



RECONSIDERING MOLAR HYPOMINERALIZATION AND “CHALKY TEETH”

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Reconsidering Molar Hypomineralization and “Chalky Teeth”: A Primer for Clinicians

Introduction

The skeleton is a mineralized tissue, giving the body structural integrity. The bones of the skeleton are comprised of a non-mineralized protein matrix with a mineralized component of calcium phosphate, in the form of calcium apatite (hydroxyapatite). The non-mineralized matrix is comprised primarily of collagen fibers, which are elastic and reduce the brittleness of bone. The organic matrix also contains regulatory proteins.

Besides bone, the other mineralized tissues in the human body are found in teeth, specifically enamel, dentin, and cementum. Enamel covers the crowns of the teeth and is a harder substance than bone. Dentin is underneath the enamel layer and contains cellular processes that are derived from cells in the dental pulp. Dentin does not have the hardness of enamel and is more susceptible to acid demineralization. Cementum covers the roots of the teeth and serves as part of the attachment apparatus of teeth to the maxilla and mandible.

When hypomineralization occurs, mineralized tissues have diminished function. Hypomineralization can occur in the skeleton, and examples include the sequelae of a deficiency of vitamin D, and hypophosphatasia. In addition, osteoporosis and osteopenia are generalized conditions characterized by reduced bone density.

Vitamin D is essential for bone metabolism and a vitamin D metabolite (1,25-dihydroxyvitamin D) is needed for proper absorption of calcium from the gastrointestinal tract. Vitamin D deficiency is associated with rickets in children and osteomalacia in adults. While relatively rare in the United States, deficiency of vitamin D is more common in developing countries¹.

Hypophosphatasia is another cause of generalized skeletal hypomineralization. Phosphate has an essential role in skeletal mineralization, as well as many other biological processes. There are multiple causes of hypophosphatasia, including deficiencies in alkaline phosphatase, an enzyme that is closely associated with normal bone function and turnover. Low levels of alkaline phosphatase in blood may indicate hypophosphatasia, a rare condition in which bones are brittle and fracture due to poor mineralization/hypomineralization.

Osteoporosis is a systemic condition in which bone mass is reduced, generally occurring in older adults. Osteopenia is an early stage of osteoporosis. Important risk factors include increasing age, female sex, and estrogen deficiency, as well as excess alcohol consumption, tobacco smoking, and a sedentary lifestyle. In osteoporosis and osteopenia there is an imbalance of osteoclastic activity (resorbing bone) and osteoblastic activity (depositing bone). The most common complication of osteoporosis is bone fracture.

Hypomineralization of the dental hard tissues can occur in association with some skeletal anomalies, but these are rare disorders, with the exception of Vitamin D-related enamel hypoplasia². In contrast to these systemically associated conditions, dental enamel is commonly affected by a unique localized type of hypomineralization, referred to as molar hypomineralization (MH).

History and Current Understanding of Developmental Defects of Enamel (DDE) (Molar Hypomineralization, “Chalky Teeth”)

As reviewed by Hubbard et. al.³, localized hypomineralization of enamel was identified more than 100 years ago. This disorder was enigmatic, as abnormal enamel occurred adjacent to normal enamel. Studies in the 1980's^{4,5} helped to define the nature of these enamel malformations. These “demarcated opacities” were different than the three other types of developmental defects of enamel (DDEs = dental fluorosis, enamel hypoplasia, amelogenesis imperfecta). Animal experiments demonstrated that MH could be the result of local causes (i.e. trauma, localized infection) or unidentified systemic conditions. Affected teeth have normal anatomy (dimension and form), but areas of enamel are not fully mineralized.

MH, which is also referred to as “chalky teeth” or “chalky enamel” occurs as demarcated opacities on molar teeth, and occasionally incisor teeth as well. Previously known as “molar-incisor hypomineralization”, the accepted term is now MH. Etiology of MH remains controversial. While consensus regarding etiology has still not been achieved, studies of abnormal dental mineralization in other conditions (i.e. amelogenesis imperfecta, dental fluorosis) have focused attention on the function of ameloblasts, the cells that are responsible for deposition of enamel³.

When considering the cause of MH, 5 key issues are yet to be settled³.

1. MH is “sporadic”, meaning that opacities can occur randomly on a tooth surface, and anywhere between one and four teeth in the maxillary or mandibular arch can be affected, without the involvement of the contralateral tooth/teeth. This would argue against the sole importance of systemic causation (i.e., systemic infection), and suggests the importance of the local environment. However, systemic perturbation with localized effects on developing enamel cannot be ruled out.
2. The predominance of hypomineralization affecting 6-year molars has not been explained.
3. The chalky defects are generally well demarcated, as opposed to other enamel defects seen in such conditions as tetracycline staining or dental fluorosis. Again, this would argue for the importance of a local mechanism in the pathogenesis of MH.
4. Epidemiological evidence about the recognized role of systemic illness or specific treatments such as the use of antibiotics has provided suggestive but inconclusive evidence for the role of such risk factors for MH.⁶
5. While studies of the etiology of MH have focused on the importance of ameloblast function, questions regarding the details of the pathologic mechanisms involved remain unresolved. What is the sequence of events that lead to reduced mineralization?

To help answer some fundamental questions related to MH, Hubbard et. al.³ have conducted research and proposed a pathologic model, based on studies of the biochemical characteristics of ameloblasts and enamel. One key early finding was that chalky enamel contains between 300% and 1500% more protein than unaffected enamel. Interestingly, the most prevalent protein was not amelogenin (which is the primary protein in development of fully calcified enamel), but was albumin, the most abundant serum protein. Further analysis indicated that albumin was trapped in the enamel opacities during development. The fetal form of albumin was detected in some opacities from 6-year molars, suggesting exposure during the developmental stage of tooth formation. Other studies have observed that albumin can inhibit enamel mineralization⁷.

Hubbard and co-workers³ also have explored why such albumin ‘contamination’ may occur, resulting in hypomineralized enamel. They proposed a potential mechanism, referred to as “mineralization poisoning”.

Both amelogenin and albumin bind to developing enamel crystals, but amelogenin is degraded by proteases (enzymes that destroy proteins), but albumin is not. The persistence of albumin in developing enamel prevents further mineralization of subsurface enamel. Mineralization continues, and as surface mineralization occurs, other enzymes degrade the more superficial albumin, resulting in a hardened surface layer of enamel. Thus, the trapped albumin results in subsurface opacities of poorly mineralized enamel.

In conclusion, the “mineralization poisoning” hypothesis helps explain the essential defect that accounts for the clinical finding. However, there is still much to be learned. For example, what accounts for the excess albumin that occurs in the environment of developing, and mineralizing, enamel? Further research to elucidate basic mechanisms that explain MH causation and pathogenesis may ultimately lead to new preventive and therapeutic approaches.

Prevalence of and Risk for Molar Hypomineralization

A review of the prevalence of molar hypomineralization observed that the prevalence of MH varies widely, due in part to different criteria used to identify affected individuals and affected teeth⁸. However, standardized criteria are now available⁹. At present, the global average prevalence rate appears to be about 20% (1 in 5 children),

clearly indicating that this condition is an important dental and public health problem (thed3group.org/prevalence).

As noted above, MH appears to have multifactorial etiology. Many identified risk factors relate to systemic illness or disturbances, likely exerting cytotoxic effects on ameloblast function during enamel development^{3,8}. Proposed causes of MH include:

- Acute or chronic illness of childhood. Evidence suggesting a role for systemic infection with supporting data from both animal models and human investigation^{10,11}.
- Environmental pollution (dioxin has been eliminated as a cause).
- Use of systemic antibiotics. However, the data supporting an association between MH and the use of amoxicillin during the period of normal enamel deposition is controversial^{12,13}.
- Complications at the time of birth, i.e., oxygen deprivation, low birthweight.
- Extended period of breast feeding.
- Genetic risk factors.

Longitudinal studies of risk factors and clinical outcomes are generally lacking, leading the field to rely on cross-sectional studies. As noted, multifactorial etiology is suspected.

Diagnosis and clinical classification:

MH manifests as discolored enamel opacities, ranging from creamy white to yellow to brown. Permanent first (6-year) molars are affected most often, followed by 2-year and 12-year molars and adult incisors. Any part of the crown of the tooth can be affected, but these opacities are most common in the occlusal/incisal part of the crown.

Several diagnostic and grading schemes for MH have been proposed, but no one system has been identified as the standard. Here are two examples:

The D3 website (thed3group.org) provides a general framework for diagnosing and grading MH. Key variables include the:

- **Patient:** consider the severity of involvement of the entire dentition.
- **Tooth:** evaluate the severity of involvement of individual teeth.
- **Pain:** an important indicator of the effect of MH on young patients. The reported level of pain may not be commensurate with clinical findings. Pain interferes with oral hygiene and the quality-of-life, such that the child is anxious about dental treatment.
- **Grading Severity:**
 - Mild: at least one mildly affected tooth. The surface of the enamel is opaque, but shiny. The color of the affected area is typically a bright white, more so than normal translucent enamel.
 - Moderate: at least one moderately affected tooth, or mild involvement with clinically significant level of pain. The enamel surface is “frosty”, that is textured but not pitted. The color can be described as “creamy”.
 - Severe: at least one severely involved tooth. The opacity is in a defined area, with a disrupted surface (pitted or degraded). The color is typically a more distinct yellow to brown.

This classification grading scheme is currently under further development, considering the important finding implicating albumin in the pathogenesis of MH¹⁴.

Another established system for clinical classification for MH has been described by Ghanim et al^{9,15}. This recording and grading system is based on the DDE Index and has been used in clinical practice and World Health Organization epidemiological research. This system was developed in response to a lack of reliable data on the global and national prevalence and characteristics of MH. Two forms were proposed – a short form for relatively rapid screening and a longer form with greater detail regarding lesion severity and distribution, as well as associated risk factors.

The short form includes evaluation of 16 teeth (2-year molars, 6-year molars, adult incisors), the eruption status of these teeth (less than 1/3 erupted vs. 1/3 or more erupted), and the clinical status of the lesions.

- 0 = no visible enamel defect
- 1 = enamel defect, other than MH
- 2 = white, creamy demarcated, yellow, or brown demarcated opacities.
- 3 = post-eruptive breakdown
- 4 = atypical restoration
- 5 = atypical caries
- 6 = missing due to MH
- 7 = cannot be scored (extensive coronal breakdown, but cause cannot be determined).

Lastly, lesion extension.

- I = < 1/3 of the tooth
- II = 1/3 to < 2/3 of the tooth
- III = 2/3 or more of the tooth

The long form includes all primary and permanent teeth, the same eruption status, but the clinical status is expanded:

- 0 = no visible enamel defect
- 1 = enamel defect, other than MH
 - 11 = diffuse opacities
 - 12 = hypoplasia
 - 13 = amelogenesis imperfecta
 - 14 = hypomineralization defect (not MH)
- 2 = demarcated opacities
 - 21 = white or creamy demarcated opacities
 - 22 = yellow or brown demarcated opacities
- 3 = post-eruptive enamel breakdown
- 4 = atypical restoration
- 5 = atypical caries
- 6 = missing due to MH
- 7 = cannot be scored (extensive coronal breakdown, but cause cannot be determined).

Specific instructions for scoring are provided in the reference¹⁵. This index has been validated for use as both a clinical and research tool⁹.

Clinical examples of MH are provided in Figure 1.

Prevention and Treatment of MH

A recent systematic review examined the variety of approaches for preventing and treating the sequelae of MH¹⁶. In addition, an earlier review by Almualllem and Busuttil-Naudi⁸ provides additional considerations for clinical management of affected patients.

Prevention:

Primary prevention of MH, which would occur at the time of tooth development, is not now possible for a variety of reasons, including a lack of a detailed understanding of the events that lead to MH, and the inherent difficulty in treating disorders that develop in utero. However, secondary prevention, which should occur once the teeth

erupt and MH is identified, is the ideal time to begin caring for persons with MH. Affected teeth have increased risk of caries and functional breakdown, and two approaches for prevention of caries and functional breakdown have emerged: fluoride varnishes and casein-based products¹⁶.

Fluoride varnish applied to affected teeth provides a high concentration of fluoride to the enamel surface. This treatment may promote limited hardening of “chalky” enamel and can reduce tooth hypersensitivity (note that true remineralization of hypomineralized enamel is not feasible). Casein-based products have also been used. Caseins are milk-derived phosphoproteins. When applied to a tooth surface, they provide a surface coating rich in both calcium and phosphate ions, which enhances re-mineralization. These products generally contain casein phosphopeptide-amorphous calcium phosphate (CPP-ACP) or casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP). Both types of products have been shown to be effective and can be used in combination.

Restorations

Almuallem and Busuttil-Naudi⁸ also note that hypomineralized teeth may be hypersensitive, and consequently it can be difficult to achieve adequate pain control when a restoration is required. A more comprehensive approach would be needed to achieve local anesthesia, including the combination of infiltration and nerve block anesthesia, and the use of inhalation sedation.

Due to the color change, esthetic concerns can be part of initial management of patients with hypomineralization of the incisal teeth. This may be most obvious when hypomineralization involves the incisal edge of anterior teeth. Tooth breakdown occurs there to a greater degree than on the direct labial surface. Suggested approaches for management of such defects include:

Microabrasion: using a mild acid and pumice, remove approximately 0.1 mm of the surface enamel. This would be followed by the application of CPP-ACP.

Tooth bleaching: at-home application (e.g., with 10% carbamide peroxide gel in a custom tray).

Etch-bleach-seal: etch with 37% phosphoric acid, followed by use of 5% sodium hydroxide, and then seal with composite or clear fissure sealant.

Resin infiltration: acid etch (15% hydrochloric acidic) followed by ethanol as a drying agent, and then resin infiltration.

Composite restoration, composite veneers and porcelain veneers: the selection of these approaches depends on the severity of the hypomineralization. Porcelain veneers are only recommended for patients 18 years of age and older.

Teeth with MH will require restorative intervention, both to remove enamel that has developed caries and remove demineralized enamel at the border of a carious lesion that would be susceptible to future decay. Clinical studies have focused on the use of composite materials. These restorations for patients with MH may need to be of the more extended classical cavity design, and not the conservative approach that has now been emphasized in treating teeth with caries in patients without MH.

A wide variety of composite materials have been utilized in the studies evaluated by Inchingolo et al,¹⁶. These include glass hybrid composites, short-fiber-reinforced composites, and glass ionomers. These studies reported positive results and no single type of material could be recommended. Further, use of crowns (either preformed metal or composite crowns for younger children, and traditional full or partial metal and porcelain crowns for older children) may be required.

In cases of severe MH with advanced decay, extraction of the first permanent molar should be considered. This will allow the second permanent molar to drift forward into the position of the first permanent molar. Such a step would be indicated for children who are between 8 and 10 years of age. When this is considered, a complete assessment of the state of the dentition is indicated, and consultation with an orthodontist may be advisable.

Other Approaches

A variety of other approaches have been reported, some that are quite innovative. These include the use of

1. A hydroxyapatite paste applied to the hypomineralized enamel. The results demonstrated reduced hypersensitivity when used to treat mild defects.
2. Low-level laser therapy, combined with fluoride varnish, resulted in an immediate reduction in tooth hypersensitivity.
3. Silver diamine fluoride was an effective treatment for hypersensitivity associated with MH. This was observed for patients treated with silver diamine fluoride alone, and silver diamine fluoride with glass ionomer sealant.
4. Biomimetic mineralization has been considered. This approach seeks to re-create the biological process of enamel mineralization. This is currently aspirational, but such a bioengineering approach will continue to be a topic of interest.

In sum, when considering clinical management of persons with MH, important knowledge gaps exist¹⁶.

1. A lack of long-term studies that evaluate the effect of different therapies on MH outcomes. By extension, there is a paucity of studies reporting the long-term follow-up of treated patients.
2. The treatment approaches vary dramatically in the published studies. This extends to the use of different products and study designs. Therefore, comparison between different clinical approaches is not possible.
3. Most of the treatment studies follow a small number of patients. Therefore, generalization to a larger population is not possible.
4. There still is no generally accepted approach to classifying patients with MH, including prevalence and extent of the disorder (number of teeth involved, severity of the involved teeth).
5. A lack of data on the prevalence of MH in different populations.

Conclusion

This review provides a primer on MH. Of particular importance for the clinician, awareness of the condition is critical. When developing a treatment plan, different clinical approaches should be thoroughly reviewed prior to initiating care. Scientific focus on MH as a clinical entity and important global health problem is due to the activities of The D3 Group (thed3group.org), and their Chalky Teeth Campaign (chalkyteeth.org). This interprofessional and international effort has brought attention to the prevalence and impact of MH, leading to both an awareness of the importance of a standardized classification scheme, and clinical management, as well as the need for prevention. Further, education is essential, including additional emphasis on MH in dental school curricula, and the continuing education opportunities for practicing dental professionals.

Recent findings on the pathogenesis of MH should stimulate research in this area. Indications that MH may develop from perinatal disruption of enamel development should also cause a reassessment of preventive strategies, which in turn will require a better understanding of risk factors associated with MH. A closer working relationship with medical providers is needed, as pediatricians should be engaged in identifying this disorder and stressing the need for a referral to a dental provider. In sum, MH provides an excellent example of the importance of medical-dental integration, from the basic research, clinical care and population health perspectives.

Acknowledgment: Mike Hubbard and Barbara Shearer reviewed earlier versions of this essay and made many helpful suggestions. Mike Hubbard also provided the clinical photographs. A wealth of additional information is available at "www.thed3group.org".

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Figure 1.



2-year molars. Left: demarcated opacity, yellow in color. The surface is intact. Considered mild involvement, unless sensitivity is present. Right: demarcated opacity, brown in color. The surface is broken. Considered severe involvement.



6-year molars. Left: demarcated opacity, brown in color, breakdown occurred during eruption. Considered extremely severe involvement. Right: sporadic distribution of hypomineralization. The molar on the right-side displays severe hypomineralization with decay. The molar on the left side shows only mild hypomineralization (arrows). Note that neither of the 2-year molars are involved, suggesting that plaque-related dental caries is not the cause.



Other teeth. Left: maxillary 12-year molars display demarcated opacities, which are brown in color. The second premolars display demarcated areas that are white in color (arrows). No hypomineralization is seen on the 6-year molars and first premolars, indicating a late onset of hypomineralization during tooth development. Right: maxillary central incisors display demarcated hypomineralization, brown in color, with post-eruptive breakdown.