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CRANIOFACIAL SKELETON (WE ROBERTS, SECTION EDITOR)

# Endemic Molar Incisor Hypomineralization: a Pandemic Problem That Requires Monitoring by the Entire Health Care Community

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## Abstract

**Purpose of Review** This review brings a major, previously under-recognized dental and general health problem to the attention of the medical and scientific community. The goals are to help clinicians make early diagnoses, thereby improving treatment outcomes, and to stimulate increasing research efforts to understand the etiology and ultimately prevention.

**Recent Findings** There are two recent systematic reviews of molar incisor hypomineralization (MIH). One reveals the global burden of the condition; mean global prevalence is 13% with 878 million people affected, with 4.8 million cases per year requiring treatment. The review into etiology found a lack of definitive knowledge, but that it is likely to be multifactorial, with childhood illness including fever possibly implicated.

**Summary** The review presents details of MIH sufficient to enable clinicians to recognize it and understand its impact on affected children, its management, and the importance of early intervention. Much further research is needed.

**Keywords** Molar incisor hypomineralization · Molar hypomineralization · Pediatric dentistry · Orthodontics · Etiology · Global burden

## Introduction

Molar incisor hypomineralization (MIH) is a common condition causing considerable pain to children, distress to their parents, and burden on health care systems around the world. All health care professionals should be aware of the condition, cooperate with the dental profession to alleviate the suffering where possible, and work toward finding the etiology and means of prevention. The aim of this review is to bring knowledge of this significant health problem to an audience beyond the dental profession, thereby improving prospects for advances in treatment and ultimately prevention.

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## Definition

Molar incisor hypomineralization is a term introduced to describe demarcated lesions of systemic origin in tooth enamel of permanent molars and incisors [1]. It may also be called molar hypomineralization (MH), as incisors are not always affected. These developmental defects vary in size, are surrounded by normal enamel, and range from white to yellow to brown opacities. Severely affected molars exhibit rapid "post-eruptive breakdown" (PEB) due to the forces of occlusion breaking down the very weak enamel. Unless affected by PEB, the enamel has normal surface contour but reduced strength and mineral content and increased protein content. The condition should not be confused with enamel hypoplasia, which has reduced enamel amount and distorted surface contour, but with normal color and strength.

There are other less common developmental defects of tooth enamel in both the primary [2] and permanent dentition [3], which have different appearance and effects. MIH also should not be confused with the very common dental caries (tooth decay) which is an environmentally acquired breakdown of tooth structure caused by acid on susceptible tooth structure. The acid is either directly from acidic food or drink

or is produced by dental plaque bacteria. Dental caries, when present, usually affects many teeth, and its initial distribution is in the pits and fissures of the occlusal (chewing) surface, as well as the interproximal and gingival margin areas. MIH, in contrast, is confined to isolated teeth and is demarcated on those teeth, usually on the occlusal half of the tooth crown, not at the gingival margin, and is likely to be on a smooth surface, not preferentially in pits and fissures as for common caries.

## Clinical Presentation

The clinical appearance of MIH on first permanent molars and permanent incisors is shown in Fig. 1, which demonstrates the different colored lesions. The darker the lesion, the less mineral is present and the weaker is the enamel. The lesions are clearly demarcated from surrounding normal enamel, and in the more severe cases on the molars, they show PEB. This PEB is where the enamel is so lacking in mineral content that it rapidly disintegrates and becomes very susceptible to the carious process. This area of the tooth is extremely sensitive because the dentin is exposed, and dentin, unlike enamel, is a cellular structure that transmits sensation from thermal, mechanical, and osmochemical (osmotic pressure chemistry) stimuli [2].

Historically, literature has described MIH as affecting the first permanent molars; upper incisors are often affected, but the involvement of lower incisors is less frequent [1]. The lesions vary in size, with the affected enamel in the most occlusal/incisal portion of the tooth, and the more gingival/apical portion of the enamel being normal. The distribution around the mouth is random and asymmetrical and can involve one or more teeth with varying severity. These teeth are beginning their mineralization at about the time of birth. The etiological factors have therefore been considered to be present in the first year of life.

More recent publications reveal that both deciduous and permanent molars are commonly affected [3]. When present in the deciduous molars, the term "hypomineralized second primary molars" (HSPM) has been proposed [4]. These teeth start cellular formation from as early as 15–22 weeks in utero with mineralization some time after that. There is a narrow neo-natal line showing the amount of enamel formed before and after birth (normally 12 μm but up to 24 μm when birth was difficult) [5]. The etiological factor causing the condition occurs in utero.

Second permanent molars have been found to be affected in reduced numbers compared to first molars, but still can be a significant burden. The second permanent molars commence mineralization at 30–36 months, which changes the required time of etiological insult to after that age [6••].

## Global Burden

In previous times, when dental caries was more widespread than it is now in developed countries, seriously broken-down permanent molars were considered to be due to caries. However, now that MIH has been identified as a condition separate from caries, epidemiological studies have demonstrated that MIH is extremely widespread around the world and is creating a major treatment burden.

A recent meta-analysis of 99 studies from 43 countries has demonstrated that there was a mean prevalence of 13.3%. The number of prevalent cases in 2015 was 878 million people, and the mean number of incident cases was 17.5 million in 2016 [7••]. There is considerable variation in the incidence

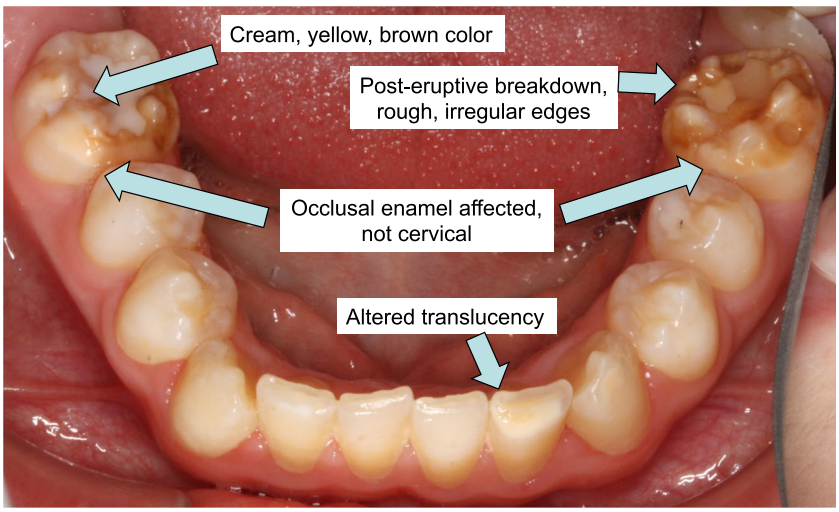


**Fig. 1** The various presentations of MIH in the same mouth of a child, with some restorative sealant present on the PEB areas on molars

and prevalence in different parts of the world. Many of the diagnosed cases are merely esthetic problems, which may not need treatment, especially for molars. However, the recent meta-analysis found 27% of diagnosed cases require treatment; this equates to 4.8 million cases per year.

A study in orthodontic practices found that there was a prevalence of 27%, with restorations or extractions due to MIH in 10% of the total population. All the extractions required a general anesthetic due to the youth and distress of the patients [8].

## Etiology

Mature dental enamel is a unique material found nowhere else in the body. It has extreme hardness with some elasticity; it is acellular with 95% mineral content, 4% water, and 1% organic matter [9]. The hardness and flexibility come from the combination of dense crystalline content with the small amount of organic material between the crystallites. Enamel is therefore very different from other mineralized tissues such as bone and tooth dentin which have less mineral and more organic matter, are cellular, and therefore are changing throughout life. These properties of enamel are necessary to withstand the forces of occlusion and mastication.

Enamel is formed by ameloblasts, which attach to the underlying developing dentin at the dentino-enamel junction. Mineral crystals gradually replace the organic matter in a regulated, complex process that is very sensitive to disruption at any stage of the process [9, 10••]. The timing of mineralization in different parts of the enamel is unclear, so it is difficult to correlate a known insult with the development of a defect.

In MIH-affected enamel, proteins are incorporated into the enamel during its formation in the first 12 months of age for first permanent molars. Blood-related protein, mostly albumin, is present, with heme in the more deeply colored lesions [11]. One hypothesis is that there is leakage of blood product into the developing matrix of the tooth, and proteins from the blood incorporate into the crystals and inhibit their growth. There is as yet no published proof of this theory [12].

It is known that some developmental dental enamel defects show strong familial heritability and genetic etiology. Amelogenesis imperfecta can be autosomal dominant or recessive, is expressed in various phenotypes, and is affected by extensive genetic heterogeneity [13]. A purely genetic etiology is expected to affect all teeth, deciduous and permanent. MIH is isolated rather than diffuse; therefore, any gene-related etiology must have a local factor varying the gene expression. A family history of enamel defects in MIH-affected subjects has been reported but it is not known if all the defects were due to MIH, so these data should be interpreted with caution [14].

It seems that there are individual thresholds making children more or less susceptible to the same insult and there may be a genetic predisposition [12].

Various health conditions during the period of enamel formation have been implicated as etiological factors. These include infections, asthma, fever, antibiotic administration, and allergies [14]. A recent systematic review evaluated the literature studying associations between MIH and various proposed etiologic factors [10••]. It found evidence that some illnesses may be implicated in the etiology of MIH, particularly fever, asthma, and pneumonia. However, there were concerns about the validity of the results in articles reviewed for a number of reasons, one being that most studies were retrospective and depended on the memory of the parent regarding previous illnesses. Prospective studies would be better, but are difficult to control. Trying to pinpoint the exact stage of mineralization and relating that to an illness are very difficult. The main conclusion of the systematic review is that MIH etiology is likely to be multifactorial, with childhood illness including fever possibly implicated.

In view of the current lack of certainty about etiology, reliable preventive measures are a long way off.

## Pediatric Dental Effects and Management

The symptomatic effect of MIH on tooth enamel can vary widely. Some affected teeth have no pain or breakdown; others can be extremely sensitive with or without PEB. Cold and sweet stimuli as well as tooth brushing may be intolerable [1, 15]. This leads to a decrease in brushing and oral health due to daily pain with normal oral activities. If there is significant enamel breakdown, the rough occlusal surface and lesion margins are retentive and easily become carious [16]. With normal tooth enamel, carious demineralization is a multifactorial and dynamic process. When MIH is present in the enamel, especially with breakdown of the tissue, the risk of carious destruction of the hypomineralized tooth structure is increased significantly [17].

When a child presents to the clinician with a sudden toothache in the back of the mouth, the parents often feel anxious and guilty that this crumbling permanent tooth could be caused by lack of dental care and good parenting. Many of these families tend to have good diets and dental hygiene using fluoride toothpaste, and the child is otherwise caries free. It is important for the clinician to relieve this anxiety from the outset by explaining that MIH is a developmental condition whose cause is not fully understood. Current data indicate that it is not linked with any type of neglect in dental care or diet.

A child who has MIH and otherwise has been caries free often has very limited dental experience. In severe cases, the pain that is experienced is acute. The use of cold water and air

from the dental equipment brings tears to their eyes, as it is equivalent to pouring vinegar on an open wound. Because of the child's often lack of experience in dental procedures and the level of pain experienced, behavioral management of the child and parent often presents a significant challenge. In order to examine the child, the clinician may use a toothbrush to clean the tooth gently and place an interim glass ionomer cement restoration to ease the pain that the child experiences whenever eating or drinking something cold or sweet. This simple initial procedure allows the child slowly to build sufficient confidence to attend the dentist and orthodontist to complete the short- and long-term treatment plan. In the most severe cases of pain and behavior management, a tube of casein phosphopeptide, amorphous calcium phosphate with fluoride (MI Paste Plus, GC Corporation, Tokyo, Japan) is given to the patient to be placed on the affected tooth repeatedly for about 2 weeks to desensitize it before the first interim restoration is placed.

Clinicians also are challenged in many cases by an inability to obtain effective local anesthesia (LA) while trying to restore an abnormal and often large lesion with PEB. This difficulty in obtaining anesthesia may be caused by the exposure to the dentinal tubules in the region of the PEB. Changes have been observed in the pulpal innervation, vascularity, and immune cell accumulation that are indicative of chronic pulp inflammation [2]. In addition to the intra-pulpal changes, there is evidence that chronic pulpal inflammatory stimuli can produce central neuroplastic changes, which may contribute to hyperalgesia.

It is difficult to obtain adequate local anesthesia under conditions of hyperalgesia, so the use of LA at this stage is not recommended. The child can become extremely phobic if this crucial step is poorly handled, especially if there is no experience with a dental procedure. There is a well-researched technique called "tell, show, do," and its use is imperative in these cases, so that the child's confidence can be gained without causing long-term dental phobias.

The MIH brown opacities are likely to break down. Children with MIH have a 1.3–7-fold higher chance of requiring restorative treatment for their first permanent molars [18]. These children often require multiple restorations on the same tooth due to the inability to successfully bond restorative materials to hypomineralized enamel. In addition, resin-based restorative materials have poor wear resistance and bond strength properties, so there is commonly a breakdown of restoration margins, thereby increasing the cost of the dental care [14, 19].

Early diagnosis of the MIH lesion is important so that timely intervention can maximize the opportunity to seal the surface of the tooth with composite resin after an initial stabilizing procedure with resin-modified glass ionomer cement. The early intervention provides tooth stability and decreasing sensitivity, allowing improved oral hygiene with fluoride toothpaste which increases mineralization. As sealants performed on MIH teeth are about three times as likely to require restoration replacement as those on normal teeth [20], constant monitoring is required.

When an MIH-affected molar's destruction is so extensive that it precludes conventional restoration, a preformed stainless steel crown can be placed as an interim measure until the tooth matures and erupts sufficiently to have a permanent crown placed, often at about 18 years of age [10••]. This option increases the cost of treatment especially since dental restorations rarely last the patient's lifetime.

When the MIH molar is so structurally compromised that the pulp is involved, the only option may be extraction [21]. An orthodontic consultation should be obtained if possible prior to extraction, so that the best treatment plan can be undertaken with the least impact on the long-term stability of the occlusion. Normally, the extraction of the MIH-affected teeth is performed with the aid of a general anesthetic. The first permanent molars are the largest teeth in the mouth, so their removal can be very traumatic for a young and inexperienced child. The provision of these general anesthetics is a significant burden on health care systems.

The psychological effects on children of MIH discolored areas on anterior teeth need to be considered by the treating dentist. PEB is rarely severe enough on anterior teeth to require the same urgent attention as is needed on posterior teeth. There are many restorative materials and techniques available, and there is a continuing stream of improved technology. However, the timing of any restoration depends on the correct sequencing of all necessary treatment and carefully considering the psychological impact of the defect on the child.

## Orthodontic Effects and Management

The study into the prevalence of MIH in orthodontic practices revealed that 4% of all patients studied required extraction of a first permanent molar [8].

Extraction of permanent molars can lead to undesirable movement of adjacent teeth toward the extraction site [22]. When adjacent teeth tip into an extraction site, interproximal spaces can develop that are food traps. The axial orientation of the tipped teeth leads to reduced ability to withstand forces of occlusion and difficulty in maintaining good oral hygiene and periodontal health. A posterior collapse of the vertical dimension of occlusion leads to concomitant posterior movement of the mandibular dentition and extrusion of upper anterior teeth producing poor alignment and deepening of the bite. If extraction of the affected first permanent molars is done soon after their eruption, some studies have shown that the adjacent teeth can spontaneously close the space, and this is more likely than when the extraction is done several years after eruption [23].

As noted above, in addition to MIH compromising first permanent molars, it can also affect deciduous molars, as well as permanent second molars and incisors. If there is PEB on the deciduous molars leading to their premature loss, there may be a need for intervention to prevent space loss by the drifting of adjacent teeth into the edentulous space. Orthodontic treatment may be indicated if loss of space has already occurred. Severe MIH with PEB has been found on second permanent molars complicating posterior occlusion. MIH on incisors rarely exhibits PEB but it causes esthetic problems.

Orthodontic treatment can be used to ameliorate the effects of permanent molar extraction when such extraction would not be used normally. However, a recent study found that treatment following extraction of first permanent molars is 2.4 months longer than if bicuspids were extracted and up to 10 months longer than in cases requiring no extraction [24]. It has been found that in some cases even after orthodontic treatment, a less than satisfactory outcome is probable [19].

If the MIH and PEB are sufficiently severe to require extraction of the molar, earlier extraction may produce fewer undesirable effects than later extraction.

An additional problem for orthodontic treatment caused by MIH is that it is more difficult to bond attachments to the affected enamel. Orthodontic attachments are generally bonded to tooth enamel by etching the enamel surface with phosphoric acid to open space between enamel rods, thereby allowing resin to penetrate into the enamel and form a strong mechanical bond. Because hypomineralized enamel does not have a normal enamel prism structure, bonding of resin is not as effective, and bond strength to hypomineralized enamel may be only two thirds that of the bond strength to normal enamel [25]. Various methods have been employed for improving the bond strength, including the use of sodium hypochlorite for deproteinization, as well as micro-etching to expose a greater surface area for bonding. These methods have met with mixed success.

MIH may contribute to insufficient bond strength for attaching fixed appliances, which extends the duration of orthodontic treatment and adds to the inconvenience for patients and practitioners.

Removal of orthodontic brackets can cause micro-fractures of the enamel [26]. When composite resin bonding material is removed from MIH-affected enamel, the bond failure is likely to be at the composite-enamel interface, as opposed to the composite-bracket interface for normal enamel. This may lead to more severe damage to the MIH-affected enamel when orthodontic appliances are removed.

## Summary

MIH is a widespread condition, which has the potential to cause severe pain and distress to children and their families. The dissemination of knowledge about the condition is important for improving monitoring to provide for early diagnosis on a consistent basis. Saving a permanent molar in the early mixed dentition (age 6–8) can prevent a great deal of distress and expense over a lifetime. School nurses, family physicians, and parents can provide an important health service by examining all children with a tongue blade and flashlight at about age 6 to assess newly erupted permanent molars. MIH is one of the more common pandemic health problems in the world, and it can be effectively controlled by early diagnosis, followed by appropriate restorative treatment. Continuing research and development are needed to prevent this important international health problem.

## Compliance with Ethical Standards

**Conflict of Interest** Paul Schneider and Margarita Silva declare no conflict of interest.

**Human and Animal Rights and Informed Consent** This article does not contain any studies with human or animal subjects performed by any of the authors.

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