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PATTERN OF MINERALISATION - A REVIEW

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Abstract

The tooth develops through different chronological stages. Collagen is the protein in connective tissue as well as in hard tissue, bone, dentin, cementum and even the mineralising ligament of the epiphyseal growth palate. Hard tissue is mineralised and has a firm intercellular framework. Tooth development and mineralisation are processes that derive from different tissues interactions, such as ectodermal and mesenchymal. These interactions are responsible for the formation of unique structures with a specific chemical composition. Despite differences, mineralized tissues are similar, deriving from highly concentrated extracellular processes involving matrix proteins, proteases, and mineral ion fluxes that regulate mineral crystal nucleation, growth, and organization. There are two theories- they are collagen template mediated mineralization and matrix vesicle mediated mineralization. Mineralized tissue are well organized hierarchical structures that adapt different stimuli to achieve a desired function. This study aims at explaining the complex chemical biological mechanism that leads to the development of dental germs and teeth. It is impossible to pinpoint the exact moment when the process drifts or the aetiological causes of important diseases, such as the MIH, without a solid understanding of this long and fascinating process.

Keywords: *Enamel; Dentin; Mineralization.*

Introduction

Fixed prosthodontic treatment deals with the replacement of teeth by artificial substitutes that are not readily The tooth develops through different chronological stages that can be summarised as follows: growth and differentiation; epithelial proliferation; histological differentiation; organogenesis; mineralisation; eruption; wear and atrophy. Collagen is the protein in connective tissue as well as in hard tissue, bone, dentin, cementum and even the mineralising ligament of the epiphyseal growth plate[1]. During amelogenesis, the enamel crystals will assemble small amorphous mineral particles all through the amorphous mature particles that are not verified experimentally. Transient amorphous mineral phases(i.e. ACP and Amorphous Calcium Carbonate) have also

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been observed to be associated with a number of other biomineralization systems[2]. Bone mineralisation, the procedure by which the natural bone network gets loaded up with calcium phosphate nanocrystals, happens in explicit, profoundly requested procedures. Mineral crystals are deposited. In organic fashion, the ECM matrix surrounding the cells provides a template for mineral deposition that defines the sites of mineralization which commence the final dimensions of crystals. There are two theories- they are collagen template mediated mineralization and matrix vesicle mediated mineralization[3]. Mineralized tissue are well organized hierarchical structures that adapt different stimuli to achieve a desired function. Studies that address the potential role of amelogenin, proteolysis, de-phosphorylation are regulating the initial enamel for mineral formation and maturation are currently going underway in the laboratory[4]. Defective mineralization of organic matrix formations is due to gene mutation and leads to the clinical spectrum of disease processes. Previously our team had conducted numerous original studies[5–11] and surveys[12–19] over the past 5 years. Now we are focussing on epidemiological surveys. The idea for this review stemmed from the current interest in our community.

HARD TISSUE OF ENAMEL AND DENTIN:

Enamel, the hardest tissue of the body, covering part of the crown of the tooth in warm blooded animals. Enamel, when developed, comprises apatite crystals containing calcium and phosphate. Enamel is not a living tissue and contains no blood vessels and nerves. The thickness of enamel over the outside of the tooth; it is hardest at the gnawing edges, or cusps. Normal enamel may vary in colour from yellow to gray. The surface enamel is harder and less soluble and contains more fluoride than the underlying enamel and is very resistant to caries[20]. Dentine is a rough, light yellow, transparent tissue coating that is just underneath enamel and cementum. Dentin constitutes the largest portion of the tooth and consists of approximately 70% inorganic matter and 30% organic matter and water[21].

ENAMEL MINERALISATION:

BIOCHEMICAL PROCESS OF MINERALISATION OF ENAMEL:

Enamel is formed by the cellular activity of ameloblasts. The ameloblasts produce two

major classes of proteins: hydrophobic proteins known as amelogenins and non- amelogenin proteins such as anionic enamel proteins namely enamelins, tuft proteins, tuftelin, enamel proteases, proteoglycans and/or sulfated glycoproteins[4] . The enamel proteins production and secretion are subordinated to the relative gene-expression in ameloblasts. The instructive signal which controls amelogenin Transcription will occurs during early cap stage. Furthermore, the inducer for tuftelin transcription is possibly different from that required for amelogenin, since

tuftelin and amelogenin are sequentially expressed and tuftelin is expressed at the bud.

These results support the hypothesis that multiple, sequential regulatory signals, provided by the dental papillae mesenchyme, control the biochemical differentiation of inner enamel epithelium into ameloblasts[22]. Enamel mineralization differs from that of bone and dentin: for example, it starts its maturation immediately after ameloblasts lay down the enamel matrix and this matrix is transient, unlike the bone and the dentin. Dental enamel forms by the deposition of non crystalline and mineral ribbons by a mineralisation apparatus related with the secretory surfaces of the ameloblast plasma membrane. The structure and orientation of enamel mineral ribbons is formed at the front of the mineralization and is not attributable to the stereospecific inhibition of mineral deposition by acidic enamel proteins on selected crystal faces. TThe hierarchical organisation of enamel ribbons into rod and interrod enamel is defined by the topographical re-configuration of the front of mineralization occurring with the creation of the Tomes cycle. The mineralisation front apparatus is the key to enamel formation, and significant advances in our understanding of amelogenesis will be achieved by gaining a better understanding of molecular events occurring at the enamel mineralisation front[23–26].

ENAMEL MATRIX:

Enamel matrix is a continuous layer formed along dentin. Enamel matrix proteins are secreted by ameloblast . Ameloblasts consist of 97% inorganic and 3% of organic. Organic part consist of proteins called Amelogenins and Non Amelogenins. An enamel matrix derivative is a sterile protein aggregate which comes from the enamel matrix, specifically from amelogenins, and is the precursor of the enamel of developing teeth. The proteins necessary for EMD are harvested from around the developing teeth by using various techniques. Enamel matrix protein derivatives are used in the restoration and regeneration of periodontal tissues and assist in the growth or further development of the periodontal ligament, root cementum, and alveolar bone. Though enamel matrix

derivatives are harvested by using various techniques, have not been shown to create a significant immune response when used in humans. The use of EMDs have also demonstrated anti-inflammatory properties. Both of these results suggest that the use of EMD is safe for humans. In addition, the results of EMD therapy are longer-lasting and have been shown to provide significant benefits to patients undergoing periodontal regeneration[27].

MINERALIZATION PROCESS:

After the initial enamel matrix is laid down, ameloblasts develop cone-like projections called Tomes' process. All enamel matrix secretions from then on occur through the Tomes' process. The enamel matrix is a partially mineralized matrix (25 to 30% calcified). The important proteins secreted by the ameloblasts are amelogenins, ameloblastin and enamelin. The secreted proteins undergo degradation by enzymes like metalloproteinases and serine proteases into smaller low molecular weight fragments[28].

AMELOGENESIS:

During the process of amelogenesis, the ameloblasts pass through a series of differentiation stages that are characterised by changes in cell morphology and function[29]. In general, cell differentiation during enamel development results in pre-secretory, secretory transitional, and maturation face ameloblasts. Cell morphology and chemical composition of the enamel extra cellular matrix are the basis for the definition of the different stages of the amelogenesis[4]. Ameloblast deposits the enamel matrix onto predentin during the advanced bell stage. In the extracellular space between the pre secretory ameloblasts and the mineralized dentin arises the complex cycle of enamel bio mineralisation. The tissue grows continuously, with the secretion of an enamel extracellular matrix, until the ameloblasts have secreted the whole thickness of the enamel matrix[30].

FORMATION OF ENAMEL MATRIX:

After the full thickness of the enamel matrix is laid down, it un- dergoes complete mineralization or maturation. During this process the ameloblasts develop villous projections on their secretory surface. They are now known as ruffle ended ameloblasts. Most of the proteins secreted (over 90%) especially amelogenins and water are absorbed. The pressure from the growing crystals squeezes out the matrix which is in the form of thixotropic gel. The crystals increase in size from 1.5 to 25 μm. During maturation the ameloblasts alternate cyclically from ruffle ended to smooth ended ameloblasts. This process is called modulation. Enamel proteins like tuftelin help in mineralization while other proteins regulate the growth of crystals. The minerals find their way first between and then through the ameloblasts to the mineralizing front. The last layer of enamel formed is not from Tomes' process, hence it is aprismatic enamel[31].

MINERALISATION OF ENAMEL:

Mineralisation of Enamel is of four types- Primary- partially mineralised enamel matrix - 30% mineralisation (innermost 8micrometer layer next to DEJ, is heavily mineralised- enamelin). Secondary- starts at the surface, sweeps rapidly into a deeper layer until the 8micrometer layer. Tertiary-rise in mineral rebounding against the enamel surface from the innermost layer down. Surface layer is 15micrpmeter side and mineralised more slowly. Quaternary- outer layer mineralizes rapidly and becomes the most mineralized part of enamel. Saliva's buffering capacity and flow of secretion are directly related to the rate and extent of demineralization[5].

AMELOGENESIS IMPERFECTA:

Amelogenesis imperfecta (AI) is a terminology for a medically and genetically heterogeneous community of disorders that, sometimes in combination with certain dental, oral and extraoral tissues, damage the dental enamel[32]. Climatic changes cannot be a reason for amelogenesis imperfecta[9]. Children who have hypomineralisation deserve a positive professional intervention but with an empathetic approach[6].

ENAMEL HYPOPLASIA:

Enamel hypoplasia (EH) is a developmental disorder that may in one of two forms impact the main and permanent teeth. It is sometimes identified as a physically missing tooth structure, and can be seen as pits, grooves or just missing parts in the crown of the tooth[33]. Maintaining a healthy disciplinary and adding supplements of Vitamin A & D to your diet can help to strengthen developing teeth which can prevent enamel hypoplasia[13].

ENAMEL HYPOCALCIFICATION:

Enamel hypocalcification is a tooth enamel deficiency in which regular quantities of enamel are formed but are hypomineralized. The enamel in this defect is weaker than usual. Some areas in enamel are hypocalcified: enamel spindles, enamel tufts, and enamel lamellae[34].

ENAMEL HYPOMATURATION:

Hypomaturation indicates a deficiency exists in the enamel 's final development and maturation. The teeth are creamy, opaque to yellow or brown. The enamel has a normal thickness, but it’s too soft, so the teeth appear mottled and may wear away and break. Hypomaturation represents between 20 to 40 percent of all cases of amelogenesis imperfecta[35].

DEVELOPMENT ALTERATIONS:

Enamel hypoplasia is a quantitative defect and it is the consequence of an altered

formation of the enamel matrix. It is caused by a reduction in the thickness of the enamel surface. It can show as: single or multiple, deep, spread or organised in horizontal rows dimples; single or multiple, narrow or wide, highlighting the absence of enamel, partial or complete furrows on a considerable portion of the dental crown. The reduction of thickness of the enamel has rounded and smooth edges and no visible demarcation line. It is however possible to observe the areas of opacity comes from its incomplete mineralisation and it is a qualitative defect. The opacity is distinct in diffused and limited lesions. Limited injuries have precise boundaries with the adjacent normal enamel and colours are white, yellow or brown. The opacity can have a linear, irregular or contiguous distribution, but boundaries are not accurate. Mineralisation is incomplete under the enamel surface that remains intact during eruption; it appears as a change of color and transparency of the glaze, whose surface may break due to a trauma produced by masticatory forces, leaving sharp edges.

At the time of the eruption, enamel thickness is normal. The enamel, at a correct degree of mineralisation, is translucent and has an index of refraction of 1.62; if there is a development defect or even a carious lesion, the enamel is more porous and has a lower index of refraction. This condition is clinically visible with a different color that varies from white to yellow, rather than brown. The color is a symptom of change of refractive index caused by an increased porosity of the enamel. It may happen that in severe cases, the surface could collapse and then look like a zone of loss of substance, which may appear similar to hypoplasia, but in hypoplasia there are smooth margins, while in this condition borders are irregular. A particular type of hypomineralisation is the MIH. This type of enamel defect is located in the first molars and incisors in secondary dentition. A number of different denominations were used for the condition with hypomineralized first permanent molars (i.e. idiopathic hypomineralisation, morbus S, cheese molars). MIH is defined as a chronological hypomineralisation of systemic origin of the first permanent molars and incisors. One or more of the molars may be affected, each with different degrees of severity. The permanent incisors may also be affected. While MIH is characterized as a temporal and general disruption, the number of first permanent molars and the degree of hypomineralisation varies greatly. Enamel in teeth affected by MIH exhibits disorganised enamel prisms.

In a polarizing microscope study, when comparing the clinical and histological presence of MIH with regular enamel, yellow⁄brown enamel opacities appear more porous than lighter[22,36–42]. Fluorosis is a qualitative defect of the enamel caused by a long-term consumption of fluoride during teeth formation. The threshold dose for the development of a mild fluorosis of permanent teeth was estimated 40-100(m) g/day of fluoride per kg of weight. It was also found that, individually, there are thresholds below which fluorosis cannot develop. The defects of enamel caused by fluorosis vary in opacity from little to white, yellow or brownish. Dental trauma can lead to sequelae that result in alterations of the enamel. The most affected teeth are the upper central incisors (30%), both deciduous and permanent. During their initial development, permanent incisors lie towards the palate and near the apex of the deciduous tooth. It follows that lesions of primary teeth can cause permanent damage to the underlying permanent tooth. The alterations are consequences of developmental disorders that occur on the follicle, whose tear will determine dysfunctions in the development of the enamel.

DENTIN MINERALISATION:

BIOCHEMICAL PROCESS OF MINERALIZATION OF DENTIN:

In regard to the biochemical process, a study on the mineral characteristic is necessary for dentin. The composition of dentin is hydroxyapatite, CaO1(OH)2(PO4)6. The mineral crystals in dentin are largely arranged with their c-axes parallel to the collagen fibers[23]. Induction of mineral crystals during mineralisation of calcified tissues such as dentin is caused by heterogeneous nucleation. Macromolecules in the organic matrix that display a specific stereochemical arrangement of reactive groups, possessing an electrical charge or other properties that lower the energy barrier, in order to form a solid phase of calcium phosphate mineral from a solution. The

stereochemical geometry and the charge distribution are supposed to mimic crystal planes of the crystal to be nucleated. Mineral nuclei formed at these nucleation sites would then grow and fuse will form mineral crystals. Because of their unique chemical characteristics, the non-collagenous dentin components, such as phosphoproteins, have come into focus as being responsible for the induction and regulation of mineral formation. Because of its pronounced anionic character, non-collagenous proteins (NCPs) like phosphophoryn (PP-H) and proteoglycans (PGs) have affinity for Ca2+ ions, suggesting that they may function as hydroxyapatite nucleators in vivo. Dentin NCPs can nucleate apatite at physiological ionic conditions.

To nucleate a mineral phase, the polyanionic macromolecules should be immobilised by some solid support; they are inductive in small amounts. The use of polyanionic macromolecules is a general motif for biomineralization[23–26] PP-H and one of the PG pools bypass predentin and they are directly transported to the site of mineral formation. The PP-H or PG, first released into the matrix, could promote the formation of the initial mineral crystals, whereas the additional accumulation of NCPs could participate in the regulation of the extent of crystal formation. The strong affinity of calcium ions with PP-H with the ions that are highly mobile on the surface of the molecule, may cause a facilitated calcium ion diffusion that would ensure a rapid formation of calcium phosphate mineral in hydroxyapatite.

DENTINOGENESIS:

Deninogenesis is the formation of dentin by mesenchymal odontoblasts located at the dental pulp periphery. Dentinogenesis is started by inductive impacts of the lacquer organ including atomic flagging pathways, for example, Wnt, Runx-2 and TGF-β. Dentinogenesis closes at the late chime phase of the molar tooth, which happens both in the crown which root zones. Separated odontoblasts oppose division and become oval spellbound secretory cells with unmistakable apical cytoplasmic tomes filaments. Tomes fibers elongate as matrix formation continues. Predentin, the first organic matrix secreted by odontoblasts, is composed of proteoglycans, glycoproteins, and collagens. Later-shaped crystallization habitats of hydroxyapatite develop and permit the change of predentin into dentin. Dentinogenesis happens both prenatally and postnatally, and can be seen less significantly all through life when auxiliary and tertiary dentin is shaped[43].

DEFECTS OF MINERALISATION:

DENTINOGENESIS IMPERFECTA:

Three sorts of dentinogenesis imperfecta: DI type 1 is related with osteogenesis imperfecta. DI type 2 has basically indistinguishable clinical radio-realistic and histological highlights from DI type 1 yet without osteogenesis imperfecta; DI type 3 is uncommon. It has been suggested that DI type 2 and DI type 3 are different expressions of the same gene[44].

DENTIN DYSPLASIA:

Dentin Dysplasia (DD), a rare anomaly is an autosomal dominant hereditary disturbance in dentin formation affecting either the primary or both the dentitions in approximately one patient in every 100,000. Type I DD is characterized by crowns appearing normal or might be slightly amber colored with no or only rudimentary root development, aberrant growth of dentin in the pulp chamber leading to reduced pulp space in permanent teeth and incomplete or total obliteration of the pulp chambers, and periapical radiolucent areas or cysts which might result in premature loss of tooth[45]. DD type II is described by yellow, earthy colored, dim golden, translucent essential teeth with complete pulpal decimation. The lasting teeth have an ordinary appearance or may be somewhat golden hued. Roots are normal in size and shape with a ‘thistle tube’ shaped pulp chamber with pulp stones[46].

CONCLUSION:

Complex chemical biological mechanisms lead to the development of tooth germs and teeth. It is impossible to pinpoint the exact moment when the process drifts or the aetiological causes of important diseases, such as the MIH, without a solid understanding of this long and fascinating process.

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AUTHOR CONTRIBUTION:

Hemanth Ragav N V carried out literature search and drafted the manuscript. Archana Santhanam supervised in preparation of the manuscript. All the authors had equally contributed in developing the manuscript.

CONFLICT OF INTEREST:

There was no conflict of interest as declared by the authors.

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