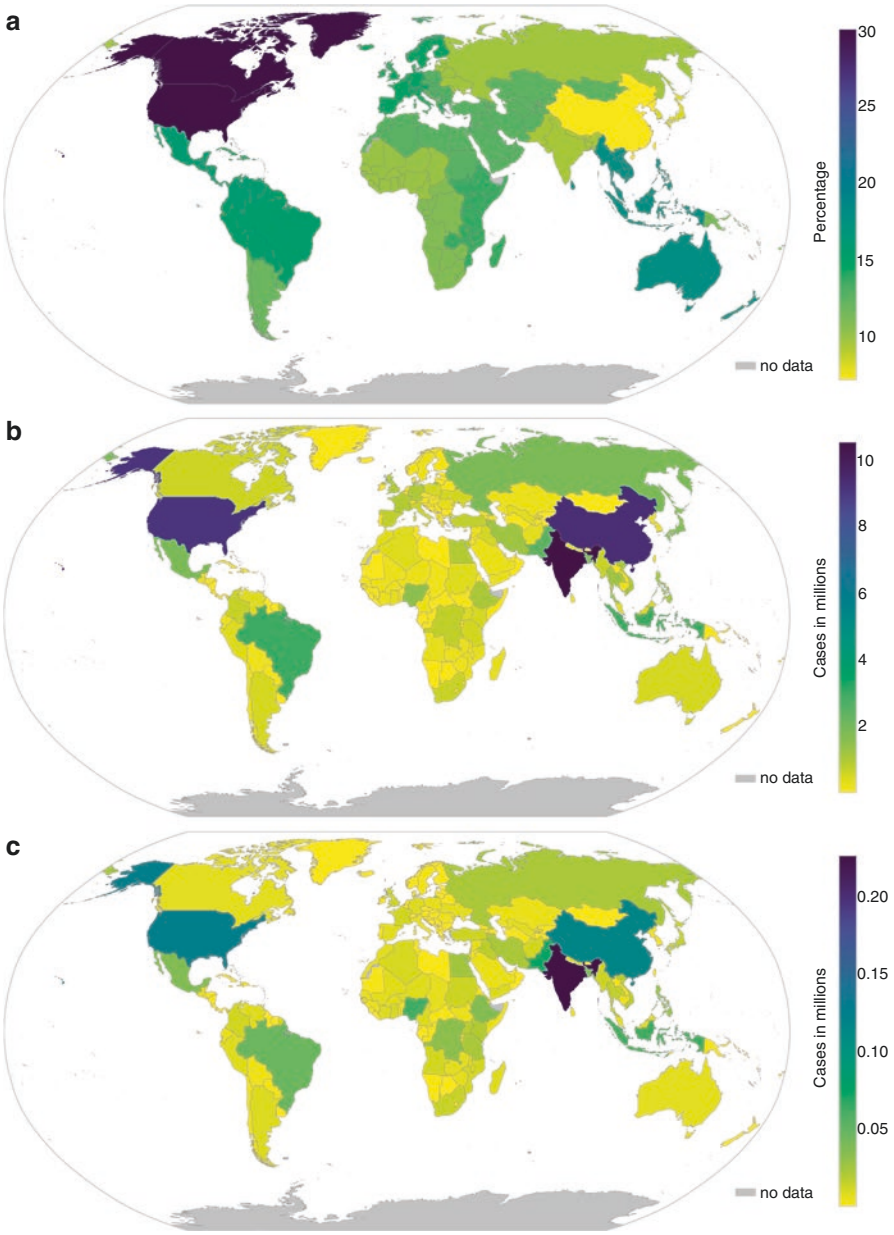

Fig. 3.2 MIH prevalence on regional level (**a**), mean number of prevalent cases in 2015 (**b**) and mean number of incident cases in 2016 on country level (**c**). (From [18])

Table 3.1 Prevalent cases in 2015 and incident cases in 2016 on super-regional, regional, and regional levels. (From [18])

GBD superregion	Prevalent cases	Incident cases	GBD region	Prevalent cases	Incident cases
Central Europe, Eastern Europe, and Central Asia	51,266,325	701,562	Central Asia	9,524,526	220,931
			Central Europe	14,994,426	162,588
			Eastern Europe	26,747,373	318,043
High income	191,396,872	2,354,845	Australasia	5,693,232	76,052
			High-income Asia Pacific	20,802,458	186,487
			High-income North America	97,115,983	1,294,819
			Southern Latin America	8,129,550	137,760
			Western Europe	59,655,649	659,727
Latin America and Caribbean	78,735,493	1,482,305	Andean Latin America	7,239,745	162,323
			Caribbean	5,705,559	107,058
			Central Latin America	35,247,762	721,087
			Tropical Latin America	30,542,427	491,837
North Africa and Middle East	61,918,666	1,533,740	North Africa and Middle East	61,918,666	1,533,740
South Asia	151,411,432	3,459,825	South Asia	151,411,432	3,459,825
Southeast Asia, East Asia, and Oceania	180,723,796	2,866,638	East Asia	98,674,522	1,235,827
			Oceania	1,131,557	32,889
			Southeast Asia	80,917,717	1,597,922
Sub-Saharan Africa	95,673,601	3,634,098	Central Sub-Saharan Africa	11,292,692	480,396
			Eastern Sub-Saharan Africa	40,036,460	1,526,477
			Southern Sub-Saharan Africa	8,875,507	224,277
			Western Sub-Saharan Africa	35,468,942	1,402,948

high-income countries, Southeast Asia, East Asia, Oceania, and South Asia. At a regional level, the highest numbers of prevalent cases were found in South and East Asia and high-income North America. At a country level, heavily populated countries such as India, China, or the United States contributed significantly to the burden of prevalent cases.

The global number of incident cases in 2016 was estimated at 16.0 million people (Fig. 3.2c). The highest numbers of incident cases at a super-regional level were found in Sub-Saharan Africa, South Asia, Southeast Asia, East Asia, and Oceania. At a regional level, the highest numbers were found in South Asia, Southeast Asia, and Eastern Sub-Saharan Africa. Growing countries such as India, the United States, China, Pakistan, or Indonesia ranked first with respect to the number of incident cases.

Table 3.2 Prevalent cases in 2015 and incident cases in 2016 on national level. (From [18])

Country	Country prevalent cases	Country incident cases
Afghanistan	3,245,732	122,509
Albania	390,681	4971
Algeria	4,086,436	100,210
American Samoa	9867	298
Andorra	11,861	134
Angola	2,493,341	115,893
Antigua and Barbuda	13,146	229
Argentina	5,017,905	93,427
Armenia	314,491	4580
Australia	5,034,433	66,368
Austria	902,273	8501
Azerbaijan	1,006,766	21,520
Bahrain	173,659	2619
Bangladesh	17,698,212	380,069
Barbados	40,775	527
Belarus	1,195,270	13,998
Belgium	1,650,366	19,673
Belize	45,928	1075
Benin	1,076,804	39,979
Bermuda	9095	113
Bhutan	94,425	1848
Bolivia	1,329,756	34,444
Bosnia and Herzegovina	616,992	5983
Botswana	257,912	6534
Brazil	29,693,560	472,252
Brunei	54,906	967
Bulgaria	247,813	2590
Burkina Faso	1,765,476	73,114
Burundi	1,139,628	49,801
Cambodia	1,660,903	42,668
Cameroon	2,382,160	91,018
Canada	5,850,975	64,101
Cape Verde	60,605	1392
Central African Republic	498,031	17,027
Chad	1,272,812	58,229
Chile	2,813,625	39,700
China	93,104,171	1,174,325
Colombia	6,798,137	119,227
Comoros	87,262	3091
Congo	479,572	18,342
Costa Rica	699,831	11,235
Cote d'Ivoire	2,208,001	81,860
Croatia	563,814	6012
Cuba	1,570,583	17,901
Cyprus	123,315	1135
Czech Republic	1,451,774	15,914
Democratic Republic of the Congo	7,537,220	319,978
Denmark	2,016,737	22,977
Djibouti	92,725	2519
Dominica	10,264	174

Table 3.2 (continued)

Country	Country prevalent cases	Country incident cases
Dominican Republic	1,354,609	30,780
Ecuador	2,104,528	46,621
Egypt	9,439,710	255,130
El Salvador	842,687	16,549
Equatorial Guinea	91,469	3139
Eritrea	531,329	20,259
Estonia	177,076	2079
Ethiopia	10,488,407	355,827
Federated States of Micronesia	12,819	340
Fiji	109,674	2487
Finland	849,278	9498
France	9,386,535	120,530
Gabon	193,059	6017
Georgia	458,925	7224
Germany	9,962,098	82,223
Ghana	2,979,959	98,855
Greece	1,565,312	16,528
Greenland	7689	286
Grenada	14,650	304
Guam	21,354	390
Guatemala	2,093,834	60,748
Guinea	1,237,978	46,377
Guinea-Bissau	186,197	6971
Guyana	99,463	1995
Haiti	1,293,136	34,020
Honduras	1,072,900	25,586
Hungary	1,401,067	13,716
Iceland	52,140	780
India	1,05E+08	2,264,940
Indonesia	29,707,968	635,506
Iran	12,377,102	229,321
Iraq	5,046,414	174,607
Ireland	693,170	11,310
Israel	1,058,069	22,787
Italy	6,774,142	60,895
Jamaica	361,509	6861
Japan	17,152,192	150,858
Jordan	1,163,428	31,674
Kazakhstan	1,959,597	45,037
Kenya	5,338,748	196,323
Kiribati	13,331	391
Kuwait	442,676	8259
Kyrgyzstan	642,369	16,932
Laos	720,357	20,083
Latvia	298,507	3036
Lebanon	654,838	7354
Lesotho	215,369	6206
Liberia	448,673	16,183
Libya	163,817	3980
Lithuania	291,349	3004

(continued)

Table 3.2 (continued)

Country	Country prevalent cases	Country incident cases
Luxembourg	84,652	914
Macedonia	251,671	2907
Madagascar	2,527,460	88,072
Malawi	1,824,063	73,304
Malaysia	4,531,900	75,975
Maldives	43,886	939
Mali	1,677,860	74,836
Malta	56,526	511
Marshall Islands	8777	271
Mauritania	390,326	13,510
Mauritius	155,374	1966
Mexico	18,267,870	371,243
Moldova	489,207	5686
Mongolia	344,959	8178
Montenegro	78,868	1042
Morocco	3,683,856	78,950
Mozambique	2,846,585	115,207
Myanmar	6,215,862	124,904
Namibia	283,947	8391
Nepal	3,508,947	82,293
Netherlands	1,721,811	19,043
New Zealand	658,799	9684
Nicaragua	805,043	18,525
Niger	1,703,047	83,088
Nigeria	15,085,053	602,667
North Korea	2,602,961	38,619
Northern Mariana Islands	14,559	205
Norway	912,624	11,161
Oman	508,640	8121
Pakistan	24,667,339	730,675
Palestine	493,646	16,613
Panama	546,573	11,192
Papua New Guinea	815,364	24,567
Paraguay	848,867	19,585
Peru	3,805,461	81,258
Philippines	11,788,776	297,714
Poland	5,194,425	57,207
Portugal	1,463,334	13,681
Puerto Rico	522,837	6931
Qatar	282,640	2661
Romania	2,604,050	28,383
Russia	18,525,645	227,012
Rwanda	1,297,845	46,006
Saint Lucia	24,828	414
Saint Vincent and the Grenadines	14,931	273
Samoa	21,791	670
Sao Tome and Principe	20,128	742
Saudi Arabia	2,443,424	51,936
Senegal	1,423,176	54,930
Serbia	1,026,495	11,424
Seychelles	11,478	227

Table 3.2 (continued)

Country	Country prevalent cases	Country incident cases
Sierra Leone	651,693	24,877
Singapore	465,359	4826
Slovakia	747,492	8009
Slovenia	419,284	4430
Solomon Islands	62,933	2110
Somalia	1,038,534	47,094
South Africa	6,364,239	140,403
South Korea	3,130,001	29,836
South Sudan	1,218,042	42,497
Spain	7,456,292	74,484
Sri Lanka	2,652,915	49,155
Sudan	3,723,103	130,565
Suriname	73,031	1434
Swaziland	148,217	4607
Sweden	1,977,210	23,942
Switzerland	1,288,527	12,869
Syria	1,919,782	58,553
Taiwan	2,967,390	22,883
Tajikistan	845,333	25,759
Tanzania	5,711,727	229,928
Thailand	12,594,679	154,058
The Bahamas	54,482	836
The Gambia	186,840	8067
Timor-Leste	120,275	4990
Togo	712,154	26,253
Tonga	12,674	379
Trinidad and Tobago	187,196	2944
Tunisia	1,184,295	21,386
Turkey	7,094,591	126,714
Turkmenistan	569,379	12,481
Uganda	4,185,238	185,783
Ukraine	5,770,319	63,228
United Arab Emirates	1,115,265	11,454
United Kingdom	9,649,377	126,151
United States	91,257,319	1,230,432
Uruguay	298,020	4633
Uzbekistan	3,382,707	79,220
Vanuatu	28,414	781
Venezuela	4,120,887	86,782
Vietnam	10,713,344	189,737
Virgin Islands, U.S.	15,096	247
Yemen	2,675,612	91,124
Zambia	1,708,867	70,766

The proportion of cases in need of care, that are those which are symptomatic (painful, hypersensitive) or with posteruptive breakdown, was estimated at 27.4% (23.5–31.7%) or 240 million existing cases and 5 million new cases each year. The resulting global burden was 2.4 million DALYs, with 0.05 million new DALYs each year.

3.4 Interpretation

Based on over 110,000 sampled individuals, the number of prevalent cases of MIH in 2015 was estimated at 811 million, and the number of incident cases in 2016 at 16.3 million. The prevalence varies significantly between super-regions and regions, while spatial-social, environmental or economic-factors are rather not well suited to explain this difference. It is possible that this has a number of reasons. First, the tested covariates may not be sufficiently associated with MIH. This is unlikely, as many of them have, using other study types, been associated in some way with the pathogenesis of MIH. Second, and more likely, ecological studies on a national level may be unable to confirm (or refute) associations, as subnational differences are in fact larger and more decisive. Current efforts to break down epidemiological analyses onto smaller spatial scale may be helpful here.

Notably, the case definition of MIH was significantly associated with the prevalence. Studies using the EAPD case definition found a higher prevalence than those using other definitions. The EAPD definition also includes sequelae of MIH, such as the presence of atypical restorations or molars missing due to MIH [25]. Hence, it may be better suited to capture the whole range of signs and symptoms of MIH; some of which may be missed when applying other definitions.

Larger countries such as India or China contributed significantly to both prevalent and incident cases. For the latter, growing countries such as Pakistan or Indonesia were also highly relevant. Generally, on an absolute level, low- and middle-income countries shoulder the main burden of MIH. As in many of them access to dental care is limited, it is unclear in how far appropriate treatment of MIH can be delivered.

In conclusion, there is great variety in prevalence and incidence between countries. Low- and middle-income countries shoulder the majority of the absolute burden.

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The Pathogenesis and Aetiology of MIH: More Questions Than Answers

4

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4.1 Introduction

The causative factors for MIH are still to be determined. Numerous researchers have identified associated factors; however, despite it being a prevalent condition in many communities worldwide, no consensus has been obtained regarding a single aetiological factor or a group of necessary factors [1–3]. Most putative factors identified to date involve childhood illness, medication taken during amelogenesis (such as antibiotics) and environmental toxins.

4.2 Amelogenesis

Amelogenesis is a complex process, and due to the stressful processes that the epithelially derived cells endure during enamel formation, the ameloblasts are sensitive to insults, both indirect and direct. There are two main phases of amelogenesis-secretion and maturation-with a transitional phase in between [4, 5].

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4.2.1 Secretion

Amelogenesis commences with secretion of several enamel matrix proteins (EMPs) by elongated ameloblasts-namely, amelogenin (AMELX), ameloblastin (AMBN) and enamelin (ENAM). The matrix is gel-like in consistency, and initial mineralization starts during this period. The tight junctions (TJs) between the ameloblasts during the secretory phase may allow movement of substances, such as mineral ions, into the developing matrix whilst separating the developing tooth from the surrounding vascular tissue [5]. The secretion phase can be affected by genetic influences or direct trauma leading to less matrix being secreted, creating a quantitative defect-hypoplastic enamel. The metallopeptidase MMP20 is expressed during secretion, and MMP20-null mice have hypoplastic and hypomineralized enamel which cleaves from the dentino-enamel junction.

The secretory phase is followed by a short transitional phase during which the ameloblasts become squatter in shape and the production of matrix proteins is ceased. This is followed by the maturation phase [5].

4.2.2 Maturation

The majority of theorization over the past two decades identifies the maturation period of the ameloblast as the most likely period for the development of MIH enamel.

The maturation phase involves an increase in mineral density of the enamel-ameloblasts secrete proteolytic agents to cleave the matrix proteins and allow increasing mineralization. The major proteinase is the kallikrein-related peptidase (KLK4) and the metallopeptidases (MMP2, MMP3, MMP9); KLK4 dominates during maturation with KLK4 null mice manifesting hypomineralized enamel of normal thickness. Other activities, such as ion transport, EMP removal, pH balance and apoptosis, occur during this phase, giving multiple potential processes in which disturbances could lead to a qualitative defect-hypomineralization [5, 6].

4.3 Aberrations During Amelogenesis

Understanding the pathogenesis of hypomineralized enamel may lead to identification of potential aetiological factors. So, what are the possible ways the ameloblast can be affected to produce demarcated hypomineralized enamel lesions?

There is a potential for errors in the production of precursor proteins and mineral deposition leading to hypomineralized enamel, such as in the several hypocalcified and hypomature forms of amelogenesis imperfecta [7].

Mineral formation causes release of protons, which are neutralized by bicarbonate secretion by the ameloblast. If the bicarbonate pH moderation system was affected and less efficient, could this lead to hypomineralized enamel? Increased carbonate, beyond levels usually found during amelogenesis, has been reported in MIH enamel [8] (Fig. 4.1).

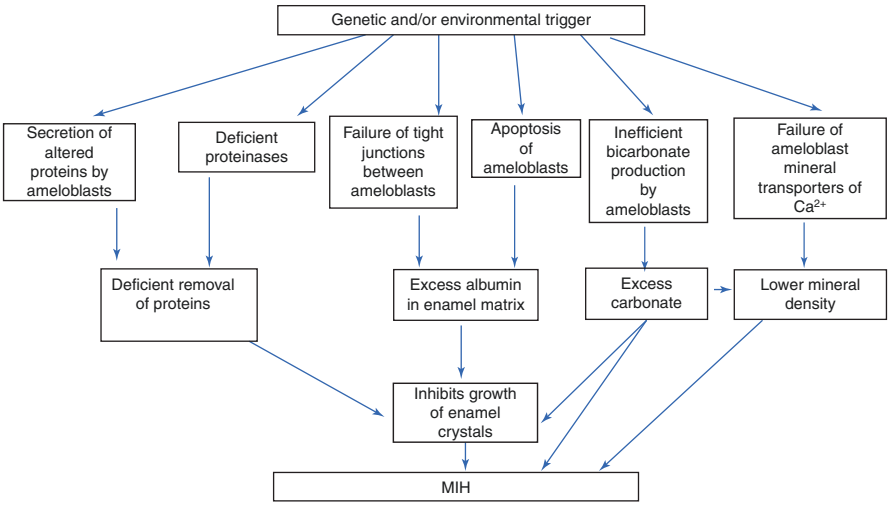

Fig. 4.1 Potential biological processes leading to demarcated opacities

There are several mineral transporters of Ca^{2+} used by ameloblasts-null mutation mice for these transporters have severely hypomineralized enamel [6]. During the mid and late maturation phase, the Ca^{2+} transport is at its greatest-and if this is affected leading to lower ionic transport, it may decrease mineral density. Of the ions found in hypomineralized enamel, Mg^{2+} is an inhibitor of mineralization [6]. Thus, there are number of potential mineral processes that, if altered, could lead to demarcated hypomineralized lesions of enamel (Fig. 4.1).

It is postulated that fluoride stresses the ameloblast (especially endoplasmic reticulum function) and, due to the effects of this stress, leads to decreased matrix cleavage and removal due to downregulation of KLK4 during the maturation phase; however, amelogenin and MMP20 are not downregulated during the secretion phase. Therefore, increased enamel porosity and decreased hardness may be due to retained proteins and peptides (mainly related to amelogenin) inhibiting crystal growth [9, 10]. It is unknown if childhood illnesses and other putative aetiological factors for demarcated defects could have a similar effect on the ameloblast as fluoride.

There is the possibility that during the secretion stage, matrix proteins are changed in structure, later leading to poor cleavage and/or reduced clearance by ameloblasts. Disruption to this endocytosis of cleaved EMPs could lead to increased residual protein content and decreased mineral density. However, this would seem unlikely as it would be expected in this case that more remnants of matrix proteins in lesion enamel would be present. While traces of amelogenin have been found in MIH-affected enamel, this was not the major protein identified; rather, serum albumin predominates with levels up to 15 times that of healthy enamel reported [11, 12].

Ameloblasts provide a well-sealed barrier between the enamel matrix and the vascular system around the developing tooth, allowing maintenance of different ionic concentrations on either side of the cells [6, 13, 14]. The TJs between the ameloblasts maintain this seal, and the intercellular permeability depends on the constituents of the TJs, which are tight in maturation but leaky in the secretory stage [6].

Albumin is not synthesized by ameloblasts; therefore, it must be of a source extrinsic to the matrix [15]: albumin leaking between ameloblasts has been discussed by Robinson and colleagues including that it is a normal minor component of the enamel matrix during the secretory phase [16]. It has been suggested that albumin can bind to developing enamel crystals and once bound inhibits further growth; however, it is believed that the crystals developing during the secretory phase are protected from this effect by the intact amelogenins surrounding them, and so the albumin is present in a free state [17, 18]. As amelogenins are degraded and removed during transition and maturation phases, albumin may gain access to the now unprotected crystals and become bound: it is postulated that excessive levels of albumin exposure during this window of mineral binding opportunity could result in Hypomineralization defects [16].

Robinson and colleagues suggested hyperaemia associated with trauma as a situation leading to excessive albumin in the maturing enamel tissue; however, TJs can also be affected by cell stressors such as fluoride [10, 14, 16]. Animal studies have found that inflammatory mediators and serum can adversely affect the function of TJs in retinal, renal and salivary gland cells [19–21]. This suggests that there is a multitude of local and systemic circumstances that could allow increased amounts of passive paracellular ion movement and blood proteins into the developing tooth germ during the maturation phase when the TJ is meant to be tight.

Additionally, cellular stress may lead not to impairment of function but rather to apoptosis of ameloblasts and therefore the possibility of unregulated ingress of ions and blood proteins into the developing enamel matrix. Although there is no evidence of this possibility at present, ameloblasts are, for a part of their lifespan, highly specialized secretory cells; in order to perform this high-load function, such cells must often employ specific coping strategies. In the case of the ameloblast, the unfolded protein response (UPR) is utilized; under more extreme circumstances, this system can switch from promoting cell survival to "cutting its losses" and promoting cell death [9].

4.4 Genetic Influences

It is becoming increasingly apparent that no single environmental cause exists and that MIH and the related hypomineralized second primary molars (HSPM) are likely to have complex aetiologies with a contribution from genetic factors [22]. In particular, as certain variants of amelogenesis imperfecta have some similarities in appearance to MIH, genetic influences have been postulated for many years. Vieira has stated that approximately 20% of MIH variation is explained by genetics [23].

However, environmental factors have been the focus of most studies with genetic studies being scarce. Family and twin studies can be used to determine the heritability, that is, the genetic contribution to the variation in a disease, as a percentage from 0 to 100 [24].

A Brazilian study of 167 pairs of twins aged 8-15 years reported identical monozygotic twins were more concordant for MIH than nonidentical dizygotic twins, suggestive of a strong genetic influence on aetiology [25]. However, a twin study of six-year-old Australian twins failed to find a similar difference, even after adjusting for known risk factors [26]. DNA-based studies have also found some, albeit weak, evidence of possible genetic aetiological factors (Table 4.1). A genome-wide association study (GWAS) failed to find any genome-wide significant results but may have been underpowered to detect anything other than very large effect sizes. The authors did nevertheless suggest a gene locus near SCUBE1 (signal peptide, CUB domain and EGF-like domain containing 1) on chromosome 22 that may be important in MIH [27].

A more targeted study of genes known to be involved in tooth development revealed an association between specific markers and MIH [28]. While some genetic variants increased the susceptibility to MIH, others appeared to be protective. Importantly, AMELX, the gene that encodes amelogenin, was not associated with MIH, suggesting that the aetiology and pathophysiology of MIH is not linked to genetic alteration of amelogenin secretion. More recently, family-based candidate gene studies seem to provide stronger evidence of a genetic influence on MIH. A number of genes (including AMELX, ENAM, AMBN and MMP20) involved in the various stages and processes of amelogenesis, including secretion and degradation of enamel matrix proteins, have been associated with MIH in this way [29].

Further, interactions between amelogenesis and immune-related genes have been suggested to have an additive effect on MIH susceptibility [30]. Inflammatory-related cytokines can induce angiogenesis in the developing tooth germ-possibly increasing the risk of entry of blood proteins into the developing tooth [31]. The

Table 4.1 Genetic studies related to MIH

Study	Study details	Findings
Kühnisch et al. [27]	GWAS of 668 children from German cohort studies	No significant associations Potential association with SCUBE?
Jeremias et al. [28]	Candidate-gene association study; 163 cases and 82 controls from Turkey, and 71 cases and 89 controls from Brazil	Associations between MIH and rs3796704 (ENAM)
Jeremias et al. [29]	Family-based candidate association study of 101 nuclear families with at least 1 child affected by MIH	AMELX, ENAM, AMBN, MMP20, FGFR1, DLX3, FAM83H, BMP2, BMP7, BMP4
Bussaneli et al. [30]	Family based candidate gene association study 101 nuclear families with at least 1 child affected by MIH	Interactions between rs6654939 (AMELX) and the SNPs rs2070874 (IL4), rs2275913 (IL17A), rs1800872 (IL10), rs1800587 (IL1A), and rs3771300 (STAT1) was observed

authors speculated that the association could be due to the regulation of KLK4 and MMP20 by TGF-β [30]. Increased prevalence of MIH has also been linked to children affected by "allergies", although the pathological mechanism is unclear [32].

The importance of epigenetics in complex diseases is increasingly recognized and may apply to MIH/HSPM. Epigenetics describes the mitotically stable modifications of genes, associated with differences in DNA expression within different tissues [33]. Aside from cell lineage specification, epigenetics appears to mediate environmental influences on the gene expression. The most commonly studied epigenetic modification is DNA methylation, the addition of a methyl (–CH3) group at the cytosine of cytosine-guanine (CpG) dinucleotides. Despite recent interest, epigenetic dental studies are rare [34]. However, a recent very small ($n = 10$) epigenome-wide association study identified differential methylation of nine genes involved in cartilage, bone, tooth and neural development that may be associated with hypodontia [35]. Further studies investigating the role of epigenetic factors in HSPM/MIH would improve understanding of the aetiology of the condition and the mechanisms by which the disease is mediated by environmental factors.

Both a genetic predisposition and an environmental systemic cause would be expected to affect teeth in a stable, temporal pattern. However, in the case of MIH and HSPM, the cause must be able to explain why teeth forming at the same time can be affected to varying degrees. The potential reasons why there are variable numbers of teeth affected by MIH and variable lesion presentation and characteristics between teeth and within single teeth remain uncertain [36]. It has been proposed that the mechanism may be related to variations in mechanical forces in the tooth germ and variable gene expression influencing specific areas of the tooth [36]. Therefore, localized factors may influence the occurrence of MIH. The distribution of MIH lesions is restricted to the occlusal two-thirds of the crown, and it has been theorized that this may be due to more dramatic changes in molecular signalling occurring during the maturation of the occlusal two-thirds involving the initiation and development of the dentine-pulp complex. Epigenetic factors can be site-specific and could potentially impart different influences on teeth forming at the same time, albeit in different locations. However, there are no epigenetic studies of MIH/HSPM, and these areas of research need further investigation.

4.5 Potential Aetiological Factors

Numerous potential aetiological factors have been proposed for MIH. Three reviews have determined that no specific factor(s) with a high-quality evidence base has been identified [1–3]. Limitations of the existing studies include lack of consistency in design and reporting and that the majority are cross-sectional and retrospective in nature, introducing recall bias and limiting any conclusions on causation. This is especially problematic given the possibility of combined factor effects and the likelihood a child might experience multiple putative factors over the relevant time frames. However, a consistent finding is that childhood illness, especially those that induce pyrexia, is associated with MIH.

4.5.1 Environmental Contaminants

The connection between breastfeeding, the contamination of breast milk with dioxin and developmental defects of enamel (DDEs) including MIH was proposed around 20 years ago by Alaluusua and colleagues in a cohort of breast-fed children [37]. This difference was corroborated in a study of adults who were children in Seveso, Italy, at the time of an accidental dioxin exposure in 1976 [38]. In a more recent study of Finnish children, a marked difference was found in prevalence of MIH between urban and rural children, and it was speculated that differences in comparatively greater urban industrialisation may play a role, with the urban children (21.3%) having close to double the prevalence of MIH compared with their rural counterparts (11.5%), putatively due to environment toxicants [39].

In a recently published paper, an increased prevalence (approximately 2×) of DDE, including demarcated hypomineralized lesions, in an area of Vietnam affected by dioxin-contaminated herbicide exposure compared with a non-affected area was reported. The limitations of the study were that it was conducted in adults and the DDE index was used; thus, specific MIH prevalence data are difficult to derive [40].

Several studies using rat models have implicated bisphenol A (BPA) as a causative factor in MIH [41–43]. Exposure of the rat to BPA increased the albumin content of the enamel and increased the expression of enamelin and decreased the expression of KLK4. A greater effect on males compared with females has also been reported-mechanism unknown [42, 44].

There was an enhanced (greater) effect of BPA with concomitant exposure to fluoride [42]. This could be because AMELX and ENAM genes are modulated by BPA, whilst KLK4 and MMP are modulated by fluoride.

One needs to interpret animal models with some caution, especially those with a continuously growing tooth used as the expression of the phenotype; however, they do shed light onto the condition in ways human experimentation could never do.

Chronic fluoride ingestion is associated with increased prevalence of diffuse hypomineralized defects of enamel, and teeth forming at the time of the fluoride toxicity to the ameloblasts will be affected-distinct from the appearance of MIH. The risk of fluorosis depends on the age and extent of the fluoride ingestion, and also genetic factors are involved [45]. There has been no positive association determined between fluoride ingestion and MIH [1, 2].

4.5.2 Birth "Complications"

Most pre-, peri- and postnatal studies are cross-sectional, and therefore claims can be made about association only. There is little evidence of association between prenatal events and MIH, although some evidence exists regarding HSPM, in vitro fertilisation and maternal smoking later in pregnancy [1–3, 26]. Maternal smoking during pregnancy has not been found to be associated with MIH [3].

There is conflicting evidence related to peripartum events such as premature birth, caesarean birth and birth complications. In their systematic review, Silva and colleagues found heterogeneity in the methodology and reporting of peripartum events, restricting the drawing of any conclusions regarding risk factors [26]. Wu and colleagues reported that premature birth and low birth weight both increased the risk of MIH; although, like Silva, they commented that the heterogeneity of data was high and there may be a publication bias for papers with positive associations [3, 46]. More recently, a positive association between increased risk for MIH and infant hypoxia during delivery as well as caesarean section was reported in a French cohort; no association was determined for prematurity [47]. In a Brazilian study, a low (<7) Apgar score was associated with diffuse and demarcated opacities in primary teeth [48]; however, in a Norwegian study, no association between MIH and an Apgar score ≤5 was determined [49].

4.5.3 Early Childhood

In early childhood, up to the age of 3 or 4, the influence of a variety of factors, especially related to health and including pyrexia/fever, chicken pox, asthma, otitis media, etc., has been investigated broadly. There has been variability in the definition of "illness", limiting the conclusions drawn [3]. Many studies have determined association of MIH with early childhood fever and "respiratory disease", which includes pneumonia and asthma.

The influence of vitamin D on dental development has been known for many decades [50]. With respect to MIH, results are conflicting. In a German study, a positive relationship between lower vitamin D (25(OH)D) levels and increased prevalence of MIH was determined [51]; however, van der Tas and colleagues reported no link between vitamin D levels at 6 years of age with MIH or HSPM in Dutch children [52]. In a recent study, a link with higher levels of vitamin D and HSPM was reported; however, the authors stated that caution should be taken when interpreting the results as they could be influenced by unknown confounding factors [26]. A recent Danish paper reported that high dose Vitamin D supplementation of pregnant women may reduce the prevalence of MIH significantly [53].

4.5.4 Medication

The association between childhood medications and MIH, like many other factors, is not specific, despite several research projects over the years [2, 54]. Antibiotics such as amoxicillin and erythromycin, as well as anti-asthma and chemotherapeutic drugs have been investigated, with a recent systematic review concluding that no specific drugs can be identified as causing MIH at this time [55–58]. The main issue is that in most cases the effect of the disease cannot be separated from the effect of the resultant medication, as the studies are either retrospective or cross-sectional; it would also be unethical to undertake a longitudinal trial and not provide appropriate medication to a control group.

4.6 Overview of MIH Aetiology

MIH aetiological factors are still uncertain. It is likely that childhood illnesses and genetic factors are involved, and possibly there is an individual threshold for susceptibility-as many children without relevant medical histories are severely affected by MIH and vice versa.

The evidence base is limited by issues with heterogeneity of existing research, especially regarding the indices used (EAPD, mDDE) and definitions of illnesses. More recently, the number of publications using the EAPD index has increased, allowing more valid comparison.

The importance of early diagnosis and appropriate treatment planning cannot be underestimated. Therefore, if a child has had HSPM, then due to increased risk, the presence of MIH should be determined as soon after the eruption of the first permanent molars as possible.

Hopefully, the aetiological factors involved in MIH (and HSPM) will be discovered; however, in the meantime, more quality longitudinal research projects are needed-both multisite and standardized.

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Part II

Considerations in Clinical Practice

Diagnosis, Classifications and Treatment Strategies of MIH-Affected Teeth

5

Katrin Bekes and Karin L. Weerheijm

5.1 Introduction

The term "molar incisor hypomineralization" (MIH) was found in 2001 [1] as a reaction to presentations given at the fifth congress of the European Academy of Paediatric Dentistry in Bergen, Norway, in 2000. Four abstracts from three working groups independently focused on permanent first molars with enamel developmental defects [2–5]. At that time, the presenters termed the defects "hypomineralized permanent first molars", "idiopathic enamel hypomineralization in the permanent first molars", "nonfluoride hypomineralization in permanent first molars" and "cheese molars" [1]. This occasion gave the signal for researchers to find a name for the phenomenon.

Since then, MIH was defined as a hypomineralization of systemic origin of one to four permanent first molars, frequently associated with affected incisors [1]. The description was chosen by the authors to put weight on the fact that molars are always involved in the phenomenon and to emphasize that a combination of affected molars with demarcated opacities of the incisors is possible but not necessary [6]. Opacities only found on incisors indicate another origin of the defect and should not be assigned to MIH [6]. Until today, global knowledge of the condition has increased, reflected by a rising number of studies focusing on this dental anomaly.

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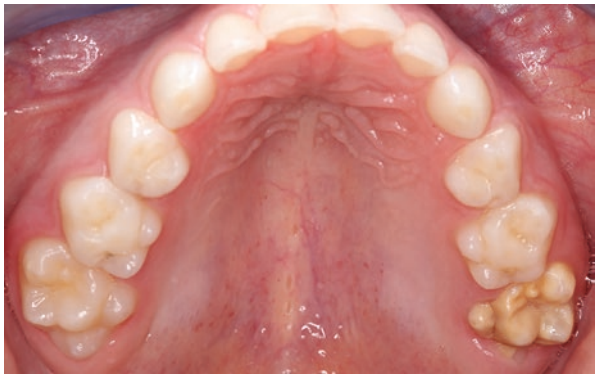

Fig. 5.1 Asymmetric appearance in molars

5.2 Clinical Presentation

Clinically, affected teeth show a hypomineralization which can be seen as an alteration in the translucency of the enamel. Hypomineralized enamel can vary in colour shade from white to yellow or brown [7], but always shows borders that are well-defined and distinct from sound enamel [8]. Porous enamel can easily chip off, especially under the influence of masticatory forces. Occasionally, enamel of affected molars breaks down facile after eruption, leaving the dentin exposed, referred to as posteruptive enamel breakdown (PEB) in the literature [6, 9]. On permanent incisors, affected enamel usually seems less severely disrupted and due to the absence of chewing forces less prone to break down. Incisal enamel defects are, however, frequently quite extensive and most common on buccal surfaces of the teeth giving rise to cosmetic concerns [10]. Expression of the phenomenon can vary not only in severity between patients but also within the mouth (Fig. 5.1).

5.3 Diagnostic Terms

In general, a variety of terms and definitions have historically been used to describe different developmental defects of the enamel (DDE). However, currently valid indices such as the modified DDE index (mDDE) [11] or the Enamel Defect Index (EDI) [11] were considered not suitable for MIH studies [6]. Therefore, separate judgment criteria for MIH in epidemiological studies were developed in 2003 [6].

In the recent past, separate clinical measures for MIH based on scientific criteria were established. Weerheijm et al. proposed that an optimum age for checking the condition would be 8 years (as all four permanent molars and most permanent incisors should have erupted) [6]. Teeth should be examined wet; however, if needed, then cotton rolls may be used to clean tooth surface to better visualise it [6, 12]. The following judgement criteria should be used to identify teeth affected by MIH (Table 5.1):

- Demarcated opacities (Fig. 5.2).
- Posteruptive enamel breakdown (PEB) (Fig. 5.3).

Table 5.1 Judgement criteria for diagnosing MIH according to Weerheijm et al. [1]

Key feature	Description
Demarcated opacities	– Clearly demarcated opacities – Variability in colour and size – Defects less than 1 mm not to be reported
Posteruptive enamel breakdown	– Defect of the surface after eruption of the tooth – Loss of enamel from an initially formed surface after tooth eruption – Frequently associated with a pre-existing demarcated opacity
Atypical restorations	– Size and shape of restorations not conforming to the temporary caries picture – Frequently extends to the buccal and palatal/lingual surfaces – Frequently associated with an opacity at the margin of the restoration – For incisors, a buccal restoration can be noticed not related to trauma
Extraction of molars due to MIH	– Absence of a first permanent molar should be related to the other teeth of the dentition – Opacities or atypical restorations in the other first permanent molars combined with absence of a first permanent molar – Absence of first permanent molars in an otherwise sound dentition in combination with demarcated opacities on the incisors
Failure of eruption of a molar or an incisor	– First permanent molar or the incisor to be examined are not yet erupted

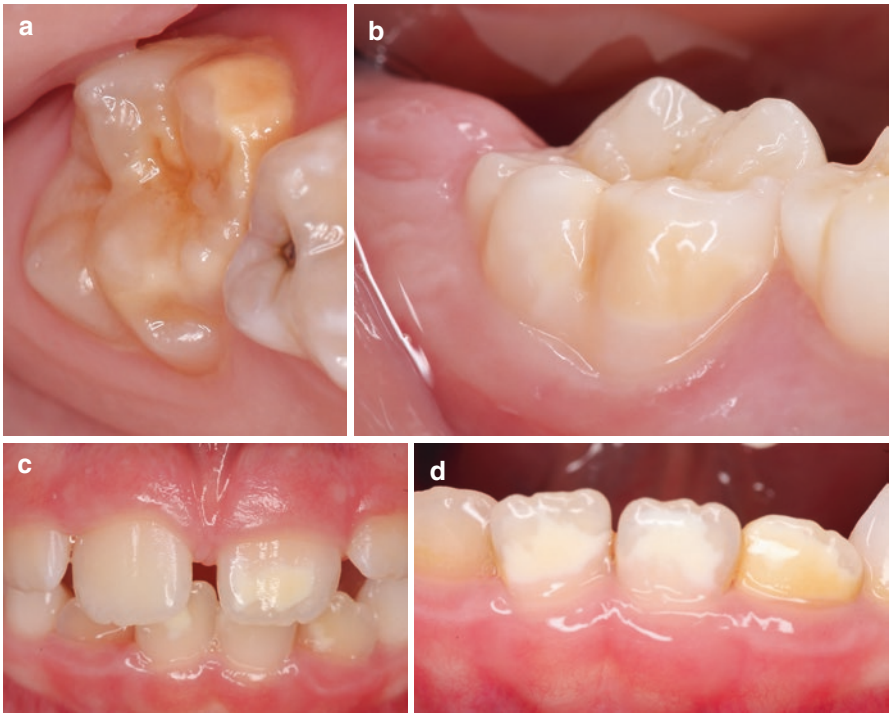

Fig. 5.2 Demarcated opacities in enamel of molars and incisors. (**a**) Tooth 16: Opacities on the occlusal, buccal and palatal surface in the mesial half. (**b**) Tooth 46: Opacity on the buccal surface. (**c**) Tooth 21, 32 and 41 showing opacities. (**d**) Tooth 32, 31 and 41: Opacities in different colours

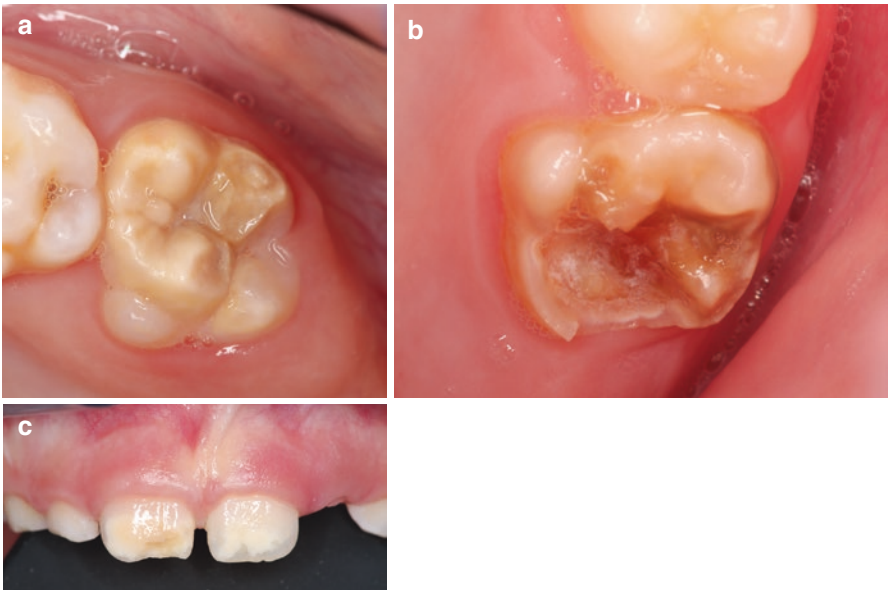

Fig. 5.3 Posteruptive breakdown of molars and incisors. (**a**) Tooth 26: Posteruptive breakdown on the mesio-palatal and disto-buccal cusp. (**b**) Tooth 26: Posteruptive breakdown affecting nearly two-thirds of the occlusal surface. (**c**) Tooth 11: Posteruptive breakdown on the upper third

- Atypical restorations (Fig. 5.4).
- Extraction of molars due to MIH (Fig. 5.5).
- Failure of eruption of a molar or an incisor.
- Diagnose MIH, at least one FPM has to be affected. European Academy of Paediatric Dentistry (EAPD) assessment criteria allow and facilitate comparisons between the findings of different studies [6].

5.4 Differential Diagnosis

Molar incisor hypomineralization may be mistaken for a range of other conditions. Therefore, it is essential to distinguish between MIH and other abnormalities in the dental structures. Besides understanding the key features which are essential for accurate diagnosis, a patient's history is mandatory for seeking acquired, environmental or genetic aetiologies.

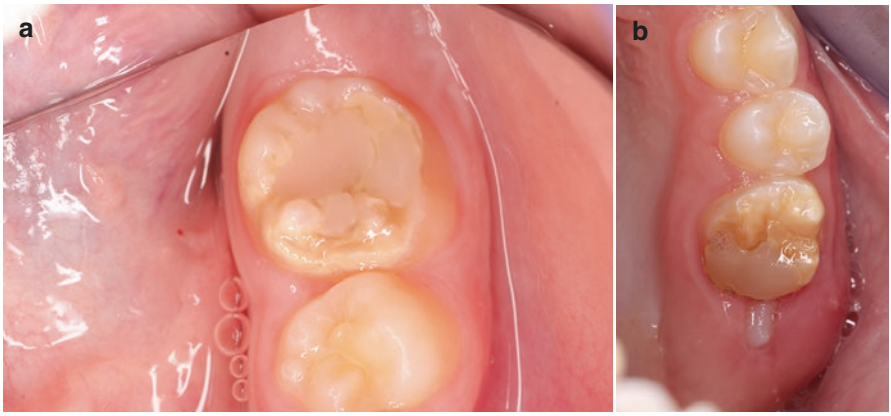

Fig. 5.4 Atypical restorations in molars. (**a**) Tooth 36: Composite restoration incorporates buccal surface. Notice the PEB at the buccal and occlusal mesial restoration margins as well as lingual and mesial opacities. (**b**) Tooth 26: Composite restoration involving the occlusal palatal and distal surface with PEB and opacities at the restoration margins

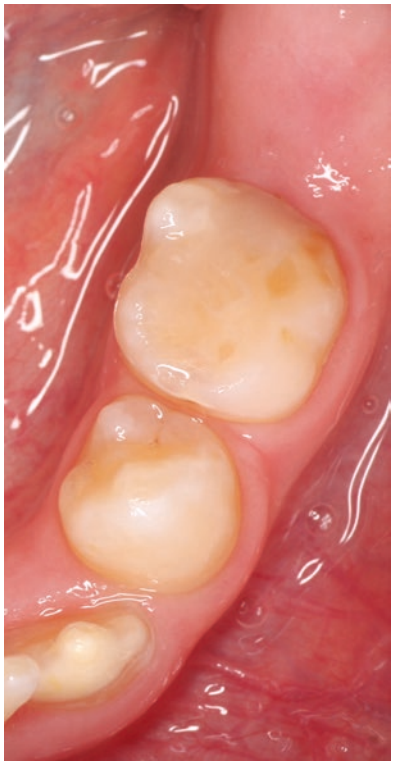

Fig. 5.5 Molar extraction due to MIH: First premolar has already erupted, but no first permanent molar can be seen

5.4.1 Amelogenesis Imperfecta

Amelogenesis imperfecta (AI) represents a group of genetic developmental dental defects that have been reported to occur at prevalence rates of approximately 1:700–1:14,000 depending on the population studied [13]. It results in enamel that is hypoplastic, hypomature or hypomineralized depending on the stage of enamel formation that is affected by the genetic defect. Due to its diverse clinical presentation, some AI cases may be difficult to differentiate from MIH [12]. Nevertheless, generalized involvement of both primary and permanent dentitions and a common familial history can help differentiate from AI (Fig. 5.6).

5.4.2 Enamel Hypoplasia

Enamel hypoplasia is a disorder concerning the quantity of enamel presenting as reduced enamel thickness including pits, grooves and/or irregular areas of missing enamel. The reduction in the enamel thickness is localized [11]. Following the fast damage to the surface of the enamel of molars affected by MIH during the posteruptive phase, the lesions might resemble enamel hypoplasia. However, margins of hypoplastic enamel lesions are mostly regular and smooth, whereas borders of MIH lesions are sharp and irregular due to posteruptive shearing of weakened enamel [12]. Examples for enamel hypoplasia are Turner's hypoplastic tooth (Fig. 5.7) or absence of enamel parts in the case of rickets.

5.4.3 Fluorosis

Dental fluorosis occurs as a result of excessive fluoride absorption during tooth mineralization [14]. Clinically affected teeth show linear, patchy, or confluent white, yellow or brown opacities without a clear boundary in the enamel [11] (Fig. 5.8). In contrast, MIH does not show diffuse opacities but demarcated opacities. Anamnesis focusing on fluoride history can also help to distinguish fluorotic lesions from opaque MIH lesions [12].

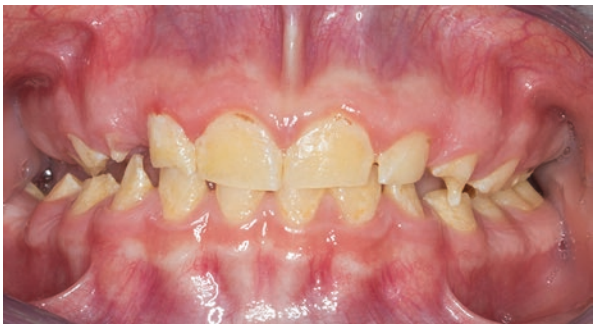

Fig. 5.6 Amelogenesis imperfecta affects enamel of all teeth. Enamel may be hypoplastic, hypomineralized or both. Teeth affected may be discoloured, sensitive, or prone to disintegration. In this case, all teeth show yellowish discoloration. Tooth surface is slightly rough in nature; no pitting is seen. In some, teeth breakdown (e.g., canines) can be seen

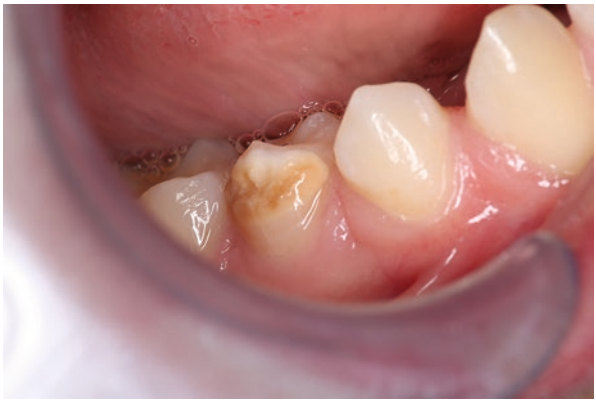

Fig. 5.7 Turner's tooth

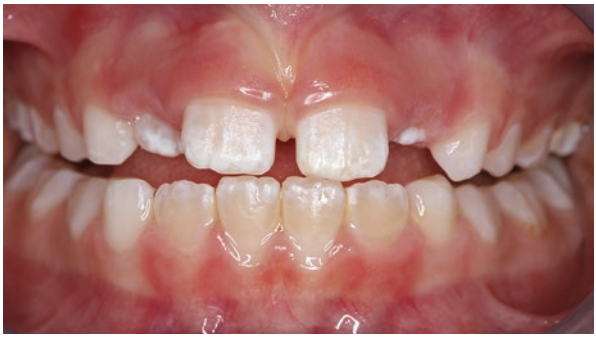

Fig. 5.8 Fluorosis. Notice the diffuse (white) opacities

5.4.4 White Spot Lesions

White spot lesions represent early signs of tooth decay. They can be seen as a result of prolonged plaque accumulation on the affected surface of the teeth. White spot lesions can be distinguished from MIH because they occur in vulnerable areas of plaque stagnation, such as the cervical or gingival margin of the tooth on an area where enamel hypomineralization rarely occurs [12].

5.5 Classifications

Currently, several approaches exist to classify the severity of MIH. In most cases, MIH is recorded as mild or severe following the graduation of Lygidakis et al. [15]. In mild cases, teeth show demarcated enamel opacities without enamel breakdown and occasional sensitivity to external stimuli but not to brushing and only mild aesthetic concerns on discolouration of the incisors. In severe cases, demarcated enamel opacities with PEB, caries, persistent/spontaneous hypersensitivity affecting function and finally strong aesthetic concerns that may have socio-psychological impact are observed.

Ghanim et al. developed a complex scoring system to quantify the severity of MIH based on the number of involved teeth as well as the type and extent of the

Table 5.2 The MIH-TNI

Index	Definition		
Index 0	No MIH		
Index 1	MIH – No hypersensitivity – No enamel breakdown		
Index 2	MIH – No hypersensitivity – Enamel breakdown	2a 2b 2c	<1/3 extension of defect >1/3 < 2/3 extension of defect >2/3 extension of defect or/and defect close to pulp or extraction or atypical restoration
Index 3	MIH – Hypersensitivity – No enamel breakdown		
Index 4	MIH – Hypersensitivity – Enamel breakdown	4a 4b 4c	<1/3 extension of defect >1/3 < 2/3 extension of defect >2/3 extension of defect or/and defect close to pulp or extraction or atypical restoration

enamel defect [16]. The proposed grading method allows separate classification of demarcated hypomineralization lesions and other enamel defects identical to MIH. It yields an informative description of the severity of MIH-affected teeth in terms of the stage of visible enamel destruction and the area of tooth surfaces affected (i.e., lesion clinical status and extent, respectively).

Recently, Steffen et al. introduced a new index, the MIH Treatment Need Index (MIH-TNI), which is part of the Wuerzburg MIH concept [17–19]. It was designed for describing treatment needs in populations and for identifying patients and providing information about the severity of MIH. The index is based on two key symptoms which are clinically considered to be the most important ones with respect to MIH: hypersensitivity and PEB (Table 5.2).

5.6 Treatment Approaches

Treatment options for teeth with MIH range from prevention, restoration to extraction. Suitability of these, however, differs depending on a number of factors. Commonly identified factors are severity of the condition, presence of symptoms, patient's dental age and child/parent's social background and expectation [15]. Nevertheless, early diagnosis and preventive intervention should always be the first treatment option with severity as a guide for the long-term treatment plan.

A first clinical approach for treating MIH was published by Williams et al. introducing a 6-step management approach [20] as follows:

– Risk identification.
– Early diagnosis.
– Remineralization and desensitization.
– Prevention of dental caries and posteruptive enamel breakdown.
– Restorations or extractions.
– Maintenance.

At the same time, another treatment decision tree was generated by Mathu-Muju and Wright [21], taking into account the level of defect severity (mild, moderate or severe) and the length of treatment time planning (short and long term). For example, in severe cases with posteruptive breakdown and sensitivity being present, glass ionomers or stainless-steel crowns serve as short-term solutions while full cast coverage is seen as a long-term treatment possibility.

As a result, Lygidakis et al. published best practical guidance and proposed an approach considering dental age and severity of the condition [15]. In early eruption stages, authors see caries prevention as an important tool as MIH teeth are more likely to have carious lesions and posteruptive breakdown due to increased porosity. In later developmental stages, when the enamel becomes more mature and if prevention has succeeded and enamel surface remained intact, the relative importance of prevention is seen to be less comparative to the necessity of restorative treatment.

Based on the MIH-TNI mentioned above, a treatment plan for each index is developed as well ranging from prophylaxis, sealing, restoration (temporary or permanent) to extraction [19]. Suitability of these treatment approaches, however, differs depending on the index with corresponding symptoms of MIH (Figs. 5.9, 5.10, and 5.11).

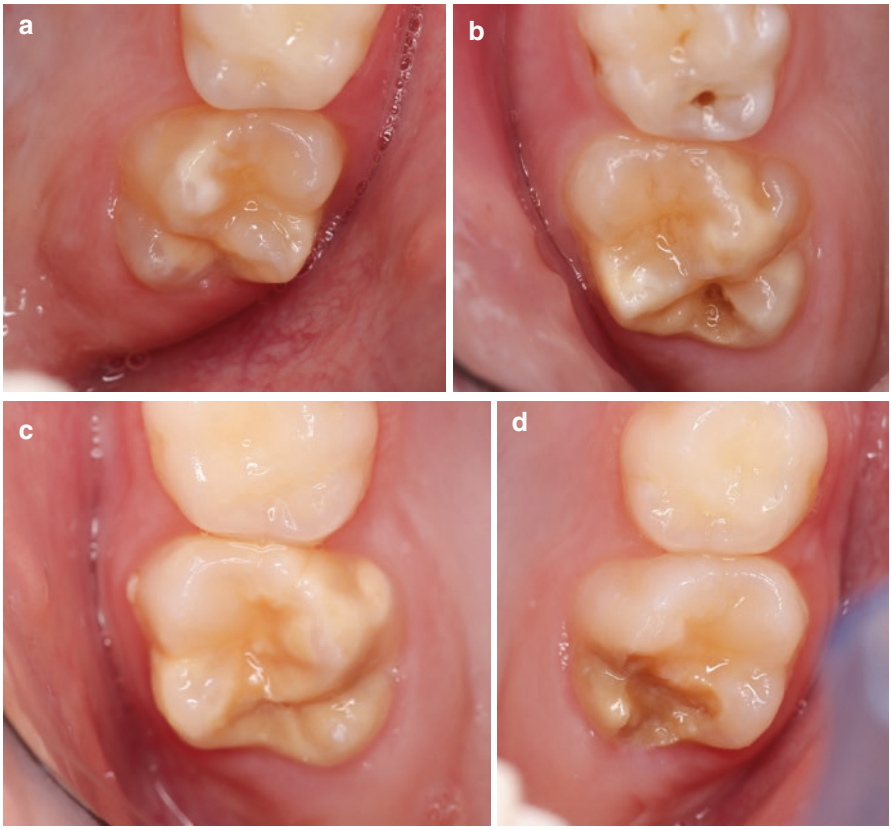

Fig. 5.9 MIH-TNI. (**a**) Index 1. (**b**) Index 2. (**c**) Index 3. (**d**) Index 4

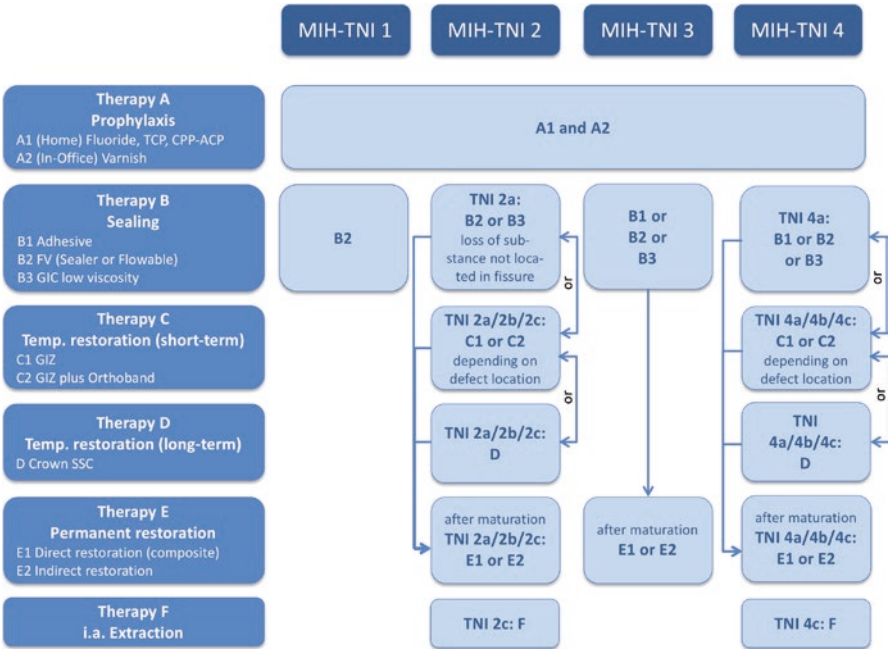

Fig. 5.10 MIH-TNI therapy plan based on the MIH-TNI in patients with low caries risk. (Original figure in German [19])

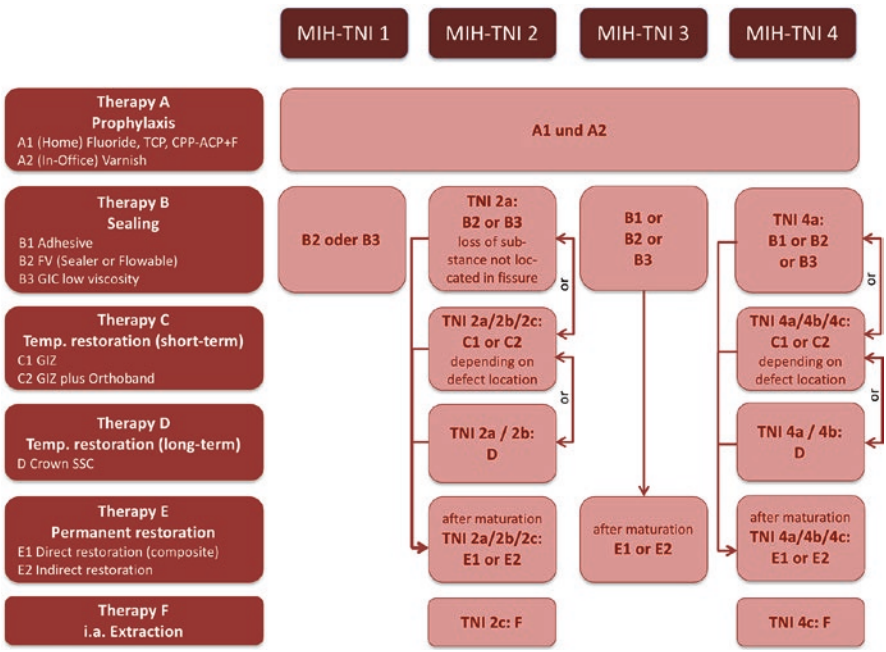

Fig. 5.11 MIH-TNI therapy plan based on the MIH-TNI in patients with high caries risk. (Original figure in German [19])

All described treatment approaches above are more or less based on a graduated plan following the goal to prevent the tooth from developing dental caries, help prevent or reduce enamel loss, restore form and function when there is enamel loss and address aesthetic issues. The following chapters of this book will focus on each treatment option mentioned and give a deeper look into each topic.

In conclusion, there is no doubt that a holistic approach should be considered formulating a treatment plan [15]. This treatment plan should incorporate a short- and long-term approach, keeping in mind the coping skills of a child and avoiding repeated treatment as much as possible. Several authors have shown that children with MIH receive much more dental treatment compared with unaffected children [22, 23]. Because of these frequent treatments, children with hypomineralized first molars may present with more anxiety and be at risk for dental behaviour management problems [22]. On the one hand, this scenario will play a significant role in the decision-making process as ideal treatment options may not be possible and alternative treatment plans are needed.

On the other hand, dentists have to be aware of their part in the whole process. Dentists can play an important role in preventing anxiety and improving coping ability in children with MIH by the following:

- Identifying MIH as early as possible (probably the most important factor).
- Expressing to the child awareness of the fact that molars create discomfort.
- Taking the severity into account for a short- and a long-term treatment plan.
- Realising that treatment of a MIH molar differs from today's tooth-saving dentistry.
- Keeping the child pain free.
- Realizing some children need remedial support during treatment.

All these things can be helpful for improving dentist/child relationships.

5.7 Summary

In summary, MIH can be diagnosed using criteria given by EAPD in 2003. Differential diagnoses comprise amelogenesis imperfecta, enamel hypoplasia, dental fluorosis and white spot lesions. Available treatment options comprise of preventive and restorative approaches and extraction. During the MIH route from eruption to a long-life functioning solution, the well-being of the child should always be taken into account.

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Association Between Molar Incisor Hypomineralization and Dental Caries

6

Gabriela C. A. Americano and Vera M. Soviero

6.1 Caries Experience in Children with MIH

Children with molar incisor hypomineralization (MIH) from both low and high caries experience populations have presented higher prevalence of caries in permanent teeth (see Table 6.1) [1–3] and higher decayed, missing or filled index (DMF index) (see Table 6.2) [1–14] than children without MIH. Children with MIH also present more teeth [14–18] and tooth surfaces with a DMF greater than zero [15, 17, 19] when only the first permanent molars are evaluated (see Table 6.3). It was also observed that multiple surface restorations are more frequent in hypomineralized first permanent molars, whilst single surface restorations are more common in non-hypomineralized molars (see Figs. 6.1 and 6.2) [15, 19]. Several studies in high caries risk populations, evaluating children in schools, have shown that children with MIH are 2.0–4.6 times more likely to have some caries experience in permanent teeth than children without MIH [1–3, 20]. In a case-control study, children with MIH from a dental clinic were 5.89 more likely to have some decayed, missing or filled permanent teeth than children without MIH [15]. Another comparative study found an odds ratio of 6.6 for children with MIH from public schools (see Table 6.4) [14].

For epidemiological purposes, the European Academy of Paediatric Dentistry recommends that the screening for MIH should be done at 8 years of age. At this

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Table 6.1 Dental caries prevalence for permanent teeth in children with and without MIH

Reference	Country	Year of publication	Age children	Dental caries prevalence (%)	
				MIH children	Non-MIH children
Jeremias et al. [1]	Brazil	2013	6–12	45.8	20.7
Pitiphat et al. [2]	Thailand	2014	6–7	35	10
Grossi et al. [3]	Brazil	2017	7–13	31.5	4.6

Table 6.2 DMF index in children with and without MIH

Reference	Country	Year of publication	Age children	DMF value	
				MIH children	Non-MIH children
Preusser et al. [4]	Germany	2007	6–12	DMF-T = 0.7	DMF-T = 0.5
Cho et al. [5]	China	2008	11–14	DMF-T = 1.5	DMF-T = 0.8
Mahoney and Morrison [6]	New Zealand	2009	7–10	DMF-T = 0.5 ± 1.1	DMF-T = 0.1 ± 0.5
Mahoney and Morrison [7]	New Zealand	2011	7–10	DMF-T = 0.6 ± 1.1	DMF-T = 0.2 ± 0.6
Jälevik and Klingberg [8]	Sweden	2012	18	DMF-T = 3.8 ± 2.9	DMF-T = 1.7 ± 2.6
Jeremias et al. [1]	Brazil	2013	6–12	DMF-T = 0.8 ± 1.1	DMF-T = 0.4 ± 0.1
Garcia-Margarit et al. [9]	Spain	2014	8–9	DMF-T = 0.5 (0.3–0.6) DMF-S = 1.2 (0.9–1.4)	DMF-T = 0.2 (0.1–0.2) DMF-S = 0.7 (0.6–0.9)
Petrou et al. [10]	Germany	2014	7–10	DMF-T = 0.2 ± 0.6	DMF-T = 0.1 ± 0.5
Pitiphat et al. [2]	Thailand	2014	6–7	DMF-T = 0.6 ± 1.0	DMF-T = 0.1 ± 0.5
Kosma et al. [11]	Greece	2016	8 14	DMF-T = 1.6 DMF-S = 4.6	DMF-T = 1.01 DMF-S = 3.46
Ulusoy et al. [12]	Turkey	2016	8–11	DMF-T = 3.4	DMF-T = 2.6
Grossi et al. [3]	Brazil	2017	7–13	DMF-T = 0.45	DMF-T = 0.07
Kühnisch et al. [13]	Germany	2018	15	DMF-T = 1.2 DMF-S = 1.5	DMF-T = 0.9 DMF-S = 1.2
Wuollet et al. [14]	Finland	2018	8–13	DMF-T = 1.17 ± 1.39	DMF-T = 0.46 ± 1.12

Table 6.3 DMF index for first permanent molars in children with and without MIH

Reference	Country	Year of publication	Age children	DMF value	
				MIH children	Non-MIH children
Jälevik and Klingberg [16]	Sweden	2002	9	DMF-T = 2.2	DMF-T = 0.4
Kotsanos et al. [19]	Greece	2005	MIH = 7.7 SD = 1.3 Non-MIH = 7.5 SD = 1.2	DMF-S = 2.8 ± 3.2	DMF-S = 0.8 ± 1.3
Muratbegovic et al. [18]	Bosnia and Herzegovina	2007	12	DMF-T = 3.5 ± 0.9	DMF-T = 2.4 ± v1.3
Grošelj and Jan [17]	Slovenia	2013	6–11.5	DMF-T = 0.9 ± 1.2 DMF-S = 1.3 ± 2.0	DMF-T = 0.6 ± 1.0 DMF-S = 0.8 ± 1.6
Americano et al. [15]	Brazil	2016	7–11	DMF-T = 1.85 ± 0.91 DMF-S = 3.78 ± 3.40	DMF-T = 1.23 ± 0.57 DMF-S = 1.40 ± 0.89
Wuollet et al. [14]	Finland	2018	8–13	DMF-T = 1.03 ± 1.25	DMF-T = 0.32 ± 0.8

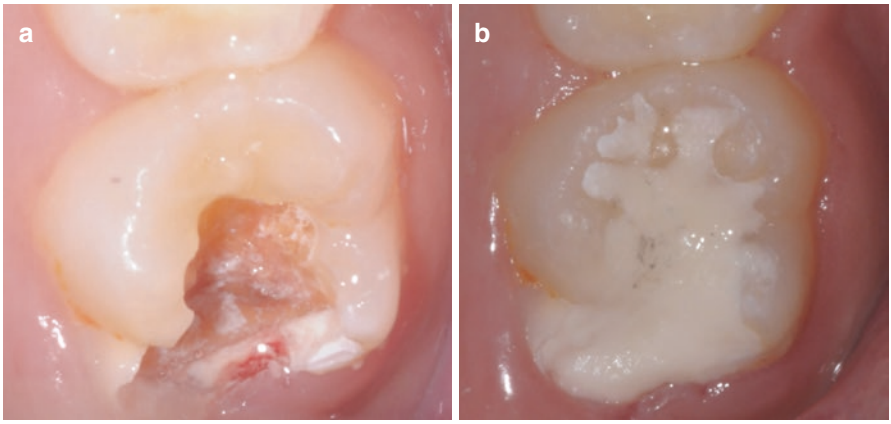

Fig. 6.1 (**a**) First permanent molar with posteruptive breakdown exposing dentin and involving multiple surfaces. (**b**) The same tooth restored and sealed with glass ionomer cement (Riva Self Cured, SDI®, Australia)

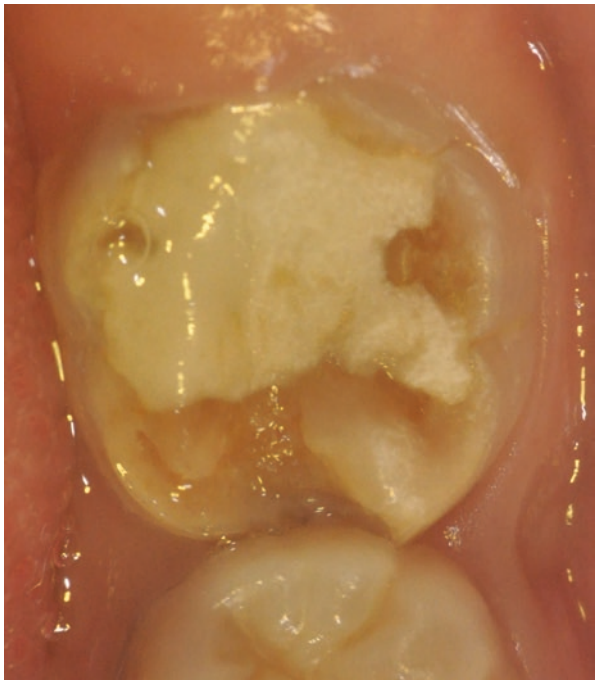

Fig. 6.2 First permanent molar with fractured restoration and involving multiple surfaces

age, it is less probable that MIH signs were masked by caries or any restorative procedure [21]. Older children have their permanent teeth exposed to caries risk factors and to MIH complications for longer, increasing the chance of dental caries development [22]. When there is posteruptive enamel breakdown [23], dental caries

Table 6.4 Odds ratio for caries experience in permanent teeth in children with MIH

Reference	Country	Year of publication	Age children	Evaluated teeth	Odds ratio (confidence interval)
Da Costa-Silva et al. [20]	Brazil	2010	6–12	All permanent teeth	Urban area: 2.0 (1.2–3.1) Rural area: 2.8 (1.4–5.6)
Jeremias et al. [1]	Brazil	2013	6–12	All permanent teeth	3.20 (2.2–4.6)
Pitiphat et al. [2]	Thailand	2014	6–7	All permanent teeth	4.60 (2.7–7.9)
Americano et al. [15]	Brazil	2016	7–11	All permanent teeth	5.89 (2.69–12.86)
Grossi et al. [3]	Brazil	2017	7–13	All permanent teeth	4.44 (2.20–8.95)
Wuollet et al. [14]	Finland	2018	8–13	First permanent molars	6.60 (3.83–11.39)

assessment in children with severe MIH can also raise DMF values, independently of the presence of caries lesions because these teeth usually require restorative intervention and therefore are counted as decayed (D) or filled (F) [22]. It was observed that the DMF means as a whole [3, 11] or restricted to first permanent molars [11] was significantly higher in children with severe MIH and ages ranging from 7 to 14 years than in children with mild MIH. Negre-Barber et al. [24] did not find significant difference in caries prevalence between children with MIH and without MIH. However, caries experience was higher in children with severe MIH than those with mild MIH, which is in agreement with another study [3]. The increase in MIH severity results in more caries lesions in dentin [3, 25] and higher DMF values in first permanent molars and incisors [24].

6.2 Does DMF Index Represent Restorative Treatment Need or Dental Caries Experience in Children with MIH?

One question is if children with MIH have higher DMF values due to more treatment need because of posteruptive enamel breakdown or indeed due to caries [15, 26]. The DMF index represents the past and/or current dental caries experience in the permanent dentition, but caries activity is not assessed [15, 22, 27]. The DMF index is based on the premise that filled and missed tooth and tooth surfaces were carious before being filled or extracted [28]. Cavities exposing dentin are recorded in the DMF index, regardless of caries activity [15]. Higher DMF values in the presence of MIH can reflect greater treatment need but not necessarily because of caries lesions [15]. In the presence of MIH, the "filled" and "missing" components of the DMF index may be restorations and tooth extractions due only to caries lesion, posteruptive breakdown of the hypomineralized enamel or a combination of both [22]. The "decay" component of the DMF index may represent caries lesions that started with or without some influence of hypomineralization [22].

6.2.1 Children with MIH and Restorative Treatment Need

A study reported that the majority of smooth surfaces of first permanent molars with DMF greater than zero had hypomineralization [15]. It is known that occlusal and smooth surfaces (i.e. distal surfaces, mesial surfaces, buccal surfaces of maxillary molars and lingual surfaces of mandibular molars) of first permanent molars are the most and the less surfaces susceptible to dental caries, respectively [29, 30]. Even mesial surfaces of first permanent molars, which are the proximal surfaces more vulnerable to dental caries in the permanent dentition, tend to remain non-cavitated during the mixed and young permanent dentition due to the decline in the dental caries progression rate observed in the recent decades [31, 32]. Thus, fractures can be the first and only reason for cavities and restorations in smooth surfaces of first permanent molars [15]. This happens, for example, when the exposed dentin of fractures remains hard in areas where dental caries development is uncommon, such as cusp tips and smooth tooth surfaces (see Fig. 6.3) [15, 29, 33]. When a cavitated caries lesion and hypomineralization are present in the same tooth surface, most of the time, it is not possible to identify if the cavity resulted from the carious process or from a breakdown of the fragile hypomineralized enamel (see Fig. 6.4) [15]. From this point of view, we cannot exclude the possibility that DMF values may be overestimated in the presence of MIH, because cavities, restorations and tooth extractions might have resulted solely from posteruptive breakdown [15, 22]. The differentiation between fillings related to MIH or not related to MIH was mentioned in one study that did not observe difference in the DMF values among children affected or not by MIH because atypical restorations were not included in the DMF index [26]. Nonetheless, independently if the cavities are associated to caries or not, children with MIH are 11 times more likely to need restorative dental treatment in

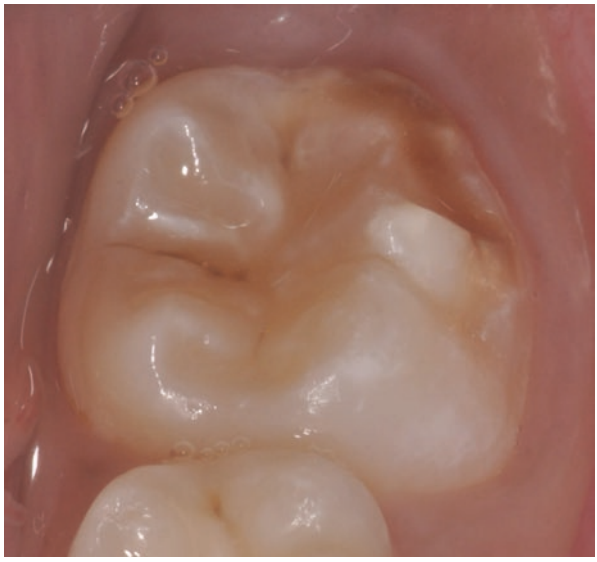

Fig. 6.3 First permanent molar with posteruptive breakdown exposing dentin where dental caries development is uncommon

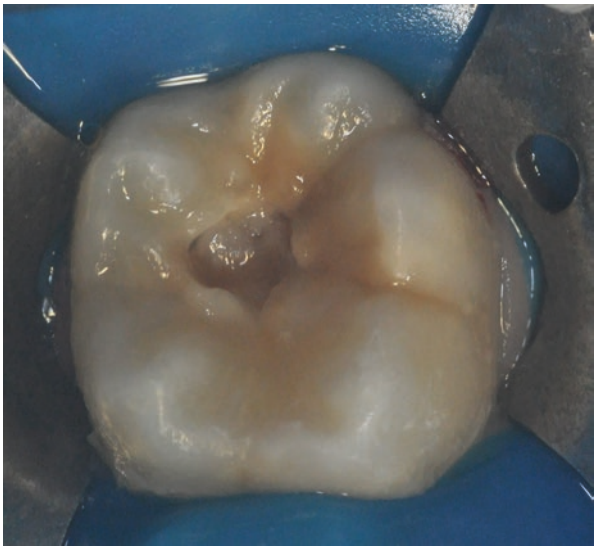

Fig. 6.4 First permanent molar with hypomineralization and cavitated caries lesion in the same tooth surface, facilitating plaque accumulation and protecting the biofilm from mechanical disturbance

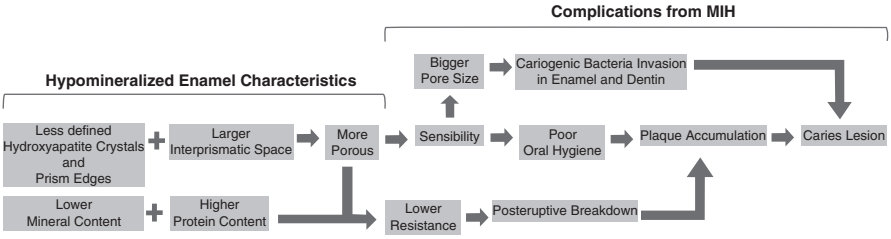

Fig. 6.5 Flowchart of the hypomineralized enamel characteristics and complications

their first permanent molars than children without MIH [19]. Higher DMF index for first permanent molars and incisors as well as its "filled" component confirm that children with severe MIH need more fillings [24].

6.2.2 Children with MIH and Dental Caries Susceptibility

On the other side, although hypomineralized teeth can be restored or extracted prior to dental caries development [22], it was reported that hypomineralized first permanent molars are more susceptible to dental caries development than non-hypomineralized molars of the same patient [3]. Hypomineralized enamel may be more prone to caries lesions due to its characteristics [15, 22], as shown the Fig. 6.5. The hypomineralized enamel is more porous because; unlike the normal enamel, prism edges and hydroxyapatite crystals are less defined; and the interprismatic space is larger [34]. Moreover, a lower mineral content and a higher protein content contribute to the lower resistance of the hypomineralized enamel [35, 36]. Thus, the

hipomineralized enamel can fracture soon after tooth eruption or later under the masticatory forces [23, 37]. Once the enamel collapses, a cavity is formed facilitating plaque accumulation and protecting the biofilm from mechanical disturbance (see Fig. 6.4) [22, 23, 37, 38]. Although, gingival index [39] and plaque index [40] were not significantly different between children with and without MIH, the MIH group presented worse gingival health parameters [12]. If the patient is not able to brush the area properly on account of sensitivity [12, 37, 38], for example, the biofilm tends to accumulate and trigger a caries lesion [22, 41]. Furthermore, the surface features of the hypomineralized enamel contribute to bacterial adhesion. Even on apparently "intact" surfaces, the pore sizes may be big enough for cariogenic bacteria to invade and destroy the enamel and dentin [35, 42].

6.3 MIH as Caries Risk Factor

Several risk factors such as sucrose intake, exposition to fluorides, salivary buffer capacity and flow rate, Streptococcus mutans counting, as well as sociodemographic and behavioural factors have been associated with dental caries. However, past caries experience has been reported as the major predictor of new caries lesions [15, 22, 43, 44]. In children, caries experience in primary teeth has been considered the best predictor for caries in permanent teeth [43–45]. However, it was observed that despite of similar mean caries index in primary teeth in children with and without MIH, children with MIH presented significantly higher DMF [3, 12, 15]. Also, in the presence of MIH, high DMF was observed in children who had no caries experience in primary teeth [15]. The mean number of teeth and tooth surfaces affected by caries in the permanent dentition were higher in MIH children [13] and first permanent molars of children with MIH seem to become affected by dental caries earlier than in children without MIH [14], suggesting that MIH is a relevant caries risk factor. Moreover, MIH was considered a superior predictor of dental caries in first permanent molars in comparison with socioeconomic status. As low socioeconomic status is associated with higher caries risk [46], this result suggests that tooth brushing and low-sugar intake are not enough to maintain hypomineralized teeth in good conditions [14]. Maybe the impact of MIH on oral health can be more evident in low caries experience populations, which the "traditional" caries risk factors are controlled [22]. From these points of view, it can be expected that the presence of MIH entails a high susceptibility to dental caries development [22].

6.4 How to Deal with MIH Children in Relation to Dental Caries?

Indeed, MIH is a worldwide clinical problem [22]. Due to its impact on caries increment, especially in first permanent molars, paediatric dentists should be aware that children with MIH demand close surveillance [22]. Not rarely, despite of good oral hygiene and low-sugar consumption, MIH children need restorative

dental treatment due to severe enamel breakdown [15]. As these children may need restorative intervention without having caries lesions, preventive approaches to maintain the hypomineralized teeth intact should be differentiated. Besides oral hygiene instructions and dietary counselling, preventive recommendations include topical fluoride application and sealants (see Chaps. 10 and 11) [23, 47]. The protection of initial enamel breakdown with high viscous glass ionomer cement seems to be a suitable strategy to protect teeth from continuous destruction [48]. Unfortunately, more studies are still needed to provide evidence of the effectiveness of preventive measures to preserve hypomineralized teeth. Certainly, early diagnosis and dental check-ups at short intervals are favourable for a better management of MIH children [14, 22, 49].

In epidemiological studies based on the DMF index, dentists should be aware that MIH can contribute to overestimate DMF values, once restorative treatment needs of MIH children might be not related to dental caries but to severe enamel breakdown [15, 22]. A follow-up study of first permanent molars since their eruption in order to report if caries lesions often develop in posteruptive breakdown can contribute to better understand the relationship between MIH and dental caries [15].

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Hypomineralized Second Primary Molars

7

Marlies E. C. Elfrink and Karin L. Weerheijm

7.1 Introduction

In the primary dentition, more or less the same characteristics as in molar incisor hypomineralization (MIH) can be noticed (Fig. 7.1a, b) [1]. Although all primary teeth can be affected [2–4] (Fig. 7.2), this MIH-like hypomineralization is most often seen in the second primary molar. For these molars, different names such as cheese five, MIH-d and deciduous molar hypomineralization (DMH) can be found in the literature [5]. Nowadays-in order to make it easier to compare research results—these molars are known by the name hypomineralized second primary molar (HSPM) [1, 6].

As in MIH, an early clinical sign of HSPM is the demarcated opacity (Fig. 7.3). These opacities can have different colours (white to yellow/brown) and appearances (dull or shiny). Hypomineralized second primary molars are defined as 1–4 second primary molars with hypomineralization [7]. The discoloured areas, especially the dull yellow/brown ones, are weaker and therefore more vulnerable not only for loss of enamel after eruption but also for caries [8].

During the clinical examination, the early HSPM signs should be noticed on an early moment in order to help the primary molar survive until exfoliation.

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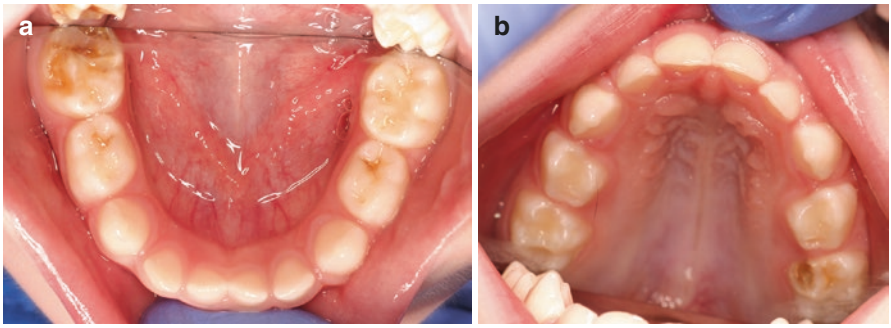

Fig. 7.1 (**a**, **b**) Upper and lower jaw of a patient with HSPM. Notice that not all second primary molars are affected in the same severity. (Photo: JSC Heijdra)

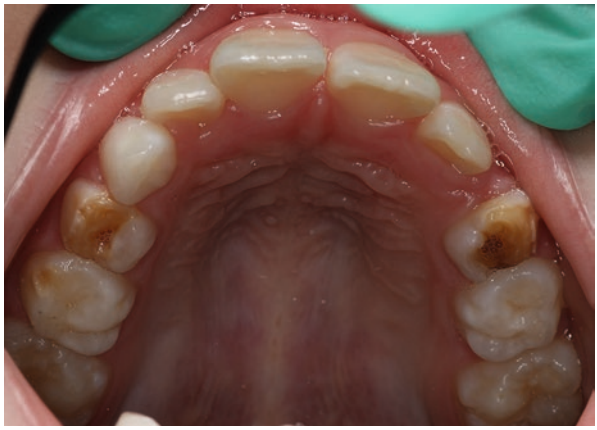

Fig. 7.2 Upper jaw showing hypomineralization defects on the 54 and 64

7.2 Clinical Appearance

The clinical characteristics are comparable to MIH. The signs can be dividing in early and late clinical signs.

7.2.1 Early Clinical Sign

7.2.1.1 Demarcated Opacity

The opacities in HSPM can be white, creamy, yellow or brown in colour. The darker opacities are weaker compared with the lighter ones. Their scoring can be split in white/creamy and yellow/brown. The enamel is of normal thickness, while the surface can look shiny or dull. The surface of the opacity is smooth (Fig. 7.3).

The demarcated opacities in HSPM show a clear border with the sound enamel. The opacities are the most commonly seen characteristic [7, 9] (Fig. 7.4).

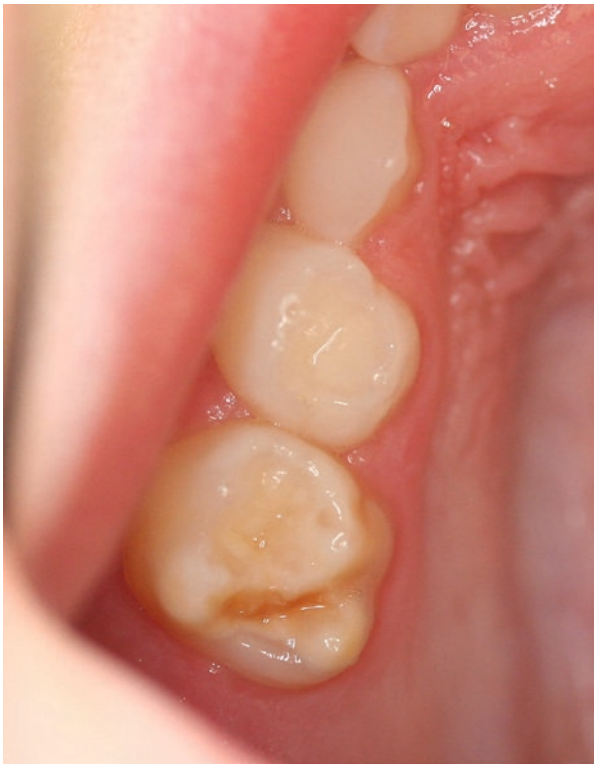

Fig. 7.3 Upper jaw showing white and yellow/brown opacities on the 55

7.2.2 Late Clinical Signs

7.2.2.1 Posteruptive Enamel Breakdown

Initially, formed enamel at the spot of a demarcated opacity is lost, most of time due to chewing forces. This loss of enamel can occur sometimes shortly after eruption and is referred as posteruptive enamel breakdown (PEB). PEB is most often seen at cusps and smooth surfaces (occlusal and palatal in the upper jaw, occlusal and buccal in the lower jaw). The borders of the defect are rough and irregular (Fig. 7.5) [1].

This PEB needs to be distinguished from hypoplasia, which is a quantitative enamel defect. In hypoplasia, the enamel is not originally formed, and the border between the formed and missing parts of the enamel is smooth (Fig. 7.6) [1].

7.2.2.2 Atypical Restauration

The hypomineralized areas are weaker and therefore more prone to caries [8]. In children with HSPM, large restorations can be noticed that does not fit in the usual picture of biofilm-related caries. For example, restorations extended to the buccal or palatal smooth surface, especially in otherwise caries-free mouths (Fig. 7.7) [1].

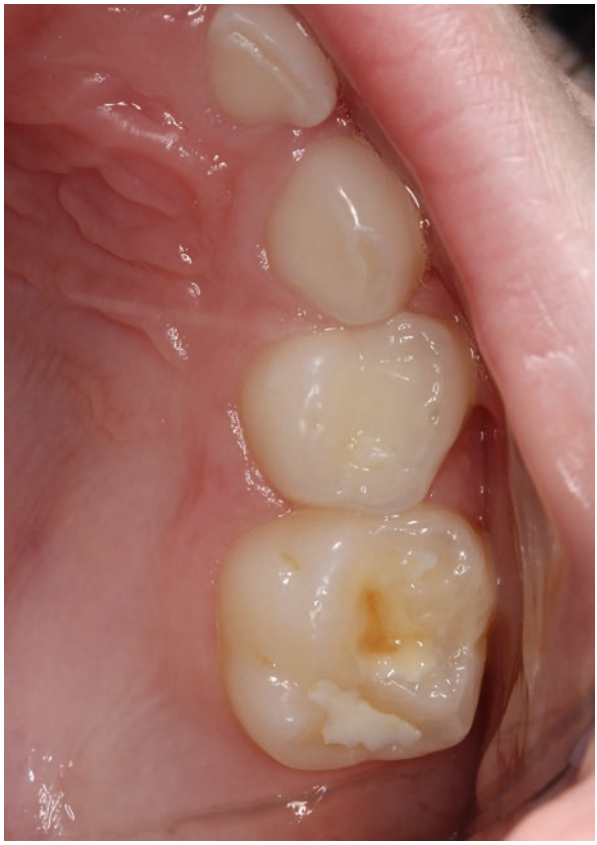

Fig. 7.4 Tooth 65 showing a demarcated opacity and a sealant in the occlusal palatal groove. (Photo: WH Kouwenberg-Bruring)

7.2.2.3 Atypical Caries

The hypomineralized areas are more prone to caries, the enamel in the opacities is weaker and the rough surface of PEB makes that those areas are difficult to clean. The atypical caries due to HSPM does not fit in the picture of biofilm-related caries. Especially with large cavities and caries on smooth surfaces in second primary molars and (almost) caries-free first primary molars, you need to think about HSPM. At the margin of the cavity, an opacity can be noticed in most cases (Fig. 7.8) [1].

7.2.2.4 Atypical Extraction

Sometimes the caries or posteruptive breakdown is very extended, the tooth is infected and the child is in pain, and the hypomineralized molar needs to be extracted. Atypical extraction of a second primary molar can be considered in an otherwise sound dentition and where other second primary molars are diagnosed with HSPM (Fig. 7.9) [1].

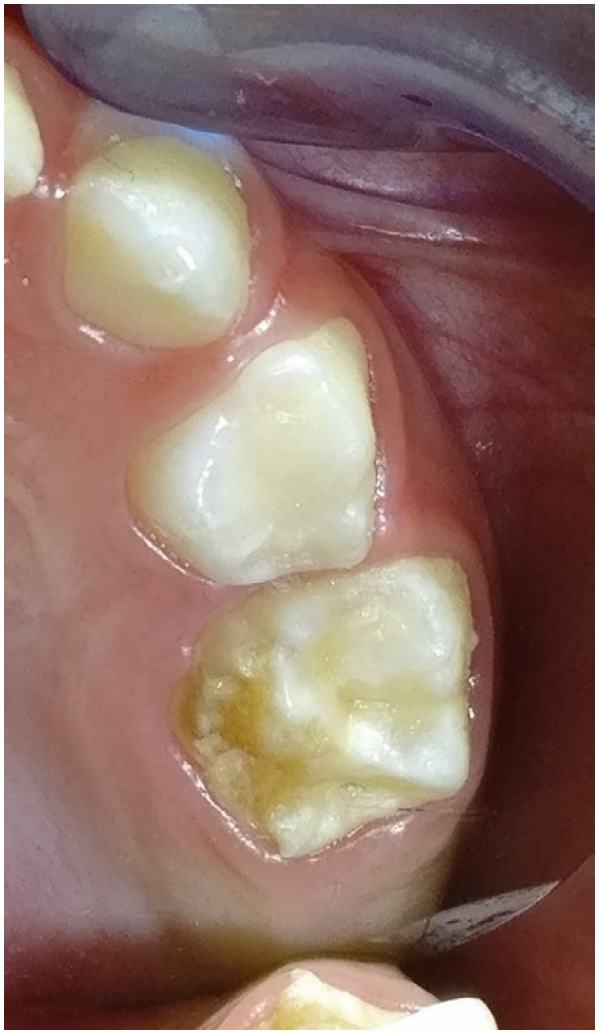

Fig. 7.5 Tooth 65 showing posteruptive enamel loss. (Photo: T. Brethouwer)

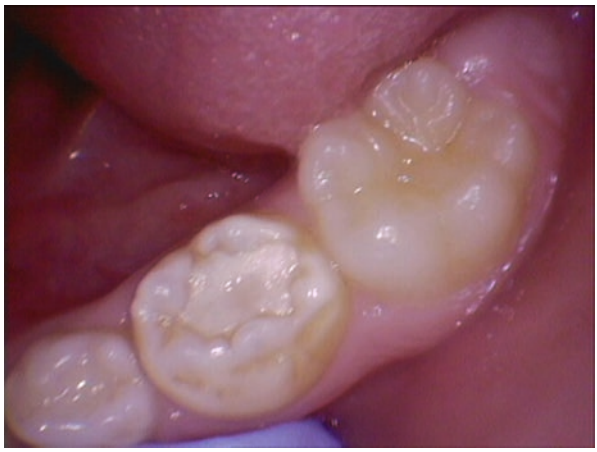

Fig. 7.6 Hypoplasia. Notice the smooth border between the affected and sound enamel

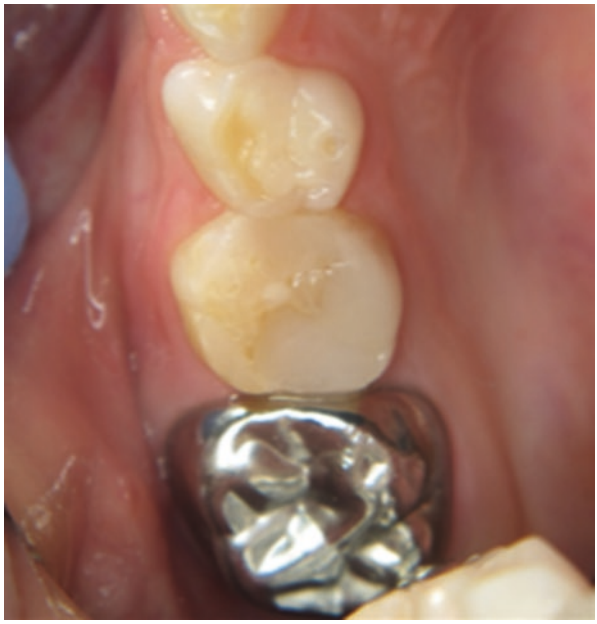

Fig. 7.7 Atypical compomer restauration in tooth 55. The 16 also has an atypical restauration due to MIH

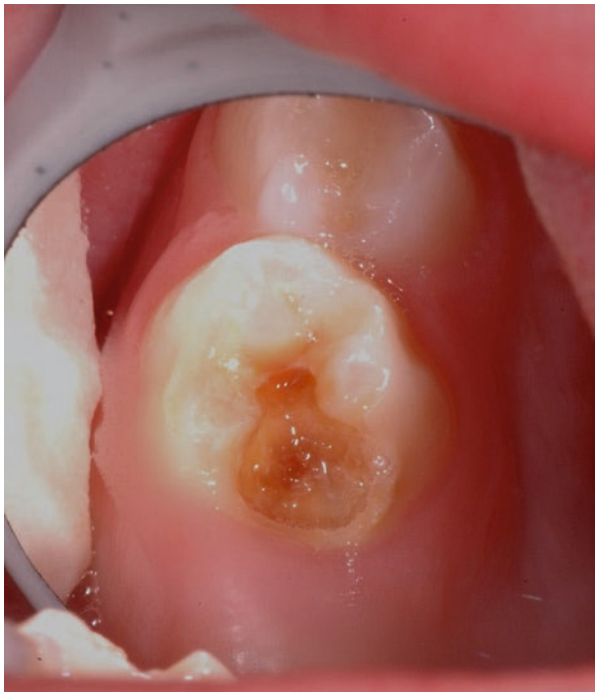

Fig. 7.8 Atypical caries in tooth 75

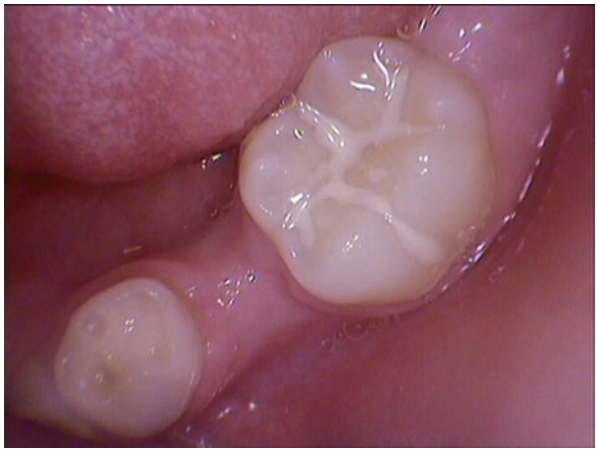

Fig. 7.9 Atypical extraction of tooth 75

7.3 Mineral Content

Hypomineralized permanent molars (MIH molars) showed around 20% lower mineral content in their enamel [10] compared with normal formed enamel. In HSPM molars, the mineral density was also investigated. In the yellow to brown opacities, a lower mineral content of 20%–22% was found when compared with sound primary molars. In white opacities, the mineral content did not differ from normal primary enamel [11].

Insight into the mineral content is important in relation with the choice of restorative material in case the molar needs treatment. Recent studies of MIH-enamel show that adhesion to hypomineralized enamel is limited [12]. More insight into the characteristics of the enamel of HSPM molars is needed to give better answers on which restauration materials be advised to use in which defect.

7.4 Prevalence

Both MIH and HSPM are commonly diagnosed problems. The reported prevalences of MIH are higher than the reported prevalences of HSPM. For both dental anomalies worldwide, figures are available. Only data from North America are missing [6].

There is a lot of variation in the prevalence figures. Partly, this can be explained by existing differences between environmental and genetic factors in the study populations but also by differences in the examination protocols and diagnostic criteria [6].

Many recent prevalence studies use the EAPD criteria and follow the EAPD advices on HSPM- and MIH-research, making the studies better comparable with each other [1, 6].

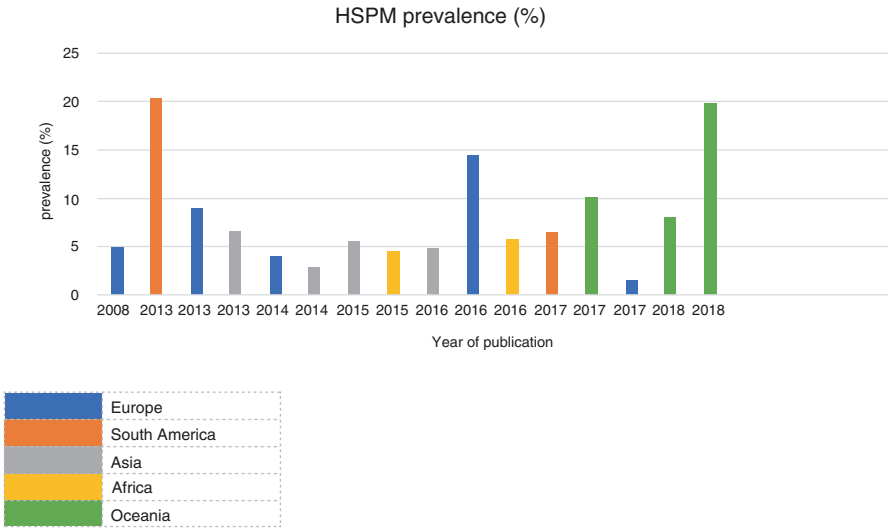

Fig. 7.10 Prevalence figure HSPM

Also, the amount of prevalence studies is strongly increased the last few years. This represents the increasing interest of (paediatric) dentists in HSPM and MIH. At the moment, for HSPM 19 prevalence studies are available [3–5, 7, 9, 13–26]. Three studies were excluded; one study did not use the EAPD index [3], in one a too select group was used [5] and one was based on the same study group as later reported data [9]. In Fig. 7.10, the prevalences of the remaining 16 studies using the EAPD criteria are shown. The overall prevalence of HSPM varies between 1.6% and 20.4% with a weighted average of 7.88%.

7.5 Relation of HSPM–MIH

Because of the similarity in clinical characteristics, a possible relation between HSPM and MIH could be expected (Fig. 7.11). This can raise the question if HSPM could be considered as a predictor for MIH.

The review article of Garot et al. [27] found five articles addressing the relation between HSPM and MIH. The mean odds ratio (OR) was 4.66 in the total group of 4662 patients included in the five studies. All studies used EAPD criteria and were comparable. However, the number of children included in the studies varied considerably: 2327 children were from the study of Elfrink et al. [9] and only 134 from the study of Costa de Silva et al. [13].

Children affected with HSPM have around five more times more chance to get MIH [27]. Especially mild HSPM is considered as a predictor for MIH. The reason for this can be that the etiological factors occur at the end of the vulnerable period of the second primary molar, which cause a mild defect. The first permanent molar

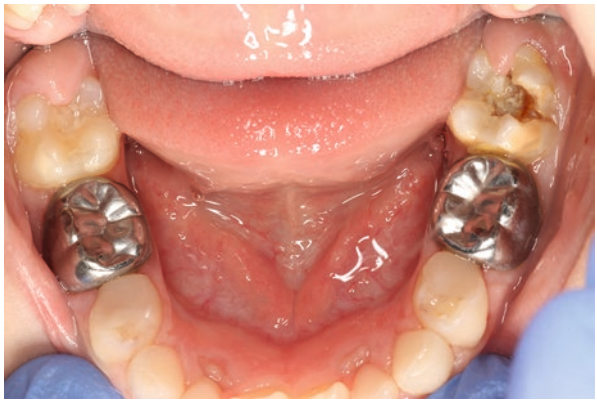

Fig. 7.11 Lower jaw showing 85 and 75 with HSPM atypical restauration and erupting 36 with MIH atypical caries. (Photo: JSC Heijdra)

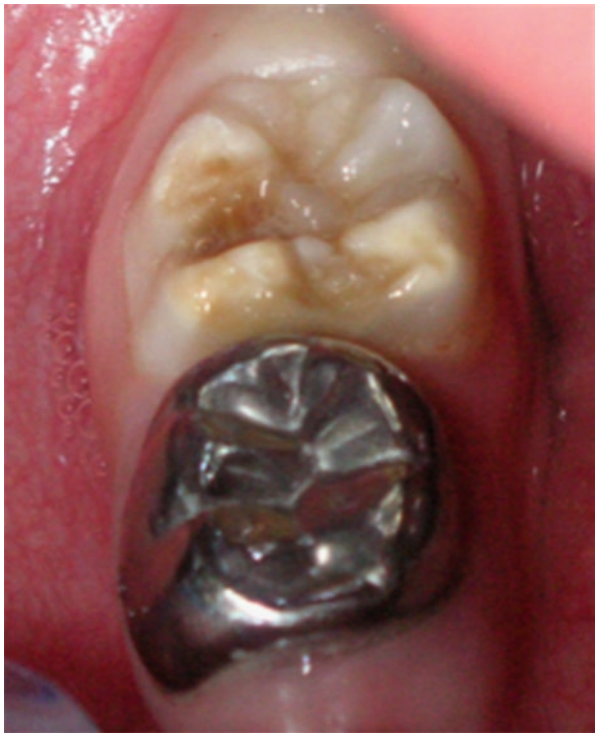

Fig. 7.12 Diagnosis of HSPM (atypical restoration 85) gives an increased risk for MIH (opacity, post eruptive enamel breakdown and caries 46). (Photo: JB Krikken)

is more affected by this etiological factor because it occurs in the beginning of the amelogenesis, affecting very active ameloblasts [27].

Also, more molars affected by HSPM gives a higher odd ratio for MIH [9, 18, 27].

The results of the abovementioned studies indicate that children with HSPM have an increased risk for MIH (Fig. 7.12). Making the diagnosis of early HSPM signs is also important for an early MIH diagnosis.

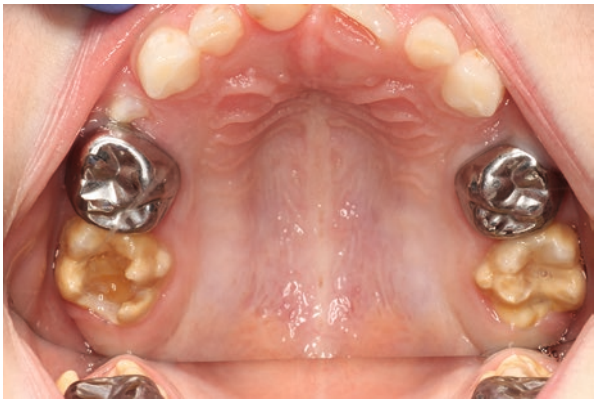

Fig. 7.13 Upper jaw with HSPM and MIH. (Photo: JSC Heijdra)

It is advisable that children with HSPM around the age of erupting of the first permanent molars should undergo clinical examinations more frequently in order to have the possibility for an early MIH diagnosis. Figure 7.13 shows the fast caries progression in a MIH molar in a child diagnosed with HSPM. The first permanent molars of this child are erupted less than 6 months.

7.6 Relation HSPM—Caries

In case of early childhood caries (ECC), teeth show caries in the eruption sequence [28, 29]. However, in many children, especially for children with a low caries prevalence, this pattern is not seen.

The second primary molar has more often caries than the first primary molar [29–35]. The largest difference can be found on the occlusal surface [30, 33]. Tooth anatomy does not seem to be of great importance for this difference [29, 30]. Thus, there has to be another reason, and HSPM was suggested as a reason for this difference [30]. Risk factors related to caries in the second primary molar are country of birth of the mother or the child and HSPM [8, 25].

When HSPM is the main reason for the caries differences, the hypomineralized areas would be found on the most caries-prone parts of the teeth. Most opacities are seen in the occlusal third of the molar, which is in line with opacities being more vulnerable to caries and rapid caries development [25, 30].

7.7 Aetiology

It is hypothesized that the possible etiological factors of HSPM are the same as the ones in MIH, although occurring earlier in life. Numerous factors have been mentioned in the literature for MIH. Pre- and perinatal factors do not seem to influence MIH highly, and they might play an interesting role in HSPM [36, 37]. The possible etiological factors for HSPM can be summarised (see Table 7.1):

Table 7.1 The possible etiological factors of HSPM

Prenatal	Perinatal	Postnatal
Medical problems	Medical problems	Medical problems
Nutrition	Prematurity	Nutrition
		Environmental factors

Table 7.2 Treatment HSPM

Treatment plan	Goal	Intervention
Short term	Pain free Gaining time	Preventive approach
Long term	Function till exfoliation	Preventive approach Adhesive restoration Stainless-steel crown Extraction

The research of Ghanim et al. [37] showed that especially pre- and perinatal factors are important in HSPM. They found medical problems during pregnancy, complications at birth, medical problems at life start, (low) birthweight, duration of breastfeeding and childhood illnesses as potential risk factors. Ethnicity of the child, alcohol consumption by the mother during pregnancy, low birthweight and fever in the first year of life of the child were found as potential risk factors in the study of Elfrink et al. [36]. The greater the amount of medical problems reported, the higher the chance of developing HSPM [37]. The possible association of medication, especially antibiotics and asthma medication, was also investigated, but no association with HSPM was found [14]. No relation was found between the timing of the potential risk factors and the location of the HSPM defect [37].

Recent research also suggests a possible genetic cause of hypomineralization defects. Genetic variation can possibly have an additional effect on the occurrence of hypomineralization [38]. Environmental factors and excessive or deficient nutrient status can have their influence on the occurrence of hypomineralization defects through epigenetics and the change in gene expression without changes in the DNA [39].

The possible association to many different factors (i.e., medical, nutritional and environmental factors) in combination with genetic variation and variation in gene expression makes it difficult to give a clear answer on the cause of HSPM already; thus, more research is needed. For the moment, the aetiology is considered multifactorial.

7.8 Treatment

The treatment strategy for HSPM resembles more or less the treatment of MIH. In both hypomineralization defects, we should focus on an early diagnosis to safeguard the molar in the short-term treatment plan [40]; in HSPM, until the time of exfoliation and in case of MIH until a definitive decision about the long-term treatment can be made (Table 7.2).

Table 7.3 Timing of treatment

Time	Sign	Clinical	Intervention
Primary dentition	HSPM Medical problems	Opacities Atypical caries PEB	Severity related: Preventive Adhesive rest Stainless-steel crown
Eruption FPM	Mild HSPM Medical history Sensitivity	Opacities: Colour Appearance: Spot and size	Preventive 3 monthly check-ups for MIH

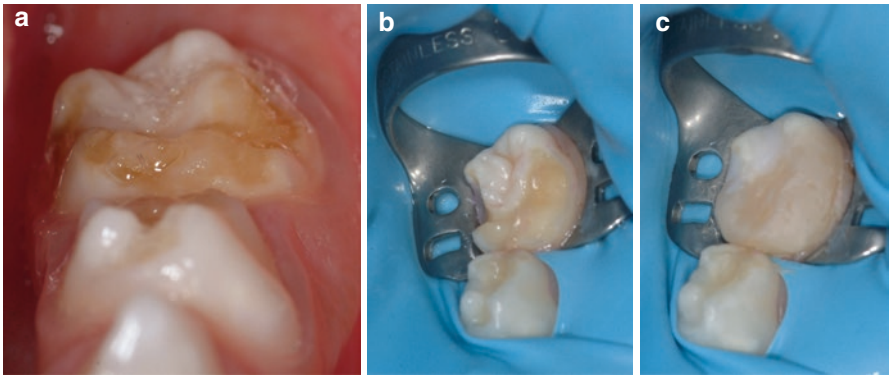

Fig. 7.14 (**a**–**c**) Tooth 75 at start, after preparation and removing all hypomineralized enamel and after restauration

The short-term plan focusses on keeping the child pain free. Therefore, the first intervention should a preventive one: brushing twice a day with a fluoridated toothpaste at home after an oral hygiene instruction, applying CPP-ACP (casein phosphopeptide-amorphous calcium phosphate) (e.g., tooth mousse®) in the evening before bed time (at home) and three monthly local application of a high concentration fluoride varnish (e.g., Duraphat®) in the dental office (Table 7.3) [41].

The next question is: Is a restoration needed, and, if the answer is yes, which restauration is needed?

The decision on whether a restauration has to be placed and which restauration depends on the sensitivity of the tooth, the severity of HSPM and the size of the affected area (PEG, atypical caries) [42].

In most cases, the restoration of first choice for a HSPM molar is a stainless-steel crown. Compomer and composite restorations can be used for small areas that need to be restored. Because the adhesion is less to hypomineralized areas of the enamel, these parts should be totally removed before placing an adhesive restoration [43]. Extraction of the HSPM molar should be avoided, if possible (Fig. 7.14a–c).

7.9 Conclusion

HSPM is, with a mean prevalence of 7.88%, a commonly seen enamel defect. Because of its relation to caries and MIH, it is important to diagnose HSPM early. Focusing on an early HSPM diagnosis is not only of importance for the primary dentition but also for the long-term survival and/or treatment option of MIH molars.

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8 Knowledge, Experience and Perception Regarding Molar Incisor Hypomineralization

Aghareed Ghanim and Karla Gambetta-Tessini

8.1 Introduction

In the past, when dental caries experience of children was particularly high, the phenomenon of hypomineralization typically went underdiagnosed [1]. Decades later, caries experience has declined in many children, leading to a focus on the prevalence of molar incisor hypomineralization disorder (MIH). There has been growing interest and research in MIH since its formal recognition in 2001 [1]. The prevalence rates vary from 2.4% to 44%, highlighting the vast disparity in the reported prevalence rates across the world, the result of a lack of internationally utilized and reliable criteria for diagnosing MIH and hypomineralized second primary molar (HSPM) [2, 3]. For HSPM, prevalence ranges between 0% and 21.8% [2]. It is reported that people at increased risk of dental caries affected by MIH or HSPM have worse outcomes regarding carious lesion development, and the condition negatively impacts their quality of life [4–6].

Recently, a new index has been developed to be used for the diagnosis of MIH/HSPM [7]. Compared with the previous criteria and indices, the MIH/HSPM index combines the principles of the European Academy of Paediatric Dentistry (EAPD) judgment criteria and modified index of developmental defects of enamel (mDDE) in order to grade the clinical status, amount of tooth surface area affected and other enamel defects comparable to MIH [7]. The new index aims to minimize misdiagnosis of MIH/HSPM, is available for a wide range of ages to explore the prevalence of MIH/HSPM and determines the prevalence changes over time. A training module

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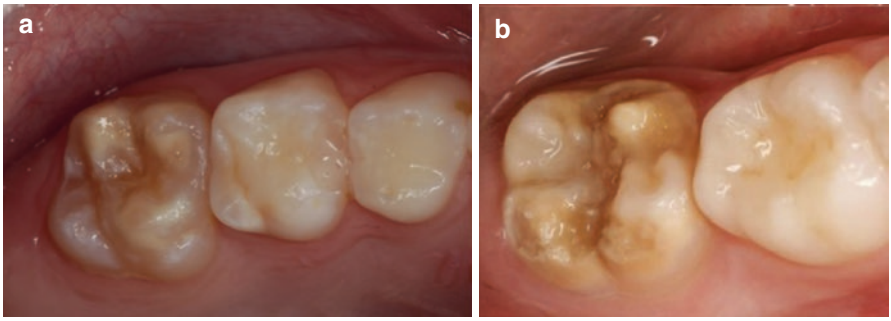

Fig. 8.1 Demarcated opacities and post-eruptive breakdown in MIH-affected molars

was developed to assist researchers in implementing the index in a standardized manner [8]. Several researchers are using/have used the index [9–14], and its properties, in terms of validity and reproducibility, have been tested. The index demonstrated adequate reliability and validity to be used for clinical assessment [15].

MIH/HSPM teeth present clinical challenges for the young patient and clinician alike. Severe hypomineralization may lead to discomfort and sensitivity for the child, which compromise normal function and oral hygiene [16–18]. Simple tasks involving mechanical stimuli to the affected teeth, such as toothbrushing, as well as air and water current, warm or cold, can lead to sensitivity and pain (Fig. 8.1) [19]. Affected children may need multidisciplinary management, including a general dental practitioner, paediatric dentist and orthodontist [20]. The long-term prognosis of affected teeth must be considered and discussed with the child and parents, and all the other associated clinical issues must be managed [18], for instance, tooth sensitivity, post-eruptive enamel breakdown (PEB) with dentine exposure, increased carious lesion susceptibility, aesthetic issues and potential early loss of first molar teeth [17, 20–22].

8.2 Dental Community Awareness

8.2.1 Knowledge Regarding Treatment

Global knowledge regarding hypomineralized teeth, particularly MIH, has been restricted to the paediatric dentistry context for a long time. Most laboratory findings regarding protein content, mineral density, microscopic appearance and physical properties of hypomineralized enamel have been published in many scientific journals, but they lack descriptions of the clinical applicability of the results [11]. Relevant information has been delivered through congresses and journals affiliated with paediatric dentistry societies [11]. However, most of the time general dental practitioners (GDPs) are in primary contact with paediatric patients or have to treat patients with severely affected teeth, presenting hypersensitivity or vast areas of enamel breakdown owing to hypomineralization.

Despite the fact that the amount of research concerning MIH has increased greatly over the past decade, GDPs still have limited understanding of the appropriate management of hypomineralized teeth. Norwegian general dentists appeared to be avoiding invasive treatment options such as extractions, and total removal of hypomineralized dental tissue was preferred by very few GDPs [23]. Evidence shows that not only GDPs but also final year dental students have reported limited knowledge, particularly regarding clinical management of hypomineralized teeth, as their clinical experience may be limited [24, 25]. Nevertheless, recent studies demonstrated that GDPs and paediatric dental specialists have selected resin composite as their preferred material for restorative treatment [26, 27], which could be indicative of increased awareness about this topic amongst GDPs. Other GDPs have reported many barriers to treatment of affected children, such as the lack of training with respect to MIH, increased pulpal sensitivity, child behaviour management challenges, premature failure of restorations and unpredictable enamel breakdown [28–33].

Oral health therapists (OHTS) have been reported to receive more information regarding MIH which also increases knowledge and awareness. However, a large number of OHTs mainly rely on glass ionomer cement (GIC) as a restorative material exclusively [31, 34]. This may be controversial, as the use of GIC in large hypomineralized lesions is considered as an interim treatment by many and advocated to reduce sensitivity and to prevent PEB in an attempt to 'stabilise' the tooth [17, 35, 36]. Training and competencies of OHTs are not sufficient to provide all restorative care necessary in severely MIH-affected children, such as preformed metal crowns (PMC); however, they feel a high level of confidence when diagnosing and treating affected children, and most importantly, they refer them to specialists for further treatment at early stages of the condition [34]. Early diagnosis and prevention of breakdown are key elements in managing MIH [37]. Medium-term and long-term treatment options for MIH teeth should include direct resin composite restorations, cast restorations, extractions and placement of PMC [18, 35, 38, 39]. Not surprisingly, the utilisation of PMC is more frequent among paediatric dental specialists than general practitioners [34, 40, 41].

8.2.2 Knowledge Regarding Prevalence and Aetiologies

Dental professionals consider MIH as a relevant clinical problem, but are still unsure about the prevalence in their communities (Table 8.1) [26, 27, 30, 31, 32, 42]. An overwhelming majority of GDPs have recommended that investigating the prevalence of MIH would be worthwhile [27, 34]. Most importantly, a significant number of GDPs perceived that the prevalence of MIH is increasing [26, 28–31, 43]. The difference in prevalence reported by GDPs from different communities could also be associated with the decreasing caries experience. Unfortunately, it is not possible to corroborate this hypothesis, as longitudinal epidemiological information of MIH and its association with dental caries is scarce worldwide.

Table 8.1 Comparison of results amongst previous studies on the dental professionals' perspectives on MIH

Authors	Year	Country/ continent	Sample and participants	Familiarity with MIH	Estimated prevalence of MIH	Preferred restorative treatment	Clinical barriers for treatment	Receiving information about MIH
Weerheijm and Mejare	2003	Europe	EAPD members ($N = 54$)	97%	3.6%–25%	NR	NR	23%
Crombie et al.	2008	Australia and New Zealand	ANZSPD members ($N = 130$)	98%	5%–25%	GIC	NR	17%
Biondi and Cortese	2009	South America	PDs, DAs ($N = 31$)	94%	NR	NR	NR	13%
Ghanim et al.	2011	Iraq	DAs ($N = 146$)	81%	6.3%–17.2%	NR	NR	NR
Bagheri et al.	2013	Iran	DAs ($N = 84$)	86%	< 10%	RC	NR	NR
Hussein et al.	2014	Malaysia	GDPs, DNs ($N = 131$)	82%	< 10%	GIC	Child behaviour insufficient training	7% - 23%
Kopperud et al.	2016	Norway	PGDPs ($N = 606$)	NR	NR	GIC	Patient anxious achieve LA	NR
Silva et al.	2016	Saudi Arabia	DS, GDPs ($N = 240$)	36%–77%	5%–10%	RC	Child behaviour	36% - 41%
Gambetta-Tessini et al.	2016	Australia and Chile	PGDPs ($N = 232$)	89%	5%–10%	GIC	Insufficient training	52%
Kalkani et al.	2016	UK	GDPs, PDs (trainees) (N = 68)	NR	NR	NR	Sensitivity child behaviour	NR
Yousif	2017	Australia	DS	96%	NR	GIC, PFM	Durability of restorations achieve LA	NR
Alanzi et al.	2018	Kuwait	KDA members ($N = 221$)	94%	10%–20%	RC	Child behaviour	65–83%
Upadhyay et al.	2018	India	PDs, GDPs ($N = 393$)	96%	PDs 10%–20% GDPs <5%	RC, PFM	Durability of restorations	NR
Tagelsir et al.	2018	USA	AAPD member ($N = 251$)	Almost 100%	<10%	PFM, RC	Durability of restorations	NR

MIH molar incisor hypomineralization. *EAPD* European academy of paediatric dentistry, *ANZSPD* Australia and New Zealand society of paediatric dentistry, *PDs* Paediatric dentists, *DAs* dental academics, *GDPs* general dental practitioners, *DN* dental nurses, *PGDPs* public general dental practitioners, *DS* dental students, *KDA* Kuwait dental association, *AAPD* American Academy of paediatric dentistry, *UK* United Kingdom, *GIC* glass ionomer cements, *RC* resin composite, *PFM* preformed metal crowns, *LA* local anaesthetics, *NR* not reported
N = number of participants

The current evidence supports a multifactorial causative theory of MIH defects, and specific aetiological factors have not been elucidated [22, 29, 44–46]. Most GDPs believed that childhood or maternal chronic and acute medical conditions were involved in the aetiology of MIH, supported by numerous investigations indicating a variety of health conditions as risk factors for MIH [45, 47, 48]. Most GDPs do not consider fluoride consumption as an important factor in the aetiology of MIH and recognize MIH as a defect distinct from fluorosis and hypoplasia [28, 29, 31, 42, 43]. Despite the amount of literature regarding the genetic influence being limited, the link between MIH and a genetic expression is also apparent [49]. Dental practitioners have recognized a genetic component as a possible aetiological factor for MIH [29, 31].

8.2.3 Training Aspects

An identified barrier to awareness is the limited delivery of accurate updated information across the dental community. Dissemination of information amongst dental professionals has been limited to MIH evidence, with little attention paid to the impact of enamel hypomineralization on the caries experience and involvement of other permanent or primary teeth [11]. Many dental professionals have reported that they are not aware of the prevalence of MIH, requiring further training in the aetiological, diagnostic and therapeutic areas [28, 29, 34]. For example, GDPs from Latin America reported limited knowledge regarding prevalence and clinical management, demonstrating that they are less confident when diagnosing and treating MIH-affected children [34]. Few studies have determined the level of recognition of hypomineralization in the primary dentition amongst dental professionals, with practitioners reporting its occurrence with a lower frequency compared to first permanent molars [28, 29, 32, 34].

Insufficient training and lack of information regarding current evidence about MIH may affect the management of children with MIH. It is expected that dental professionals develop the ability to have life-long learning to search out answers and solve problems using evidence. However, many GDPs have reported not receiving adequate information [29, 34]. It is important that health authorities and research centres consistently and effectively disseminate scientific evidence and provide clinical management guidance for GDPs. This may help to decrease the treatment burden associated with MIH in the future [29]. It is essential to expand the availability of MIH information not only to those professionals who are specialists (e.g., paediatric societies, paediatric dentistry postgraduate students and dental academics) but also to those practitioners who are in the position to diagnose this condition initially. Information and education on MIH should be discussed similarly across all oral and medical health professionals, as associated risk factors include common childhood illnesses (e.g. fever episodes) [11, 49]. Continuing education programs might disseminate MIH knowledge and clinical management amongst dental professionals to increase confidence when diagnosing and treating children with MIH. This information should be also extended to the consumer/community, and an

increased awareness will lead to early attendance for dental examination and early management of MIH-affected teeth before PEB occurs or ensuring timely extraction of severely affected teeth.

Establishing the perceptions and clinical conduct of health practitioners relating to MIH seems essential to orientate local health authorities regarding the dissemination and inclusion of scientific information and evidence into the clinical guides. The inclusion of up-to-date evidence in the guidelines, particularly in regard to MIH definition, prevalence, aetiology and clinical management, may support practitioners in their decisions and increase their awareness and understanding about MIH [50].

8.3 Conclusions

Over the last 13 years, studies have been conducted in a range of countries that evaluate the perceptions and knowledge of practicing clinicians regarding MIH; however, considerable variation in knowledge and perceptions exists. Across all the studies, the majority of the clinicians surveyed were familiar with MIH or had encountered MIH in practice, but few knew the prevalence of MIH. The disparities in the reported prevalence of MIH across these studies highlight the need for valid and reliable international criteria for diagnosis. Effective management is contingent on understanding of the MIH disorder and the severity of the condition. Treatment planning needs a preventive basis, and management plans must be individualized, with the clinician weighing up the advantages and disadvantages of different restorative options. Management of MIH-affected teeth is inherently unpredictable, and more research is required. However, comprehensive, evidence-based treatment planning that considers the long-term prognosis can improve patient outcomes.

Education programs for oral care providers should include training in identifying and diagnosing demarcated lesions for the purpose of optimal management. Increasing oral health professionals' knowledge base about MIH causative factors is the ideal springboard for decreasing the incidence of the defect. Although it is recognised that knowledge itself is not sufficient to reduce the defect occurrence; accurate knowledge and information is necessary for the oral health professionals to identify the problem and to decide on the best treatment options.

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Part III

Treatment Approaches

9 Treatment of Children with MIH: A Challenge in Pain Control and Behaviour Management

Richard Steffen

9.1 Introduction

Since the term molar incisor hypomineralization (MIH) was defined in 2001, the many publications on this topic have largely dealt with the aetiology and prevalence of this disease [1, 2]. Just as often, publications are pointing out the difficulty of distinguishing MIH-affected teeth from other structurally damaged and carious teeth [3–6]. Significantly less publications are dealing with the therapy, with most of them only giving a theoretical overview of how teeth affected by MIH can be treated [7, 8]. Preventive, regenerative and restorative treatments are recommended in mild MIH cases, and preventive, regenerative, temporary restorative approaches or extraction followed by orthodontic treatment modalities are recommended in severe cases [7]. William and co-workers distinguish between younger and older children in the treatment of MIH-affected patients, and they also mention the need for good patient management and pain control, but how this pain control should be executed was not explained [9]. In the literature, the difficulties about successful and sufficient local anaesthesia of MIH teeth are only marginally discussed [10–12]. For practitioners in paediatric dentistry in daily practice, however, this is a major problem, especially when it comes to a treatment of younger patients which have already a history of chronic pain and, which is the worst, associated caries at these MIH molars. MIH-specific pain control and a special treatment protocol therefore is indispensable (Fig. 9.1).

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Fig. 9.1 Although no treatment has been performed by the dentist yet, tears are already running down the face of this child with MIH teeth. He will cooperate, but the pain memory is already reporting warning signals based on experience

9.2 Pain and Children

9.2.1 Definition of Pain and Fear

Pain is a stimulus-induced, subjective feeling of discomfort. The intensity is influenced not only by the strength of the stimulus but also by gender, age and former pain experience. Social origin, religion and philosophical attitudes also play a role in the perception of pain. Stimuli are triggering pathophysiological processes that produce pain perception. There is a distinction between acute and chronic pain. While acute pain is ending by self-limitation, chronic pain persists for months and years [13].

Fear is a more or less strong, vague feeling of discomfort, concern or threat. Anxiety in children is, among other things, influenced in its manifestation and target projection by the developmental age, the social environment and the unpleasant initial experiences. Without the help of the social environment (coping strategies, direct help), sometimes children fears are triggered by pain can become chronic persistent fears [14, 15].

9.2.2 Peculiarities of the Child's Perception of Pain

Depending on the age of the child, very specific problems arise with childlike pain. Contrary to long-standing claims, children of all ages have experience with pain. Typical problems with pain perception of children are limited by the ability to communicate, by cognitive problems with the allocation of pain, by a lack of

experience and by an incomprehensible social environment, which also has a strong effect on the pain memory [14, 16].

9.2.3 MIH-Induced Pain

Pain induced by MIH-affected teeth usually manifests at the earliest when the hypersensitive MIH tooth erupts. In the child's psyche, a transition from a "magical" world view to a "more realistic" picture takes place between the ages of 5–6 years. MIH experiences of pain therefore usually influence this transition period and affect the understanding of pain of these children. Childlike experiences, such as inexplicable pain in the mouth, are difficult for the children to put into the right context without help and understanding of the social environment [4, 14].

In a large part of the severely hypoplastic first molars, constant more or less strong chronic pain sensations are described on these teeth from the eruption onwards [17]. In addition to spontaneous enamel breakdown with perhaps additional rapidly progressing caries, the strong hypersensitivity of the MIH molars is a leading symptom of MIH [4, 9, 18]. Therefore, hypersensitivity has been implemented as one of the two main factors of the MIH-treatment need index (MIH-TNI) (see Chap. 2) (Fig. 9.2).

The consequences of a chronic hypersensitivity are often major restrictions in oral hygiene, problems with the intake of cold and warm food, chronic pain and sudden anxiety episodes during the day and simultaneously a clearly limited ability to cooperate with the dental treatment (Fig. 9.3).

Dentists repeatedly report that with hypersensitive MIH molars, a painlessness dental treatment is very difficult or even impossible to achieve. In clinical everyday

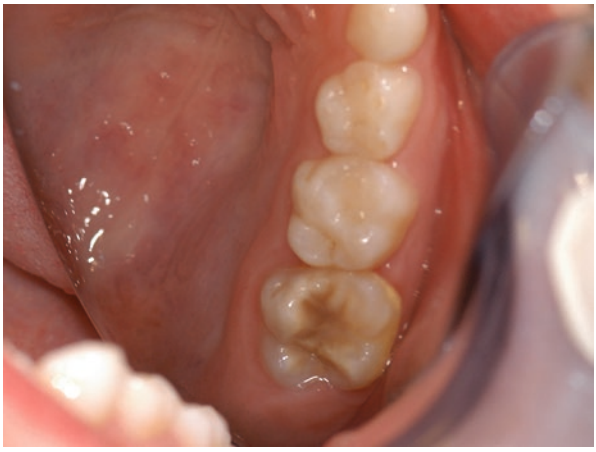

Fig. 9.2 A 7-year-old and 6-month-old caries-free child with MIH-TNI 3 without enamel disintegration on tooth 26. Despite good oral hygiene overall, only limited brushing is possible on this MIH tooth

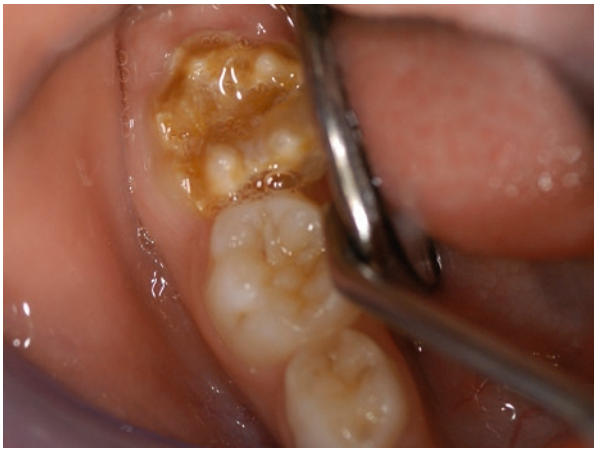

Fig. 9.3 A 7-year-old and 2-month-old child with severe MIH, enamel disintegration and associated caries on tooth 46, whilst all other teeth have no caries. Oral hygiene is almost impossible with this hypersensitive MIH tooth, and any intake of cold or warm food is painful

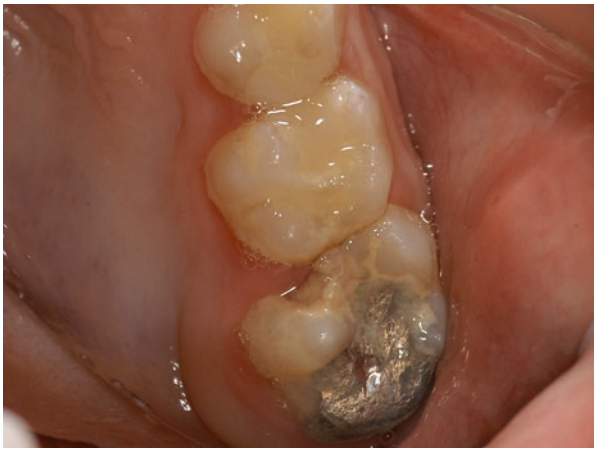

Fig. 9.4 A 7-year-old and 1-month-old child with severe MIH. Despite several treatment attempts, tooth 26 is still insufficiently treated, and adequate oral hygiene is still not possible due to hypersensitivity. Here even an experienced dentist has been helpless

life, treatment sessions with MIH teeth often have to be interrupted, and because of the ineffective anaesthesia, despite repeated and high-dose local anaesthesia application, sufficient pain reduction could not be achieved [10, 11]. A Greek study showed that MIH molars are as worse restored the more severe the hypersensitivity of the treated MIH teeth was [19] (Fig. 9.4).

The cause of this hypersensitivity appears to be chronic pulp inflammation. The porous hypomineralized enamel and dentin layers do not sufficiently protect the pulp tissue of hypoplastic teeth against the permanently occurring physical, chemical and thermal stimuli in the oral cavity. This phenomenon occurs almost exclusively in the first permanent molars, primary molars are rarely affected and incisors almost never [6] (Fig. 9.5).

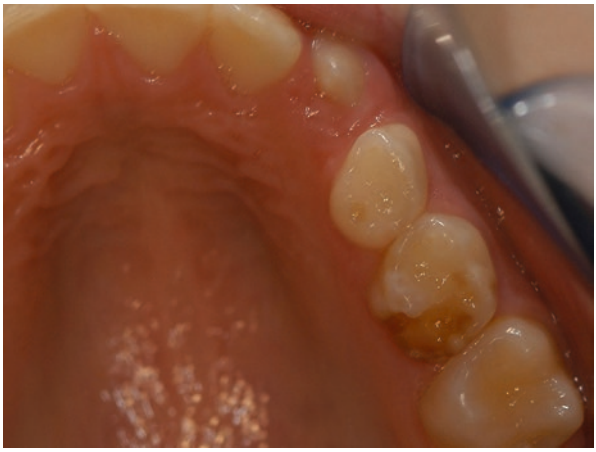

Fig. 9.5 A 10-year-old and 11-month-old child with a hypomineralized upper second primary molar; the tooth additionally shows caries but no signs of hypersensitivity

Fig. 9.6 Behaviour management: Joint training of patient and dentist of the stop signal

9.3 Basics of Child Treatment

9.3.1 Behaviour Management Control and Treatment Protocols for Children with MIH

Treatment protocols adapted to children and protocols for behavioural management are basic prerequisites for the successful treatment in paediatric dentistry (Fig. 9.6). In addition to the classical tell-show-do technique, there are other methods to influence the psyche of the younger patients. Classical conditioning, positive reinforcement, distraction and attention control, systematic desensitization and cognitive modelling are just a few of them [2, 20]. However, these techniques are very sensitive to disturbing additional factors [15, 21]. The social environment, especially

parents and educational supervisors, have a very large influence on the effectiveness of our behaviour management techniques. Invasive techniques such as active restraint, voice control with coercion (e.g., hand over mouth technique) and corporal punishment, also by parents [15, 22], all have a negative mental impact, and therefore these are absolutely not recommendable for paediatric dentistry.

9.3.2 Key Moments for a Painless Clinical Examination and Treatment of Hypersensitive MIH Teeth

To achieve a comprehensive and as perfect as possible painless dental clinical examination and build on that a traumatic treatment for a child suffering from chronic painful MIH teeth, it is a basic prerequisite to follow these recommendations:

- Painless examinations and confidence-building measures.
- Local anaesthesia: Intraoperative pain control as perfect as possible.
- Premedication in cases where local anaesthesia alone is not sufficient.
- Postoperative pain control.
- Additional sedation for children, which have developed deep unconscious fear.
- General anaesthesia in cases with bigger and unpleasant interventions (i.e. multi extractions).

9.3.3 Everything Starts with a Painless Examination

Starting with the initial examination, MIH-affected teeth must be treated with caution. If necessary, the teeth may only be dried with cotton wool rolls and thermal stimuli, such as cold instruments, warming surgical lamps or air syringe must carefully be taken into account and perhaps their use must be dispensed with altogether (Fig. 9.7). For children who already have had experienced painful episodes during

Fig. 9.7 Auxiliaries for drying hypersensitive MIH teeth, during examinations without air blower insert

former dental check-ups, confidence-building measures may be necessary at this stage. Greatest possible pain control in all dental interventions provides us with the basis for successful treatment of traumatised MIH patients [20].

9.3.4 Local Anaesthesia, Special Technics and Optimized Equipment

Difficult successfully applied anaesthesia of chronically inflamed MIH molars has turned out to be a serious clinical problem [11, 18]. In the literature, there are no publications about the frequency of anaesthesia failures in MIH teeth, but before the introduction of a MIH-Optimized anaesthesia technic in our clinic, up to 50% of the hypersensitive molars to be treated were affected by insufficient local anaesthesia. Following our clinical experience, there also seems to be a linear relationship between the strength of hypersensitivity of MIH teeth and the frequency of anaesthesia failures.

9.3.4.1 Local Anaesthesia in Children

For any restorative treatment, the sensation of hypersensitive MIH teeth must be controlled by effective local anaesthesia. Suitable local anaesthetics block the Na ion channels for Na^+ and lead to a reversible pharmacological elimination of the pain receptors and pain conduction. This process is clearly impaired in chronic hypersensitive MIH teeth. Local anaesthetics must be selected according to the general medical condition, the desired duration of action and depth of anaesthesia. Today, articaine (4%) with a small amount of adrenaline (epinephrine) is mostly used as an anaesthetic [23]. Articaine is available in three formulations: Ultracain® with an epinephrine addition of 1:100,000, 1:200,000 or 1:400,000. All three formulations can be used in children with hypersensitive MIH teeth [23]. The proportion of the vasoconstrictor does not lead to a better depth of anaesthesia but above all has an influence on the duration of the anaesthesia. Thus, for MIH children, concentrations of epinephrine in the dilution of 1:400,000 can be used, and therefore we can achieve a lower systemic load due to epinephrine. Instead, the dose of articaine may be higher than in "normal" not chronically inflamed teeth. Without doubt, it is very important to maintain the individual daily maximum dose, which depends primarily on body weight and not only on the age of the child to be treated. Important note:

For children, the recommended daily dose is 5 mg/kg [23].

Adverse drug reactions in children occur very rarely and are usually caused by neglecting the dosage guidelines.

9.3.4.2 Optimized Clinical Anaesthesia Technique

Needles with a counter-section, which are very a-traumatic and a deliberately slow injection technique are especially important for a painless local anaesthesia. All normally used local anaesthesia forms can be used in MIH-affected teeth, but the effect of the anaesthetic is faster due to the more permeable childlike compacta. Basically, sufficient infiltration anaesthesia is usually both in the upper and in the lower jaw. To

Table 9.1 Conventional and special anaesthesia techniques to eliminate pain in hypersensitive MIH teeth

Conventional anaesthesia techniques	Description	Useful for MIH
Terminal anaesthesia	Injection of a local anaesthetic into the submucous tissue as close as possible to the bone and the tooth to be anaesthetized	Yes, with partially insufficient effect on hypersensitive MIH teeth
Anaesthesia with nerve block	Injection of a local anaesthetic near a peripheral nerve trunk	Yes, with partially insufficient effect on hypersensitive MIH teeth
Intraligamental anaesthesia	Injection of a local anaesthetic into the periodontal ligament	Yes, with partially insufficient effect on hypersensitive MIH teeth
Intraosseous injections	Rotating needle systems or special drills used to provide access through the bone compacta for infiltration anaesthesia	Yes, with almost no inadequate anaesthesia

anaesthetize the puncture site, a depot is first placed, and then the required amount of local anaesthetic is infiltrated very slowly. The better permeability of the child's jaw structures also allows the use of special anaesthesia techniques [23].

Table 9.1 gives an overview of the common types of local anaesthesia.

9.3.4.3 Optimized Technical Equipment

It may be advantageous to anaesthetize MIH molars using the CIA technique (crestal intraosseous approach technique) instead of a conventional anaesthesia. This technique is particularly atraumatic and effective especially when performed using a computer-controlled injection system.

The STA Wand® Plus is a pen-like electronic anaesthesia system, and the infiltration of the local anaesthetic is computer controlled. Because of its extra thin needle, the anaesthesia is less painful, and the device does not look like a classic syringe. The anaesthetic is administered drop by drop either in the slow-flow method, in which a drop of the local anaesthetic is administered every 2 s and is particularly suitable for single-tooth anaesthesia, or in the fast-flow method, in which the anaesthetic is administered within double speed. The infiltration speed and the very effective automatically aspiration of the injection system can be controlled by a foot pedal. The conventional nerve block and infiltration techniques both are suitable as anaesthesia methods. Infiltration especially with the CIA technique has less effect on the soft tissues, which may be of great benefit to children. Because the Wand® system uses the porosity of the bone, individual teeth can be anesthetised more precisely, and nerve block anaesthesia is therefore less necessary (Fig. 9.8).

The QuickSleeper® device (Dental Hi Tec. Cholet, France) uses a particularly well-cutting needle with the help of a special application handpiece first cutting and then rotating for intraosseous anaesthesia.

The system allows controlled injection through the cortical bone of the local anaesthetic into the more permeable cancellous bone of the alveolar process.

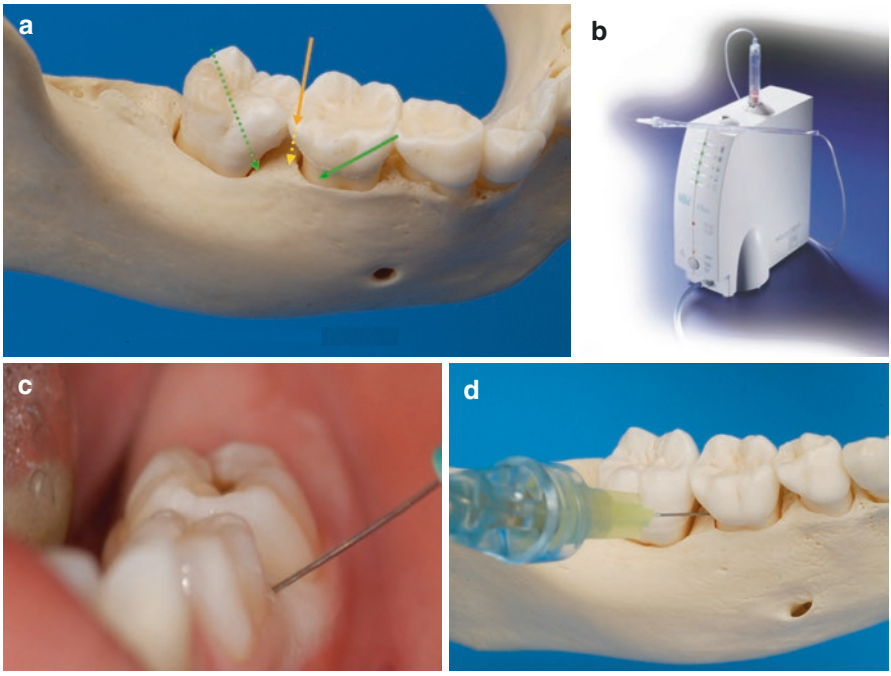

Fig. 9.8 CIA injection method (**a**, **c** and **d**) using the computer-controlled injection device STA Wand (**b**)

The Quickspleeper can be compared to the STA Wand system, but is superior in that it does not use a cost-intensive disposable handpiece, but normal dental injection needles or special DHT needles (Dental Hi Tec). The disadvantage, however, is a somewhat chunkier handpiece.

The DHT needles make it possible more to cut than to perforate the mucosa, with that more gently than more sharply. By applying the local anaesthetic to the alveolar bone near a hypersensitive MIH tooth, deeper and much more reliable anaesthesia is achieved with less anaesthetic and therefore less toxic load.

The QuickSleeper is currently the only computer-controlled device on the market that enables with a rotating needle a targeted perforation through the cortical bone, so that even MIH molars, which are difficult to anaesthetise, can be treated repetitively well (Fig. 9.9).

9.4 Premedication

It is likewise a great help to treat children with hypersensitive MIH teeth with an analgesic premedication before an upcoming treatment. For a real painless MIH treatment protocol, it is sometimes crucial to take premedication with selected analgesics into account. Such a treatment protocol is based on the findings in the

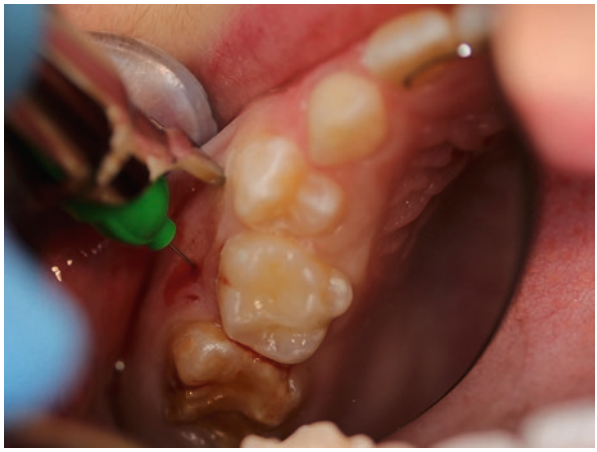

Fig. 9.9 Quicksleeper intraosseous injection system, at the moment when the corticalis is perforated at region 16

treatment of patients with chronic back pain. Premedication allows better to push a chronic inflammatory condition below an acute threshold [24].

The MIH premedication protocol differs significantly from conventional analgesia and is based on the following principles:

- The use of the most effective analgesic for premedication.
- Very high but short-term dosage of analgesic medication (1–2 days).
- Targeted effect of the prestaggered analgesic to repress chronic pain (between 48 and 24 h before dental treatment).
- Long-term and too much repetitive analgesic treatment cycles (more than 3–4, max 2–3 days) doses must be avoided at all costs [24, 25].

If there is any doubt about the dosage of analgesic medication, then for further help, specialists (i.e., paediatricians) should be consulted about the dosage and type of medication that should be used.

Drugs used for premedication and postoperative pain control are usually the same. In addition to the analgesic effect, an anti-inflammatory effect is also desirable in MIH premedication [25].

From the large selection of established drugs for pain relief, the following analgesic substances are available and can be used for premedication in MIH (Table 9.2).

This list only gives a brief overview, is incomplete and does not contain any conclusive therapy recommendations. Decisions as to which drugs should ultimately be used for the analgesic premedication of MIH children must always be made according to the current state of pharmacology [25].

9.5 Postoperative Pain Control, Medication After the Treatment

A special postoperative pain control is usually not necessary with any selected medication. In the case of particularly painful procedures (e.g., extraction of the 6-year molars), the analgesic already administered for premedication can be scheduled a little longer.

Table 9.2 Special intraosseous anaesthesia techniques, their application and advantages in treatment of hypersensitive MIH teeth

Special intraosseous anaesthesia techniques	Application	Advantages for hypersensitive MIH teeth
CIA: Crestal intraosseous approach	45° angle from buccal under interdental papilla (into cancellous bone) or root furcation	Little pain, high reliability, little soft tissue anaesthesia
PASA: Palatal anterior superior alveolar nerve block	45° angle from palatal into the palatal mucosa at the level of the incisors	Little pain, high reliability, little soft tissue anaesthesia
AMSA: Anterior middle superior alveolar nerve block	45° angle from palatal into mucosa at the level of the first premolars	Little pain, high reliability, little soft tissue anaesthesia

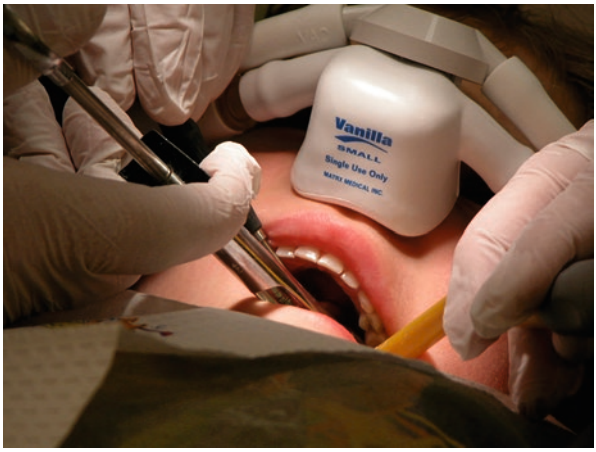

Fig. 9.10 Nitrous oxide/oxygen sedation and simultaneous injection in the left lower jaw for the treatment of MIH tooth 36

9.6 Sedation

Sedation can influence the threshold of pain and consciousness in children [26]. While drug sedation can be used especially in very young patients, sedation with a nitrous oxide oxygen mixture will be the medication of choice for five- to seven-year-olds. The efficacy of nitrous oxide/oxygen sedation in MIH patients who have already experienced various treatment failures cannot be overemphasized [26–28]. Inhalation sedation can be applied in a medium dosage (30–50% N_2O content), showing a low analgesic but an even greater sedative effect. If nitrous oxide sedation is applied correctly, then it can be used to set existing anxieties into a new context, establish treatment protocols and also avoid anxiety-induced gag reflexes (Fig. 9.10) [20, 27–29].

9.7 General Anaesthesia

In selected cases, if the clinical effort required for pain control and anxiety management is so extreme that treatment is not appropriate for the patient's age and is clinically correct, then the patient may need to be treated under general anaesthesia [30].

9.8 Conclusions

As the prevalence of MIH seems to increase with a simultaneous decline in caries, paediatric dentists working in restorative dentistry will increasingly be confronted with the problems of MIH teeth needing restorative approaches. Existing hypersensitivity of MIH molars may represent a major clinical problem if early restoration is required. Competent and pain-free care of MIH patients must therefore include child-oriented behaviour control and safe and proper pain control. Dentists must be aware that children with teeth affected by MIH suffer significantly more from hypersensitivity, dental anxiety and secondary caries. Attributing blame for this condition to the parents is almost always inappropriate.

The following principles should be strictly observed when controlling behaviour and pain [18, 20]:

- Avoid pain at every step of treatment.
- Use the best possible pain control.
- Pay strict attention to the behaviour feedback from MIH patients.

In the treatment of MIH patients, a concept must be developed that takes into account optimal pain control and behaviour control. Such a concept must be individually adapted to the degree of discomfort of MIH patients. The MIH-TNI provides practitioners with such a treatment protocol that also takes into account the sensitivity of MIH teeth to pain.

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Prophylaxis and Desensitizing of MIH Teeth

10

Spyridon N. Papageorgiou and Hubertus van Waes

10.1 Introduction

Molar incisor hypomineralization (MIH) is a form of developmental defect of enamel with systemic origin that affects at least one first permanent molar and is often associated with affected incisors [1]. The prevalence of MIH ranges from 4% to 25% [2] according to the assessed population and set criteria [3].

Although MIH is considered to be an idiopathic condition, its concise etiology remains unclear. On the one hand, the proposed risk factors for MIH include prenatal (maternal smoking or maternal illness/infection), perinatal (infant hypoxia, low birthweight with/without premature birth, caesarian delivery, birth complications, or calcium shortage), and postnatal factors (breastfeeding, nutrition, dioxins, childhood illnesses, medications) [4, 5], but none of these can be considered causative [6]. On the other hand, MIH has been recently proposed to be a multifactorial genetic, not an idiopathic, condition, and that if additional gene variations are also present, then it may result in involvement of permanent canine and premolars additional to molars and incisors [7].

Teeth affected by MIH show considerable histological, mechanical, macroscopical, and clinical differences to healthy teeth. Histologically, MIH-affected teeth show less distinct prism sheaths and a lack of arrangement of the enamel crystals. Mechanically, affected enamel shows impaired mechanical properties, in terms of reduced hardness and modulus of elasticity compared to healthy enamel [8, 9]. The enamel of MIH-affected teeth is characterized by increased amounts of proteins such as serum albumin, type I collagen, ameloblastin, a1-antitrypsin, and antithrombin III, which have been reported to inhibit the growth of hydroxyapatite crystals and the enzymatic activity during enamel maturation, thereby resulting in an overall

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reduction of minerals content of the enamel [10, 11]. From a clinical aspect, MIH-affected teeth seem to be more prone to dental caries due to the enamel's increased porosity and brittleness, which makes MIH-affected teeth sensitive to thermal or mechanical stimulation and makes oral hygiene difficult to perform adequately [5]. Additionally, MIH-affected teeth are also more prone to rapid breakdown under the exposure of the masticatory forces [12]. Children with MIH undergo dental treatment of their first molars nearly 10 times as often as unaffected children [13], which leads often to increased prevalence of behavioral management problems or dental fear and anxiety [14].

10.2 Conservative Management of MIH-Affected Teeth

The management of MIH is challenging as the clinical appearance and individual need for treatment varies widely, with a broad spectrum of treatment modalities being available, ranging from prevention of enamel breakdown or caries, management of hypersensitivity or pain, restorative treatments, to extraction with or without subsequent orthodontic alignment of adjacent teeth [2, 3, 15]. The decision as to which of these options is suitable needs to be made individually considering the severity of the lesions, the symptomatology of the affected tooth, and the patient's dental age and expectations [15]. Identification of patients at risk of MIH and early diagnosis can lead to more effective and conservative management [16, 17]. Based on the available evidence, children at risk of MIH are those with poor general health during early childhood and/or those with hypomineralized second primary molar(s) [15–18]. There are currently no guidelines available for the management of MIH; however, the European Academy of Paediatric Dentistry published a consensus paper in 2010 as "best clinical practice guidance for clinicians dealing with MIH" [15]. The current chapter focuses solely on preventive and desensitizing conservative measures for MIH-affected teeth.

10.3 Preventive Treatment Approaches

Preventive treatment following the diagnosis of MIH should be individually tailored to each patient, taking into account factors such as the patient's caries risk, the lesion's posteruption breakdown, any symptoms the patient might have and their severity, and the extend/severity of the demarcated lesions. Clinical decision-making depends to a large extent on the number of teeth involved and the severity of the lesions (depth, size, color, and enamel breakdown) [19]. For example, mild cases of MIH might not necessarily need to be treated with extensive treatment approaches. It is however very important to commence enhanced prevention as soon as MIH teeth erupt as they are prone to posteruptive enamel breakdown and caries due to the greater porosity of enamel and its lower mechanical resistance especially in severe MIH lesions [20, 21]. Affected children and their parents should be provided with the appropriate dietary and preventive advice to limit cariogenicity and

erosivity of the child's diet. They should be encouraged to use fluoridated toothpaste with at least 1450 ppm F to reduce caries risk and tooth sensitivity.

Apart from the usual oral care with a fluoride-containing toothpaste, many dental clinics include in their preventive protocols the sealing of the all MIH-affected molars' fissures. If the enamel surface of MIH-affected molars is intact, resin-based fissure sealants might be used in conjunction with adhesive application before placement in order to increase fissure sealant retention [20, 22]. However, results regarding the use of an adhesive prior to fissure sealant application are conflicting [23–26]. Increased bond strength for fissure sealants might be also attained by using de-proteinizing agents such as 5% sodium hypochlorite or papain-based Papacarie gel for 60 s after etching [27]. If the MIH-affected molars are only partially erupted, hypersensitive, or have posteruptive enamel breakdown, then glass ionomer cement fissure sealants might be preferable [20, 28], even though these sealants will serve only as temporary management option due to the material's poor retention. Therefore, the application of such sealants varies from that of typical resin-based ones and often covers the entire occlusal surface coverage. As a general rule, applied fissure sealants should be regularly monitored and replaced when lost [28], while additional regular professional applications of fluoride varnishes/gels might be used as a part of the enhanced prevention protocol and to reduce tooth sensitivity [20].

Both in vitro and in vivo studies indicate that remineralization of MIH-affected teeth posteruption seems to be clinically possible, but complete resolution of the symptoms is not always feasible due to the extent, depth, and thickness of these lesions [29–31]. In an effort to remineralize MIH-affected teeth and reduce tooth sensitivity, a wide variety of materials have been applied on the enamel lesions.

Topically applied fluorides, delivered in the form of concentrated varnishes or gels, can act as a reservoir for fluoride ions. These fluorides can be redepositioned as fluorapatite on the tooth surface during remineralization and reduce tooth sensitivity, while also enhancing the tooth's resistance to demineralization [16, 32, 33]. One of the most commonly used fluoride varnishes is Duraphat (Colgate-Palmolive, Manchester, UK) containing 50 mg NaF/mL (2.26% F, 22,600 ppm F), which binds to enamel and plaque, acting as a slow-release fluoride reservoir. Another less-concentrated treatment gel, Gelkam (Colgate-Palmolive, New York, NY), containing 0.4% SnF (3000 ppm Sn and 1000 ppm F) can be applied as a single drop on a cotton bud by the parent (told to "paint on the molar like nail polish") several times per week after brushing and flossing. The parent must be very responsible and fully compliant in undertaking this task, as regular swallowing of this product prior to eruption of the permanent incisors could promote anterior fluorosis [16, 33]. Restrepo et al. [34] and Ozgul et al. [35] reported the reduction of dental hypersensitivity in MIH-affected teeth after application of fluoride varnish. These results are similar to those found by other authors [36, 37] in patients without MIH, who reported a decrease in dental hypersensitivity after the use of fluoride varnishes. Weekly topical application of fluoride gel or varnish might improve the tooth's resistance to demineralization, decrease tooth sensitivity, or enhance enamel remineralization and posteruptive maturation [19]. Thus, fluoride varnish treatments may be considered a therapeutic option in cases of MIH-related dental hypersensitivity.

This treatment might be appropriate especially for newly erupted permanent first molar with moderate hypomineralization and no disintegration of the surface enamel, where a survey indicated that the majority of Norwegian dentists (51.2%) preferred treatment with fluoride varnish for such lesions [38].

Successful full enamel remineralization and reduction of a tooth's sensitivity has also been reported with the use of bioactive glass-containing toothpastes. An example for such a toothpaste is the Novamin toothpaste (GlaxoSmithKline, Weybridge, Surrey, UK) [39], which includes a very fine bioactive glass particulate with a particle size of ~18 μm used as an active repair agent. This material remineralizes tubules in the dentine by the formation of apatite leading to reduced fluid permeability and thereby tooth sensitivity [39]. Multiple studies suggest that NovaMin containing toothpastes have better remineralization capability than the widely-used casein phosphopeptide amorphous calcium phosphate (CPP-ACP) paste as the former attaches to the enamel surface more compactly [40–42]. Such bioglass-containing dentifrices can be simply applied by the patient in Essix-style retainers overnight.

Arginine-containing toothpastes have been also proposed for the treatment of MIH-affected teeth to reduce the associated hypersensitivity [43]. Arginine promotes the sealing of the dentinal tubules and thereby decreases the number of sensory afferents exposed and blocks the hydrodynamic pain mechanism [44]. A recent meta-analysis of dentin hypersensitivity in general [44] indicated that arginine-containing toothpastes provided a superior desensitizing effect in terms of tactile hypersensitivity test or air-blast test compared to toothpastes containing fluoride, strontium, or potassium. These results are consistent with the observations of Bekes and colleagues [43] who found a significant decrease in hypersensitivity 8 weeks after two applications of an arginine desensitizing paste on teeth with MIH. Such results suggest that arginine paste can be recommended as a desensitizing agent for MIH-affected teeth.

CPP-ACP nanocomplexes are casein-derived peptides in which ACP is stabilized by CPP, and these nanocomplexes act as a calcium and phosphate reservoir when incorporated into the dental plaque and on the tooth surface [45]. CPP-ACP has been shown to effectively reduce demineralization and remineralize carious lesions in both in vitro and in vivo setting. This process might be particularly helpful at early-stage lesions, where the enamel surface of newly erupted teeth has not completely matured [29, 31, 46]. The CPP-ACP nanocomplexes help increase the bioavailability of calcium and phosphate within the saliva and therefore encourage remineralization and desensitization of MIH-affected teeth [20, 28, 47, 48]. CPP-ACP has the ability to bond strongly with the biofilm on teeth and also can stabilize calcium, phosphate, and fluoride ions within saliva by the presence of CPP which prevents spontaneous precipitation and allows penetration of these ions deep into the subsurface lesion; these factors are effective in improving the remineralization process throughout the body of lesion, whereas the fluoride-alone products tend to mainly remineralize the surface layer [31, 49, 50]. The most commonly used CPP-ACP products include a topical tooth creme (Tooth Mousse or MI Paste, GC Corporation, Tokyo, Japan), a sugar-free chewing gum (Recaldent Pty Ltd., Melbourne, Australia), or lozenges (Adams/Cadbury Schweppes, Morris Plains,

NJ) containing CPP-ACP as Recaldent (Recaldent Pty Ltd., Melbourne, Australia) [16, 20, 51]. From the other side, it might be important to know that CPP-ACP-containing products have casein and therefore might be contraindicated in children with allergy to milk [31]. Existing evidence indicates that CPP-ACP is effective in the remineralization of enamel subsurface lesions [45] or white spot lesions [52, 53] and in the prevention of dental erosion caused by wine consumption [54]. Specifically for MIH, CPP-ACP was found to be effective in reducing the sensitivity of MIH-affected teeth [48], while microscopically the defective rods of MIH-affected molars transform into a more geometric, mature, and mineralized prism [29]. Therefore, these products can also be recommended to patients with mild pain to external stimuli [20].

Another CPP-ACP containing product often recommended for the treatment of MIH-affected teeth is the MI Paste Plus (GC Corporation, Tokyo, Japan), which contains 10% CPP-ACP plus 0.2% NaF (900 ppm F). The combined use of fluoride and CPP-ACP has been shown to give enhanced benefits than using either agent alone [49, 55]. Another effective product that can be used is Enamelon Treatment Gel (Premier Dental, USA), which contains both fluoride (970 ppm F) and ACP. Studies have shown that this product provides substantive amounts of fluoride and ACP ions to enhance remineralization with similar benefits when compared to 5000 ppm fluoride products [56].

10.4 Existing Evidence from Clinical Studies

Insights on the clinical performance of various interventions can be best gleamed in an evidence-based manner through well-designed clinical longitudinal studies on humans. As the main scope of treatment of MIH-affected teeth is to assess the absolute or relative success of treatment and any adverse effects that treatment might be accompanied with, the ideal study designs for this research question are comparative (multiple group) randomized or nonrandomized studies and single-group longitudinal cohort studies on humans. The evidence basis for this chapter consisted of a literature search of multiple databases (MEDLINE through Pubmed, the Cochrane Library, Embase, Scopus, Web of Science) up to April 2019 with the search strategy: ("molar incisor hypomineralization" AND (treat* OR therap* OR random* OR blind* OR effectiven* OR efficac* OR efficienc* OR "atraumatic restorative" OR casein OR amorphous OR arginine OR fluoride OR restoration OR sealant* OR crown OR amalgam OR composite OR "glass ionomer" OR compomer OR veneer* OR microabrasion)). Previous systematic reviews on the matter were also consulted to check for any missing studies. The internal validity (risk of bias) of any identified studies was assessed according to their design [57, 58] according to the recommendations of the Cochrane Handbook [59] and analyzed qualitatively.

A total of seven clinical studies published between 2011 and 2018 were identified (Table 10.1). These were two randomized clinical trials and five nonrandomized studies, which were all performed in university clinics in Argentina, Austria, Brazil, Italy, and Turkey. Two nonrandomized studies included only an active

Table 10.1 Characteristics of clinical studies on the treatment of MIH-affected teeth

Study	Design, setting, country[a]	Patients (M/F); age[b]	Teeth; severity	Treatment	Follow-up	Outcome
Bakkal et al. [31]	uNRS; Uni; TUR	38 (NR); (7.0–12.0 years)	38 NR tooth; any sensitivity	G1: CPP-ACP G2: CPP-ACFP	1 month	Mineral content (LF)
Baroni and Marchionni [29]	pNRS; Uni; ITA	30 (NR); (6.0–9.0 years)	30 MOLs; NR	CPP-ACP	36 months	Enamel morphology
Bekes et al. [43]	pNRS; Uni; AUT	19 (10/9); 8.2 years	56 MOLs; SCASS≥2	Arginine paste	2 months	Sensitivity/pain (SCASS/WBFS)
Biondi et al. [60]	uNRS; Uni; ARG	55 (NR); (6.0–17.0 years)	92 NR; mild/moderate lesions	G1: F-varnish G2: CPP-ACP G3: F-TCP-varnish	1.5 month	Mineral content (LF)
Özgül et al. [35]	RCT; Uni; TUR	33 (NR); (7.0–12.0 years)	92 INCs; sensitivity ≥30 VAS	G1: F-varnish G2: F-varnish + ozone G3: CPP-ACP G4: CPP-ACP + ozone G5: CPP-ACFP G6: CPP-ACFP + ozone	1 month	Sensitivity (VAS)
Pasini et al. [48]	uNRS; Uni; ITA	40 (NR); (8.0–13.0 years)	40 NR; NR	G1: CPP-ACP G2: Control (F-toothpaste)	1 month	Sensitivity/pain (SCASS/VAS)
Restrepo et al. [34]	RCT; Uni; BRA	51 (35/17); 10.3 years	51 INCs/MOLs; diameter > 2.0 mm	G1: F-varnish G2: Control (usual care)	1 month	Mineral content (QLF)

CPP-ACP casein phosphopeptide amorphous calcium phosphate, *CPP-ACFP* casein phosphopeptide amorphous calcium phosphate including fluoride, *F* fluoride, *G* group, *INC* incisor, *LF* laser fluorescence, *MIH* molar-incisor hypomineralization, *MOL* molar, *NR* not reported, *pNRS* prospective non-randomized study, *QLF* quantitative light-induced fluorescence, *RCT* randomized clinical trial, *SCASS* Schiff Cold Air Sensitivity Scale, *TCP* tricalcium phosphate, *Uni* university clinic, *uNRS* nonrandomized study with unclear design, *VAS* visual analogue scale, *WBFS* Wong Baker Faces Scale

[a]Country given with its three-letter ISO code

[b]Age given either as mean (one value) or as range (two values in parenthesis)

treatment group, while the remaining five randomized/nonrandomized studies compared two or more different groups that included arginine toothpaste, fluoride varnish, fluoride-tricalcium phosphate (F-TCP) varnish, CPP-ACP paste, CPP-ACFP, ozone therapy, no treatment (usual care with fluoride toothpaste), or a combination thereof. The treated MIH-affected teeth were followed for periods ranging from 1 to 36 months, and the outcomes assessed included enamel composition, enamel mineral content, tooth sensitivity, or patient-reported pain.

The methodological robustness and the risk of bias among the included clinical studies was problematic for most existing randomized and non-randomized studies, as confounding, selection bias, performance bias, detection bias, and selective reporting bias were not handled adequately in many of them (Table 10.2). Therefore, the risk of bias for almost all existing studies was judged as high for at least one domain. The sole exception was one non-randomized trial that did not provide adequate information to assess its robustness.

The results of identified clinical studies give some insights about the efficacy of existing methods to treat conservatively MIH-affected teeth (Table 10.3). Performance for each treatment is judged both in terms of absolute efficacy (i.e., does the treatment result in a significant improvement of MIH-affected teeth) and in terms of comparative efficacy (i.e., does one treatment work better for MIH-affected teeth)—the latter expressed with the mean difference (MD) and its 95% confidence interval (CI).

As far as absolute efficacy is concerned, there is evidence that the mineral content of MIH-affected teeth as seen by fluorescence techniques can be significantly improved both with usual dental care (i.e., use of a fluoride-containing toothpaste twice per day) and with the use active ingredients such as fluoride varnish, F-TCP varnish, CPP-ACP paste, or CPP-ACFP paste ($P < 0.05$). The same observation was made using energy dispersive x-ray spectrometry that indicated that use of

Table 10.2 Methodological robustness/risk of bias assessment of comparative clinical studies on the treatment of MIH-affected teeth

Study	Design	Tool used	Problematic domains	RoB
Bakkal et al. [31]	NRS	ROBINS-I	Confounding, selection bias, detection bias	High
Biondi et al. [60]	NRS	ROBINS-I	Confounding, selection bias, detection bias, outcome reporting bias	High
Özgül et al. [35]	RCT	Cochrane RoB	Unclear randomization sequence generation, missing allocation concealment, missing blinding of outcome assessor, incomplete outcome data reporting	High
Pasini et al. [48]	NRS	ROBINS-I	Unclear	Unclear
Restrepo et al. [34]	RCT	Cochrane RoB	Unclear randomization sequence generation, missing allocation concealment, missing blinding of outcome assessor, incomplete outcome data reporting	High

RCT randomized clinical trial, *RoB* risk of bias, *ROBINS-I* risk of bias in nonrandomized studies of interventions, *NRS* nonrandomized study

Table 10.3 Results of clinical studies on the treatment of MIH-affected teeth

			Absolute effects	Comparative effects	
Study	Treatment	Outcome	Change (95% CI)	MD (95% CI)	*P*
Bakkal et al. [31]	G1: CPP-ACP G2: CPP-ACFP	Mineral content (LF)	G1: −1.9 (−2.9, −0.9)[a] G2: −2.6 (−3.4, −1.8)[a]	G2-G1: −0.7 (−1.9, 0.6)	0.28
Baroni and Marchionni [29]	G1: CPP-ACP	EDX peak for C	G1: −8.2 (−12.0, −4.4)[a]	–	–
		EDX peak for P	G1: 3.3 (−19.4, 26.0)[a]	–	–
		EDX peak for Ca	G1: 6.4 (2.0, 10.8)[a]	–	–
		EDX peak for O	G1: 2.1 (0, 4.2)	–	–
		EDX peak for Na	G1: 0.2 (0, 0.30)	–	–
		EDX peak for Mg	G1: 0 (0, 0.1)	–	–
		EDX peak for Ca/P ratio	G1: 0.2 (−0.1, 0.6)	–	–
Bekes et al. [43]	G1: Arginine paste	Sensitivity (SCASS)	G1: −6.8(−8.3, −5.3)[a]	–	–
		Pain (WBFS)	G1: −2.9 (−3.9, −1.9)[a]	–	–
Biondi et al. [60]	G1: F-varnish G2: CPP-ACP G3: F-TCP-varnish	% change in LF (mild lesions)	G1: −19.6% (NC)[a] G2: −9.3% (NC) G3: −28.3% (NC)[a]	G3-G1: −8.7% (NC) G3-G2: −19.0% (NC) G2-G1: 10.3% (NC)	<0.01
		% change in LF (moderate lesions)	G1: −36.6% (NC)[a] G2: −6.6% (NC) G3: −19.8% (NC)[a]	G3-G1: 16.8% (NC) G3-G2: −13.2% (NC) G2-G1: 30.0% (NC)	<0.001
Özgül et al. [35]	G1: F-varnish G2: F-varnish + ozone G3: CPP-ACP G4: CPP-ACP + ozone G5: CPP-ACFP G6: CPP-ACFP + ozone	Sensitivity (VAS)	G1: −2.0 (NC) G2: −2.4 (NC) G3: −4.3 (NC) G4: −4.6 (NC) G5: −3.1 (NC) G6: −2.5 (NC)	–	0.02

Table 10.3 (continued)

			Absolute effects	Comparative effects	
Study	Treatment	Outcome	Change (95% CI)	MD (95% CI)	*P*
Pasini et al. [48]	G1: CPP-ACPG2: Control (F-toothpaste)	Sensitivity (SCASS)	G1: −1.3 (−1.5, −1.1)[a] G2: −0.1 (−0.3, 0.1)	G2-G1: −1.2 (−1.4, −1.0)	<0.001
		Pain (VAS)	G1: −4.0 (−4.3, −3.7)[a] G2: −0.3 (−0.7, 0.1)	G2-G1: −3.7 (−4.2, −3.2)	<0.001
Restrepo et al. [34]	G1: F-varnish G2: Control (usual care)	ΔF (QLF)	G1: 1.2 (1.0, 1.3)[a] G2: 0.8 (0.6, 1.0)[a]	G2-G1: 0.4 (0.1, 0.6)	0.001
		ΔQ (QLF)	G1: 0 (−0.1, 0.1) G2: 0.1 (0, 0.1)	G2-G1: −0.1 (−0.2, 0.1)	0.25

CPP-ACP casein phosphopeptide amorphous calcium phosphate, *ΔF* difference in fluorescence, *ΔQ* difference in lesion extension, *EDX* energy dispersive X-ray spectroscopy, *F* fluoride, *G* group, *LF* laser fluorescence, *MIH* molar incisor hypomineralization, *NC* non-calculable, *QLF* quantitative light-induced fluorescence, *SCASS* Schiff Cold Air Sensitivity Scale, *TCP* tricalcium phosphate, *VAS* visual analogue scale, *WBFS* Wong Baker Faces Scale
[a]Statistically significant changes from baseline at 5%

CPP-ACP leads to a phosphorus/calcium supplementation of MIH-affected enamel. Sensitivity and/or pain among patients with MIH-affected teeth was found to improve after a 1–2 months application of arginine paste, fluoride varnish, CPP-ACP, or CPP-ACFP, while a potential additive effect of ozone was also observed. This phenomenon might be explained by the fact that ozone seems to increase the diameter of dentin tubules, which could facilitate the ingress of the desensitizing minerals [61].

As far as comparative performance of desensitizing agents is concerned, very limited data are currently available. First, compared to usual oral care (i.e., use of fluoride toothpaste), the use of CPP-ACP paste was found to be superior in terms of reduction of tooth sensitivity to both thermal (MD = −1.2; 95% CI = −1.4 to −1.0; $P < 0.001$) and mechanical stimuli (MD = −3.7; 95% CI = −4.2 to −3.2; $P < 0.001$) [48]. This scenario agrees with Krithikadatta et al. [52] who highlighted that fluoride in combination with ACP-CPP was more effective in the treatment of white spot lesions than fluoride alone, because calcium and phosphate ions are present to form the fluorapatite. Likewise, the use of a 5% NaF varnish (Duraphat, Colgate Palmolive, Hamburg, Germany) was associated with significant improvement in the enamel's mineral content (seen as increased fluorescence) compared to the usual oral care with 1.450 ppm fluoride-containing toothpaste (MD = 0.4; 95% CI = 0.1–0.6; $P = 0.001$), even though the lesion area was unaffected ($P = 0.25$) [34].

Several materials have been found to be effective as remineralizing/desensitizing agents on absolute terms but perform differently on terms of relative effectiveness. Biondi and colleagues [60] found greater improvements in enamel fluorescence of MIH-affected teeth with the use of either a fluoride varnish (Duraphat, Colgate Palmolive, Hamburg, Germany) or an F-TCP varnish (ClinPro, 3 M ESPE, Seefeld, Germany) compared to a CPP-ACP paste (Tooth Mousse; GC, Tokyo, Japan). On the one hand, both varnishes consistently performed better than the CPP-ACP paste (Tooth Mousse; GC, Tokyo, Japan) both for teeth with mild MIH lesions (MDs of 10.3% and 19.0% compared to CPP-ACP paste) and for teeth with moderate MIH lesions (MDs of 13.2% and 30.0% compared to CPP-ACP paste). On the other hand, Ozgul and colleagues [35] found that CPP-ACP paste (Tooth Mousse; GC, Tokyo, Japan) provided a better desensitizing effect than a fluoride varnish (Bifluorid 12, Voco Chemie GmbH, Cuxhafen, Germany) in the short- or mid-term (up to a month after application). Any differences were diminished in the long-term follow-up of 3 months post-application, even though adjunct use of ozone slightly prolonged their duration.

Finally, Bakkal and colleagues [31] found that addition of fluoride in CPP-ACFP (MI Paste Plus; GC, Tokyo, Japan) does not offer a statistically significant advantage over CPP-ACP (Tooth Mousse; GC, Tokyo, Japan) in its remineralization efficacy, as seen through DIAGNOdent reading ($P = 0.28$). The same observation was done by Ozgul and colleagues [35], who found no short- or long-term difference in tooth sensitivity between the use of CPP-ACP (Tooth Mousse; GC, Tokyo, Japan) and CPP-ACFP (MI paste Plus; GC America Inc., Alsip, Ill., USA). This case is in accordance with Krithikadatta et al. [52] who observed that fluoride incorporated into CPP-ACP did not improve the degree of remineralization of white spot lesions when compared to 10% CPP-ACP alone.

10.5 Concluding Remarks

Current evidence from clinical studies indicates that various approaches might be effective in the remineralization/desensitization of MIH-affected teeth including usual oral care with a plain fluoride toothpaste or an arginine-containing toothpaste and use of fluoride varnishes or CPP-ACP pastes. Limited comparative evidence hints that both fluoride varnishes and CPP-ACP pastes might be more effective than usual oral care. It remains unclear how do fluoride varnishes and CPP-ACP pastes compare to each other, as contradictory results exist in the literature regarding their remineralization and desensitization effects. Additionally, it has been shown that demarcated opacities related to MIH tend to fracture over time, and currently, there is no evidence that preventive measures, such as topical application of fluoride or CPP-ACP, reduce the chance of the occurrence of enamel breakdown in hypomineralized teeth [12]. Finally, most of currently available recommendations stem from nonrandomized studies with methodological weaknesses and low internal validity, which makes our confidence in these questionable [62]. Therefore, well-conducted randomized trials assessing the mineral content of MIH-affected enamel, the tooth's sensitivity, and enamel breakdown are needed to form robust clinical recommendations.

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The Use of Fissure Sealants in MIH-Affected Posterior Teeth

11

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11.1 Introduction

Pit and fissure sealants have been used for nearly 50 years to prevent and control fissure caries, by preventing bacteria biofilm growth that can lead to dental decay. When applied on occlusal surfaces of permanent molars, they are effective for preventing caries in children and adolescents, while their effectiveness is closely related to the longevity of sealant coverage (i.e. clinical retention). There is moderate-quality evidence that 48 months following placement, resin-based sealants reduced caries by between 11% and 51% when compared to no sealant placement; longer follow-up periods, however, have reduced quantity and quality of evidence [1].

First permanent molars affected by MIH require preventive care, as there is a high risk of posteruptive breakdown and acidogenic challenges of the oral cavity. Once the breakdown occurs, the subsurface enamel and/or dentin is exposed, resulting in sensitivity to cold, heat and brushing and possibly in further accumulation of plaque and development of caries [2, 3]. Moreover, MIH-affected enamel exhibits disorganized enamel prisms, porous structure, low mineral content and loosely packed crystallites, characteristics correlated with reduced strength and hardness [4–6]. These features can explain the risk of rapid caries development and restoration failures. Molars that are affected by MIH undergo dental treatment nearly 10 times more often compared with molars without MIH [7].

As a result of the previous, it is very important to start an enhanced preventive program as soon as MIH teeth erupt [2, 8]. In addition to other preventive approaches (e.g., fluoride varnishes, casein products, etc.,) resin sealant treatment for MIH molars is considered a valuable and effective preventive measure [8]. Fissure sealants should be placed before breakdown occurs and when the tooth is fully erupted

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and moisture control is adequate. In such cases of not adequate isolation during eruption, glass ionomer cements (GIC) can be considered as an interim preventive option [1, 2, 8]. An early diagnosis combined with the evaluation of the severity of the condition and the patients' dental age and expectations will facilitate proper timing for sealant placement.

The few clinical studies in the literature have shown that for intact hypomineralized molars, resin-based fissure sealants with adhesive application prior to placement are recommended, and for patients with spontaneous hypersensitivity of posterior teeth, sealants and professional application of fluoride varnishes are reported as the appropriate preventive approach [2, 3, 8].

11.2 Clinical Procedure

11.2.1 Isolation

Adequate isolation is the most critical aspect of fissure sealant application. If the enamel porosity created by the etching procedure is filled by any kind of liquid, the formation of resin tags in the enamel is blocked or reduced and the resin is poorly retained. Salivary contamination, during and after acid etching, also allows the precipitation of glycoproteins onto the enamel surface, greatly decreasing the bond strength of the fissure sealant [9]. If this occurs, re-etching is needed [10, 11]. The use of rubber dam is obviously the safest way of securing optimal moisture control, but in young and newly erupted teeth, this is usually not practical as it demands the use of local analgesia for the clamp placement. Additionally, there is sufficient evidence that careful isolation with cotton rolls gives similar retention results compared to rubber dam [9, 12]. The maintenance of a dry field can therefore usually be achieved using cotton rolls and isolation shields, in combination with a thoughtful use of the water spray and suction. However, the isolation procedure may occasionally be extremely challenging, particularly in the partially erupted teeth or in those children with poor cooperation.

11.2.2 Pretreatment

11.2.2.1 Mechanical Cleaning and Etching

Before etching, teeth should be cleaned with a bristle brush in a slow handpiece to remove any plaque or debris from the surface. Although mechanical cleaning of fissures using a round bur no. ¼ in a slow handpiece has shown conflicting results of better sealant retention in sound molars [13], its use in MIH molars might considerably enhance the retention rates of sealants. Removal of possibly defective enamel from the fissures allows better flow of the adhesive to their bottom, thus increasing sealant retention [12, 14]. Recently, the study of Hasanuddin et al. on fissure sealants in permanent molars with dental fluorosis, a defect with some structural similarities with MIH, reported higher retention rates for resin-based sealants when mechanical fissures preparation was included prior to the conventional etch and seal technique [15].

Following any type of occlusal surface cleaning, enamel is then etched with 37% phosphoric acid as usual. SEM studies have shown that regardless of the etching time, exposure of hypomineralized enamel to phosphoric acid fails to produce similar etching patterns seen in sound enamel [16]. This microstructural difference was attributed to the excess proteins in the hypomineralized enamel [4]. However, it needs to be stressed that most of the in vitro studies examine defective enamel and not the areas adjacent to the enamel defect, which have been shown to be less defective [17, 18]. Therefore, etching patterns in less defective areas might be closer to those of sound enamel, and this is probably the reason for increased retention rates when adhesives are used as it is shown below. Finally, previous findings in a classic study by Seow and Amaratunge in Amelogenesis Imperfecta hypomineralized variants reported that the etching patterns in these types of AI may occasionally resemble those of normal enamel despite the presence of hypomineralization abnormalities and morphological changes at the crystallite level [19].

11.2.2.2 Deproteinization

Few studies suggest that application of 5% sodium hypochlorite (NaOCl) for 60 s after etching (deproteinization) enhanced enamel bonding in teeth affected by MIH by removing excess protein content from the tooth surface [20–22]. The above studies looked at shear bond strength and success rates of composite restorations when NaOCl is applied following etching of the hypomineralized enamel. However, differences in both materials and methods used in the studies do not allow clear conclusions.

Kraemer et al. in a recent in vivo study showed that following etching, additional pretreatment of affected enamel with NaOCl did not enhance enamel bonding, while previously Gandhi et al. showed that when NaOCl is used before etching, there seems to be no difference compared to the conventional etch and bond technique [23, 24]. Crombie et al. also showed failure of pretreatment with NaOCl to promote deeper penetration of resin infiltrant materials into the hypomineralized enamel [25].

As only a few studies have been conducted in this area with conflicting results, it is difficult to draw definitive conclusions. Even if some of them support deproteinization for the placement of composite restorations on teeth with hypomineralized enamel, there are no studies investigating the use of deproteinization for sealant application [26]. Hence, further high-quality in vivo and in vitro studies are needed in this area.

11.2.2.3 Adhesion/Bonding

For hypomineralized enamel which during treatment undergoes chemical, mechanical and morphological alterations, adhesion is a key factor for the success of any resin restoration or sealant application [5, 26]. The literature on adhesion in hypomineralized enamel is still limited, especially regarding its use in sealants [14, 23, 26].

Bonding to hypomineralized enamel of MIH-affected teeth is very challenging [8, 27]. The enamel-resin adhesive interface has been found to be weaker in

MIH-affected first permanent molars, compared to sound teeth, possibly because of limited interprismatic enamel dissolution, higher porosity, greater organic content and lower microtag formation in affected enamel [4, 16, 21, 28]. However, in vitro research has shown that adhesion to hypomineralized enamel although less effective is still possible, as the enamel surrounding clinically defective lesions is less affected [4, 17, 18]. The use of modern adhesive systems may further enhance bonding to the hypomineralized enamel, increasing the success rates of composite resin restorations and sealants to MIH teeth.

Results regarding the use of an adhesive prior to fissure sealant in MIH molars are conflicting [29]. In one of the first studies on fissure sealant retention following adhesives application, it was clearly shown that these factors helped substantially in sealant retention in cases of molars with enamel "alterations" as they were described that time [30]. Lygidakis et al. reported that fissure sealants applied using a fifth-generation adhesive after the etchant had a higher retention rate than those applied without it and that by using adhesives, sealant retention rate in MIH molars approached that of sound teeth (Table 11.1) [8, 14]. A possible explanation for this result would be that the currently available single-bottle adhesives have a great ability to flow deeply into capillary-like spaces of the etched enamel surface and promote an optimal resin tag penetration and enhanced adhesion. The hydrophilic monomers present in the contemporary bonding agents increase the surface wetting and resin penetration [26].

The type of adhesive used for bonding to hypomineralized enamel may also play a role. William et al. suggested that self-etching adhesives have superior bond strength to hypomineralized enamel compared with all-etch single-bottle adhesives possibly attributed to omitting of rinsing, thus eliminating the interference of residual water on the bond [16]. However, the hydrophilic properties of acetone included

Table 11.1 Clinical trials on resin-based sealants (RBS) retention on MIH-affected teeth

Authors (year)	Participants (no. of teeth)	Intervention	Materials/ technique used	Follow-up (months)	Results
Kotsanos et al. (2005)	I: 35 treatment II: 90 control	I: RBS on MIH teeth II: RBS on control teeth	N/A	I: 33 II: 55	I: 77.1% retention II: 82.3% retention
Lygidakis et al. (2009)	I: 47 treatment II: 47 control	I: RBS on MIH teeth with use of fifth-generation adhesive II: RBS on MIH teeth without the use of adhesive	Mechanical fissure cleaning using a round bur no. ¼ Fissurit® One-step®	48	I: 70% fully sealed, 30% partially sealed II: 26% fully sealed, 45% partially sealed, 29% failed
Fragelli et al. (2017)	I: 16 treatment II: 25 control	I: RBS on MIH teeth II: RBS on control teeth	Fissurit®	18	I: 72% retention II: 62% retention

in some of the single-bottle adhesives systems may play the same role for removing the residual water from the etched enamel, increasing the available for bonding enamel surface [2, 14]. Finally, the recent study by Kraemer et al. showed that a two-step self-etch adhesive revealed lower values of microtensile bond strength compared with two- and three-step etch-and-rinse adhesives, while the systematic review of Ekambaram and Yiu further concluded that there is no sufficient evidence to prove that self-etch dental adhesives bond better to hypomineralized enamel [23, 26].

11.2.3 Sealant Application

The selected pit and fissure sealants are applied and photopolymerized according to the manufacturer's instructions [14]. The surface is checked for deficiencies, and sealant is added if needed. Regarding the type of sealant used, Hasanuddin et al. evaluated the retention of fissure sealants in permanent molars with dental fluorosis, defect with some structural similarities with MIH, reporting significantly higher sealant retention when applying resin based than when using glass ionomer sealants [15]. However, the Cochrane Database systematic review by Ahovuo-Saloranta et al. concludes that, regarding sound molars, "the relative effectiveness of different types of sealants is unknown, due to very low-quality evidence" [1]. There is no evidence concerning the use of different types of sealants in MIH-affected teeth.

11.3 Success Rates

The effectiveness of resin-based sealants is related to their retention, which in normal teeth appears high in many studies. At 12 and 24 months follow-up, resin sealants are retained completely on average in 80% of cases. After 48–54 months, most studies reported 70% retention of sealants [1]. On the contrary, in MIH molars, enamel alterations leading to inferior enamel-sealant bond strength result to lower retention rates, as confirmed by the systematic review of Elhennawy and Schwendicke [31].

There is conflicting evidence however on the success rate of resin-based sealants on molars with MIH compared to sound molars, as to date there are only three studies evaluating the retention of resin-based sealants [29]. Kotsanos et al. and Fragelli et al. compared success rate of sealants on MIH-affected molars with sealants on sound molars, while Lygidakis et al. compared sealants on MIH, with or without the use of fifth-generation adhesives (Table 11.1) [14, 32, 33].

Kotsanos et al. performed a retrospective study evaluating 35 teeth with MIH, 52.2 (±34) months after application of resin-based sealants and compared them with 90 resin-based sealants on unaffected molars, which were evaluated after 53.5 (±25.1) months. From the MIH group, 22.9% of the sealants needed retreatment, while on the control group, 17.7% needed retreatment. Sealants in MIH molars were found to need retreatment almost 2 years earlier than sealants in the control

group and were three times more at failure risk compared to those on control teeth [32]. The characteristics of that study were the inclusion of the sealed MIH molars within a larger-scale study including all types of restorations on affected molars, the diversity of follow-up period of affected and control teeth and the absence of technique and materials details. Considering however the period this study was performed, most possible treatment approach would have been the "standard" etch and seal technique.

Fragelli et al. in a prospective study evaluated 41 MIH molars 18 months after application of fluoridated resin-based sealants using rubber dam. All molar teeth had mild defects with white, yellow, and brown opacities and received a weekly application of fluoride varnish for a month before application of the sealants. Sealants were applied with a "standard" etch and seal technique and revealed a retention rate of 62% on sound molars and 72% on molars with MIH, presenting no statistical difference. During the follow-up period, from the 13 sealant failures observed, only 2 were associated with caries, both in the MIH-affected group [33]. Findings regarding caries highlight the greater risk of developing carious lesions in patients with MIH [34]. It was concluded that sealant application may be an effective approach to preventing carious lesions in MIH-affected first permanent molars [33]. The characteristics of that study was the pretreatment of the molars with four weekly applications of fluoride varnish, the use of rubber dam for isolation during treatment of sealed molars and the use of the "standard" etch and seal technique.

Lygidakis et al. in a double-blind split mouth study evaluated prospectively 94 molars with mild MIH, 4 years after application of a fluoridated resin-based sealant using cotton roll isolation, mechanical cleaning of the fissures and with or without the use of adhesive prior to sealant placement. In the end of the study period, treated molars were recorded as fully sealed, partially sealed and with sealant lost. When the resin-based sealant was applied without the adhesive, 26% molars remained fully sealed and 45% partly sealed after 4 years, while total sealant loss was seen in 29% of the molars. When resin-based sealant was applied using the fifth-generation adhesive prior to sealant placement, then the retention rate was significantly better at 70% fully sealed and 30% partly sealed molars, without any case of total sealant loss [14]. The later 4-year results are compatible with those described previously for the retention rate of light-cured resin-based sealant to sound molars using the "standard" etch and seal technique [1, 9]. It seems safe to speculate that the use of single-bottled adhesives increases substantially the retention rates of sealants in MIH molars. A possible explanation has been given above in the section of "adhesion/bonding".

Previous studies in sound molars have also shown that sealant retention can be improved if a clinician applies a bonding agent that contains both an adhesive and a primer between the previously acid-etched enamel surface and the sealant material. A recent thorough systematic review and meta-analysis that evaluated five clinical studies from 2009 to 2016 has concluded that fifth- and sixth-generation adhesive systems beneath fissure sealants had "a significant positive effect on retention rates." Regarding the type of adhesive used, it was concluded that the use of etch-and-rinse systems is preferable to that of self-etching systems. The authors speculated that the better results with these adhesive systems can be attributed to the wetting quality of

monomers such as hydroxyethylmethacrylate or to the newer functional monomers such as 10-MDP, which favour the diffusion process and improve adhesion to either dry or moist enamel. In addition, in the case of difficult isolation, the volatile solvents of adhesive systems such as ethanol or acetone can displace the trapped water to promote adhesion of sealant to the tooth [35].

Further research is needed on the use of sealants for MIH-affected first permanent molars for the (a) application at different stages of eruption, (b) use of different sealant materials and (c) use of etch-bond-seal technique. In addition, methodology of the studies should aim for high internal and external validity and longer follow-up periods, while split mouth design appears a very good method to compare interventions, such as sealants or restorations on MIH teeth, with a control in the same patient. This way, any outcomes (success or failures) obtained would most likely be a result of the tested intervention and not of the patient-related confounding factors [26].

11.4 Conclusions

- Fissure sealants should be placed in fully erupted MIH permanent molars, before breakdown occurs, and when moisture control is adequate. In cases of inadequate isolation during eruption, glass ionomer cements can be considered as an interim preventive option.
- Implementing the evidence presented above, the following clinical options should be considered for enhancing sealant retention in the hypomineralized enamel of MIH molars:
  - The use of mechanical cleaning of fissures using a round bur no. ¼ and a bristle brush in a slow handpiece.
  - The application of fifth- or sixth-generation adhesive systems according to the manufacturer's instructions, following enamel etching (i.e. etch-bond-seal technique).
  - Conflicting research results on enamel deproteinization with NaOCl does not support at present its regular use.

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Direct Restorations of MIH-Affected Teeth

12

Norbert Krämer and Roland Frankenberger

12.1 Introduction

The restoration of teeth affected by molar incisor hypomineralization (MIH) is a major challenge in today's dental practice. An increasing number of patients consult specialists in order to restore discoloured, defective, and/or hypersensitive teeth and expect an appropriate therapy [1].

Due to the fact that etiology of these defects is still not fully understood, an even further increase in case numbers is expected. Unfortunately, to date, no official guidelines are available for the restoration of MIH-affected teeth. Furthermore, the considerable variety of observed anomalies and pain symptoms require special attention and make it difficult to give simple recommendations for treatment. Facing this background, authors from Germany, Austria, and Switzerland met to give structured advice based on treatment needs.

There are different ways of restoring these teeth, and every possibility is desperately welcome. However, compared to indirect restorations, the authors argue in favor of directly applied restorations in order to preserve a maximum amount of sound tooth hard tissues.

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12.2 Special Requirements

The restoration of MIH-affected teeth is influenced by the factors surface (S), pain (P), pulp (P), and behavior (B). These have significant impact on treatment measures:

- Surface: The enamel surface suffers comparably lower hardness, being characterized by cracking and considerable roughness (Fig. 12.1) [2–4]. Chippings are a typical observation already shortly after eruption of these teeth, when first occlusal loads are present (Fig. 12.2). Sometimes MIH teeth show cracks already during eruption when apatite formation was terminated (Fig. 12.3). This makes it necessary to stabilize the weakened enamel by remineralization and/or restoration, allowing for appropriate oral hygiene.

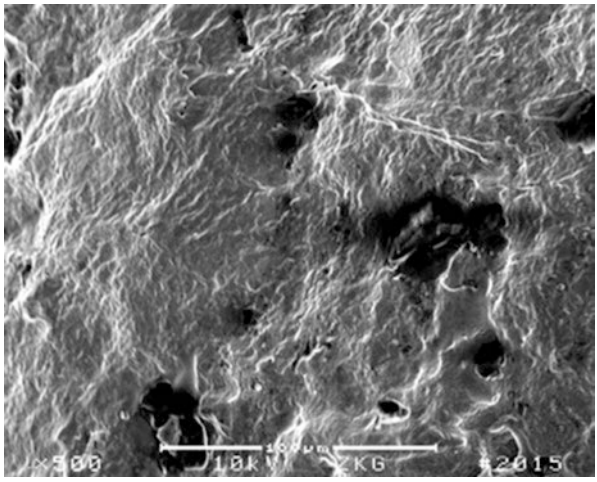

Fig. 12.1 SEM image (500×) of an enamel surface of an untreated MIH tooth displaying roughness and porosities

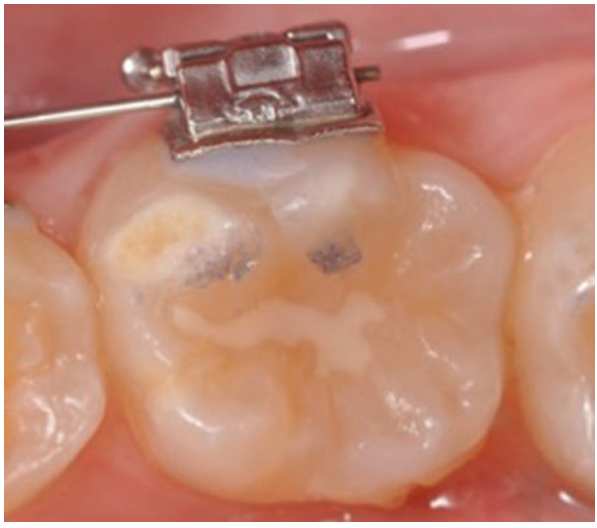

Fig. 12.2 Flaking in MIH enamel at the occlusal contact area (OCA)

- Pain: Especially in severe cases of MIH, chronic pain is expected (Fig. 12.3) [5]. Teeth are sensitive to cold or even tactile impacts (e.g., tooth brush contact). This is caused by the mentioned porosities extending from the enamel-dentin junction to the very surface (Fig. 12.4). Facing this background, the chronic pain has to be stopped by effective sealing of accented surfaces/areas. It is important that the

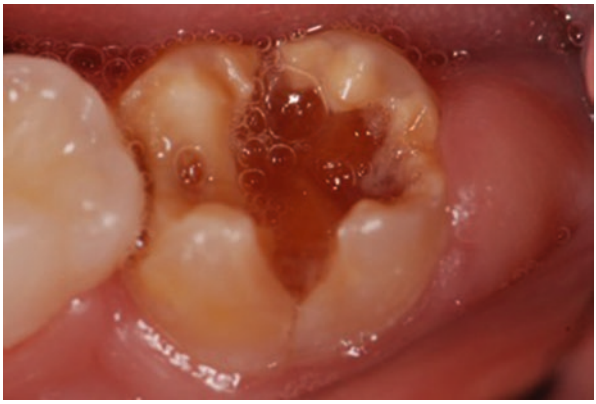

Fig. 12.3 Incompletely mineralized lower first molar approximately 1 year after eruption. The distinct defect clearly promoted caries progression. The remaining yellowish-opaque alterations still give a hint of the MIH structure

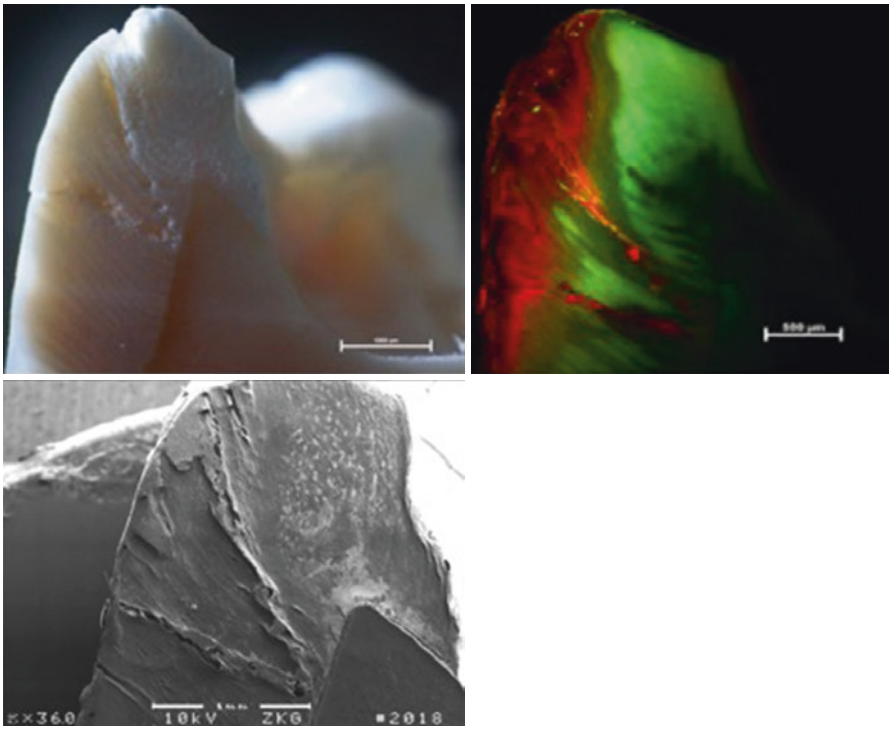

Fig. 12.4 Cut MIH specimen (left side above, original; right side above, indirect staining under a confocal laser scanning microscope; below, SEM, 360× magnification). It is clearly visible that the porosities are present throughout the enamel

tooth receive appropriate isolation in order to cut the persisting pain stimulation. According to the individual symptoms, these individuals are graded as emergency patients and therefore should be immediately treated.

- Pulp: In extreme cases, primarily when MIH teeth remained untreated for a long time, the pulp may be irreversibly damaged (Fig. 12.5). Here, the limit of conservative dentistry may be reached earlier compared to unaffected teeth [6].
- Behavior: Compliance of the children is crucial for treatment options. Children with severe MIH often do not show good compliance [6]. Due to massive pain symptoms, also measures for quick and easy temporary sealing have to be found. In extreme cases and intense treatment need, also general anesthesia may be necessary, making it obvious that treatment has to be finished in one session (Fig. 12.6).

All four factors are decisive for MIH treatment and were therefore the base of the Würzburg treatment need index (TNI) [7]. The indications for direct restorations are displayed in Fig. 12.7.

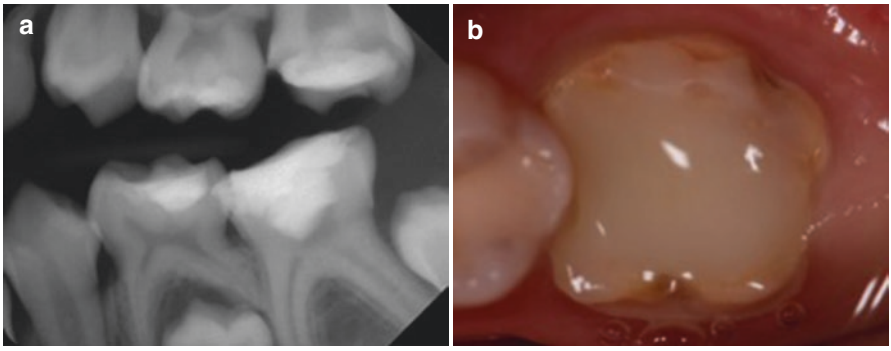

Fig. 12.5 (**a**) Lower first molar in a 10-year-old boy not having been adequately restored over 3 years showing signs of percussion. (**b**) Clinical view of the same tooth. Extraction under general anesthesia was indicated due to limited compliance for endodontic treatment

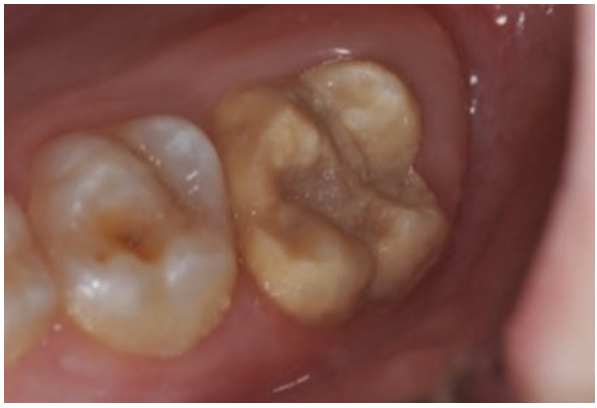

Fig. 12.6 Treatment need for all four first molars, restoration was carried out under general anesthesia

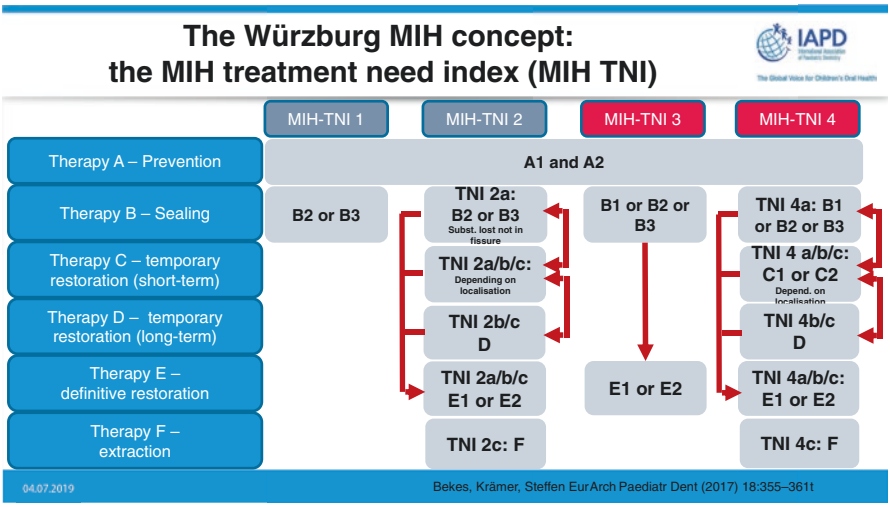

Fig. 12.7 Direct restoration listed under therapy C (temporary restoration; short term) and therapy E (definitive restoration) [7]

Therapy C involves measures being conducted under emergency conditions (TNI 2 b, c) and/or suffering hypersensitivity (4 a–c). Definitive direct restoration is indicated when compliance is given and with defects without hypersensitivity (TNI 2 a–c) or with hypersensitivity without lesion (TNI 3) or with lesions (TNI 4a–c). Direct restorations show the advantage that treatment is accomplished in one session. A further important aspect is that direct restorations always are adapted to the defect and not vice versa; thus, normally it is possible to preserve a reasonable amount of sound tooth hard tissues. Due to the MIH microstructure, also defective restorations have to be expected; thus, simple and effective repair should be possible [7].

Altogether, the direct restoration of MIH teeth show the following requirements:

- Stabilization of tooth hard tissues.
- Good isolation against thermal and painful stimuli (i.e., absence of pain directly after treatment).
- Effective sealing of enamel porosities.
- Anatomical reconstruction of surfaces, cusps, etc.
- Possibility of repair.
- Preservation of sound tooth hard tissues.

12.3 Micromorphological Features: Is Adhesion Actually Possible?

There is no doubt that treatment outcomes are often unsatisfactory when teeth are displaying typical MIH characteristics (i.e., well-defined opacities ranging from white to yellow/brown, posteruptive surface breakdown, and hypersensitivity) and

are treated in exactly the same way as carious lesions. The predominant limiting factor here is the lack of appropriate bonding mechanisms to MIH-affected enamel in the context of restorative treatment.

12.4 Different Enamel Microstructure

The fundamental background to this issue is that the enamel of MIH-affected teeth is characterized by a lower mineral and higher protein content, resulting in higher porosity and significantly reduced microhardness compared to sound enamel. The darker the enamel, the softer it appears to be. The prismatic structure of the affected enamel is described as being less dense with wide empty structures and loosely packed apatite crystals. These microstructural anomalies lead to a dramatic reduction of a tooth's mechanical properties (i.e., surface hardness, wear behavior, fracture toughness, etc.), of course also resulting in little resistance to masticatory forces. In addition, the inhomogeneous surface structure which is lacking a regular pattern in the distribution of available apatite provides overall unfavorable bonding conditions (Figs. 12.8, 12.9, 12.10, and 12.11) [4].

In other words, there is no chance for stable micromechanical interlocking because the cohesive strength of the bonded MIH enamel is not high enough to withstand both polymerization shrinkage and occlusal forces. Furthermore, any chemical bonding does not work reliably facing the limited availability and irregular distribution of calcium in MIH enamel.

As a consequence, bonded restoration margins tend to disrupt, marginal cracks and fractures occur more often, and a loss of retention is also frequently observed—something which is extremely rare in conventional adhesive dentistry.

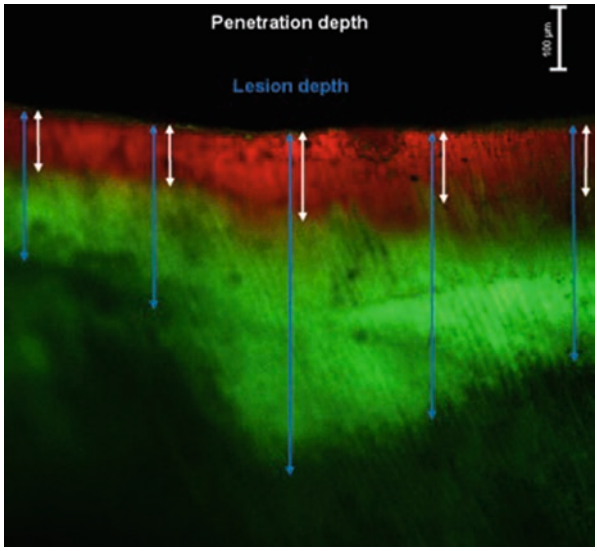

Fig. 12.8 CLSM image of lesion depth and infiltration depth in a MIH tooth

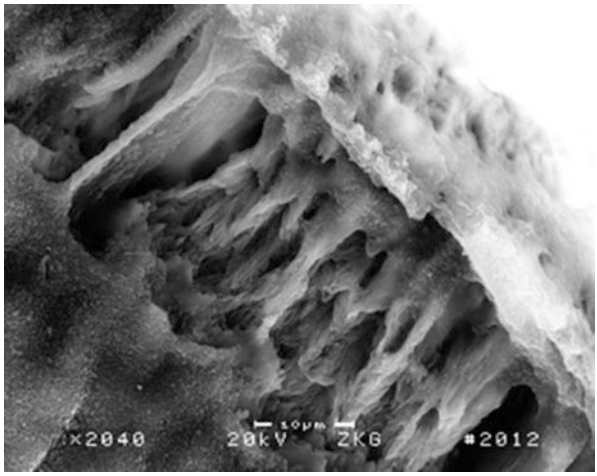

Fig. 12.9 SEM image (2040×) clearly showing enamel porosities from bottom to surface

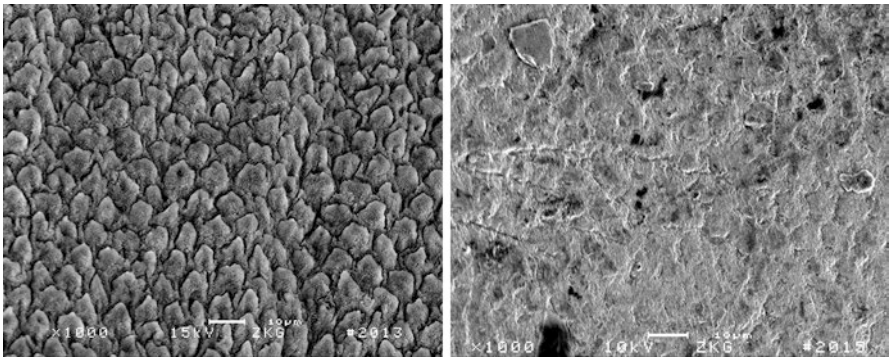

Fig. 12.10 Enamel etching pattern following 30 s phosphoric acid etching on sound enamel (left) and MIH enamel (right) under a SEM (approximately 2000× magnification)

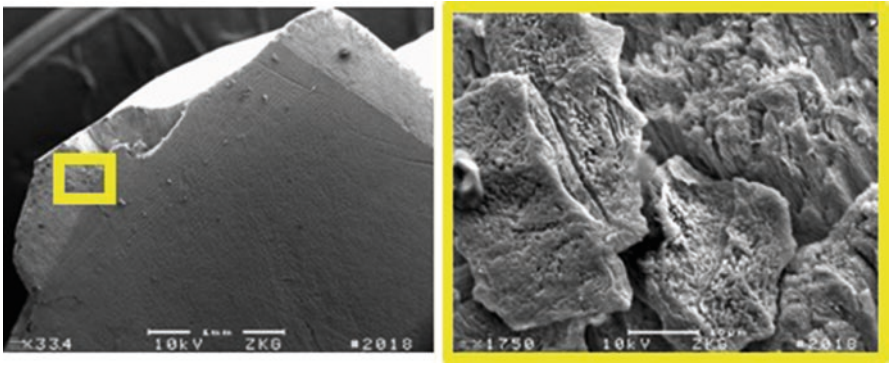

Fig. 12.11 Damaged enamel surface in a SEM overview (left) and 1750× magnification (right)

By contrast, dentin bond strength is usually unaffected in MIH teeth; thus, the risk of a complete adhesive failure is not increased. The compromised marginal seal caused by inferior bonding to MIH enamel, however, has a negative effect on restoration longevity, as the risk of bacterial invasion and caries development at the margins increases so that repair or replacement of a restoration is often necessary. As a result, patients with MIH are frequently in need of restorative treatment in daily dental practice.

The clinical observations regarding an inferior marginal integrity of adhesive restorations are in line with the results from shear bond testing [9, 10]. The in vitro experiments show that-independent of the bonding agent and the adhesive technique used (self-etch vs. etch and rinse)-a significantly lower bond strength is obtained on MIH-affected enamel than on sound enamel. Bond quality to affected dentin, by contrast, has not been reported to be compromised.

12.5 Bonding Strategies

As it seems quite impossible to establish a strong and durable bond to MIH-affected enamel, alternative strategies should be taken into account. One potentially suitable approach is stabilization of the porous and soft MIH enamel. This approach might be possible by thoroughly filling or infiltrating the large porosities in the MIH enamel structure prior to the application of the bonded restorative material. This strategy was evaluated in an in vitro study [9]. Here, the MIH-affected enamel was treated with sodium hypochlorite in order to dissolve the protein followed by application of a caries infiltrant before the actual restorative procedure was carried out. However, this measure did not enhance enamel bond strength, and it furthermore seemed difficult to predict the depth of MIH enamel infiltration (Fig. 12.12). At the moment and with available infiltration materials, infiltration depth for MIH porosities is definitely too shallow. Additionally, resin infiltration is considerably disturbed by proteins (serum albumin, antitrypsin, or serum antithrombin) inside the porosities. Therefore, further investigations toward MIH-enamel restabilization are required in this field.

Facing unsatisfying results and uncertain clinically proven approach for the stabilization of MIH-affected enamel being available to date, there remains only one possible clinical recommendation. Whenever feasible without sacrificing too large portions of tooth structure, cavity preparations should be extended until the margins are located in sound enamel. In this way, it is possible to ensure a durable marginal quality of the adhesive restorations as a fundamental prerequisite for their long-term success. In this context, it is recommended to use a modern universal adhesive containing MDP [9]. These MDP containing adhesives should be used in a selective enamel etch or etch-and-rinse mode. Based on our studies, reliable results are obtained. The performance is comparable to that of a multi-step adhesive [9].

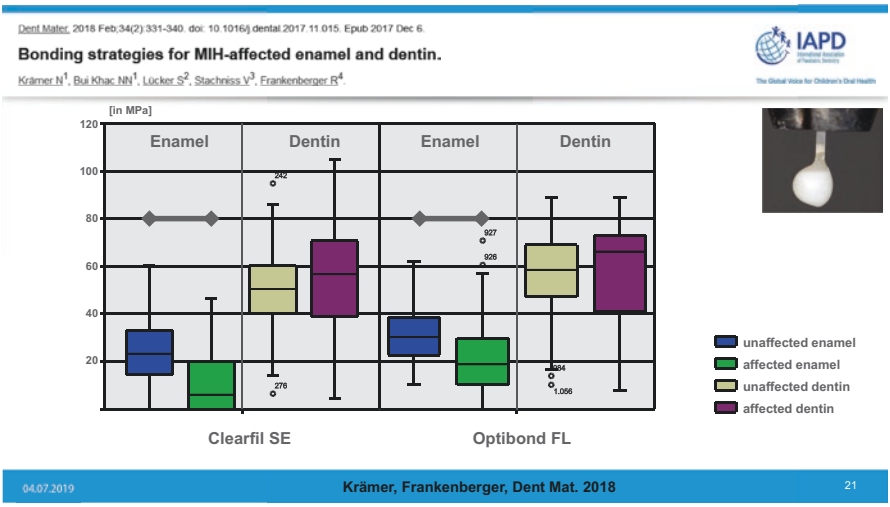

Fig. 12.12 Bond strengths to sound and MIH-affected enamel and dentin. By contrast to MIH enamel, MIH dentin bond strengths are not affected [9]

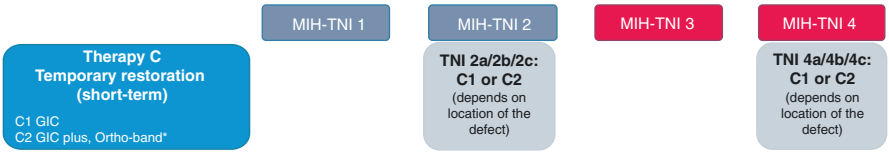

Fig. 12.13 Temporary restoration (short term): Indication and options [7]

12.6 Temporary Restoration

Temporary restorations as direct measure are indicated when teeth suffer defects immediately after dentition (TNI 2 a–c) and/or the tooth shows hypersensitivity (Fig. 12.13).

Also, insufficient compliance for complex adhesive treatment makes temporary restorations necessary. Due to the severity of defects and their pain symptoms, any therapy is urgently indicated and may not be postponed [7].

Provisional restorations are normally carried out using glass ionomer cements (GIC) or resin-modified GIC [11]. GICs are easy and quick to handle, they furthermore serve as effective sealing of sensitive MIH teeth, and finally release substantial amounts of fluoride. Less favorable are inferior adhesion, especially to MIH enamel, and low flexural strength causing chippings and fractures clinically [11–13].

Prior to application, the tooth has to be cleaned. GICs are applied on softened, but not carious, dentin without further preparation. This process requires only a limited time for good isolation of the field. According to our experience, low-viscous GICs are favorable here, because both rough surfaces and pits and fissures are sealed appropriately. In order to save the material from early overdrying, a varnish or simply bonding agent is used for covering [14] (Figs. 12.14, 12.15, and 12.16).

The provisional restoration aims to gain some time until teeth are completely erupted and to omit complex treatments under general anesthesia. The indication for extraction of these teeth is way too early at this point. Normally, 1–4 years longevity should be achieved. Scarce hints in the literature show annual failure

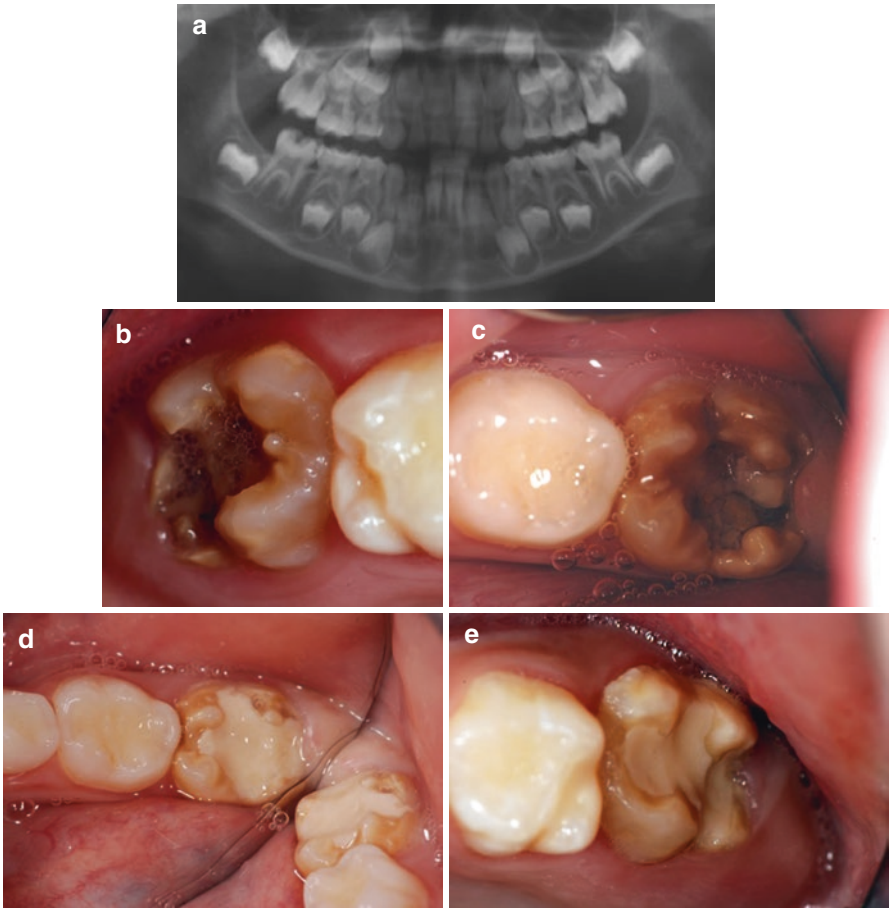

Fig. 12.14 (**a**) Orthopantomogram of a 7-year-old with MIH in all first molars. (**b**) Upper first molar being hypersensitive already after eruption. (**c**) Same patient, drying for taking photographs was impossible. (**d**) 6 months after primary treatment with intact occlusal GIC with chipping buccally. (**e**) GIC restoration in another MIH molar

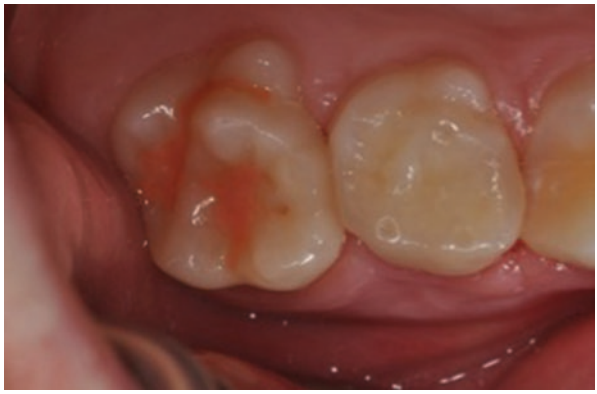

Fig. 12.15 Low-viscosity GIC (here: Fuji Triage, GC) have the advantage that hypoplastic areas plus pits and fissures are sealable for a certain amount of time

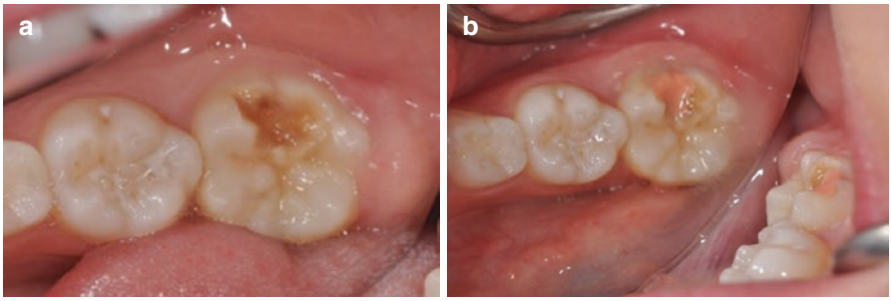

Fig. 12.16 (**a**) Hypoplastic and hypersensitive molar. (**b**) The cavity was just cleaned and then filled with Fuji Triage leading to substantial reduction of sensitivity

rates of 12% [11]. However, often low numbers, missing of controls, and short terms limit the published papers [15]. Main failure reasons are gaps, fracture, and fillings needing repair [8, 16]. This case requires regularly conducted recalls.

12.7 Adhesive Restoration

Direct adhesive restorations are the treatment option of choice in the vast majority of clinical cases involving MIH-affected adhesive substrates (Fig. 12.17). Due to the abovementioned factors, a primarily minimally invasive procedure may cause early retreatment due to marginal fractures caused by weak enamel structures. Therefore, the following strategy is feasible:

After appropriate local anesthesia with considerably longer waiting time, the affected tooth has to be thoroughly cleaned with a course polishing paste in order to remove plaque which is normally thicker due to persisting hypersensitivities of MIH teeth. Beside caries, also affected enamel has to be removed until sound margins are achieved. For the case of still intracoronal restorations, a conventional resin composite layering may be applied (Figs. 12.18, 12.19, 12.20, 12.21, and 12.22) or

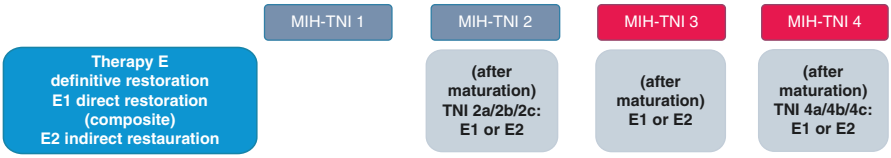

Fig. 12.17 Definitive direct restoration: indication and options [7]

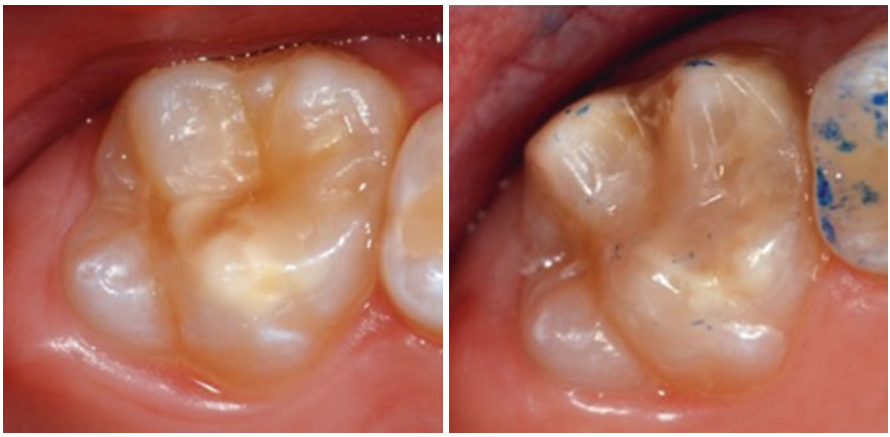

Fig. 12.18 Adhesive restoration before and after treatment

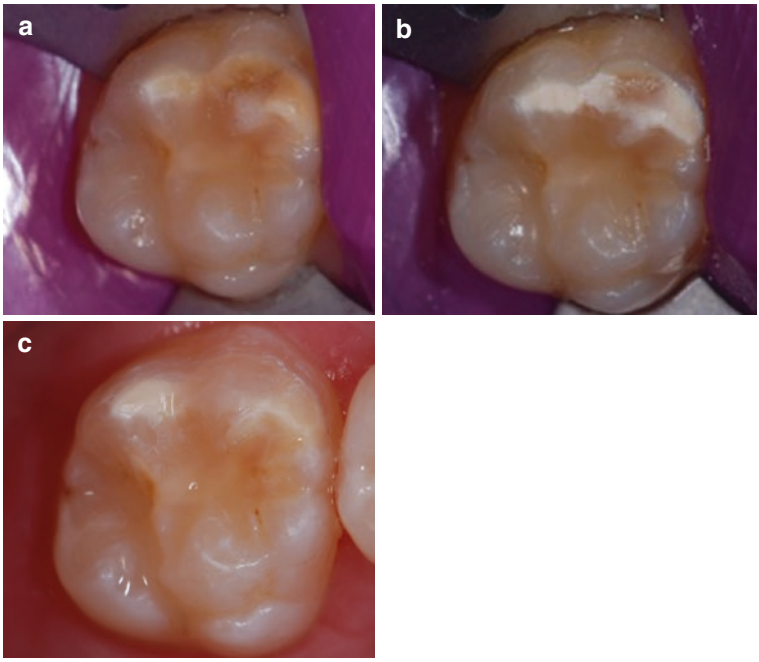

Fig. 12.19 (**a–c**) Adhesive restoration step-by-step

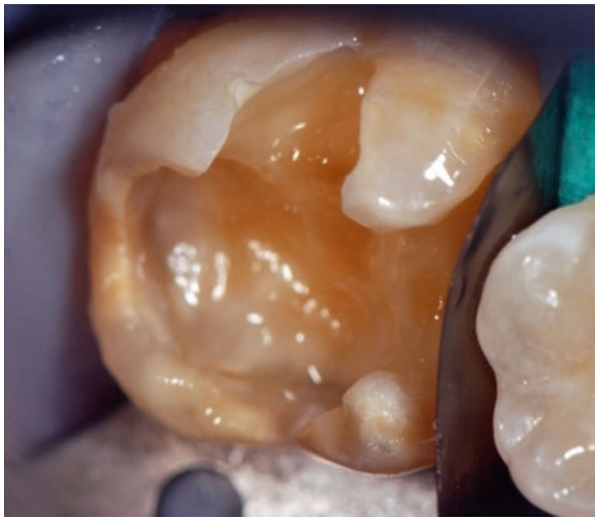

Fig. 12.20 Extended defect having been adhesively pretreated

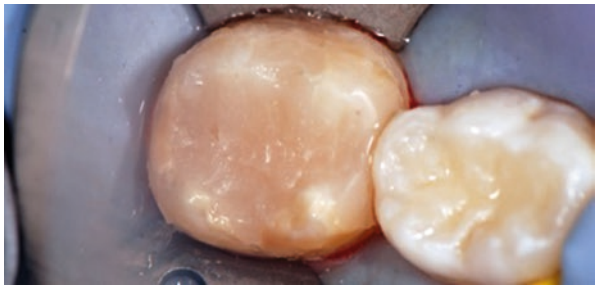

Fig. 12.21 Restoration immediately after placement

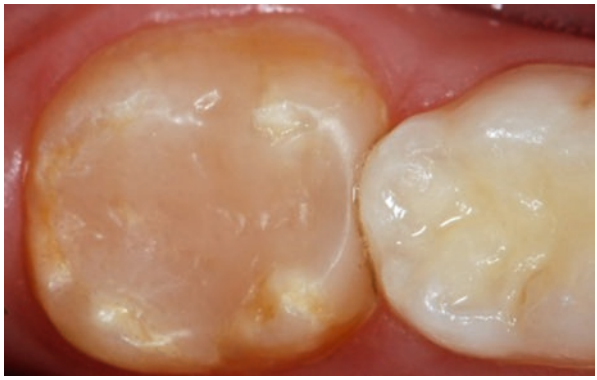

Fig. 12.22 Restoration after 1 year. A small defect at the load-bearing cusp

a bulk-fill composite. For the case that one or more cusps have to be replaced, it is reasonable to make a lining with a flowable resin composite or a flowable bulk fill composite, covered by a sculptable resin composite.

12.8 Repair

For repair of restorations in MIH-affected teeth, it seems to be logical to apply the same rules as in conventional resin composite repair. One of the most important findings of our research regarding resin composite repair is that the filling-inside-filling approach may be the most promising. In former times, it was often speculated that despite a circumscribed defect such as a chipping of a resin composite restoration, it may be feasible to extend the repair cavity to sound enamel due to superior bonding characteristics when enamel is etched and bonded. However, cutting an additional adhesive substrate without any need did not show better results in vitro, and clinical findings are confirming this more defensive approach.

For marginal defects of MIH restorations, this method does not work because here the reason for failure is predominantly too defensive initial preparation, which is often more correlated with the compliance of the young patients than the skills of the operator. When MIH restorations show marginal defects, it is always mandatory to transfer the preparation margin into sound enamel and then to carry out conventional repair procedures for the remaining resin composite (i.e., sandblasting with 50 μm aluminum oxide particles followed by adhesively bonded repair restorations being applied in the same as was described above) (Figs. 12.23, 12.24, and 12.25).

12.9 Chances and Limitations of Direct Restorations

There remains a clear lack of knowledge about the ideal treatment approach for the dental practitioner in order to preserve a maximum amount of tooth hard tissues on one hand and on the other hand to create restorations with stable margins and good retention rates over time.

At the moment, adequate longevity of direct adhesive MIH restorations can only be ensured when the restoration margin is placed in sound enamel. However, this

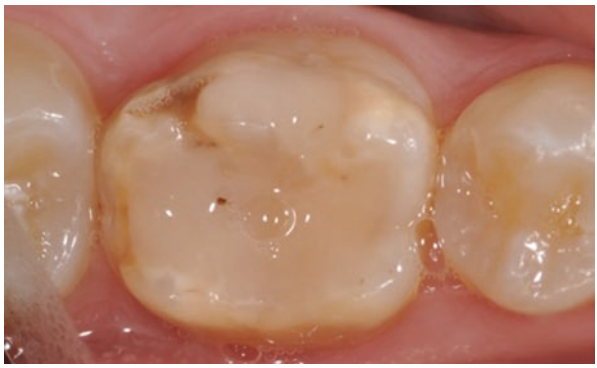

Fig. 12.23 Defect adjacent to preexisting restoration in a MIH tooth

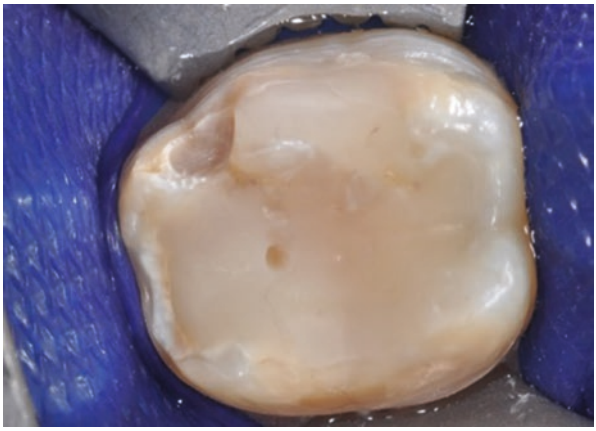

Fig. 12.24 Adhesive pretreatment including sandblasting of resin composite margins

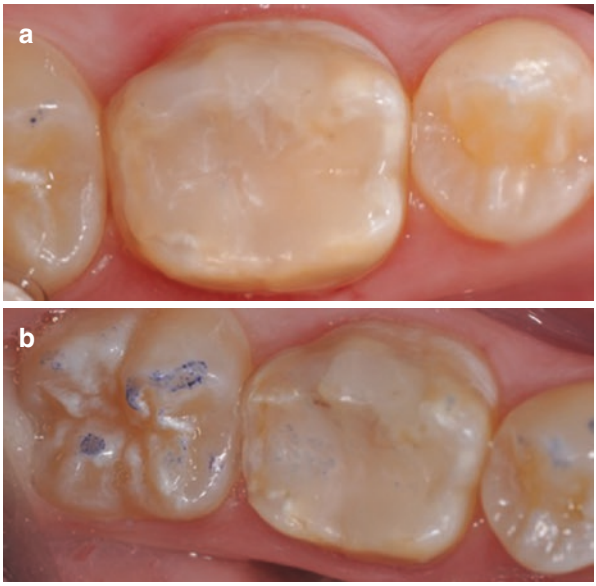

Fig. 12.25 (**a** and **b**) Restoration immediately after placement and after 4 years

often means to cut considerable amounts of occlusal areas with consequently higher demands for the operator in an anyway difficult treatment environment. Alternative treatment approaches are currently investigated, and it is particularly important to leave this task to scientists when children are involved.

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Indirect Restoration Approaches for MIH-Affected Teeth

13

Katrin Bekes

13.1 Introduction

As described in previous chapters, qualitative, demarcated developmental hypomineralized defects of one or more permanent first molars, with or without signs of lesions on the incisors, are defined as molar incisor hypomineralization (MIH) [1]. Hypomineralized enamel can vary in colour shade from white to yellow or brown [2], but always shows borders that are well-defined and distinct from sound enamel [3]. Thereby, opacities present as microscopically porous [3]. Affected enamel presents with less distinct prism sheaths. The crystals are disorganized, loosely packed with enlarged interprismatic space [4]. Moreover, a higher carbonate content, decreased mineral content, and increased amounts of proteins can be found [5, 6]. Porous enamel can easily chip off, especially under the influence of masticatory forces. Occasionally, loss of enamel occurs rapidly after eruption, leaving the dentin exposed [7, 8].

Clinically, affected molars can represent a spectrum of severity and extension of the defect from hardly visible opacities to severe destruction of the enamel. It is possible that intact opacities can be found on one molar, while in another molar large parts of enamel may breakdown soon after eruption [7]. Moreover, MIH could be considered a progressive defect over time as affected teeth have the tendency to accumulate more severe defects over time. Among factors that are associated with this increase in severity of MIH, the colour of enamel opacity seems to be a good predictor for a posteruptive breakdown of the hypomineralized enamel [9]. Hence, early detection, intervention, and appropriate therapy is necessary to prevent severe complications and improve both masticatory function and esthetic.

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13.2 Restorative Management of Hypomineralized First Permanent Molars

The available treatment modalities for teeth with MIH are extensive, ranging from prevention, restoration, to extraction [10]. The suitability of these modalities, however, differs depending on a number of factors. Commonly identified factors are severity of the condition (e.g., extent of the defective enamel and quality of both defective enamel and unaffected parts of the tooth), presence of symptoms (with or without association of hypersensitivity), patient's dental age, and child/parent's social background and expectation [11].

Severe cases of MIH with cavitated structural defects can be restored directly (temporarily using glass ionomer cements and definitive usually using resin composite) or indirectly (using ceramic, composite, or metal restorations). Thereby, glass ionomer or resin-modified glass ionomer cement restorations provide a treatment option in early posteruptive stages. They can be used as intermediate treatment in less-than-ideal conditions of moisture control [11, 12]. On the contrary, composite materials become more important later as long-term restoration when the child grows. Composite performs best in MIH teeth where defective enamel is well demarcated, confined to one or two surfaces with no cusp involvement, and has supragingival margins [13]. The more extensive the defect and the restoration, the more increased is the risk of failure. Moreover, one must consider that when restoration margins are in hypomineralized enamel, there is greater possibility of future structural loss and marginal leakage due to the low mechanical resistance of the tissue and low bond strength to this tissue [14].

Preformed metal crowns (PMC) can be used from early to late posteruptive stages for MIH molars with breakdown, especially in cases with not enough tooth structure being present to support composite restorations [11]. This restoration technique ranks among the more definitive approaches, albeit it is still a temporary medium-term solution. Finally, partial and full coverage indirect restorations may be considered for MIH in the late mixed and permanent dentitions [15]. This modality of treatment is not suitable for the teeth soon after eruption due to placement difficulties associated with short crowns, large pulps, long treatment time and high cost, and the child's limited cooperation [16]. It is applicable years later when the final occlusion has settled.

Both options — direct and indirect — have a number of advantages and disadvantages. On the one hand, composite restorations do not require substantial tooth hard tissue removal, but have a significantly lower survival probability in MIH than nonaffected molars. On the other hand, indirect restorations usually require additional preparation (substance loss), but have high survival probabilities [4].

13.3 Preformed Metal Crowns

13.3.1 Indications

A preformed metal crown (PMC), more commonly known as a stainless steel crown (SSC), is a prefabricated metal crown form that is adapted to the individual tooth and cemented with a luting agent [17]. SSCs have a very long history of use, although its greatest use is in the primary dentition. Complete coverage with a stainless steel crown prevents further tooth loss, reduces sensitivity, prevents cusp fractures, and helps maintain space and crown height [16]. It is not costly and requires little time to prepare and insert [11]. Generally, indications for use in permanent teeth comprise interim restoration of broken down or traumatized teeth, teeth of young patients with developmental defects (Fig. 13.1), and restoration of a permanent molar which requires full coverage but is only partially erupted [18].

For MIH molars with extensive defects, especially where there is significant cuspal involvement, preformed metal crowns often provide an expedient and effective medium interim solution. The term "interim" refers to any time period ranging from a few months to a decade and beyond [19]. SSCs can preserve molars with MIH until cast restorations are feasible [20]. Furthermore, these crowns can be placed in molars with poor prognosis where extraction is the treatment of choice. The MIH tooth can be preserved at an early stage while waiting for the ideal extraction time.

In conclusion, preformed metal crowns can be used from early to late posteruptive stages for MIH molars with breakdown, especially on those that do not have enough tooth structure to support composite restorations [11].

13.3.2 Placement Procedures

The stainless steel crown for the permanent molar is designed in such a way that it closely resembles the anatomy of a first permanent molar tooth and it also obtains its retention mainly from the cervical margin area [18]. Preparation in permanent molars

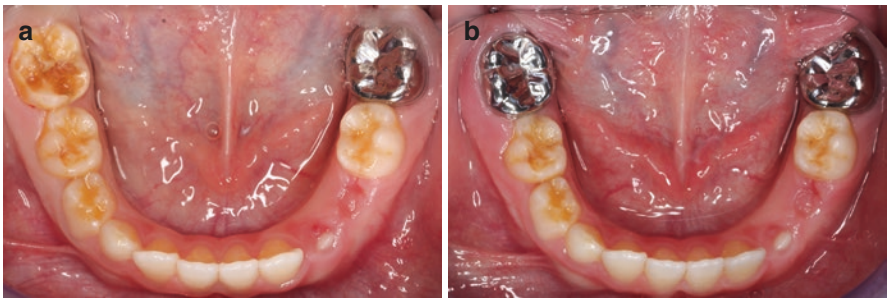


Fig. 13.1 Patient with MIH in both lower first permanent molars showing PEB and severe hypersensitivity. Breakdowns were progressing rapidly. (**a**) Tooth 36 already restored with a SSC; tooth 46 still unrestored. (**b**) Both first permanent molars restored with SSCs

is essentially the same as for a cast metal crown but with a reduction in the amount of tooth tissue removed [18]. Potentially future preparation for indirect restorations should be considered. An occlusal reduction of 1.5–2 mm is needed. Performing this first step enables the proximal reduction to be done more easily [19]. As recommended by Radcliffe and Cullen (1991), only preparation of proximal slices but not of buccal and lingual sides should be done. This procedure allows the extra option of future placement of an onlay rather than a full coverage crown [20].

The SSC should establish a good contact area with neighboring teeth and snap into place cervically. When there is no adjacent tooth, proximal tooth reduction should still be performed to avoid an excessive crown overhang. This procedure is especially important on the distal surface prior to eruption of the second permanent molar. Any overhang could displace the eruption path. If necessary, the margin of the crown can be trimmed with crown scissors or abrasive wheels [19].

One potential alternative to keep removal of sound tooth tissue to a minimum is placement of orthodontic separators 1 or 2 weeks prior to preparation.

13.3.3 Clinical Outcomes

Clinical studies focusing on SSCs in MIH molars are only limited to short-term studies.

Zagdwon et al. (2003) compared SSCs and nickel chrome (NiCr) alloy cast crowns for restoration of permanent first molars affected by amelogenesis imperfecta (AI), severe enamel hypoplasia, or MIH. Around 42 restorations were placed (19 SSCs, 23 NiCr crowns) in 17 adolescents with a mean follow-up of 17 months. A good success rate was reported, and only one failure of 19 PMCs placed over a 2-year period was observed. There was no statistically significant difference between the two types of restorations in terms of quality or longevity. However, the authors concluded that although it was possible to do a minimal preparation design for NiCr crowns, it was more technique sensitive, required multiple visits, and was less cost effective compared to traditional SSC [21].

Kotsanos et al. [22] retrospectively investigated management of first permanent molars in children with MIH attending a paediatric dental practice. In total, 136 interventions (sealants, fillings, SSCs) were placed in 133 molars. Authors reported no replacement was needed for preformed crowns placed on 24 molars for a period of 3–5 years.

13.4 Indirect Restorations

13.4.1 Indications

Indications for performing indirect restorations are primarily situations where it is possible to use remaining dental hard tissues, while there is such a level of degradation that classical composite reconstruction would fail to meet its basic functional and aesthetic performance [23]. Indirect treatment options for MIH include partial coverage restorations or classical treatment approaches such as crowns. However,

laboratory fabricated full crowns should be viewed with caution. They are not recommended for young children because of short crown height and large pulp size with prominent pulp horns in immature teeth [24]. Pulp requires attention as an increased risk of iatrogenic exposure of the pulp chamber during preparation and irreversible irritation of the pulp tissue due to preparation trauma given. Radiographs should be taken for adequate assessment of extension of the pulp chamber prior to preparation, and preparation itself should be as minimally invasive as clinically possible [25]. All in all, this approach may be considered for MIH in the late mixed and permanent dentitions [11]. For fabrication of these restorations, tooth-coloured materials (including composite and ceramic) and metal alloys may be used.

13.4.2 Metal Alloys

Available studies for this treatment option in MIH cases are scarce. Successful use of indirect restorations using metal alloys or ceramic is mostly published for other enamel defects (e.g., amelogenesis imperfecta) [26].

Gaardmand et al. (2014) analyzed 57 cast adhesive gold copings in 33 children with MIH. Four restorations were lost to follow-up, and one was lost after 3 months and was re-cemented. Caries was diagnosed in relation to two CACs after 43 and 68 months, respectively. One of these was later treated with a conventional filling, and the other was extracted. Authors reported no pulpal damage or infection in any of the restored molars. More than 40% of CACs could be followed for more than 3 years. All in all, after a mean observation period of 38.6 months (SD 28.9), 56 restorations (98.2%) were still functioning [27].

As mentioned above, Zagdwon et al. (2003) investigated cast adhesive copings (nickel chrome alloy) and stainless-steel crowns in permanent molars affected by AI or severe enamel defects (including MIH). In 17 adolescents, 42 restorations were placed (23 cast copings, 19 SSCs). The mean follow-up was 17 months (range of 12 to 24 months). Compared to one SSC, two CAC (at 2 and 19 months) failed and required replacement. There was no significant statistical difference between the two types of restorations for quality and longevity [21].

In a retrospective study, Koch and Garcia-Godoy (2000) evaluated clinical performance of cast gold crowns and tooth-coloured composite or ceramic crowns placed on 41 first permanent molars with developmental defects in children 6–8 years of age. After 2–5 years, all crowns were fully retained. Marginal adaptation of 39 out of 41 crowns was rated excellent. All treated teeth were vital and asymptomatic at all evaluation points. No secondary caries was recorded. Neither gingival inflammation nor loss of vertical dimension was observed in any case. Authors reported all crowns were well accepted by patients and their parents [24].

13.4.3 Composites

Due to evolution of adhesive technologies and restorative materials, approaches and treatment plans for restoring posterior teeth have been considerably innovative [28]. Although gold has demonstrated persistent clinical success and biocompatibility,

tooth-coloured restorations are increasingly replacing metal restorations not only for aesthetic concerns but also for more conservative preparations [29].

Modern composite resins may also serve as an alternative in these young patients as they demonstrate the necessary hardness, strength, and wear resistance for successful clinical performance. Laboratory-processed composite restorations are more resistant to occlusal wear than direct composites, particularly in occlusal contact areas, and show a reduced polymerization shrinkage which is limited to the thin luting layer [30]. Any necessary occlusal adjustments post insertion can be more easily and effectively polished, and chips or fractures may subsequently occur and can be repaired relatively easily [31].

To our knowledge, clinical studies focusing on this treatment option are only available in case reports. Feierabend et al. described a case series of 34 restorations in 8 patients (6–15 years) with enamel defects (including 3 patients and 7 teeth with MIH) followed for 2–48 months with all restorations being in situ. Patients with MIH reported a strong decrease or complete absence of hypersensitivity [32]. This is in accordance with recently published data by Dhareula et al. (2018) who used minimally invasive indirect composite onlays for rehabilitation of 10 molars affected by MIH in children aged 8–14 years [33]. At 30–36 months (mean 34.8 months) follow-up, all onlays were found to be in place with complete elimination of pre-treatment sensitivity. Marginal integrity and anatomic form remained unaltered over time. Depreciation in colour stability and evidence of cavosurface marginal discoloration at 30 months was evident in only one of the restored onlays. Both studies conclude that indirect resin onlays may serve as an aesthetic, conservative, restorative alternative for MIH-affected molars with favorable outcomes.

13.4.3.1 Case

A healthy 12-year-old male presented to the Department of Paediatric Dentistry on referral complaining of pain in the upper jaw due to MIH in both first permanent molars (Fig. 13.2a–c). Clinical examination revealed tooth 16 showed white, yellow, and brown areas of opacity with posteruptive breakdown (PEB) on the distobuccal side. Tooth 26 also presented white to brownish opacities affecting two-thirds of the occlusal surface and PEB as well. Hypersensitivity was reported. Treatment planning comprised of laboratory-made composite restorations for both molars to protect dental structure, reduce sensitivity, and improve masticatory function.

Premedication was used 24 h before starting preparation procedures (see Chap. 9). Teeth 16 and 26 were prepared without undercut after local anesthesia was applied. All hypomineralized enamel was removed, and, in this case, supragingival margins were possible (Fig. 13.2d–g). Impressions were taken using polyether (Impregum, 3M, Germany). Afterwards, provisional fillings were applied using a light-cured material (Clip, Voco GmbH, Germany). The elastic consistency assures an easy removal.

A microfiller composite resin was used by the technician (SR Adoro, Ivoclar Vivadent, Liechtenstein). It has a weight percentage of 65% inorganic fillers, a flexural strength of 125–150 MPa, and an e-modulus of 7000–7500 MPa.

In the second appointment following local anesthesia, provisional fillings were removed with a scaler, followed by cavity cleaning with a polishing brush and an oil and fluoride-free cleaning paste (Proxyt, Ivoclar Vivadent, Liechtenstein). A rubber

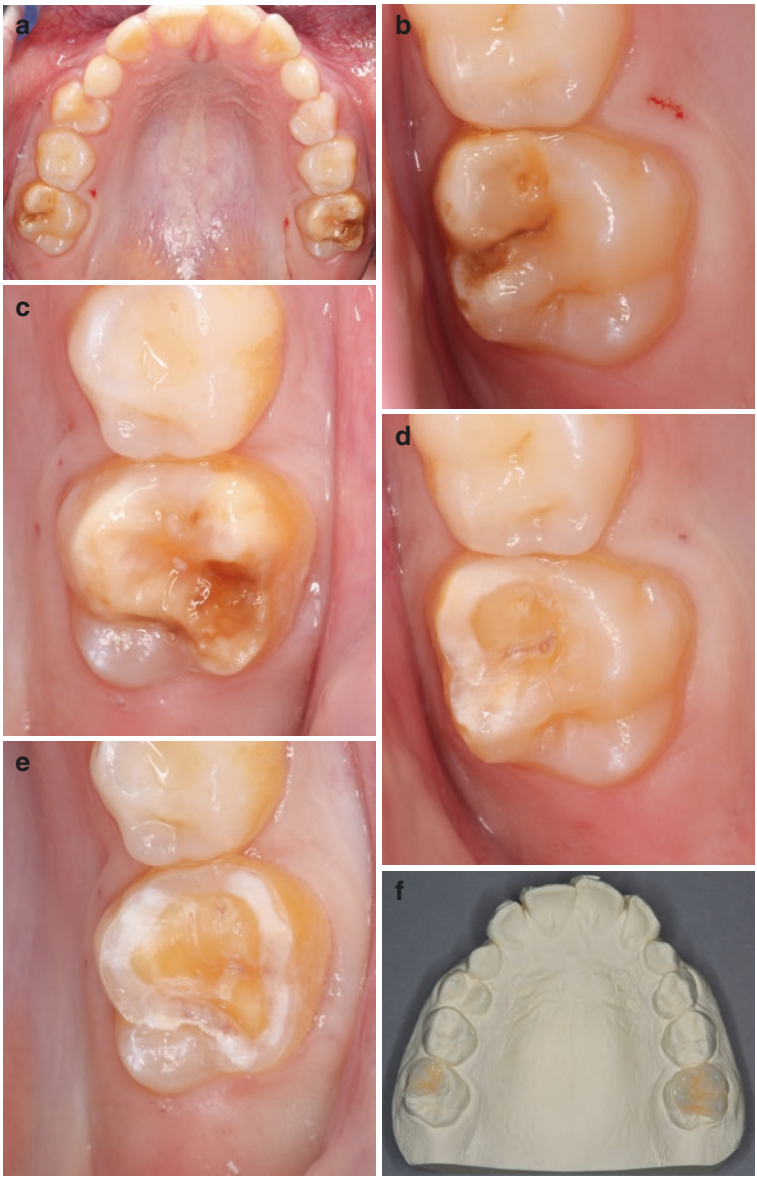
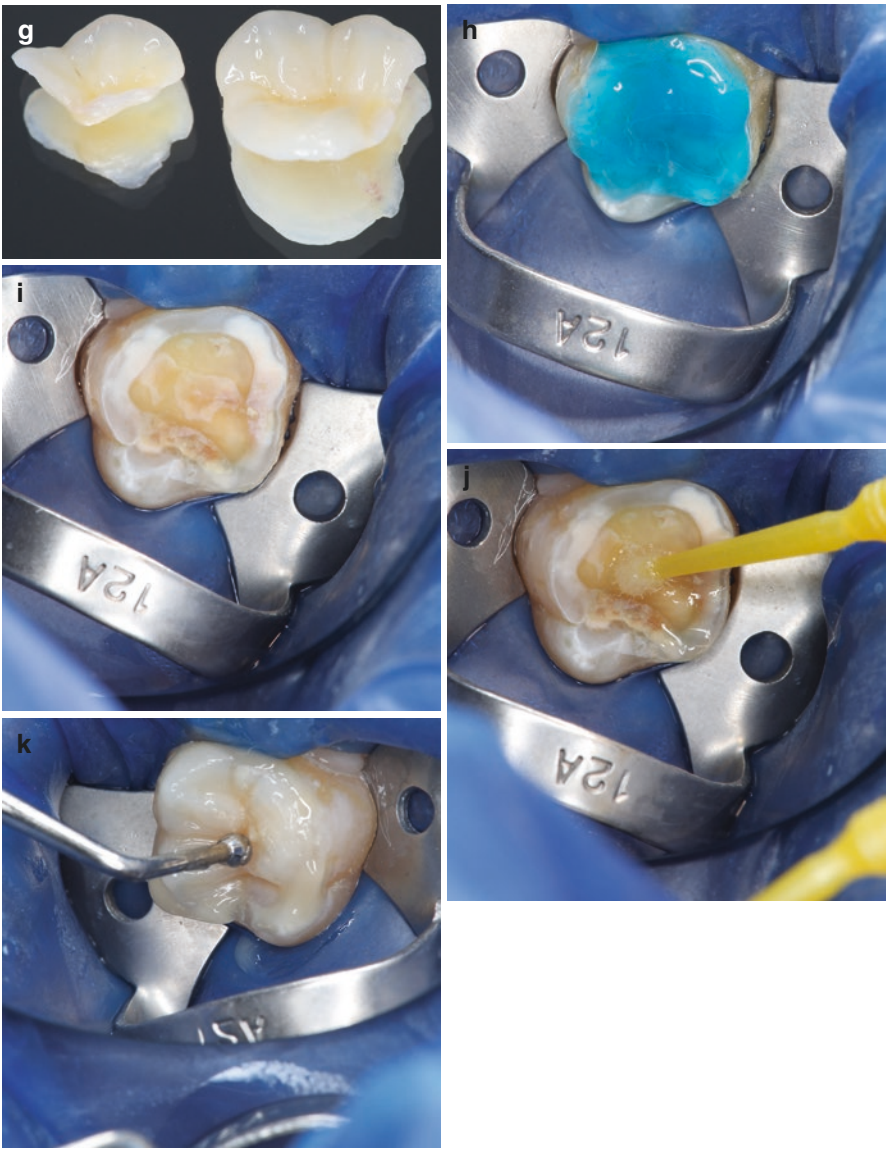


Fig. 13.2 A 12-year-old patient showing MIH with PEB in both upper first permanent molars. The patient complaints severe hypersensitivity. (**a**) Occlusal view of the upper jaw. (**b**) Tooth 16 in detail. (**c**) Tooth 26 in detail. (**d**) Tooth 16 after preparation. (**e**) Tooth 26 after preparation. (**f**) Laboratory-made composite restorations for both teeth shown on the plaster model (Karl Halbleib, N.I.C.E. Zahntechnik, Wuerzburg, Germany). A microfiller composite resin was used (SR Adoro, Ivoclar Vivadent, Liechtenstein). (**g**) Laboratory-made composite restorations for both teeth (Karl Halbleib, N.I.C.E. Zahntechnik, Wuerzburg, Germany). (**h**) Rubber dam application and etching of the tooth surfaces (37% phosphoric acid). (**i**) Tooth as it was seen after conditioning. (**j**) Application of the primer (Multilink A+B, Ivoclar Vivadent, Liechtenstein). (**k**) Insertion of the restoration before removing excess cement. (**l**) Tooth 16 after removal of excess and cleaning. (**m**) Tooth 26 after removal of excess and cleaning. (**n**) Occlusal view of the upper jaw after insertion of both restorations



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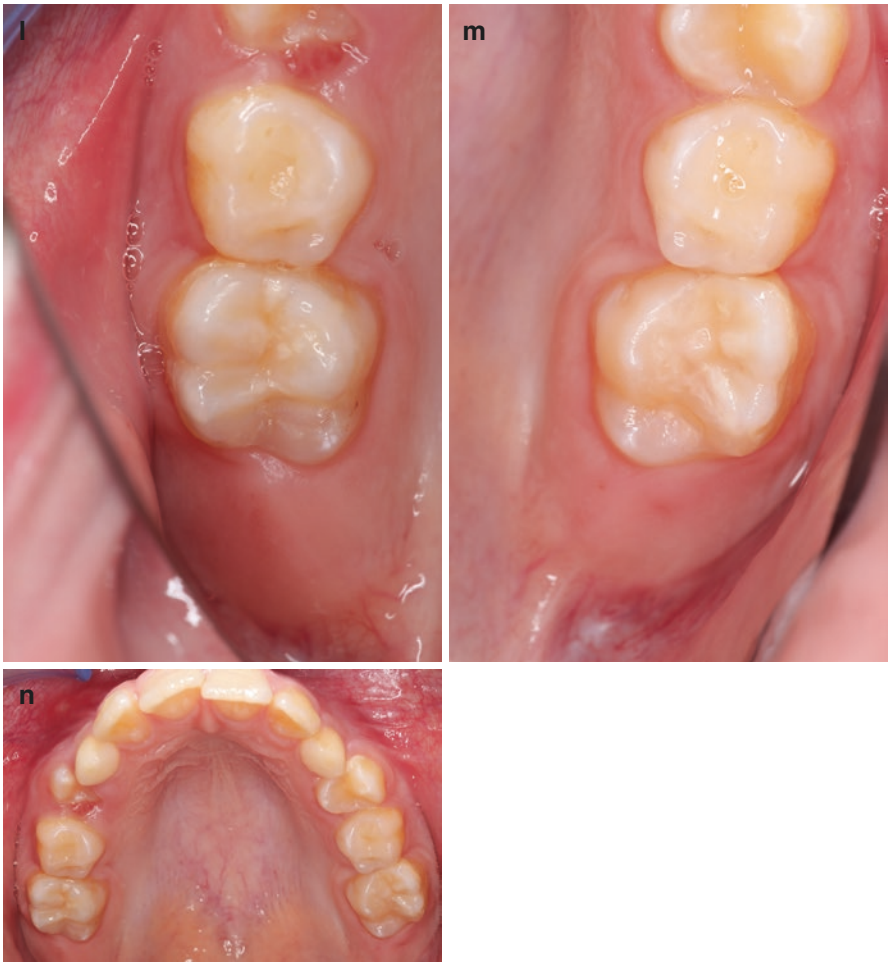

Fig. 13.2 (continued)

dam was applied (Fig. 13.2h). After that, the cavity was rinsed with a water spray and dried with air. Overdrying was avoided.

Next, inner restoration surfaces were sandblasted with aluminum oxide (grain size 100 µm and pressure of 1 bar). Afterwards, a single-component silanizing agent (Monobond-S, Ivoclar Vivadent, Liechtenstein) was applied for 60 s. Simultaneously, teeth were conditioned with etch–rinse technique (37% phosphoric acid, Ivoclar Vivadent, Liechtenstein). The enamel and dentin were etched for 30 s and 15 s, respectively (Fig. 13.2h, i). Subsequently, mixed Multilink Primer A/B was applied onto the entire bonding surface using a microbrush, starting with the enamel surface. It was then scrubbed into the surface for another 30 s (Fig. 13.2j). Excess was dispersed with blown air until the mobile liquid film was no longer visible. As the

primer is solely self-curing, no light curing was necessary. Following this scenario, restorations were inserted with Multilink Automix cement. The restoration was seated in place and secured (Fig. 13.2l). Excess material was immediately removed with a foam pellet and dental floss. Subsequently, all margins were light cured for 20 s (1000 mW/cm^2, Bluephase Style, Ivoclar Vivadent, Liechtenstein).

Finishing and polishing were performed with various silicone burnishers (Fig. 13.2l, m).

13.4.4 CAD/CAM

Nowadays, there are many ways to produce indirect restorations based on ceramics or composite. Conventional fabricated restorations compete against computer-aided design and computer-aided manufacturing (CAD/CAM) procedures. With regard to pediatric dentistry, CAD/CAM restorations have become a common method of treatment for permanent teeth in children [34]. Combining this technology with the use of digital impressions might be a further advantage as well. Data have shown adolescents feel more comfortable with scanning, although these scanners can require more chair-side time than traditional impression methods [35]. Nevertheless, with respect to MIH cases, literature is rare with only one case report being published using ceramic blocks [36].

13.4.4.1 Case

An 11.5-year-old female patient presented at the Department of Paediatric Dentistry complaining of pain due to a MIH-affected left lower permanent first molar with PEB (Fig. 13.3a–c). Clinical examination revealed the tooth showed severe hypersensitivity. Treatment planning comprised a CAD/CAM restoration for the affected molars to protect dental structure, reduce sensitivity, and improve masticatory function.

Premedication was used in this case as well, and local anesthesia was applied. Cavity preparation was performed in accordance with conventional rules for all ceramic restorations (e.g., rounding off interior corners and edges). Digital impressions were taken using an intraoral scanner (3Shape Trios, 3Shape, Denmark) (Fig. 13.3d, e). After that, a temporary restoration was applied using Clip (Voco GmbH, Germany).

Data of intraoral scans were transferred and 3D designs prepared. For manufacturing, a nano-ceramic hybrid CAD/CAM block was chosen (Grandio bloc, Voco GmbH, Germany) (Fig. 13.3f, g). Characteristics were 86% filled for enhanced strength and wear resistance and toothlike elasticity. Finalized restoration was blasted on the luting surface with aluminum oxide (50 µm) at 2 bar, cleaned using a steam cleaner, and then dried with oil-free air.

Following local anesthesia, the provisional filling was removed and restoration was tried in. After that, a rubber dam was applied, and pretreatment of the restoration could start. The luting surface was treated with a silane coupling agent (Ceramic Bond, Voco GmbH, Germany) for 60 s. The processed restoration was luted with a composite-based, adhesive luting agent (Bifix QM, Voco GmbH,

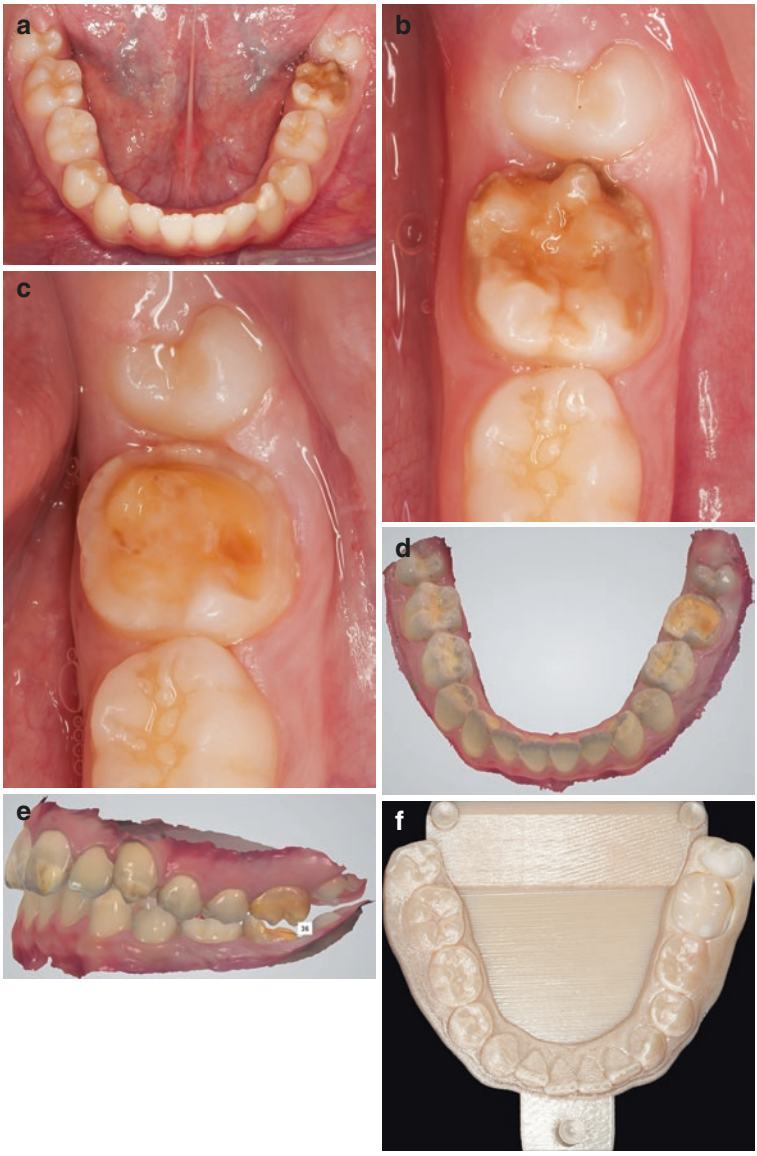

Fig. 13.3 A 12-year-old female patient showing MIH with PEB in the lower first permanent molar, complaining severe hypersensitivity. (**a**) Occlusal view of the lower jaw. Tooth 36 severely affected by MIH and PEB. (**b**) Tooth 36 in detail before preparation. (**c**) Tooth 36 after preparation. (**d**) Digital impression taken with the intraoral scanner, showing the lower jaw (Christoph Kurzmann, Medical University of Vienna, Austria).[1] (**e**) Digital impression of both jaws on occlusion so that the size of preparation can be checked.[1] (**f**) CAD/CAM restoration milled and situated on the model.[2] (**g**) CAD/CAM restoration in detail.[2] (**h**) Restoration cemented and rubber dam removed. (**i**) CAD/CAM restoration in detail. (**j**) Occlusal view of the lower jaw after restoration of tooth 36

[1]Digital impressions taken by Christoph Kurzmann, Medical University of Vienna, Austria

[2]CAD/CAM restoration constructed by Tom Vascovic, Medical University of Vienna, Austria

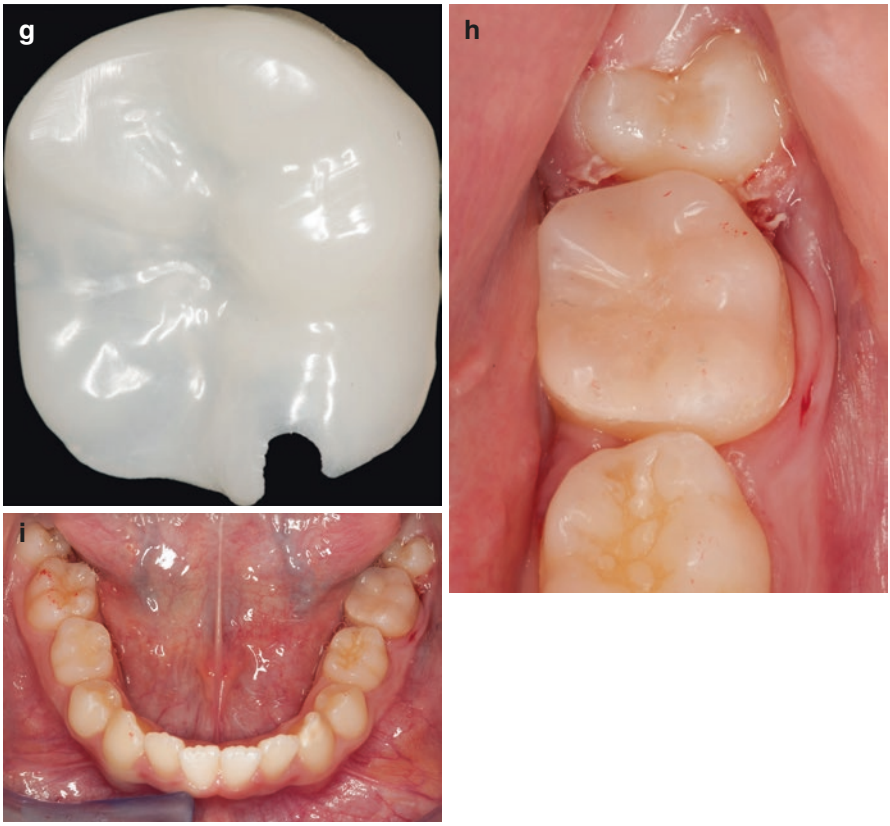

Fig. 13.3 (continued)

Germany). Simultaneously, the tooth was bonded with universal adhesive (Futurabond U, Voco GmbH, Germany). Excess material was immediately removed after insertion of the restoration with a foam pellet and dental floss. Subsequently, all margins were light cured for 20 s (1000 mW/cm², Bluephase Style, Ivoclar Vivadent, Liechtenstein). Finishing and polishing was performed with various silicone burnishers (Fig. 13.3h, i).

13.5 Conclusions

In conclusion, indirect restorations provide a feasible and useful method for restoration of affected molars with demarcated opacities and posteruptive surface loss. Case reports indicate laboratory-made composite resin restorations might be an alternative to cast metal or adhesive copings when the indication for direct composite restorations is exceeded. However, RCTs are needed focusing on this topic.

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14 Aesthetic Management of Molar Incisor Hypomineralization: Staged Strategies for Affected Incisors

Clarence P. Tam and David J. Manton

14.1 Introduction

Molar incisor hypomineralization (MIH) is an aesthetically, structurally and occasionally functionally debilitating condition affecting the enamel of first permanent molars with often affected maxillary incisors. These structural changes seem to occur in a sporadic fashion affecting one or more incisors to varying degrees. Depending on the nature, colour and depth of the lesions, various modalities of treatment are available to neutralize and correct the aesthetic handicap affecting the lives of many worldwide. Various treatment options will be discussed with a focus on desirability of non- or minimally invasive options prior to macroreduction and corrective resin layering, following the theme and protocol of responsible aesthetics. This chapter will define the current best practice protocol for addressing the sequential clinical techniques to treat incisor hypomineralization.

MIH is often misdiagnosed with other developmental lesions of enamel, most frequently enamel hypoplasia. It is important to note its deficiency in the post-secretory phase, that is, the stage following the enamel matrix deposition during its subsequent mineralization by ameloblasts. The deficiency in enamel hypoplasia is localized to the enamel secretory phase or enamel matrix formation. In MIH, as the surface breakdown occurs post-eruption, lesion margins become characteristically irregular, leading to exposed dentin and accelerated caries formation, particularly in

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molars. Lack of functional masticatory forces on labial enamel surface opacities leads to a greater maintenance of surface integrity in MIH-affected incisors. An additional functional load may indeed be the reason why lesion severity generally is greater on molars relative to incisors; however, interestingly the palatal surfaces of incisors are rarely affected, possibly indicating a different pathogenesis. MIH lesion border morphology is in contrast to enamel hypoplasia, where, phenotypically, these lesions are already visible upon eruption into the oral cavity and feature smooth peripheral margins [1].

Genetically, MIH contrasts with amelogenesis imperfecta (AI), which features a wide variety of genetically based developmental enamel conditions affecting all teeth (primary and permanent) with no dependence on chronological, biological or environmental stimuli or events. Inheritance for various subtypes have been found to include autosomal-dominant, autosomal-recessive, sex-linked recessive and sporadic inheritance, affecting one or more of the following enamel matrix proteins amelogenin, ameloblastin, enamelin, tuftelin and amelotin and enzymes such as MMP-20 and KLK4 [2].

MIH can be confused with the hypomature and hypocalcified variants of AI. MIH can also be misdiagnosed as Turner's tooth, which is an area of hypomineralization and/or hypoplasia which often only affects a single tooth in the mouth and features a location-specific infective or traumatic aetiology to the preceding primary tooth during the first 5.5 years of life, which is the time when the crown formation is complete for the maxillary lateral incisors [3, 4].

MIH can be mistaken for fluorosis, the distribution of which is dependent on the chronologic excess presence of systemic fluoride during enamel matrix formation [5]. Fluorosis affects enamel forming at the time of the ameloblast toxicity and is not limited to the first molars and incisors, but is expressed temporally in all the forming enamel. The treatment of fluorotic lesions of enamel, especially mild lesions, is different to that of MIH as the fluorotic hypomineralized lesions tend to be shallower and have a smaller mineral deficit [6].

14.2 Biomechanical Considerations

As the integrity of enamel matrix formation is compromised, at eruption, the resulting surface not only is more porous, irregular in ultrastructure and deficient in volume, microscopically the hydroxyapatite crystals are characterized with visually indistinct, unorganized rod sheaths which makes adhesive bonding and ultimate microtensile shear bond strength less predictable relative to normal enamel [7, 8]. This permeability may be the origin of bacteria detected in the dentine below what appears to be clinically intact hypomineralized enamel [1]. This phenomenon may be responsible for the presence of a heightened immune cell density observed in the pulp horns and sub-odontoblastic region of hypomineralized teeth as relative to increased inflammation [1]. Biomechanically, there is often a significant reduction in both elastic modulus and surface microhardness, paired with a propensity to absorb stain. Crombie et al. (2013) analyzed the mineral content of affected enamel in MIH cases and quantified this at 58.8% (vol%

mineral), where a level of 86% is seen in unaffected enamel [9]. As a result, the Vickers microhardness was also significantly reduced in affected enamel. The surface layer of demarcated hypomineralized lesions of enamel can also remineralize and approach the mineral density and hardness of healthy enamel if the oral environment is healthy [10].

14.3 Strategies for Optimizing Adhesive Strength

MIH-affected enamel is softer and more porous than healthy enamel. The mineral density can be significantly reduced, although this case varies considerably between and within affected teeth. Bonding is often compromised as there is an increased proportion of organic matrix relative to inorganic matrix, especially using fourth- and fifth-generation total-etch adhesives. As such, if prudent, the conservative macroreduction of affected areas to expose as much normal tissue as possible must be considered to increase the relative proportion of mineralized substrate in the underlying areas [11]. The downside of this approach is that in severely affected teeth, this may represent more than 2/3 of the tooth surface enamel. A recent systematic review failed to show any significant advantage of self-etching adhesives compared to etch and rinse adhesives relative to bond strength [12].

Adhesion to enamel is most effective to the ends of the rods, not the lateral aspects. As the organization is irregular, with likely random areas of dentine exposure, it is prudent to consider air abrasion as a pretreatment to MDP-based adhesive bonding protocols using 27 μm aluminium oxide to increase the surface area for potential bonding. Motisuki et al. [13] noted a significant difference in microtensile shear bond strength when dentin surfaces were treated with micro air abrasion (27 μm aluminium oxide particles) relative to bur-cut dentine.

It stands to logic that a microroughened surface features more surface area for both increased micromechanical retention and for enhanced chemical adhesion. A study by Chay et al. revealed that oxidative pretreatment of hypomineralized enamel with a 5.25% NaOCl (aq) solution for 1 min resulted in significantly higher microtensile shear bond strengths relative to control and indeed was not statistically significantly from the bond strength of normal enamel. The use or non-use of resin infiltration did not have any significant impact on increasing the microtensile shear bond strength of hypomineralized enamel [7]. Kumar et al. did not find any statistically significant increase in Knoop hardness when comparing resin-infiltrated hypomineralized enamel with uninfiltrated enamel [10].

14.4 Restorative Considerations

Posteriorly, the average age of first permanent molars featuring a poor prognosis is 8.5–9 years [11]. As such, prior to the eruption of the permanent second molars at 12 years, such teeth may be considered for exodontia and replacement therapy by the second and third molars in course.

Anteriorly, the extent and severity of opacities is widely variable and frequently asymmetrical. The breakdown of enamel is less common anteriorly as there is a lack of direct functional loading on the labial surface, but the poor aesthetics are a driver for patients to seek aesthetic solutions as often social interactions and self-confidence are affected [14].

14.5 Modalities of Treatment in Order of Staging

14.5.1 Remineralization Strategies

The methodology of increasing mineral density of a lesion is termed remineralization. The remineralization function of the active molecule, casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) crème relative to the restoration of mineralization, morphology and porosity has been well-documented in the literature in its treatment of hypomineralized white spot lesions with calcium and phosphate levels recovering to almost that of normal, mature enamel at the 3-year mark [15].

Reservations of effectiveness are due to the theory whereby the use of a supersaturated solution of Ca^{2+} and PO_4^{3-} ions is believed to rapidly deposit mineral ions on the surface of the lesion, limiting penetration and diffusion of these ions deeper in the lesion body. One solution is to stabilise the Ca^{2+} and PO_4^{3-} ions by creating complexes such as CPP-ACP or CPP-ACFP which congregate at the surface and maintain high ion gradients, which then obviate spontaneous precipitation, instead allowing for a slow ion release over time into the lesion body of neutral ion complex CaHPO4 [16].

Overall, there is little doubt that the action of CPP-ACP is statistically significant in vivo on remineralization metrics of white spot lesions and early carious lesions. This effect is long term in nature, however, does not appear to be statistically different from fluorides, and there is conflicting evidence in the literature regarding the clinical effectiveness of CPP-ACP in conjunction with fluoride. Relative to anterior teeth, the ultimate question is whether statistical significance translates from a cost–benefit and risk–benefit ratio standpoint into clinical significance relative to visible lesion reduction [17].

14.5.2 External Vital Bleaching

Molar incisor hypomineralization presents with an array of lesion morphologies and colours. For the chromatically affected lesion with significant background lesion contrast, there has been reported effectiveness in improving lesion appearance with the use of carbamide peroxide in custom nightguard or bleaching trays. This is unlikely to improve or decrease the underlying opacity; however, the mechanism of action is to decrease the contrast between the background colour and the often chromatically discoloured, opaque lesion. Affected patients usually are discontent with the colour of their teeth, so this provides a noninvasive and often visually dramatic

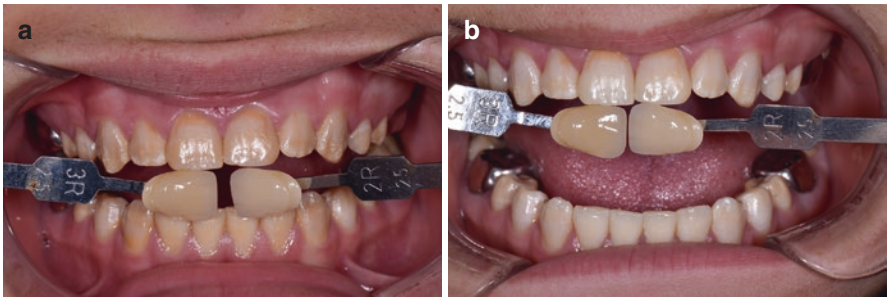

Fig. 14.1 (**a**) Baseline bleaching shade acquisition. (**b**) Overnight vital bleaching in custom cervical seal trays with 10% carbamide peroxide (Opalescence, Ultradent, UT) at the 2-week bleach check. (**c**) Bleach shade check at the 1-month mark. End of active treatment

treatment option to improve outcomes and bolster motivation. The result is possible when a 10% carbamide peroxide solution is used without deteriorating chemical and mechanical properties of both normal and hypomineralized enamel [18].

14.5.2.1 Case 1

A 15-year-old healthy male with generalised hypocalcified or hypomature enamel (Fig. 14.1).

Case comments: The patient was given the options of vital bleaching to decrease the contrast of both the chromatic and hypocalcified maverick features, for which he was being teased at school. Since vital bleaching, his self-confidence has increased, and the teasing has stopped. Further treatment to further reduce the visibility of the now-minor white specks was not desired by the patient. He was instructed to use CPP-ACP crème in his bleaching trays overnight for an additional two weeks to bolster the surface quality of the bleached teeth.

An alternate protocol for combined use of remineralizing CPP-ACP crème in conjunction with external vital bleaching was presented by Mastroberardino et al. [19]. Custom bleaching trays are fabricated for the patient, with instructions to use CPP-ACP crème in the trays, worn on the teeth for 2 h each day for a three-month period. Following this period, for two consecutive days out of a 7-day week, a 20% carbamide peroxide solution is applied to the custom bleaching trays for 2 h per day. The remineralizing agent, CPP-ACP, would be used instead of the peroxide gel for the remaining 5 days of the particular week. This protocol was executed for 2 months to comprise 14 days of vital bleaching as per the manufacturer's recommendation. There was a visible improvement in aesthetic condition reported.

14.5.3 Surface Microabrasion

Incisor hypomineralization lesions found in anterior teeth are sometimes characterized as ultrastructurally located throughout the entire thickness of the enamel down to the dentin-enamel junction (DEJ) [11]. As a result, microabrasion, both in chemical and mechanical air and pumice-driven forms, are often limited in their ability to

decrease lesion visibility. The concept of removing white spot lesions chemically was pioneered by Kane in 1926 using 36% hydrochloric acid. Since then, mechanical assistance from a rotary handpiece was utilized in the 1970s using a mixture of 18% hydrochloric acid, hydrogen peroxide and ether and finally paired with an abrasive agent in 1982 by Murrin et al., who utilized 36% hydrochloric acid paired with pumice in a micromotor handpiece. Over time, the acid concentrations tested decreased and were paired with the abrasive suspended in a water-soluble mixture for safety and ease of removal. To increase lesion permeability and to remove aprismatic enamel, some authors have suggested the use of surface macro abrasion using an extra-fine diamond bur prior to the use of chemomechanical abrasion [20].

Modern microabrasion formulations are supplied by companies such as Ultradent Products Inc. (Opalustre) (6.6% HCl + silica carbide abrasive) and Premier Dental Company (Prema Compound) (10% HCl + silica carbide abrasive). Relative to fluorosis, where the lesion may be located more superficially, enamel microabrasion works well to improve visual appearances. Sundberg found an average of 5–10 applications of microabrasive systems that have been found to result in loss of 25–200 μm of enamel, which is clinically acceptable. This range in enamel loss corresponds to the application of Opalustre on the tooth for 1-min cycles for a total treatment range between 1 and 10 iterations of microabrasion.

The transillumination technique works well for judging the presence of hypomineralized lesions [21]. With an LED source on the palatal aspect, a more opaque/dark appearance of the lesion with ill-defined borders signifies that it is deeper from the surface towards the DEJ relative to one which is a more translucent/light lesion featuring neatly defined borders. If the lesion extends superficially enough (remember that MIH lesions always start at the dentinoenamel junction), the surface layer removal by decalcification (Icon-Etch, DMG, Hamburg) sometimes in conjunction with microabrasion used often to remove superficial stain may provide a better candidate for resin infiltration effectiveness (discussed in Sect. 14.5.4) [22]. The "view from an extreme lateral aspect" technique involves judging the depth of the lesion from extreme mesial or distal angles to ascertain the depth of penetration visually through the enamel volume. White spot lesions that appear to be "painted" on the surface may be more superficial in position and thus better microabrasion candidates than those that display opacity or diffuse lesion bodies penetrating deeper in the enamel volume.

Often a concern revolves around post-treatment residual enamel microroughness and plaque/stain accumulation. Bertoldo et al. reported natural enamel rehardening via the presence of chloride and silica ions from the microabrasion compound (Opalustre, Opalescence). Chloride ions are strongly linked with enamel rehardening, accounting for the bulk of saliva's ionic strength. The use of this mixture allows the formation of a bioactive compound (Ca_3SiO_5) that is reported to induce a new apatite layer on acid-etched enamel. The clinical stability of this apatite layer is unknown but suggests this passive approach should be considered over the use of reductive polishing discs and wheels [23].

The simultaneous mechanical, compressive and acid erosive effects on the enamel rods has been found to result in a surface layer similar to aprismatic enamel, a highly mineralized layer with altered optical properties that has greater reflective character. This may be advantageous in helping to camouflage subsurface lesions. This

"abrasion effect" can be achieved with the use of both phosphoric and hydrochloric acid, which despite concentration differences have a very similar erosive effects on opening surface interprismatic spaces with no effect on the subsurface structure [24].

14.5.3.1 Case 2

An 18-year-old healthy female with unsightly hypomineralized spot on the labial surface of tooth 43 (Fig. 14.2).

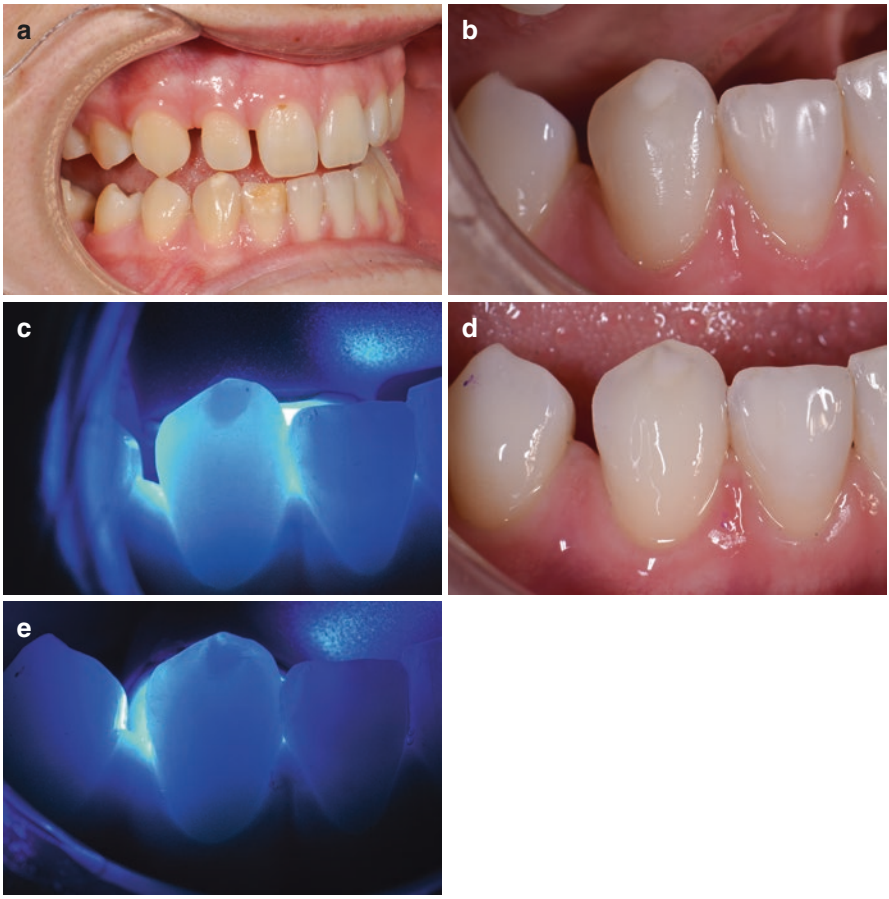

Fig. 14.2 (**a**) Hypomineralization noted on 42 and 43 buccoincisal aspect. Transillumination revealed that treatment of 43 may be partially successful using microabrasion; however, the depth of the enamel dysplastic defect on 42 required a subtractive–additive restorative approach. (**b**) Overnight bleaching in custom trays using 10% carbamide peroxide was utilized prior to the composite bonding on 42. Pre-microabrasion situation on 43BI. (**c**) Transillumination reveals partial translucency of the lesion, which makes it a candidate for microabrasion. (**d**) Post-microabrasion using a 6% hydrochloric acid solution impregnated with silica carbide particles (Opalustre, Ultradent, UT). Three cycles of 1 min each were utilized with moderate pressure. (**e**) Post-operative transillumination assessment reveals portions of the lesion that are subsurface in nature and more proximal to the dento-enamel junction. Penetration to this depth may require resin infiltration

14.5.4 Resin Infiltration

Hypomineralized enamel lesions have increased porosity and therefore could be suitable for the resin infiltration method originally designed for carious lesions. This approach is microinvasive and one that requires two components: Firstly, chemomechanical treatment to remove the more highly mineralized surface layer to increase penetration of the infiltrant. Secondly, under desiccated conditions (as no carrier or primer can be evaporated within the body of the lesion), a low viscosity resin may be infiltrated into the body of the lesion with both mechanical and active diffusion mechanisms. Although the degree of visual lesion improvement varies drastically between cases [25] and even between teeth in the same mouth, this represents the last resort of noninvasive options and may be considered with or without composite layering depending on whether there is a physical defect or deficiency with the area. This variability is reflected in the study completed by Kumar et al. [10], who determined that 11 out of 21 samples tested exhibited a positive visual change with resin infiltration.

If chromatically discoloured lesions exist, a consideration is the requirement of vital nightguard bleaching prior to lift the colour value of the tooth and lesion, often perceived as a positive therapeutic outcome. It is imperative to allow the requisite 7–10 day stand down period to permit full oxygen radical leaching from the teeth before any resin bonding technique is employed. Schoppmeier et al. demonstrated an increased visual masking ability of resin infiltration as discussed below when the teeth were pre-bleached using a 25% hydrogen peroxide solution 2 weeks prior to the resin infiltration technique, suggesting the possibility of a synergistic effect between bleaching and infiltration [26].

Full rubber dam isolation often with ligature ties is ideal as the standard in patient protection and dental isolation prior to any adhesive restorative procedure. Occasionally, for anterior teeth in younger individuals where there are insufficient posterior anchor points or crown height/angulation for the rubber dam clamps, a more localised gingival protective measure is a compromise (OpalDam, Ultradent Products, Inc.), with an application similar to that of in-chair whitening procedures. This may be utilized in gag reflex-affected individuals also with the use of a lip-retracting device (OptraGate, Ivoclar Vivadent).

The use of a 15% hydrochloric acid solution for etching of the enamel results in a degree of enamel loss. Hydrochloric acid is preferred over phosphoric acid as the latter does not completely remove the hypermineralized surface layer. Meyer-Lueckel et al. noted an average loss of enamel thickness of 77 μm after a 4- × 2-min cycle protocol. For the 960 measurements used in the study, only 11 exceeded 120 μm, which indicates that over-etching and substantial enamel volume loss is hard to achieve even with increased cycle iterations [27]. What is important to note is the actual surface layer thickness as pertains to hypomineralized enamel. Kumar et al. [10] determined the average surface layer lesion thickness of MIH enamel to be 58 ± 29 μm. The average depth of acid erosion with a 15% HCl (aq) solution was 58 ± 12 μm. Arnold et al. noted the use of 15% HCl (aq) over a 2-min period resulted in a thickness loss of 34.02 μm [28]. For reference, it is known that the average thickness of enamel in the cervical region averages between 300 and 500 μm, in the middle third 500–700 μm and incisal third 700–1000 μm in anterior teeth. Usually, etching

cycles occur in tandem with a total of between 2 and 4 cycles on average. With this increase in etching, each cycle increases the erosive depth between 13.28 and 15.16 μm ($p < 0.05$) with the median enamel surface loss being 77 μm. Arnold found no significant difference on surface roughness between acid-treated surfaces and control [28].

The action of surface corrosion removes a hypermineralized layer that is an obstruction to the porous body of the lesion, improving access of the infiltrant to the subsurface region. This inadvertently also changes the optical refraction of enamel, and as desiccation is achieved, water is lost and air is gained. Water has a refractive index of 1.33 and air 1.00. Hence, the corresponding reflective index is inversely proportional in nature, and thus the lesions and teeth appear even whiter than baseline during treatment.

TEGDMA is the preferred monomer for this technique as it has been found to infiltrate to a greater extent than bis-GMA. It needs to, however, be pretreated with ethanol [29] to desiccate the lesion.

Resin infiltration has physical benefits to the hypomineralized enamel in addition to optical gains. Paris et al. [30] noted an increased resistance to demineralization and microhardness with respect to resin-infiltrated carious enamel. This case is achieved only with two applications of the resin infiltrant.

Penetration depth and microhardness of the enamel following resin infiltration used in carious hypomineralization with Icon (DMG, Hamburg) was found to be the highest in all measured outcomes when compared to the use of CPP-ACP and a conventional bonding agent (10). The mean penetration depth of Icon was 26.32 ± 4.61 μm. This is often different to the porous ultrastructure dimension of MIH enamel. Crombie et al. discovered that infiltrant penetration extended to 670 ± 390 μm. Crombie discovered increased Knoop microhardness of infiltrated lesions relative to adjacent uninfiltrated hypomineralized lesions on the proportional magnitude of 2.2 ± 2.5 times that of control [10, 25].

Although resin infiltration with Icon can produce optical improvements by way of increased penetration coefficients and increased surface microhardness, it has been found to be more susceptible to staining than other restorative options. As such, increased home hygiene vigilance and dietary awareness needs to be practiced by the patient [31].

14.5.4.1 Case 3

A 57-year-old female with medical history significant for a mild form of multiple sclerosis presented to my service for aesthetic enhancement of her smile. Anatomically, her anterior dentition featured a congenitally missing upper right lateral incisor (tooth 12) and enamel dysplastic spot lesions which were not chromatic in nature (Fig. 14.3).

14.5.4.2 Case 4

A healthy 10-year-old male presented to the practice on referral for aesthetic improvement of his upper anterior teeth, for which he was being teased. History was significant for three dental impact subluxation accidents as a child, which in all cases the teeth eventually firmed up again according to the parent. The situation may represent hypomineralization with or without the influence of a Turner's tooth

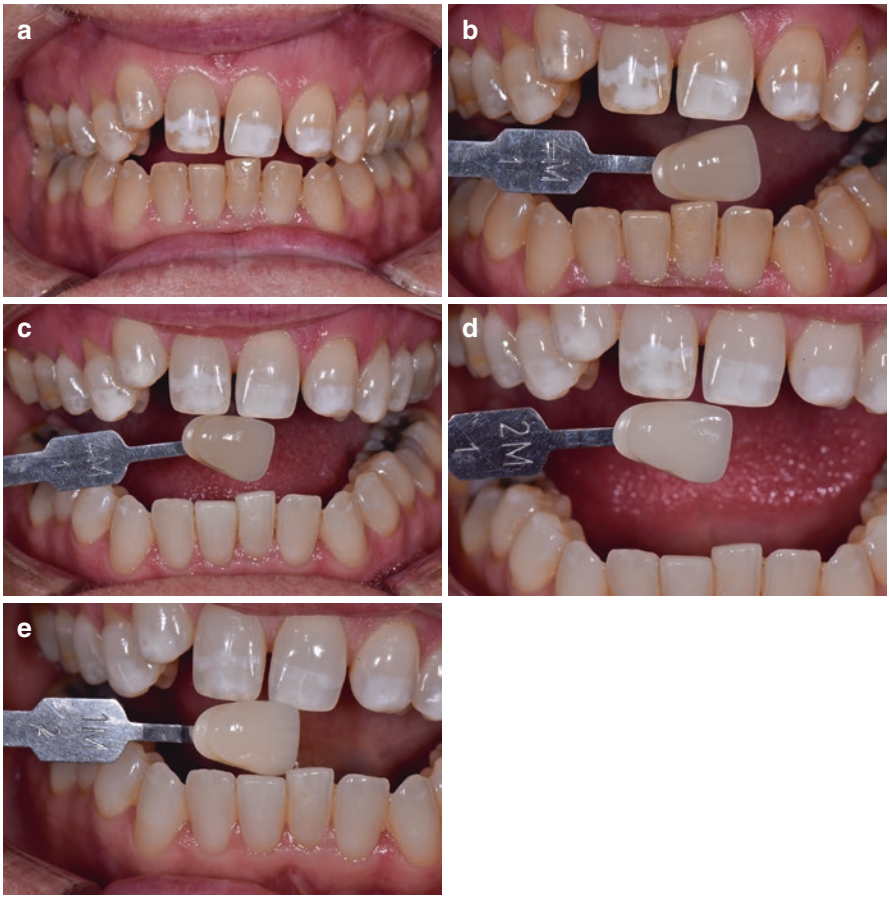

Fig. 14.3 (**a**) Baseline situation. Banding is noted in the upper posterior sextants on the buccal aspect indicating a possible interaction with tetracycline-based antibiotics during dental development. The white intensives are visible and most intense in the anterior region. (**b**) Baseline bleach shade. (**c**) Overnight bleaching using 10% carbamide peroxide (Opalesence, Ultradent Products Inc., UT). A 3-week bleach shade check. (**d**) Bleach shade check after 1 month, 3 weeks of overnight vital bleaching. (**e**) Bleach shade check after 2 months, 3 weeks of overnight vital bleaching. (**f**) Baseline situation pre-resin infiltration using Icon (DMG, Hamburg). (**g**) Cross-polarized photo taken using Polar_Eyes (Bioemulation, Germany) revealing true extent and intensity of internal hypomineralization. (**h**) Placement of 15% hydrochloric acid on tooth surface for 2 min before thorough rinsing with water for 1 min and air drying. (**i**) Application of ethanol to the surface for 1 min (Icon, DMG, Hamburg) and thorough desiccation. The etch–rinse–dry–ethanol–dry cycles were completed over 4 cycles. (**j**) Situation prior to infiltration with TEGDMA-based resin: 2 cycles of 3 min scrub and dwell, air thin, floss, 40-s cure, reinfiltrate, 3-min dwell time, air thin, floss, 40-s cure. (**k**) Unpolarized and cross-polarized photos of immediate post-operative situation. Degree of visual intensive reduction noted with areas of residual hypocalcification. (**l**) A 1-week post-infiltration reassessment photo. Significant aesthetic improvement

Fig. 14.3 (continued)

situation. Indeed, due to his frequent skateboarding, his scarred lip indicates that this type of injury continues to the present day (Fig. 14.4).

14.5.5 Macroreduction and Aesthetic Layering

Macroreduction is used alone or, as this protocol defines often, in conjunction with and following the use of the aforementioned procedures only if a visible or structural defect remains [11]. Depending on the position of the residual lesion, further tooth reduction even after resin infiltration may need to be undertaken, both to physically eliminate aspects of the lesion and provide adequate restorative space for planned aesthetic composite layering and/or indirect procedures. As such, rubber dam isolation in conjunction with retraction cord is requisite to maximize the prognosis of these restorations.

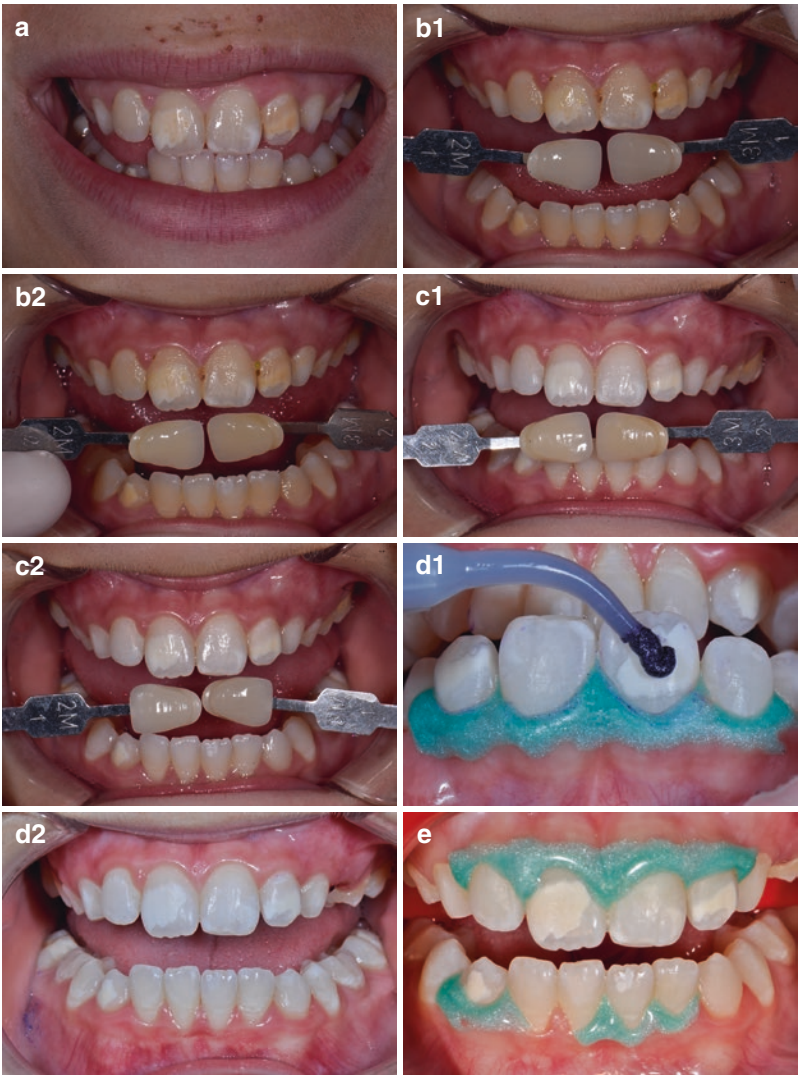

Fig. 14.4 (**a**) Baseline smile depicting clear and well-defined intensives in the upper anterior sextant. (**b**) Baseline shade prior to overnight vital bleaching using custom cervical seal trays and 10% carbamide peroxide (Opalescence, Ultradent Products Inc., UT). (**c**) Situation after 2 weeks of overnight vital bleaching. Intensives are still present in the teeth, but dramatically improved in position without the chromatic effects. (**d**) Situation after microabrasion using Opalustre (6% HCl with silica carbide particles) (Ultradent Products Inc., UT) × 3 cycles of 1 min. Minimal effect on white intensives. (**e**) Isolation for resin infiltration using a TEGDMA-based resin infiltrant (Icon, DMG, Hamburg). Full rubber dam isolation would have been ideal, however the strong gag reflex of the patient obviated placement. OpalDam (Ultradent, UT) was used instead for gingival protection in junction with an OptraGate (Ivoclar Vivadent). (**f**) Immediate post-operative situation. The etch–rinse–dry–ethanol–dry cycles were completed over 4 cycles. Infiltration with TEGDMA-based resin: 2 cycles of 3 min scrub and dwell, air thin, floss, 40-s cure, reinfiltrate, 3-min dwell time, air thin, floss, 40-s cure. (**g**) A 1-week post-operative reassessment of the lesions. Dramatic reduction of both chromatic and white hypomineralized intensives via the aforementioned combination therapy approach. Status update: no more teasing at school

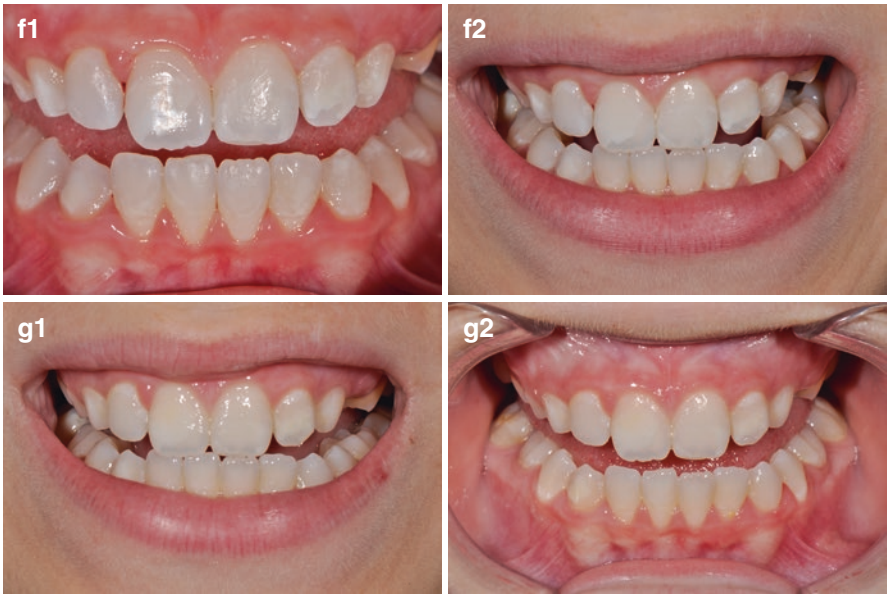

Fig. 14.4 (continued)

This is considered an irreversible restorative approach, and will require maintenance and replacements over time as composite restorations have a limited service lifetime. The approach requires the prudent use of infinity and/or starburst bevels to increase the surface area both for bonding and blending of resins into the surface of the adjacent enamel. Surface preparation and decontamination with particulate micro air abrasion is also beneficial in gaining micromechanical retention prior to the adhesive procedure.

If the need for composite addition or layering is known, it is paramount that a colour map is generated and recorded photographically prior to dental anaesthesia being administered. This will ensure the best chance of matching the tooth shade parameters in the pre-dehydrated state.

If there is a deficiency in outline form or primary anatomy of the affected tooth, it is important to restore the shape using a diagnostic wax-up guided or freehand approach to building the lingual or palatal shelf. A self-cured addition silicone material is used (i.e. Exaflex, GC America) to capture the palatal aspects extending to the facio-incisal line angle of the wax-up. Usually, a chromatic or achromatic semi-translucent or milky-white translucent enamel-like composite is used for this layer, usually averaging 0.3 mm in thickness. This layer should approximate the palatoaxial angle or inclination of the adjacent teeth, providing adequate space for layering of subsequent composites facially.

Opaquers may need to be utilized (i.e. Masking Liner, Essentia, GC America) in thin layers to visually occlude/mask discoloured regions of the tooth preparation. The hue, value and chroma of the tooth is reflected in the chosen dentin shades. These opaque shades approximate closely the pre-dehydrated target shade in the cervical aspect of the tooth, for the reason of the dentin being the most visible in the area where the enamel is thinnest. The dentin layer is sculpted anatomically with the

incisal aspect developing into dentin mamelons, with usually 2 to 3 dominant lobes depending on the anterior tooth to be restored. These mamelons are further splayed into smaller subheads, with subtle connections of small strands of these subheads at sporadic intervals to the incisal edge. The most important angle to judge layer thickness is from the incisal view. In this way, space remaining for subsequent layers can be preserved to avoid "overbuilding" the tooth facially, which often can be aesthetically disastrous after finishing back to the correct tooth buccolingual tooth volume.

Following placement of the dentin/opaque layers, the incisal aspect features the aforementioned dentin mamelons, which are a series of undulating areas. It is important to allow this area to feature visibly in the final product, hence the need for an application of a clear translucent material in this region. Often, a clear or amber translucent material is used for the bulk of the incisal edge, leaving room for a blue translucent or grey translucent application on the proximal and/or proximoincisal aspects of the incisal 1/3. It is critical not to overbuild this layer and leave adequate room for your enamel layer.

Once the translucent layer is cured, occasionally the colour map indicates the presence of minor hypocalcified streaks, spots or clouds in the adjacent teeth along with areas of increased chroma and/or crack lines. Tints or stains can be applied at this time with the principle that "less is more". It is important to ignore any increased appearance of hypocalcification in the adjacent teeth as dehydration changes the refractive index of the enamel, as mentioned before. Stick to your guns, meaning stick to your original colour plan.

The enamel layer is usually composed of either a single chromatic layer or two blended layers of a chromatic enamel cervically and an achromatic enamel incisally. This is built and sculpted to full form, ensuring adequate material and volume in the transitional facioproximal line angle regions. This is critical to ensure adequate visual "separation" of the teeth and accurate reproduction of the primary anatomy of the tooth.

The primary anatomy is refined using a series of abrasive discs (Sof-Lex Extra Thin, 3M ESPE) before the three planes of facial reduction defined using a red-stripe fine diamond bur. Cervical overhangs are removed completely. A flat to slightly concave area on the facial plane exists in the incisal to middle thirds between the position of the facioproximal line angles. This area is created using a red-stripe fine diamond bur. The secondary anatomy is planned using an HB lead pencil and is inscribed on the surface of the tooth as a contouring map before placement using a series of needle-point diamond, football-shaped diamond and chamfer burs to create a smooth, undulating surface reflecting the lobes of the respective tooth. Once this process is complete, the use of medium and fine Sof-Lex discs pressing slightly into the depressions helps to remove macro scratches.

The tertiary anatomy often consists of the placement of perikymata, which is achieved with the use of green-stripe or coarse diamond burs, run at stall speed and light pressure in a single direction across the tooth. The restoration is then polished to high shine using a pre-polisher followed by diamond-impregnated silicone polishing cups and discs. A final luster can be imparted by the use of a 1 μm aluminium

oxide paste (Enamelize, Cosmedent) with a felt plastic-backed single-sided disc mounted on a mandrel (Flexibuff, Cosmedent).

A number of studies have corroborated the longevity of composite restorations on young permanent incisors. Peumann et al. investigated the success of composite additions on maxillary central and lateral incisors over a 5-year period with an 89% success after the 5-year observation period [32]. Macroreduction and aesthetic layering is an approach when used in a minimally invasive manner and following use of the aforementioned techniques can result in a maximally aesthetic result to the patient's benefit.

14.5.5.1 Case 5

An 8-year-old healthy female was referred to me to support and treat the aesthetic and functional impairment with teeth 32, 31, 41 and 42. On examination, enamel dysplasia was noted with hypoplastic and hypomineralized features: localized advanced on 32, 42 MIDBL, localized moderate on 31, 41 BIL aspects. It features very thin buccolingual dimensions (0.5 mm). The plan was to complete bonded composite restorations to restore natural anatomical dimensions of enamel which would function to bolster the residual functional strength of the tooth (Fig. 14.5a–d).

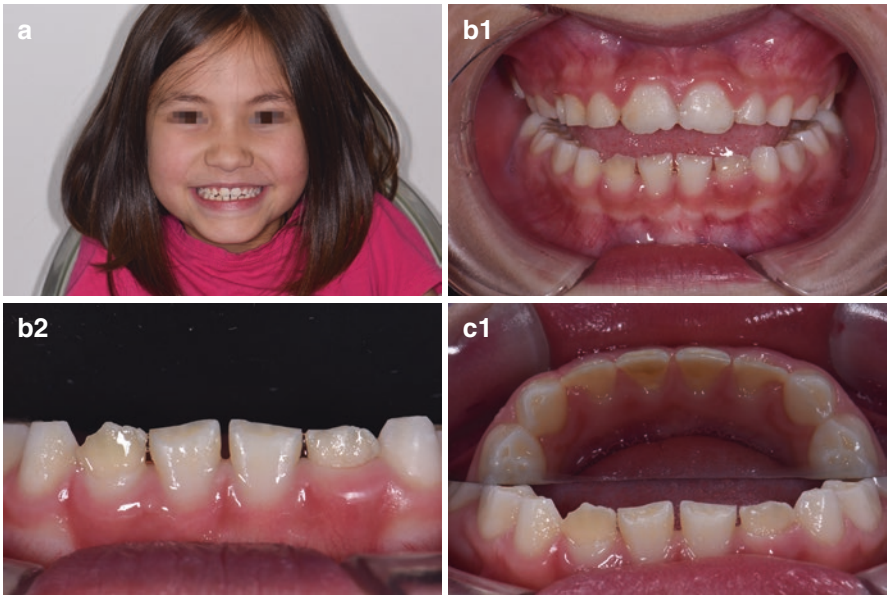

Fig. 14.5 (**a**) Baseline photo showing presence of hypoplastic and hypomineralized lower anteriors in a case requiring no required tooth structure reduction. (**b**) Frontal retracted photographs showing lower incisor appearance. (**c**) Combination frontal and incisal view showing extremely compromised buccolingual thickness of teeth 32 and 42 with susceptibility to fracture. (**d**) Postoperative views of no-preparation additive composite bonding to protect compromised tooth structure and simultaneously enhance aesthetics

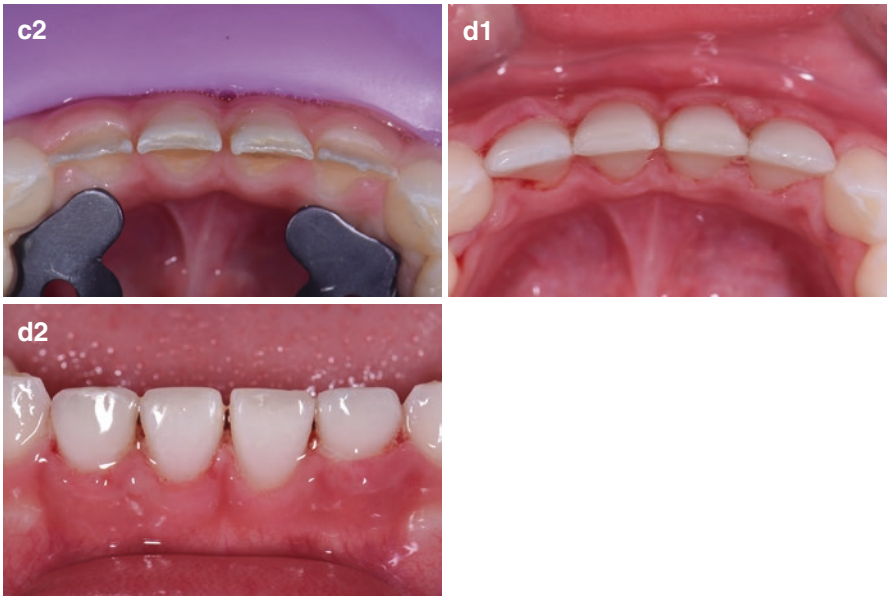

Fig. 14.5 (continued)

14.5.5.2 Case 6

A healthy 26-year-old female presented to the practice for aesthetic improvement of the chromatic incisor hypomineralization lesions particularly in her upper central incisors and a stained horizontal and vertical hairline fractures featured on the labial surface. There is presence of hypomineralization or enamel dysplasia in her other teeth, with a generalized distribution relative to lesion intratooth position and intertooth position. After gaining foundational restorative stability via elimination of dental caries, custom home bleaching trays were fabricated for the patient, and she used a 10% carbamide peroxide solution overnight over the course of a month until the individually maximal value attainable was reached. Whitening resulted in a lessened appearance of the brown fracture lines and the chromatic patches on the teeth, although the horizontal craze lines and 11MIB chromatic patch was still intensely visible. The decision was made to complete conservative facial reduction to allow for reduction of the superficial aspects of the lesion and simultaneously provide layering space. The restoration was micro air abraded using 27 μm aluminium oxide before a total-etch adhesive technique using Peak Universal Bond (Ultradent Products Inc., UT). The composite veneer was constructed to mask the unsightly areas, modify the value of the teeth further and impart subtle hints of hypomineralized specks and streaks throughout the teeth that would enable them to blend into the adjacent teeth (Fig. 14.6a–o).

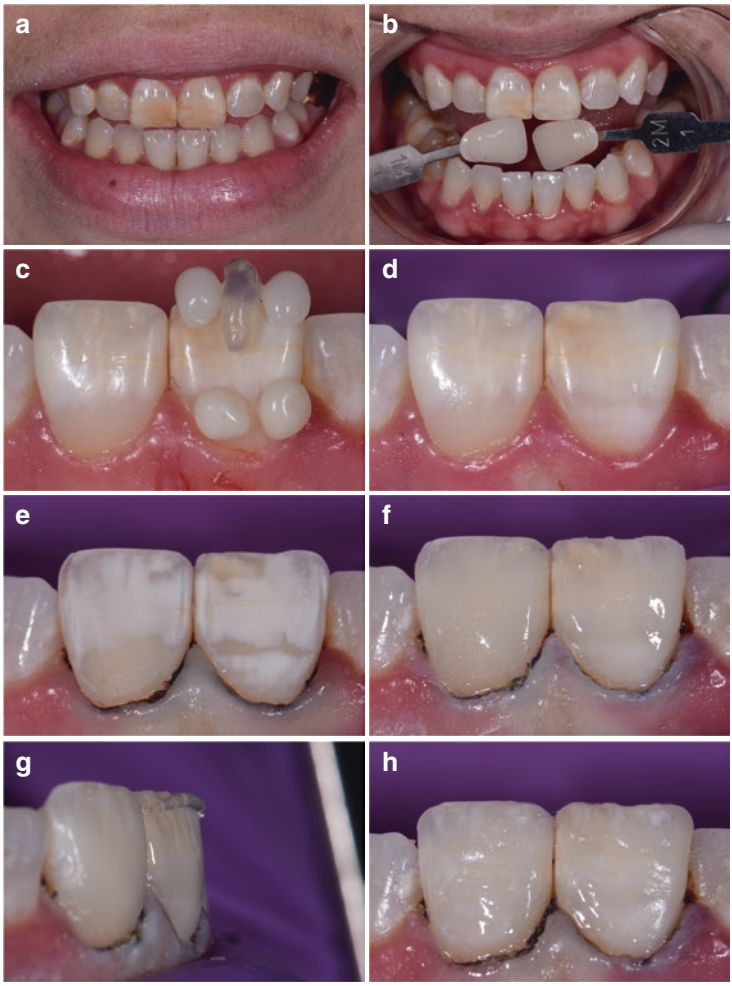

Fig. 14.6 (**a**) Baseline situation with chromatic incisor hypomineralization and stained comminuted hairline fracture pattern. (**b**) Situation following 4 weeks of overnight bleaching using 10% carbamide peroxide (Opalescence PF, Ultradent, UT). (**c**) Baseline situation prior to composite veneer placement on 21, 11. Shade selection via the shade button technique using various shades of enamel and dentin as well as an iridescent blue effect shade from Vit-l-escence (Ultradent, UT). (**d**) Split rubber dam isolation-initial situation prior to composite veneer placement. The residual chromatic fracture lines and patches can be appreciated. (**e**) Veneer preparation maintaining bulk of preparation within enamel. (**f**) Following total-etch adhesive application, the dentin layer was applied using A1 (Vit-l-escence, Ultradent Products Inc., UT). (**g**) The incisal irregularities of the intentionally created dentin lobules were filled using an iridescent blue translucent material (irB, Vit-l-lescence, Ultradent, UT). (**h**) A white tint was applied to the restoration to impart hints of hypomineralization that would enable the restorations to blend harmoniously with the adjacent natural teeth. (**i**) Following placement of the enamel layer to full volume (Pearl Neutral, Vit-l-escence, Ultradent Products Inc., UT), primary and secondary anatomy were developed. (**j**) Following finishing and polishing, the adjacent teeth are dehydrated and become brighter in value with more intense opacities. (**k**) On indirect lighting, the internal effects imparted can be appreciated. The unsightly chromatic patches and craze lines have disappeared. (**l**) Oblique view reveals harmonious presence of secondary anatomy which permits a harmonious blend into the surrounding dentition. (**m**) Post-operative reassessment reveals acceptable aesthetics and resolution of the patient's chief concerns. (**n**) Post-operative reassessment. Oblique View

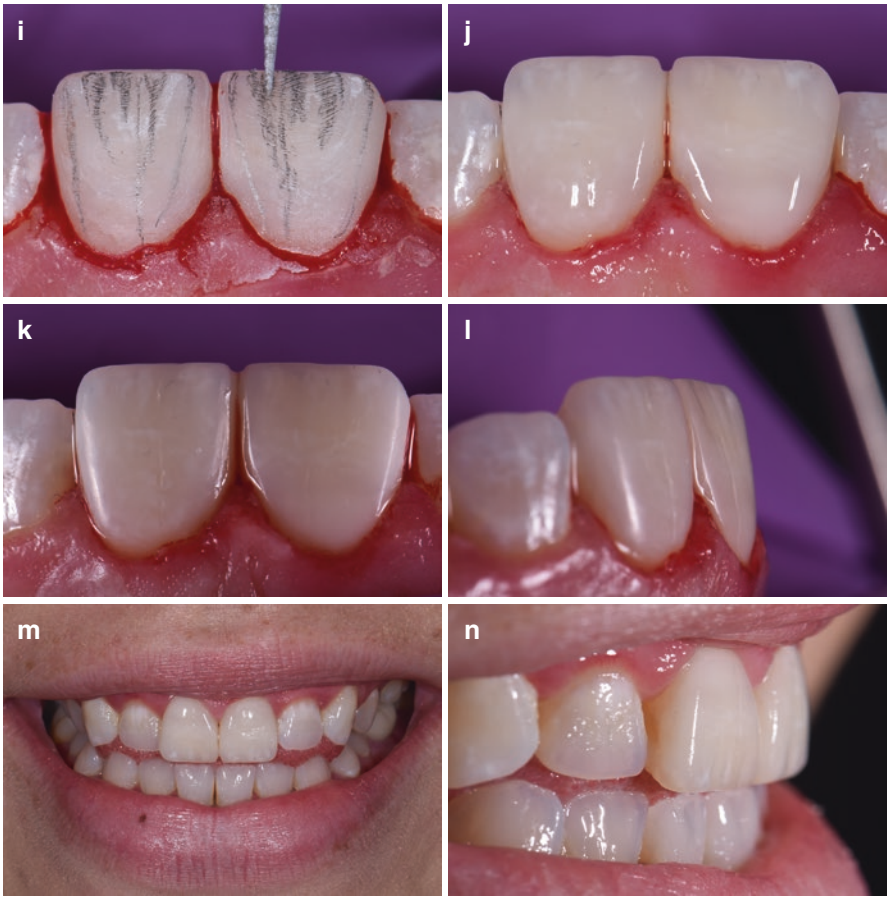

Fig. 14.6 (continued)

14.6 Conclusion and Remarks

Incisor hypomineralization is an aesthetically and structurally-significant, emotionally debilitating condition that often affects the confidence of affected individuals. Treatment modalities can range from ultraconservative to invasive, depending on the degree of hypomineralization and/or structure loss. A protocol for staged treatment is presented in this chapter. Often, mild, generalized cases should be investigated for initial noninvasive treatment via tooth whitening in order to decrease the contrast between the background and lesion colours. Often, a side effect is the elimination or lessening of chromatic aspects of the lesions. Following this scenario, localized residual visible lesions of concern should be investigated for treatment via remineralization via CPP-ACP sometimes completed in conjunction with

microabrasion, if suitable. Failing this, the ability of the TEGDMA monomer allows significant visual and functional improvement of the affected tooth via a resin infiltration technique. The techniques mentioned up to this point are non- or minimally invasive in nature. Finally, if the resin infiltration technique is not completely successful in eliminating problem areas, conservative macroreduction can be utilized and composite layering to achieve aesthetic improvement.

It is comforting that with modern techniques, the ability of the clinician to stage the treatment via this protocol allows a responsible approach that will not only gain the patient's trust but also ensure that a maximum volume of healthy tooth structure is preserved to ensure a maximal prognosis into the future.

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Extraction of MIH-Affected Molars and Orthodontic Space Closure

15

Christian Kirschneck and Peter Proff

15.1 Introduction

In this chapter, we discuss the extraction of MIH-affected molars and subsequent orthodontic space closure as possible treatment option in patients with severe MIH and corresponding prerequisites, timing and treatment strategy. Extraction therapy needs to consider not only the MIH pathology itself but also the entire dental and orthodontic status of the patient in question to achieve maximum patient benefit and the individually optimal treatment with minimal adverse effects. Due to the complexity of correct decision-making and therapy, the (paediatric) dentist, paediatrician and orthodontist should work together in identifying and administering the best treatment option available for the patient, minimising treatment time [1].

15.2 General Considerations for Extraction of Permanent Teeth in Orthodontics

Before a decision in favour or against an extraction therapy with subsequent orthodontic space closure can be made, comprehensive orthodontic diagnostics are required, consisting of a proper general, dental and orthodontic anamnesis, clinical examination, intraoral photo documentation, functional status, photo-static analysis, orthodontic model analysis and radiological imaging (panoramic and lateral cephalometric radiograph and — if necessary — dental radiographs), as an orthodontic closure of the extraction space can affect both function and aesthetics of the entire stomatognathic system [2]. Several general, local and secondary parameters have to be considered [2]. If unfavourable conditions based on these parameters are

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identified, the extraction of permanent teeth is discouraged [2, 3]. If it is unavoidable in these cases due to poor prognosis of MIH-affected teeth, an (implant-)prosthetic restoration of the extracted tooth should be preferred instead of opting for orthodontic closure of the extraction space.

General parameters in favour of orthodontic extraction therapy with subsequent space closure are as follows [2]:

- Convex facial profile with prominent lips, unobtrusive nose and decreased nasolabial angle.
- Short upper lip and "gummy smile".
- Vertical growth pattern, open bite or reduced overbite.
- Young patients during the mixed dentition, as guided tooth eruption facilitates space closure.
- Absence of functional or TMD problems.

Local parameters in favour of orthodontic extraction therapy with space closure are as follows [2]:

- Severe dental crowding and loss of space within the dental arch.
- Proclined upper teeth and Angle class II/1, if dental compensation is desired.
- Small skeletal/apical jaw base or large tooth material.
- No tooth aplasia and no previous extractions of permanent teeth.
- Presence of third molars (germs) with the possibility of alignment.
- Favourable topography of the maxillary sinus (no deep recesses) allowing mesialisation of molars.

Secondary parameters in favour of orthodontic extraction therapy with space closure are the following [2]:

- Limited socio-economic circumstances of the patient due to generally high follow-up costs for (implant) prosthetic treatment and maintenance.
- Good patient compliance and oral hygiene due to the otherwise elevated risk of enamel decalcifications and periodontal bone loss during prolonged fixed orthodontic therapy in extraction cases.
- Patient preference (caution: if general or local parameters are largely not in favour of orthodontic extraction therapy, then no such treatment should be undertaken only based on patient preference).

15.2.1 Indications for the Extraction of MIH-Affected Molars

In general, orthodontic indications for the extraction of permanent molars to resolve primary or secondary crowding are very limited. Hotz and A.M. Schwarz postulated that there is no orthodontically justified indication for the systematic removal of the

first permanent molars except for pathological reasons including dental caries, endodontic and periodontal problems, as well as hypomineralizations such as MIH [4], which do not allow a preservation of the tooth. First permanent molars should thus only be extracted, if their preservation until the third decade of life seems unlikely [5]. As an exception to this basic rule, which is still valid today, a systematic extraction of the first permanent molars was advocated in patients with an open bite and sole occlusal contact at these teeth to close the bite — this approach, however, has been dropped, as long-term success was poor [5, 6], most likely due to the skeletal aetiology of the open bite in most of these cases, which does not allow dento-alveolar compensation [6]. Applying the basic molar extraction rule of Hotz and A.M. Schwarz to MIH-affected molars, these molars may be extracted for orthodontic reasons, if long-term prognosis of these teeth is poor and prognosis of orthodontic treatment success achieving good oral function and aesthetics is favourable (Fig. 15.1) [7].

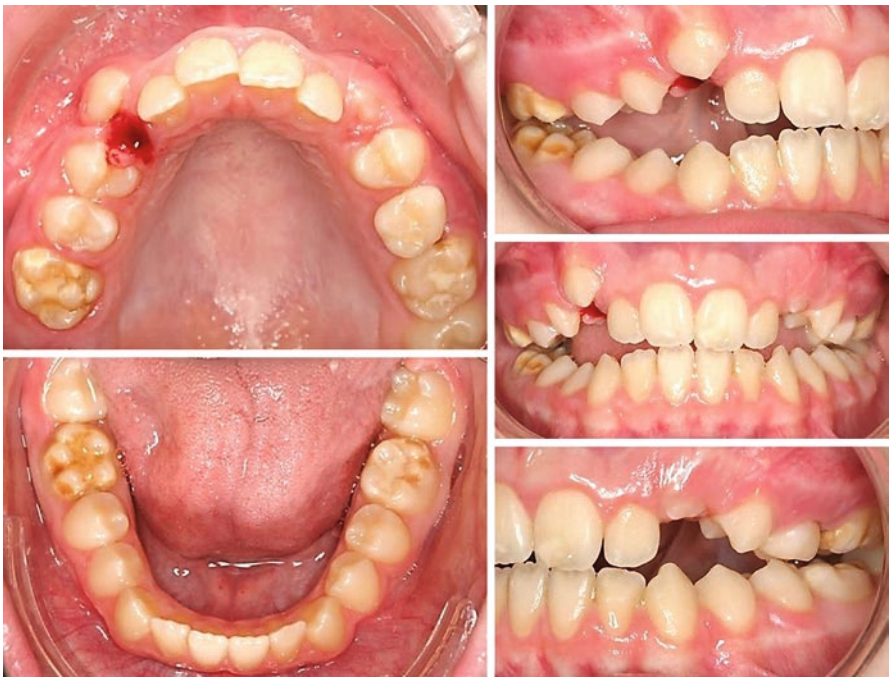

Fig. 15.1 Baseline intraoral status of a patient with lateral open bite, reduced overbite and molar incisor hypomineralization (MIH) of all four first permanent molars without involvement of the incisors. MIH severity level was high with pronounced susceptibility to pain and loss of tooth substance progressing quickly due to mechanical spallings. Except for the late timing after eruption of the second molars, excluding the possibility of spontaneous space closure, conditions for orthodontic extraction therapy with space closure were otherwise favourable, because there was no aplasia of teeth, hypodontia or previous extraction of permanent teeth and suitable general, local and secondary extraction parameters were present

Poor long-term prognosis of MIH-affected molars can be assumed as follows:

- At a high MIH severity level, comprising large-scale hypomineralization, pronounced yellow–brown discolouration, loss of enamel and change of crown morphology, temperature hypersensitivity and porosities reaching into the dentine.
- If loss of tooth substance progresses quickly due to mechanical spallings [8].
- In case of incontrollable endodontic or periodontal problems such as irreversible pulpitis, apical or advanced periodontitis or high susceptibility to pain [9–11].
- After repeated unsuccessful conservative-prosthetic treatment [9, 10].
- In case of severely limited oral hygiene (e.g. due to a distinctly elevated temperature and pain hypersensitivity of MIH-affected teeth) [8].

A favourable prognosis of orthodontic treatment success achieving good oral function and aesthetics can be assumed as follows:

- If there is no aplasia of teeth, hypodontia or previous extraction of permanent teeth [8].
- At a (dental) age of 8–11.5 years at the time of molar extraction and subsequent orthodontic treatment [3, 12, 13].
- If there is (primary or secondary) crowding within the dental arch in question [8, 11].
- If favourable general, local and secondary extraction parameters are present such as a vertical growth pattern with tendency to develop open bite (high-angle cases) [2, 13].

15.3 Extraction Timing of MIH-Affected Molars in Absence of Dental Crowding

Timing extraction therapy of MIH-affected molars correctly is essential or even decisive for its success [5]. In order to facilitate the orthodontic space closure necessary after molar extraction, the best age from an orthodontic point of view is between 8 and 11.5 years, if no distinct anterior or secondary crowding is present [11–14]. Due to individual discrepancies in chronological and dental age [15], timing of molar extraction should also be based on radiological findings on tooth development (orthopantomogram, panoramic radiography) with all age information for extraction timing given in this article referring to dental age. These include fully visible crowns and an appearance of the root furcation of the second molars [16]. An early extraction between the (dental) age of 8 and 10 in the resting phase of the mixed dentition is to be preferred in the upper dentition [3, 8, 11–13, 17, 18], because eruption of the lateral incisors occurs during this period, whereas this is not yet the case for the second premolars and molars [14, 19]. If the extraction takes place before the second molar eruption (at the age of 12), their eruption is accelerated up to 3 years together with the third molars and occurring in a more mesial position, filling part of the extraction space, which makes orthodontic space closure easier or even sometimes unnecessary (self-compensation) [5, 11, 19]. Baume [20] arrived at this conclusion already in 1939/1940 and carried out extensive studies on

tooth migration after extraction of premolars and first molars and found that a "guarantee of absolute space closure and avoidance of tipping of the second molars in the lower dentition can be given only at an extraction age of 9-10 years. Extraction of the lower first molar after the age of 13 almost always leads to severe occlusion disorders". Despite the importance of molar extraction in the lower dentition prior to the age of 13 and thus complete eruption of the second molars, as stated by Baume, extraction of MIH-affected molars in the lower dentition should be delayed until eruption of the second premolars around the age of 11 [13], if there are no crowding problems to be resolved, because there is an increased risk of distal migration of the second premolar tooth germs [5], which occurs at a much faster rate than migration of erupted premolars and also faster than mesial migration of erupted molars [13, 20].

15.4 Extraction Timing of MIH-Affected Molars in the Presence of Dental Crowding

Exceptions to the general rule that extraction of MIH-affected molars between 8 and 11.5 years of (dental) age is best are patients with distinct anterior or secondary crowding in the upper dentition and patients with Angle class II/1 [1, 12]. In these cases, the extraction space gained in the upper dental arch can be utilized to resolve the crowding present or to retract the upper front compensating class II/1 occlusion. This is only possible if the extraction space resulting from the extraction of upper MIH-affected molars is not depleted by mesial movement of the second molars. For this reason, extraction in the upper dentition should be delayed in these cases until the (dental) age of 12 (eruption of the second molars) and an orthodontic anchorage of second molars considered after extraction (e.g. by using a TPA, Nance appliance, headgear or skeletal anchorage) [4, 5, 13, 20]. In the lower dentition, on the other hand, an early extraction between the (dental) age of 8 and 10 should be preferred in case of an existing crowding problem, because mesial movement of lower second molars is only half as fast as in the upper dentition [20] and an early distal migration of the premolar germs can be used to resolve the crowding [5, 13]. An exception to this rule is patients with Angle class II/2 and a horizontal growth pattern, as these cases have a tendency of further bite deepening. Extraction of molars in these patients should thus be delayed, especially in the lower dentition [18, 19].

15.5 Consequences of Late Extraction of MIH-Affected Molars

If MIH-affected first molars are extracted late, that is, after the second molars have fully erupted (around the age of 13), then fixed orthodontic treatment with a multibracket appliance is unavoidable (Fig. 15.2), since spontaneous mesial movement of second molars only occurs incompletely with mainly mesial tipping and rotation, particularly in the lower dentition [3, 20]. Distal tipping and rotation of the second premolars is also possible [13, 19], substantially increasing orthodontic treatment efforts. Furthermore, the risk of persisting occlusal disturbances, periodontal

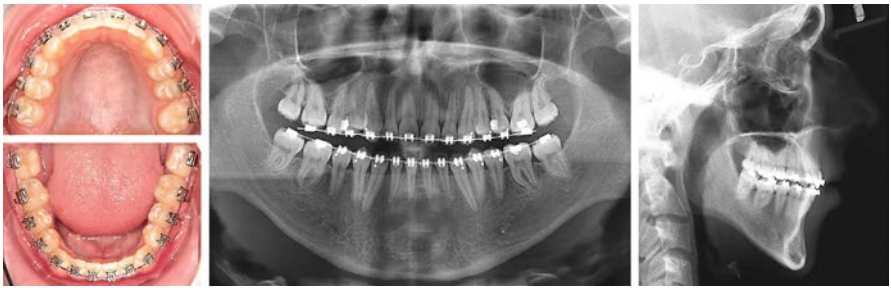

Fig. 15.2 Orthodontic extraction therapy of all four first permanent molars and space closure by orthodontic mesialisation of second and third molars with a fixed multibracket appliance (intraoral images, panoramic and lateral cephalometric radiograph). The patient shows a pronounced vertical growth pattern

damage and large residual extraction spaces with atrophy of the alveolar bone in the long-term is distinctly increased [3, 5]. In the lower dentition, however, no complete self-compensation without additional orthodontic measures is to be expected, even with early extraction of MIH-affected first molars, because of the extent of the extraction space, the more compact bone structure and lower mesial migration tendency of the lower second molars [5].

15.6 Consequences of Premature Extraction of MIH-Affected Molars

Premature extraction of MIH-affected first molars before the (dental) age of 8 is unfavourable, as immigration and rotation of the second molars into the extraction space will occur. In the presence of anterior or secondary dental crowding, a lack of space will persist, because extraction space is used up by the second molars and unavailable for alleviation of crowding. In patients without dental crowding problems, premature molar extraction is also problematic, as distal migration and rotation of premolar germs is likely to occur, generating undesired anterior spacing, retroclination of anterior teeth and alveolar midline displacement [3, 5, 19, 21]. Premature molar extraction is also associated with an increased risk of bite deepening due to the lack of vertical support [5]. In addition, before the age of 8, presence or aplasia of third molars cannot be assessed [19]. Aplasia of third molars, however, is no contraindication for extraction therapy of first molars [3].

15.7 Importance of Choosing the Correct Timing of Orthodontic Extraction Therapy

Adherence to the correct extraction time making use of spontaneous tooth movement tendencies greatly facilitates space closure after orthodontic extraction therapy of MIH-affected molars and improves prognosis. A study by Jacobs et al. (2010) shows that extensive active orthodontic mesialisation of already erupted second molars by

means of fixed mechanics without skeletal anchorage resulted in significant retrusion of the incisors with corresponding soft tissue and profile changes [22]. Therefore, comprehensive fixed orthodontic treatment with skeletal anchorage (mini-implants, miniplates etc.) is recommended to achieve space closure without adverse effects on the anterior dentition and a favourable treatment result [4, 18, 22], particularly in the lower dentition, as complete spontaneous space closure is unlikely.

15.8 Balancing and Compensatory Extraction Therapy

In orthodontic extraction therapy of MIH-affected first molars, possible balancing and compensatory extractions also need to be considered. It is the responsibility of the orthodontist to decide, based on the malocclusion present, whether an additional balancing extraction is required, that is, a removal of the contralateral tooth in the same dental arch, or a compensatory extraction, that is, the removal of the corresponding antagonist tooth in the opposite dental arch. Which of the two possibilities is more effective for a given indication has not yet been clearly established [13, 19], but symmetrical (compensatory) extraction, especially in the presence of crowding, may reduce the risk of dental arch asymmetries and midline shifts [1, 13]. Evidence on this matter, however, is limited — especially if no crowding is present [3, 19]. If a lower first MIH-affected molar is to be extracted, then a compensatory extraction in the upper dentition in patients with class I occlusion should be considered to not leave the antagonist first molar without occlusal support with risk of its long-term elongation; in class II occlusion, this is only necessary, if the lower second deciduous molar is lost. Alternatively, a corresponding retainer should be inserted in the upper dentition holding the upper first molar without occlusal contacts in place to prevent elongation [3, 13, 16, 19], which is not a problem in the opposite situation due to the continuous occlusal support of the lower first molar by the second upper premolar [3].

15.9 Prognosis for Orthodontic Space Closure After Extraction of MIH-Affected Molars

Clinical studies by Mejàre et al. (2005) and Jälevik and Möller (2007) attested orthodontic extraction therapy of permanent first molars a favourable prognosis (Fig. 15.3), because space closure achieved in the majority of patients (up to 87%) was good or acceptable, if timed prior to complete eruption of the second molars [23, 24]. If extraction is timed between 8 and 10.5 years of age, then spontaneous space closure by mesial movement of the second and third molars is to be expected in 81% (upper dentition) and 50% (lower dentition) of cases, whereas for patients aged 10.5–11.5 years at the time of extraction, this is achieved only in 55% and 59% of cases [12, 13]. By contrast, if molar extraction is performed before the age of 8, only 69% or 34% of patients (upper/lower dentition) can expect a good spontaneous space closure [12, 13]. The same is true for extraction therapy started beyond the age of 12 with good spontaneous space closure by mesial movement of molars to be expected in only 56% and 44% (upper/lower dentition) of patients. Resolution of anterior and secondary crowding using the extraction space, by contrast, always

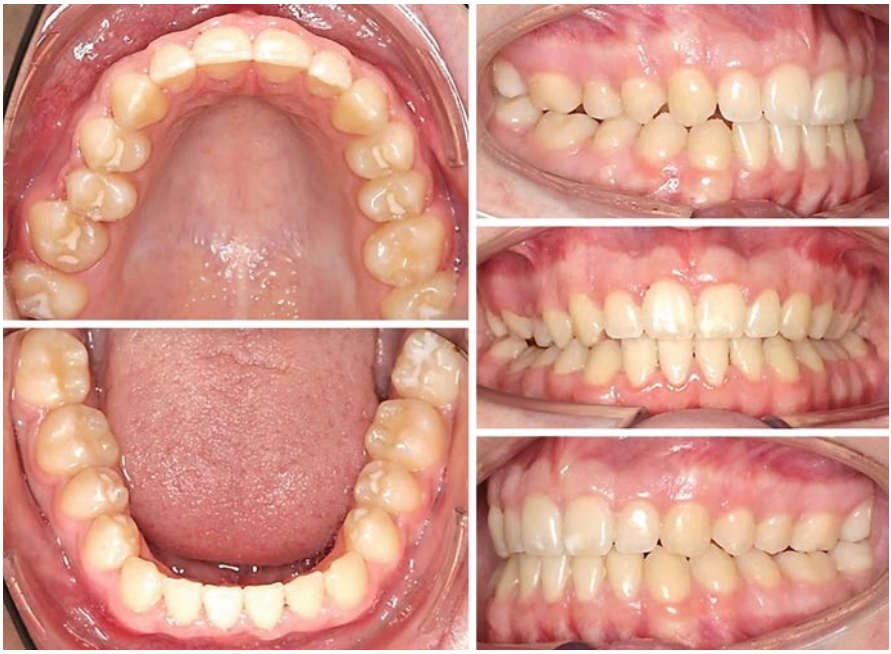

Fig. 15.3 Intraoral status after completion of fixed multibracket therapy. The second permanent molars could be successfully mesialized substituting the extracted MIH-affected first molars with third molars also mesialized in position of the second molars. Despite the loss of the first molars, a complete row of teeth in good class I occlusion could thus be re-established in both dental arches. For continued settling of occlusion and stabilisation, the patient received a removable orthodontic retention appliance

requires additional fixed orthodontic therapy [1]. In the upper dentition, the prognosis of molar extraction appears more favourable due to the disto-buccal to mesio-palatal direction of the eruption path of second molars, whereas in the lower dentition, mesial tipping is more likely to occur and usually requires adjuvant orthodontic therapy [12, 13].

15.10 Advantages of Orthodontic Extraction Therapy of MIH-Affected Molars

Orthodontic extraction therapy seems to have advantages over restorative therapy, because in patients of comparable baseline parameters, additional prosthetic treatments such as renewal or repair of restorations were reported to be necessary in 48% of cases following prosthetic restoration [23], which is likely due to enamel breakdown below restorations [25].

15.11 Prognosis for Eruption of Third Molars After Extraction of MIH-Affected Molars

Extraction of the first molars can significantly improve the available space for eruption and mesial alignment of the second and third molars and their angulation [21, 26, 27]. This way, alignment of the third molars into a good position is facilitated [21] and the probability of their retention reduced to 10% (compared to 45% in premolar extraction cases) [3, 26, 27]. The dentition can thus in many cases be completed again despite the iatrogenic loss of the first molars [19]. Upper third molars seem to profit more from orthodontic extraction therapy of first molars than lower third molars regarding favourable effects on their angulation [26].

15.12 Summary

Inconsiderate extraction of hypomineralized molars is not justified from an orthodontic point of view. However, given a certain severity of hypomineralization with poor long-term prognosis and favourable factors for orthodontic treatment success, it represents a valid treatment approach, offering certain advantages over prosthetic–restorative therapy [7]. The decision to extract MIH-affected first molars, however, should not be made by the (paediatric) dentist, orthodontist or paediatrician alone, but always in conjunction after comprehensive interdisciplinary diagnosis and joint treatment planning, taking into account general, local and secondary factors. For the success of orthodontic extraction therapy in molar incisor hypomineralization, choosing the optimal time for molar extraction — between 8 and 11.5 years of (dental) age — is essential [7]. An early referral of children affected by MIH to the orthodontist and an orthodontic examination in the early mixed dentition is thus recommended to allow for correct timing of orthodontic extraction therapy and space closure in patients, which would benefit from this treatment approach.

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Health Economic Evaluation of Management Strategies for MIH

16

Falk Schwendicke and Karim Elhennawy

16.1 The Need for and Types of Health Economic Evaluations

As discussed earlier, MIH is a highly prevalent condition, with at least every fourth case being in need of treatment given clinical symptoms (such as cavitated structural defects, hypersensitivity or pain as well as aesthetic impairment) [1]. Consequently, a range of treatment options are available, indicated according to the lesion's severity (mild to severe) and symptoms (with or without the association of hypersensitivity). For mild cases (i.e., those without breakdown and/or hypersensitivity), as well as for cases with mainly aesthetic impairment, no health economic evaluations are available. Hence, this chapter will mainly deal with the management of severe cases. We will first layout why health economic evaluations may be needed.

All healthcare is provided within a system where care generates costs and resources are limited. The costs are either covered by an insurer or the patient itself. Besides only considering costs for the initial treatment (which is-by itself-already a complex endeavor in some cases), decision makers should also consider the

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long-term benefits of the treatment and the costs associated with complications occurring long term. Four different types of health-economic analyses are available; these types are discriminated by the health outcome used as follows [2]:

- Cost of disease studies do not assess health benefits, but only the costs associated with a disease. These costs can be direct medical costs (e.g., those for diagnostics and treatments, such as for staff, materials, drugs). Direct medical costs are usually relevant from a payer's or a provider's perspective, who shoulder these direct costs (i.e., the costs associated with medical procedures). Note that in many healthcare systems, payers do not pay exactly the costs generated (these can only be precisely determined when assessing a range of items and the used units), but pay providers for procedures using fixed fees. These systems are oftentimes nevertheless based on or related to times and efforts of the provided procedure.
- Costs can also be direct non-medical or indirect/opportunity cost. The first are costs not directly associated with the medical procedure, such as transportation costs. The latter are costs for lost opportunities either due to the disease itself, such as productivity losses at work (presenteeism) due to pain or sickness, or costs for time off in work or school (absenteeism). Estimating these costs is less straightforward, as the valuation of the lost opportunity is not easy (how much is a lost hour worth?). Non-medical and indirect/opportunity costs need to be considered when taking a societal (and not only a payer's) perspective.
- Cost-effectiveness studies assess the effectiveness of a treatment (with effectiveness being a clinical outcome, such as tooth retention time, restoration survival, or pain) and weigh effectiveness against the treatment costs. These studies usually use the cost-difference between two interventions and relate it to the effectiveness differences. This is called the incremental cost-effectiveness ratio, ICER. A treatment can be more expensive, but also more effective, for example. This cost-effectiveness difference can be expressed as ICER.
- Cost-utility studies investigate the utility of a treatment, which is oftentimes measured as quality- or disability-adjusted life. Utilities express the severity of a disease (or any health state) and the time an individual experienced it (suffered from it). Determining utilities is not always easy; a range of methods are available (many using questionnaires). For many health states in dentistry, such as a sound versus a filled tooth or a retained versus a replaced tooth, no utility values have been set so far. Also, note that these values are culturally sensitive and need to be validated in different settings. For MIH, no such values have been defined. One could assume that the negative impact of a painful MIH tooth is similar to that of untreated dentin caries lesions. For such lesions, the so-called disability weight (i.e., indicating the severity of suffering) is 0.010 [3]. As a comparison, the disability weight of severe heart failure is 0.179 (i.e., nearly 20-fold higher); however, one may suffer for shorter time from untreated severe heart failure than from untreated MIH or caries. Using utility values allows analyses across diseases (which is an advantage of disease-specific analyses, e.g., avoided pain in MIH cases cannot be sensibly compared with avoided falls in elderly people).
- Cost–benefit studies transform effectiveness or utility, i.e., the health outcome, into a monetary value. Again, this allows to compare different diseases (as their effectiveness is measured on the same scale—money). Notably, it is also useful

to capture non-health and health outcomes and allows transparent decision-making (for cost-effectiveness and utility analyses, one needs to assign a willingness-to-pay for effectiveness or utility to make commissioning decisions). In cost–benefit analyses, improved health outcomes are translated into monetary savings, these costs may then be compared with costs for an intervention, and decisions may be made from an economic-only point of view. These studies are ambiguously discussed at present and have only very sparsely been applied in dentistry so far.

16.2 Health Economic Analyses

Health economic analyses build on two main methodologies; these analyses may be used on their own or combined: The first involves conducting a primary data collection similar to a cohort study or a clinical controlled trial (e.g., comparing two strategies for restoring MIH lesions and collecting costs data alongside). Based on this study, costs and effectiveness within the studied sample can be determined.

This type of analysis has the advantage that costs can be assessed in depth and for this very specific setting, for example, by measuring staff costs (staff hours factorized with the costs per hour for different staff) and materials costs (costs for restorative materials used to restore MIH molars, e.g., multiplied with amount of material used). This "micro-costing" allows very detailed and realistic cost estimation also from a provider's perspective. It further enables to collect data on indirect/opportunity costs (by collecting travelling and treatment times and by knowing the patients' occupational status, etc., and hence being able to assign money to an hour of lost work). Such analyses have further advantages, such as being able to collect efficacy or effectiveness data in the same setting as the cost data (mixing costs data from one source, such as a university clinic, with effectiveness data from another source, e.g., a dental practice, has obvious limitations and might lead to erroneous conclusions as to the true cost-effectiveness of a treatment in both settings).

The second method uses mathematical models. Modeling studies aim to simulate the natural path of (MIH) teeth or patients (children with MIH) throughout their lifetime. Teeth or patients are initially placed in a certain health state (e.g., a severely affected MIH molar) and can move from one to another health status (e.g., this molar being restored using composite, this composite failing and being replaced, the tooth eventually being removed, etc.). The probability of every move ("translation") is based on data obtained from other studies, oftentimes systematic reviews or large cohort study. For each translation, a treatment (e.g., restoration) is assumed to be provided and costs are generated. These costs are estimated based on various data sources, such as previous clinical studies (which might have used micro-costing) or fee item catalogues. Note that it is more difficult to realistically determine indirect and opportunity costs in these studies, and usually modeling studies need to make certain assumptions in this regard.

Modeling studies make use of the best available data and combine these in a way which allows to follow teeth or patients in longer sequences of events (MIH molar ➔ carious surface in MIH molar ➔ restoration ➔ replaced restoration ➔ extracted tooth ➔ implant, etc.)-oftentimes much longer than original studies! Their

advantage compared with original studies is that they are less costly, allow to assess the long-term sequels of initial decisions (clinical studies will not be able to estimate the lifetime costs following the placement of a restoration), and also easily compare a larger range of therapies (e.g., no treatment, sealing, sodium fluoride varnish, CPP-ACP to manage hypersensitivity of MIH molars).

All modeling studies can only be as valid as the input data. Moreover, and as touched, modeling studies usually require a number of assumptions to be made both in the construction of the model and the parameters used for modeling. Thus, all modeling studies are subject to uncertainty. This uncertainty can be evaluated, for example, by using univariate sensitivity analyses. Such analyses vary one aspect of the study, for example, a structural component of the model (e.g., the simulated sequence of events, this case is called structural uncertainty), an input parameter (e.g., the costs for a restoration of an MIH molar, this is called parameter uncertainty), or the individual profile of a patient (e.g., MIH severity, gender, lifetime, caries risk, this case is called heterogeneity). Moreover, many models are analyzed via more advanced mathematical simulations, which allow to introduce the uncertainty of many variables at the same time (which is why this case is called joint probability sensitivity analysis). This is done via simulating a number of patients (e.g., 1000), with transition probabilities (or other uncertain parameters) being randomly sampled from a certain range of each parameter (e.g., the costs of a restoration in different countries). The sampling is repeated for a series of times (e.g., 1000), allowing to estimate both the per-patient and per-population variance. This allows to quantify the overall uncertainty of the findings and to conclude as to their robustness.

Quantifying uncertainty is crucial in these analysis, and uncertainty is something we may accept and even investigate: the findings from a study might be robust despite great uncertainty being present (as long as, e.g., composite for restoring a severe MIH lesions is always both more effective and less costly than restoring it using a glass ionomer, the exact size this advantage is of limited relevance if one has to decide between these two). If uncertainty, however, affects the ranking of strategies (composite being more effective, but more or less costly than glass ionomer depending on the data input), the decisions to be made will be uncertain, too. It is thus relevant to highlight and quantify this uncertainty.

16.3 Assessing the Cost-Effectiveness of Severe MIH

As discussed elsewhere in this book, for severe MIH cases (those lesions with cavitated structural defects in the enamel), dentists can either (1) restore the defects directly (usually using resin composite); (2) restore them indirectly (e.g., using ceramic or metal restorations), usually after temporization of the molar, for example, using preformed metal crowns; or (3) remove the tooth, followed by spontaneous or orthodontic alignment of the adjacent teeth [4]. Spontaneous alignment has been found in up to 82% and 63% of the adjacent teeth in the maxilla and mandible, respectively, under certain conditions and appropriate timing [5–8].

Each of these options has a number of advantages and disadvantages: (1) Resin composite restorations do not require substantial tooth hard tissue removal, but have a significantly lower survival probability in MIH than non-MIH molars [4]. (2) Indirect restorations usually require additional preparation (substance loss), but have high survival probabilities. They are also more expensive than resin composites and are unsuitable soon after eruption, but years later (when the final occlusion has settled). As discussed, MIH molars planned to receive indirect restorations usually require temporization. (3) Removing the teeth is the most invasive option, but may achieve the best long-term prognosis: MIH molars have significantly increased treatment needs, and after repeated re-interventions, extraction may be required. In this case, spontaneous or orthodontic alignment of adjacent teeth might not be feasible any longer, with replacement of the tooth (via bridges or implant-retained crown) being necessary.

The early treatment decision made for a molar with severe MIH has long-term consequences both clinically and economically: As described, certain treatments (such as resin composites) are initially far less costly than others (such as indirect restorations or removal and orthodontic alignment). They might, however, require more follow-up treatments and come with earlier tooth loss, which increases long-term costs. Assessing these long-term consequences and weighing costs and effectiveness against each other is thus relevant to support decision makers.

A recent cost-effectiveness analysis [9] compared resin composite and preformed metal crown placement followed by placement of an indirect restorations and tooth extraction plus (if needed) orthodontic treatment for managing severe MIH molars. The outcomes were costs (in Euro) and the effectiveness, measured as tooth retention time of the tooth in the position of the first molar (if the first molar was extracted and the second molar moved into the position of the first molar, the retention time of this second molar was assessed).

A model-based analysis was used, which allowed to follow patients and molars over their lifetime. Three main pathways were modeled as follows (Fig. 16.1):

1. Removal and alignment with or without active orthodontic treatment. It was assumed that the tooth was extracted at the optimal age, where the chances of spontaneous alignment were 83% and 63%. Given that this was a model-based evaluation, the authors varied this age, increasing it to 14 years and assuming no spontaneous alignment at this age any longer. The MIH molar was temporized using a preformed metal crown, the failure of which was modeled, too. After removing the MIH molar, the sound second and third molar were assumed to be orthodontically aligned if needed, with space closure to be attempted from distal, which requires minimum anchorage. For this alignment, a number of orthodontic alternatives were modeled. After alignment, the second molar was assumed to be subject to caries increment, the sequels of which were modeled, too, including restorative and endodontic complications. If the aligned second molar needed, at some state during the patient's life, extraction, tooth replacement was assumed via implant-supported single crowns. Implants were assumed to experience restorative complications (requiring re-cementation or renewal of

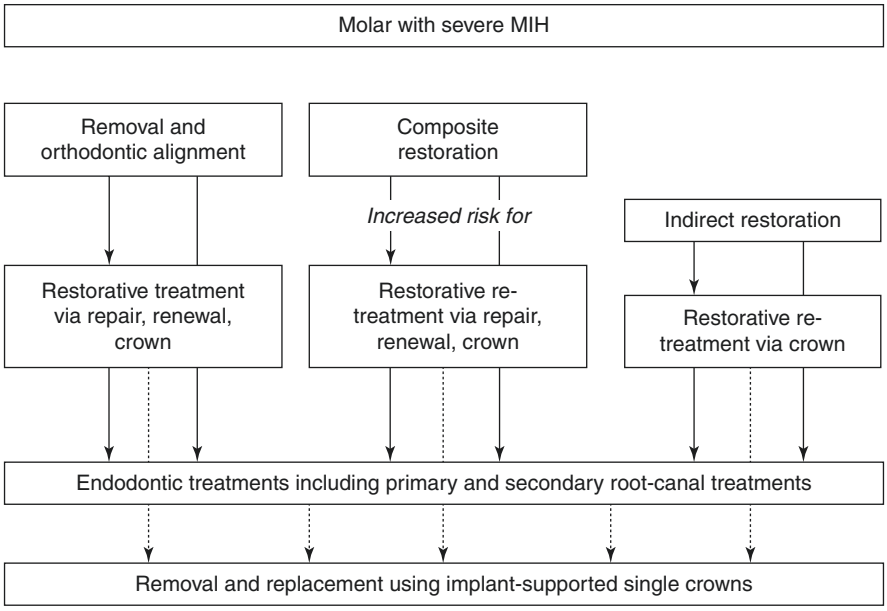

Fig. 16.1 The model used to assess the cost-effectiveness of strategies for managing severe MIH. (From [9])

crowns) and biologic (e.g., peri-implantitis) or technical complications (e.g., abutment or implant fracture). The study performed modeling analyses for 1, 2, 3, or 4 MIH-affected molars.

2. If MIH molars were retained and restored using resin composite, these could experience restorative and endodontic complications [4].
3. If MIH molars were retained and restored using indirect restorations, the assumption of temporization being required between age 6 and 18 was made, as indirect restorations would not place commonly in early childhood, but late adolescence. Temporization was assumed using a preformed metal crown, again with certain risks of failures. Afterwards, indirect restorations were placed, also coming with risks of failure.

The used model is illustrated in Fig. 16.1. In summary, and as described in brief above, this model aimed to allow, in silico, to follow MIH or adjacent teeth long-term over different stages. Translation between these stages occurred by treatment. The probabilities of these transitions were extracted from systematic reviews, larger cohort studies, and some assumptions needed where also supported by lower evidence levels. Note that the construction of these models—an important aspect in modeling—is, for example, mainly guided by the developers (i.e., experts' opinion—the lowest level of evidence). Thus, it is of great relevance to communicate the decisions made when constructing the model transparently and to also assess if a different model construction greatly impacts on the modeling results.

16.4 Cost-Effectiveness of Different Strategies for Managing Severe MIH

As described, a model-based cost-effectiveness of resin composite, preformed metal crown placement followed by placement of an indirect restorations, and tooth extraction for managing severe MIH molars was performed. If teeth were removed at the optimal age, extraction was the least costly and most effective option, requiring the least follow-up treatments and retaining the second molar much longer than alternative strategies which retained the first molar, at lower costs. Resin composite and preformed metal crown placement followed by placement of an indirect restorations were more costly and less effective. Figure 16.2 displays the simulated costs and effectiveness of the three options for 1000 patients with one mandibular MIH molar being treated.

Notably, if extraction was not performed at the optimal age, and spontaneous alignment less likely, the costs for extraction increased significantly (as more cases required orthodontics), with resin composite then being a valid option, being less costly (but not more effective) than extraction. Especially in individuals with only treated 1 MIH molar, extraction then showed low cost-effectiveness (being far more costly than composite). By contrast, if more than one MIH-affected tooth was to be managed, the costs for orthodontic therapy were generated at the patient level and hence distributed over the affected teeth, while restorative treatments generated costs per tooth.

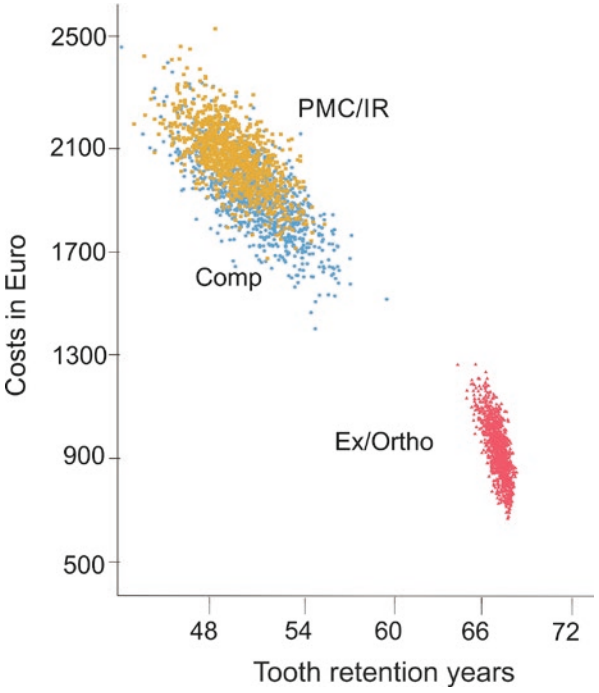

Fig. 16.2 Cost-effectiveness plan for managing one mandibular molar with severe MIH (From [9]). The costs and effectiveness of different treatments are plotted. Extraction plus, if needed, orthodontic treatment (Ex/ortho) is least costly and most effective compared with resin composite (Comp), and the placement of a preformed metal crown followed, some years later, an indirect restoration (PMC/IR)

16.5 Interpretation and Critique

As healthcare resources are limited, the cost-effectiveness of any intervention has relevance for decision-making on multiple (clinical, policy) levels. As the assessment of MIH-a problem which is managed in children, who will experience the sequels of the provided treatment for decades-requires a long-term perspective, a long-term analytic horizon, for example, using a modeling approach, seems needed. Based on this approach, it was found that for managing MIH molars, both a direct composite restoration and an extraction (with or without orthodontic treatment) are options to consider. Two factors were the most important drivers of cost-effectiveness: the timing of extraction (and the associated need for orthodontic alignment, generating significant costs) and the number of molars per patient to be treated.

If MIH molars were extracted at the ideal age, extraction was both least costly and most effective, mainly as the oftentimes self-aligning second molar shows a very good long-term prognosis, while the initial treatment was affordable and easy to perform. If, however, orthodontic treatment is required, it should be considered that such treatment is time consuming and requires a specific amount of compliance from the patient. Moreover, before attempting extraction and possibly "risking" the need for orthodontic alignment, a range of factors, such as the general orthodontic situation (number of present teeth/hypodontia, crowding, presence and type of malocclusion, etc.), should be considered.

More so, in case of late tooth extraction (after the eruption of the neigboring second permanent molar) or for the management of a single MIH-affected tooth, placing a direct resin composite restoration was the least costly option. This was due to resin composite avoiding expensive orthodontic treatment costs [10]. Resin composites can be placed without additional loss of sound tooth substance, as they can be adhesively bonded. However, given the structural abnormality of MIH enamel, the unusual cavity formation, the endodontic complications arising from inflamed pulps, and the limited compliance of the patients [11, 12], composites show more failures in MIH than non-MIH teeth, with annual failure rates of 2%–3% for MIH molars [4]. Their indication should hence also carefully be decided.

Temporizing the tooth and placing an indirect restoration in early adulthood was not cost-effective in any scenario. The advantages of the lower risk of failure of indirect restorations (annual failure rates of 1% have been reported for MIH molars) [4] and the associated lower risk of restorative re-interventions do not seem to outweigh the initial treatment costs. Moreover, many re-interventions needed on such indirect restorations are relatively expensive (e.g., replacement or even more escalating restorative or prosthetic options), highlighting once more the need to avoid an unnecessary acceleration of the restorative cycle [13].

16.6 Conclusions

Health economic assessments gain relevance in dentistry, as in all medical fields. Health economics uses a comprehensive set of methods and outcomes. On MIH, data on the cost-effectiveness of different management options are sparse. We have

described the only existing study on the cost-effectiveness of managing severe MIH molars and discussed aspects affecting the cost-effectiveness of such management in general. Health economics on MIH interventions can, in the future, assist a transparent and explicit decision making, allowing to choose the most effective and/or cost-effective option. Generally, the uncertainty around a decision should be considered, and health economic evaluations provide a range of tools to do so.

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