

# Amelogenesis imperfecta: a diagnostic and pathological review with case illustration

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## SUMMARY

Amelogenesis imperfecta is an inherited disorder of enamel development, which results in morphological defects of both the primary and secondary dentition, usually in the absence of systemic involvement. Mutational defects involving the genes that encode for enamel matrix proteins and proteinases are implicated in this disorder. The phenotypic expression is variable, spanning a spectrum from barely discernible changes to severe aesthetic and functional enamel defects. The specific type and location of the genetic mutation, as well as the mode of inheritance, determine the clinical presentation. Clinical recognition and early therapeutic intervention are required for the most successful outcome. An essential component of the treatment process includes patient counselling and education. Patient management requires a dedicated multi-disciplinary approach. The disorder is reviewed here with emphasis on the clinical significance for the oral healthcare worker. In addition, a case is presented in order to provide an example of treatment planning and dental management.

## INTRODUCTION

Amelogenesis imperfecta (AI) is an inherited disorder of dental enamel formation. Several genes, mutations of which result in disordered enamel structure, regulate the process of amelogenesis. The clinical features of the defective enamel depends on the involved gene, the location and type of mutation, as well as the mode of inheritance.<sup>1</sup> AI usually affects the dentition in isolation with rare reports of associated systemic involvement.<sup>2</sup> AI has also been described as a component of certain syndromes.<sup>1,2</sup> The clinical appearance of AI is highly variable and results in teeth smaller than normal and enamel which is irregular and discoloured, with associated dental hypersensitivity. The inherent strength of the enamel is compromised and the affected teeth are prone to fracture and tooth decay. There is generalised involvement of both the deciduous and permanent dentitions.<sup>1</sup> The combination

## ACRONYMS

AD:	Autosomal dominant
AI:	Amelogenesis imperfecta
AIT:	Amelogenesis imperfecta with taurodontism
BOP:	bleeding upon probing
CAL:	clinical attachment loss
ENAM:	enamelin gene
OHCW:	oral health care worker
PPD:	periodontal probing depths
TDO:	tricho-dento-osseous syndrome
VDO:	vertical dimension of occlusion

of functional and aesthetic concerns may have a profound psychological effect on the affected individual.

The aim of this article is to review the clinical, radiographic and pathological features of amelogenesis imperfecta in order to facilitate early diagnosis. A clinical case is presented to illustrate the principles and importance of a multi-disciplinary approach.

## CASE REPORT

### Clinical history

A 45-year-old female patient was referred to the Department of Prosthodontics at the University of Pretoria, with a main complaint of severely worn and discoloured teeth, associated with difficulty in eating. Her dental history revealed her primary dentition to be weak and discoloured. She had no medical history of significance and there was no history of previous restorative dental treatment.

Intra-oral examination revealed severe, generalised occlusal wear and yellow-brown discoloration of the enamel. Microdontia of the anterior teeth was marked (Figure 1). Complete loss of enamel due to chipping had, in some areas, resulted in exposure of the underlying dentine. Teeth 26, 36 and 37 were missing and carious lesions were noted on teeth 17, 18 and 28 (Figure 2). In addition, peri-apical pathology was present in association with tooth 12. An overbite of 6mm with an overjet of 1mm and a freeway space of 4mm was recorded. Teeth 15, 16 and 27, 28 were in cross bite with, respectively, teeth 46 and 38; there was an overlapping of teeth 11 and 12; and teeth 24 and 38 were rotated. Canine guidance was observed on lateral excursive movements with anterior guidance on protrusion.

A comprehensive periodontal examination was performed, which included the charting of periodontal probing depths (PPD), clinical attachment loss (CAL), bleeding upon probing

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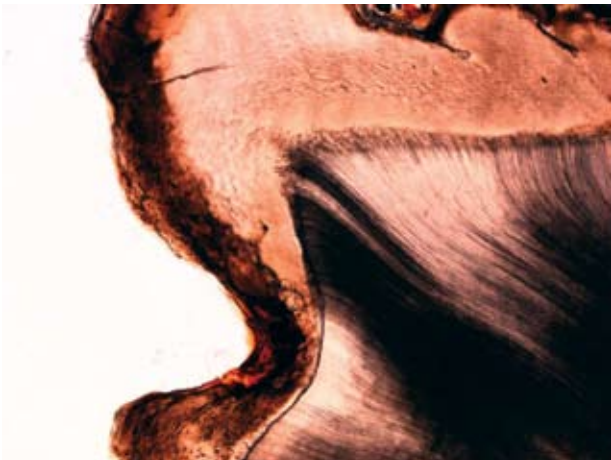
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**Figure 1:** Intra-oral photograph showing generalised enamel defects with associated discolouration, microdontia and open contacts.



**Figure 2:** Pre-operative panoramic radiograph showing evidence of microdontia and generalised loss of enamel which appears to be normally mineralised.



**Figure 3:** Hypomineralised enamel viewed on ground section of molar tooth.

(BOP), and plaque control. The plaque index was 42% and the BOP was 40% at the initial examination.

### Diagnosis

The periodontal diagnosis was that of a localised slight chronic adult periodontitis (American Academy of Periodontology) / generalised minor, localised moderate, adult periodontitis (Van der Velden classification).<sup>3</sup>

The main clinical differential diagnosis included dental fluorosis and amelogenesis imperfecta. There was no history to suggest geographic exposure to excess fluoride content in drinking water. The patient confirmed that several family members were afflicted by similar dental abnormalities. A panoramic radiograph was taken and teeth which were subsequently extracted, were submitted for histological evaluation of the ground sections.

Radiographic examination showed generalised dental involvement in which all of the teeth showed variable enamel

thickness and radio-density. The enamel present was irregular in appearance, with smaller crowns noted in support of the clinical appearance of microdontia. Open contacts were evident between the upper and lower anterior teeth. The underlying dentine appeared radiographically sound with normal pulpal morphology (Figure 2).

Ground sections of the extracted teeth showed normal dentinal and cemental morphology. The enamel was reduced in thickness and comprised a disorganised, haphazard arrangement of hypo-mineralised, aprismatic dental hard tissue (Figure 3). Occasional voids were identified.<sup>4</sup>

The diagnosis in this case was based on the clinical history and presentation, radiographic features and tooth morphology, as viewed on ground sections of the teeth. The lack of dentinal abnormalities and the generalised involvement of the dentition are supportive of the diagnosis of a hypomature form (Type II) of amelogenesis imperfecta.

## PATIENT MANAGEMENT

### Preparations for chair side treatment

The main aims of the final treatment plan, in descending order of importance, were the removal of pain and sepsis, correction of the dental malocclusion, restoration of masticatory function and improved aesthetics. Diagnostic waxed-up models of the maxillary and mandibular arches were articulated pre-operatively, to assess the options and to enable a predictable outcome. The diagnostic wax-up was used to fabricate splinted provisional maxillary and mandibular crowns.

### Periodontal treatment

The initial cause-related therapy included full-mouth debridement and root planing of all pockets with attachment loss. The patient's home plaque control practices were assessed and modified as needed.

Significant improvement of the periodontal status was achieved within 6 weeks, at which time resolution of the PPD was noted and the new plaque-index was recorded to be 28% with a bleeding index of 20%.

The surgical phase of treatment was performed under general anaesthesia. Full-mouth clinical crown lengthening was carried out, to provide increased retention and accessibility to deep sub-gingival margins.<sup>5</sup> The third molars and tooth 12 were extracted due to caries. An endosseous tissue level dental implant was inserted in the 36 region (Straumann® SP 4.1x10mm). Anti-inflammatory medication (Ibuprofen 400mg tablet tds po) and an anti-bacterial oral rinse (Chlorhexidine gluconate oral rinse solution 0,12% bd) were prescribed and post-operative instructions were issued.

One week post-surgery, the sutures were removed. Healing was satisfactory and uneventful. A three month healing period was allowed for re-establishment of the dentogingival complex after the crown lengthening and for osseous integration of the dental implant.

### Restorative Treatment

Following adequate soft tissue healing and osseointegration, the remaining teeth were prepared for full coverage ceramic crowns. Provisional restorations were cemented with non-eugenol zinc oxide cement (TempBond NE; Kerr Corp, Orange, Calif) to the new vertical height. There was a 3mm increase in the vertical dimension of occlusion (VDO). The patient showed no evidence of pain or discomfort over a 48-hour period associated with the adjusted VDO. Endo-



**Figure 4:** Post-operative view of cemented prostheses with improved aesthetics.

dontic treatment was performed on tooth 46, due to pulpal exposure during tooth preparation.

Impregum™ (3M ESPE) was used in non-perforated special trays to obtain the final impressions. The crowns were manufactured, following confirmed compatibility of the new VDO, using the BruxZir® Solid Zirconia material and the anterior crowns were veneered with porcelain for optimal aesthetics.

All traces of provisional cement were eliminated ultrasonically, following removal of the provisional restorations. The marginal fit and occlusion of the definitive crowns were fully evaluated, prior to permanent cementation. The crowns were cemented with Relyx™ Unicem (3M ESPE) (Figure 4). An occlusal guard was fabricated for nocturnal use.

The possibility of orthodontic treatment was considered in the initial work-up of this patient, however, owing to patient time constraints and disinterest, this option was not further pursued.

## DISCUSSION

Enamel is derived from ectoderm and is deposited during the process of amelogenesis. Ameloblasts differentiate during the pre-secretory phase of this process and proceed to deposit soft enamel matrix during the secretory phase. The organic and water content of the enamel matrix is replaced by a hydroxyapatite mineral component during the maturation stage. The clinical features of the dentition in AI will depend on the stage that is affected during the amelogenesis process.<sup>6</sup> If insufficient enamel matrix is laid down, the enamel will be thinner than normal, with abnormal development of the dentino-enamel junction. A normal thickness of enamel may

be present with insufficient mineralisation or a combination of these factors may be present. Thinner or weaker enamel is irregular in its microscopic structure and results in aesthetic compromise and functional defects.<sup>3</sup>

The classification of AI is complex and is based on a combination of clinical and genetic features. The complexity of the classification systems in existence is a reflection of the wide spectrum of clinical presentations. Hypoplastic, hypocalcified and the hypomature forms are the three main forms of AI with a fourth form described as a hybrid lesion, seen in association with taurodontism (Table 1).<sup>2,3</sup>

Patients with AI frequently experience dental hypersensitivity and present with discoloured and weak teeth. The attendant psychological problems associated with severe forms of the disorder have led to patient requests for full clearances followed by full denture construction at a young age. The oral health care worker (OHCW) should be familiar with the clinical spectrum of enamel changes occurring in AI and should be knowledgeable enough to allow for early recognition and dental management.<sup>7</sup>

At present, the diagnosis is based on the clinical presentation. The diagnostic criteria include the following:

- i. Clinical identification of an enamel disorder / disorder of amelogenesis
- ii. Elimination of all possible extrinsic causes of enamel hypoplasia
- iii. Establishment of familial involvement
- iv. Generalised involvement of both the primary and secondary dentitions

Although the genetic basis of AI is well established, the diagnosis in milder forms of disease, or in sporadic cases may not always be clinically possible.<sup>1,2,8</sup> Molecular genetic testing may be of use in such cases, although, at present, such tests are not available for diagnostic purposes.<sup>2</sup> An additional factor, impeding early clinical recognition is the variable clinical presentation, even in members of the same family. Autosomal dominant (AD) forms of amelogenesis imperfecta tend to affect at least one member within each generation of affected families. The most important feature to recognise in this genetic subgroup is hypoplastic enamel, which is thinner than normal. The teeth are smaller than normal and resemble teeth which have been prepared to receive crowns. There are large spaces and open contacts. The enamel is discoloured, rough and often pitted or grooved.<sup>9</sup> Some forms of AD AI present with enamel hypo-mineralisation, whilst the enamel may be normally mineralised in others. The enamelin gene (ENAM) is typically involved in AD cases.<sup>10</sup> ENAM, kalikrein 4 (KLK4) and matrix metalloproteinase-20 (MMP-20) are genetically implicated in recessive forms of AI. Both hypomature and hypoplastic forms are identified with variable clinical appearances. Males, inheriting a defective X-chromosome in X-linked forms of AI, present with full expression and severe phenotypic abnormalities of the dentition. Females are somewhat protected by the lyonisation process and often present with vertically grooved teeth. The vertical ridges and grooves in these cases are the result of alternating deposition of normal and abnormal enamel protein. The AMELX gene is implicated in these forms of disease.<sup>11</sup>

Most cases of AI present with isolated dental involvement; however, it has been noted in association with other syndromes. This occurs with whole chromosome defects as exemplified in cases of AI seen in association with cone-rod dystrophy.<sup>12</sup> The occurrence of taurodontism in cases of AI (AIT) is well documented and has been included in many of the classification systems.<sup>3</sup> AIT has overlapping features

**Table 1:** Classification of Amelogenesis imperfecta\*

Category	Phenotypic subtypes	Mode of inheritance
Type I Hypoplastic	Pitted	AD <sup>1</sup>
	Local	AD, AR <sup>2</sup>
	Smooth	AD, X-linked dominant
	Rough	AD
	Enamel agenesis	AR
Type II Hypomature	Pigmented	AR
	Generalised	X-linked recessive
	Snow-capped teeth	X-linked, AD
Type III Hypocalcified	Generalised	AD, AR
Type IV Hybrid (hypomature & hypocalcified)	Associated with taurodontism	AD

\* Adapted from Witkop 19888,  
<sup>1</sup> – Autosomal dominant, <sup>2</sup> – Autosomal recessive

with tricho-dento-osseous syndrome (TDO), in which the additional features of wavy hair and skeletal abnormalities are observed. The DLX3 gene is mutated in cases of TDO syndrome, which is not always the case in AIT. These two forms of disease are considered separate entities.<sup>13</sup>

AI needs to be distinguished from extrinsic forms of enamel hypoplasia, most notably dental fluorosis. The enamel defects, attributed to dental fluorosis, tend to be more random and show marked opacities. A band-like pattern of staining is seen, which often coincides with times of increased fluoride uptake. Furthermore, the chronological sparing of certain teeth, may be the most essential clinical feature, by means of which the distinction from AI may be made.<sup>2</sup>

Dental treatment in affected patients is mandatory and should include some form of genetic counselling. Patients will want to know what the chances are of their children being affected. Although molecular testing is not routinely performed for diagnostic purposes at present, the OHCW should be armed with sufficient knowledge to be able to at least convey the relative risk of inheritance to the patient.<sup>2,14</sup>

The most critical aspect of early clinical recognition is the early institution of dental therapy. Children diagnosed with AI will need to undergo a series of provisional restorative procedures. It is only once the permanent dentition has erupted completely that the dentist may consider placement of definitive restorations. Multiple, frequent dental visits are required. The malocclusions resulting from shifting of teeth and collapse of the dental arch due to premature enamel loss, also requires close co-operation with the orthodontist.<sup>7,15</sup>

The use of all-ceramic restorations for these patients has increased, owing to improved aesthetics, physical properties and biocompatibility. The potential advantages of solid sintered zirconia crowns include increased strength and toughness, decreased elastic modulus and the ability to undergo transformation toughening.<sup>16</sup> Longterm follow-up is essential to assess the bond between tooth and restoration. There is always a risk of bond-failure, particularly where dentine is exposed with resultant micro-leakage and pulpal exposure.<sup>17</sup>

The OHCW needs to be well-informed of the clinical features of AI, in order to implement the most appropriate dental treatment for the patient's age and state of dentition. Finally, patients with AI should be treated holistically, incorporating a multi-disciplinary team of practitioners for restoration of aesthetics, function and self-esteem.

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