Caries Process, Prevention, and Management: Demineralization/Remineralization

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Conflict of Interest Disclosure Statement

- Dr. Nascimento reports no conflicts of interest associated with this course. She has no relevant financial relationships to disclose.

Short Description – Forensic Dentistry

This is part 5 of a 10-part series entitled Caries Process, Prevention, and Management. In this course, the dynamic process of demineralization and remineralization is discussed, paying particular attention to tooth hard tissue structure, the role of acid production by cariogenic bacteria, and the critical pH at which tooth enamel begins to dissolve, typically around pH 5.5. The role of acid-neutralizing bacteria, saliva's buffering capacity, and fluoride in tooth hard tissue remineralization will also be explained.

Course Contents

Overview

Caries is characterized by the progressive chemical dissolution of the hard tooth structures - enamel and dentin - by the acid produced when the bacteria in dental plaque ferment carbohydrates. The development of caries is dependent on the interplay between processes that cause demineralization of tooth enamel, and those which cause remineralization. Only when factors favor a sustained acidic environment, typically below a critical pH threshold, does the dissolution of enamel exceed the remineralization process, leading to caries formation.

Learning Objectives

Upon the completion of this course, the dental professional should be able to:

- Explain the differences in how tooth enamel and dentin structure are affected by demineralization.
- Describe the role of bacterial acid production in the demineralization process.
- Understand the concept of critical pH and its relationship to the onset of demineralization.
- Identify the five zones of carious dentin in an advanced lesion.
- Discuss how demineralization impacts different populations, including young children, the elderly, and other special populations.
- Be familiar with the factors that promote remineralization and their role in caries prevention.

Glossary

acidogenic – Something that produces acid, such as cariogenic bacteria that ferment sugars to produce acids.

aciduric – Capable of growth in an acidic environment, often referring to acid-tolerant bacteria that can survive and proliferate in the low pH conditions created by cariogenic bacteria.

buffering agent – A substance that adjusts the pH of any solution, such as saliva or plaque fluid, and can resist pH fluctuations. Beneficial in the prevention of dental caries by maintaining a neutral pH that minimizes demineralization.

carbonated hydroxyapatite – The hydroxyapatite in human enamel is not pure and contains carbonate ions. The presence of carbonate ions makes the enamel structure much more soluble and less resistant to acid dissolution. Chemically, the hydroxyapatite that comprises enamel is often described as a calcium-deficient carbonated hydroxyapatite, which is more prone to demineralization.

cariogenic bacteria – Bacteria present in the oral biofilm (dental plaque) that, when provided with fermentable carbohydrates, produce acids that lead to the occurrence of carious lesions when other necessary factors are present (such as low pH and insufficient remineralization).

demineralization – The chemical process by which minerals (mainly calcium and phosphate) are removed from the dental **hard**

tissues - enamel, dentin, and cementum. This occurs through dissolution by acids produced by bacteria or by chelation. The rate of demineralization depends on the degree of supersaturation of the immediate environment of the tooth and the presence of fluoride, which can slow the process. In optimal circumstances, the minerals can be replaced through the process of remineralization.

dental plaque – An organized community of many different microorganisms that form a biofilm and is found on the surface of the tongue and all hard surfaces in the oral cavity. Dental plaque is present in all individuals and can vary from being comprised of health-related microorganisms (commensals) to being highly harmful (pathogenic), predisposing the patient to dental caries or periodontal diseases. Dental plaque must be removed by mechanical methods, such as toothbrushing or professional dental cleaning (prophylaxis), as it cannot be eliminated by rinsing or chemical agents alone.

fluorapatite – A crystal structure in tooth mineral (Ca10 (PO4)6 F2) resulting from the replacement of hydroxyl ions (OH-) in the hydroxyapatite structure with fluoride ions (F-). Fluorapatite (also commonly referred to as fluoroapatite, fluorhydroxyapatite or fluorohydroxyapatite) is stronger and more acid resistant than hydroxyapatite.

GERD – Gastroesophageal reflux disease; the reflux of hydrochloric acid generated in the stomach that travels to the mouth. Erosion will occur upon the acid's contact with enamel surfaces. glycolysis – Glycolysis is essential to all living organisms and is the process whereby energy is released from sugars by the formation of pyruvate. This pathway is crucial for bacterial metabolism, especially in cariogenic bacteria, which produce acid as a byproduct.

hydroxyapatite – Crystals of calcium phosphate – (Ca10 (PO4)6 OH2) that form the mineral structure of teeth and bone. Enamel comprises approximately 98% hydroxyapatite (by weight). Much of the hydroxyapatite in enamel, however, is a calcium-deficient carbonated hydroxyapatite, the crystals of which are readily dissolved by acids. The addition of fluoride creates fluorapatite, which is less soluble and more acid-resistant.

ions – Atoms or molecules that carry either a positive or a negative electric charge in a solution. For example, sodium chloride (NaCl, common table salt) in water dissociates into Na+ and Cl– ions.

pellicle – A layer of salivary glycoproteins that forms on the tooth surface and is present within minutes of oral hygiene or professional prophylaxis. The pellicle layer is protective against caries as it slows the diffusion of calcium and phosphate ions away from the tooth surface. Sometimes referred to as the Acquired Pellicle, it varies in thickness in different parts of the mouth and is reduced during oral hygiene or by dietary acids. In addition to protecting against caries, it is the layer to which microorganisms first attach to the tooth surface in the formation of the dental plaque.

remineralization – The chemical process by which minerals (mainly calcium and phosphate) are replaced into the substance of the dental hard tissues – enamel and dentin. The process requires an ideal environment that includes supersaturation with calcium and phosphate ions, and adequate buffering. In the presence of fluoride, remineralization is enhanced by the formation of fluorapatite, which is more resistant to acid attack.

translucent – Permitting the passage of light; especially transmitting and diffusing light so that objects beyond cannot be seen clearly.

white spot lesion – The earliest clinical signs of dental caries, appearing before cavitation occurs. At this stage, the disease process is reversible through remineralization, provided favorable conditions are present - such as the use of fluoride and adequate availability of calcium and phosphate ions.

Introduction

Dental caries is a biofilm-mediated, sugar-driven, multifactorial, and dynamic disease characterized by alternating phases of demineralization and remineralization of the dental hard tissues.[1] The pH and carbohydrate availability are key environmental factors affecting the physiology, ecology, and pathogenicity of the oral biofilms colonizing the teeth.[2] The acidic environment that triggers the **demineralization** of tooth enamel results from the metabolic activity of cariogenic bacteria, such as Streptococcus mutans, which ferment dietary sugars and produce acid as a byproduct.[3] Changes in environmental pH occur following the consumption of dietary sugar. Specifically, organic acids produced by the fermentation of dietary carbohydrates by cariogenic bacteria elicit demineralization of tooth enamel. These periods of acid challenge to the tooth are followed by periods of alkalization, which neutralizes plaque pH and promotes remineralization of tooth enamel.[4]

In discussions of the caries process, particular attention is given to the enamel - the hard, outermost layer - because it is the primary contact with **cariogenic bacteria** and the starting point of the demineralization process that can lead to caries development. Enamel is composed predominantly of hydroxyapatite crystals, which are vulnerable to acid dissolution, especially when there is a loss of calcium and phosphate ions.[5] Many beneficial oral bacteria can tolerate short periods of low pH, but their growth is inhibited by prolonged or frequent exposures to acidic conditions.[6] Enamel is also the only tissue of the tooth that does not have the ability to grow or repair itself after maturation, making it even more crucial that its demineralization is prevented. Once enamel is demineralized, it cannot regenerate on its own without intervention, which is why maintaining its integrity is essential in caries prevention. Caries can also develop in dentin, the hard layer under the enamel, so understanding the chemical composition of this layer, and how it is affected by demineralization, is also important.

The process of **remineralization** - the replacement of lost minerals in hard dental tissues - can halt, slow down, and, in some cases, reverse the caries process.[1] Saliva and fluoride are two key players in remineralization. Saliva contains calcium and phosphate **ions**, which help restore lost minerals and strengthen the tooth structure. Saliva also plays a key role in maintaining oral pH at around neutrality, which is optimal for the growth of most health-associated oral microbiota. Fluoride can be incorporated into the tooth structure to form **fluorapatite**, which is more resistant to acid dissolution than hydroxyapatite.[5] For caries prevention, factors in the oral cavity must be highly favorable for remineralization to occur, so that this process can be effective. If the environment is more favorable for demineralization, such as in the presence of low pH or high bacterial acid production, the remineralization process may have little or no influence, or not occur at all; and caries will develop.

Clinical Significance Snapshots

How does understanding the demineralization-remineralization cycle help me prevent or arrest the caries process in my patients?

The 'demin-remin' cycle is like the ebb and flow of money in a checking account. If too many withdrawals are made and too few credits received, the account becomes overdrawn. When deposits (remineralization) match or exceed the withdrawals (demineralization), a healthy balance is maintained. The same applies to the balance of calcium, phosphate, and fluoride ions entering and exiting the tooth. Some loss of these minerals inevitably occurs during mealtimes, as cariogenic bacteria in the biofilm on the surface of the tooth metabolize the sugars in the diet of minerals caused by sugar-containing foods and beverages. Foods rich in calcium, such as yogurt, cheese, or milk, can help remineralize enamel. These foods are particularly beneficial at the end of meals to help neutralize acids and promote remineralization.

Why is the use of fluoride agents so prominent in the prevention of dental caries?

Hydroxyapatite crystals in enamel are naturally impure due to the presence of carbonate ions. These carbonate ions weaken the crystal structure, making it more vulnerable to dissolution by acids produced during the fermentation of carbohydrates by cariogenic bacteria. Fluoride ions can replace some of the carbonate and hydroxyl ions in hydroxyapatite, forming fluorapatite. Fluorapatite is structurally stronger and more resistant to acid dissolution than carbon-hydroxyapatites. This conversion significantly enhances enamel's resistance to demineralization, effectively tipping the demineralization/remineralization balance in favor of remineralization. Fluoride should be available in the oral cavity daily in low concentrations, ideally through the use of toothpaste with proven bioavailability of fluoride (ADA Seal of Acceptance), to consistently promote enamel health and prevent caries. For patients who are at higher risk of caries, such as those with frequent sugar consumption or reduced saliva flow, additional forms of fluoride application should be considered. These may include fluoride rinses (daily or weekly depending on concentration), and professional application of fluoride varnish, gels or foams, which offer higher fluoride concentrations for enhanced protection.

Tooth – Hard Tissue Structure and Enamel

Enamel is the most mineralized tissue of the body, forming a very hard, thin, **translucent** layer of calcified tissue that covers the entire anatomic crown of the tooth. Enamel's remarkable hardness is due to its composition, which is primarily inorganic. Approximately 95% of enamel consists of calcium and phosphate ions that combine to form strong **hydroxyapatite** crystals ($Ca_{10}(PO_4)_6(OH)_2$). These hydroxyapatite crystals are highly organized, giving enamel with its strength and resistance to mechanical wear.

Hydroxyapatite crystals are dynamic and can incorporate trace minerals into its crystal lattice. These ions can be negatively charged, such as fluoride or carbonate, or positively charged, such as sodium, zinc, strontium, or potassium. The concentration and type of these trace minerals influence the solubility of enamel. For example, the presence of fluoride in the crystal structure strengthens enamel and reduces its solubility, making the enamel more resistant to demineralization. On the other hand, the incorporation of carbonate increases enamel solubility, making it more susceptible to acid dissolution. It has been shown that the outer layers of enamel are richer in fluoride and poorer in carbonate than the inner layers, making the enamel surface more resistant to acid dissolution than the deeper layers. This gradient in mineral content plays a critical role in the enamel's ability to resist environmental challenges, such as acid exposure from dietary sources.

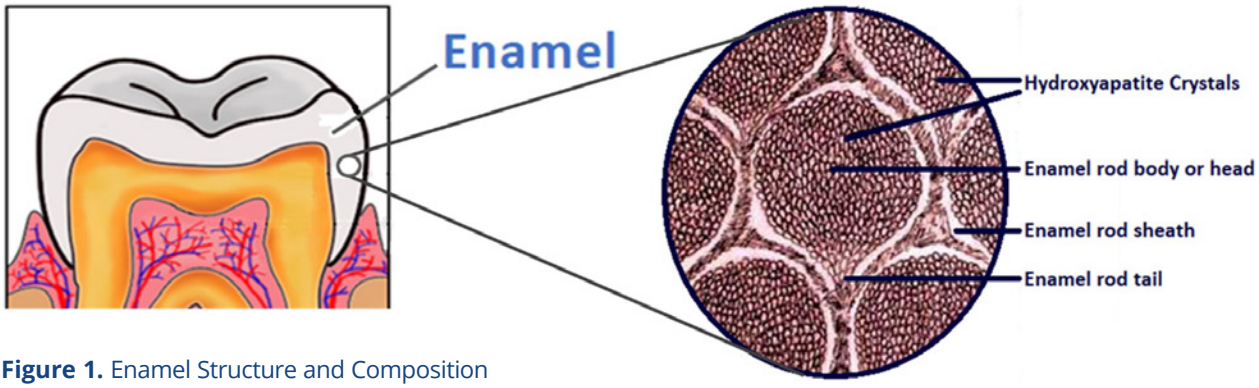

Figure 1. Enamel Structure and Composition

Approximately 1% to 2% of enamel consists of organic materials, primarily enamelins, which are specialized proteins that have a high affinity for binding to hydroxyapatite crystals, facilitating enamel mineralization and organization. The remainder of enamel's composition is water, which accounts for approximately 4%.

The inorganic, organic, and water components of enamel are highly organized: Millions of **carbonated hydroxyapatite** crystals are arranged in long, thin prisms (or rods) with diameters ranging from 4 to 8 µm.[7,8] These rods are aligned perpendicular to the dento-enamel junction (DEJ), which separates enamel from the underlying dentin. Viewed in cross-section, these rods appear as keyhole-shaped structures, with each rod surrounded by a sheath made of enamelin proteins. The interrod enamel, or interrod cement, lies between the rods and has the same crystal composition, but with different orientations of the crystals.

The number of enamel rods varies depending on the tooth, with estimates ranging from 5 million in the lower lateral incisor to 12 million in the upper first molar. These structural features are critical for the mechanical properties of enamel, as they contribute to its hardness and resistance to mechanical wear. However, minute spaces, or pores, exist between the rods, where crystals are absent. These spaces contribute to enamel's permeability, enabling fluid movement and diffusion within the enamel, which is vital for processes such as remineralization and demineralization. However, these pores also lead to variations in density and hardness, making enamel more prone to demineralization, especially when the oral pH becomes acidic due to the presence of cariogenic bacteria.

When the pH of the oral environment drops below a critical threshold (typically around pH 5.5), demineralization occurs, where calcium and phosphate ions are leached from the enamel, weakening the structure. This process is exacerbated by the acidic byproducts of bacterial metabolism, particularly lactic acid produced by **acidogenic** bacteria during the fermentation of dietary carbohydrates.

Enamel Formation

Enamel is formed by specialized epithelial cells called ameloblasts during tooth development. Just before a tooth erupts from the gums, the ameloblasts are disrupted, which leads to the loss of enamel's ability to regenerate or repair itself. This means that when enamel is damaged by injury or decay, it cannot restore itself naturally. Furthermore, enamel is not fully mineralized at eruption, and to achieve complete mineralization, calcium, phosphate, and fluoride ions are taken up from saliva, which adds a layer of 10 µm to 100 µm of enamel over time.[7] This mineralization process is crucial for strengthening the enamel and increasing its resistance to acid dissolution.

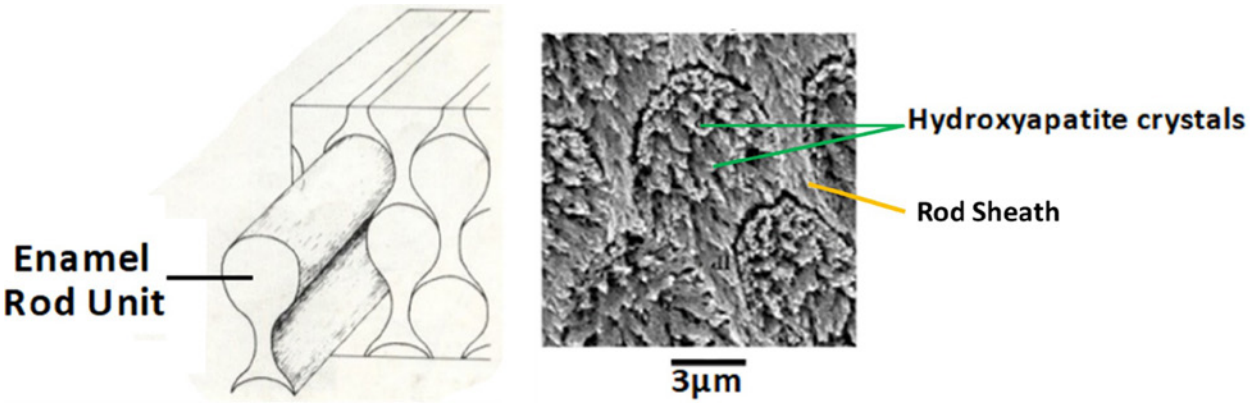

Figure 2. Enamel rod cross-section
Images adapted from: Enamel / orthodontics courses (slideshare.net)

Dentin

Dentin is a hard, light yellow, porous layer of tissue directly beneath the enamel and cementum. Dentin constitutes the largest portion of the tooth and consists of approximately 70% inorganic matter and 30% organic matter and water. The inorganic component consists primarily of calcium and phosphate ions, which form hydroxyapatite crystals. While these crystals are similar to those in enamel, they are approximately 30 times smaller, making dentin softer and more flexible than enamel.[9]

Unlike enamel, dentin is a living tissue with the ability for constant growth and repair. This is facilitated by the presence of odontoblasts, which are specialized cells located on the outer layer of the pulp. These cells are responsible for the continuous formation of new dentin throughout life. Tiny dentinal tubules extend from the cementoenamel junction (the interface between enamel and the cementum covering the root) to the pulp, aiding in the regeneration process. Odontoblast extend into these tubules, allowing them to produce new dentin and mineralize it over time. In addition to this regenerative function, the dentinal tubules also carry nerves, which enable dentin to transmit pain, a feature not found in enamel.[8]

Demineralization

Bacterial Acid Production

Bacteria aggregate in **dental plaque** on the surface of teeth, where they convert glucose, fructose, and sucrose into acids through a process called glycolysis. This is the primary energy-generating pathway in all bacteria, including the caries-associated *Streptococcus mutans*. In Figure 4 below, the monosaccharides glucose, galactose, and fructose enter the **glycolysis** pathway at the points shown in the diagram. The dotted lines in the pathways indicate that there are additional intermediate steps. *Streptococcus mutans* is capable of further metabolizing pyruvate (pyruvic acid) to generate additional energy and more acid byproducts. When excess sugars are available, *S. mutans* favors the lactate dehydrogenase pathway to produce lactic acid, which significantly lowers the pH in the immediate environment of the tooth. This drop in pH makes saliva and the interbacterial fluid in dental plaque more acidic, creating an environment that promotes enamel demineralization.

The rate at which acid is produced is influenced by the microbial composition of dental plaque. In general, the more acidogenic and **aciduric** bacteria, such as Streptococcus mutans, are present in plaque, the faster acid is produced. **Sucrose** is metabolized rapidly by *S. mutans*,

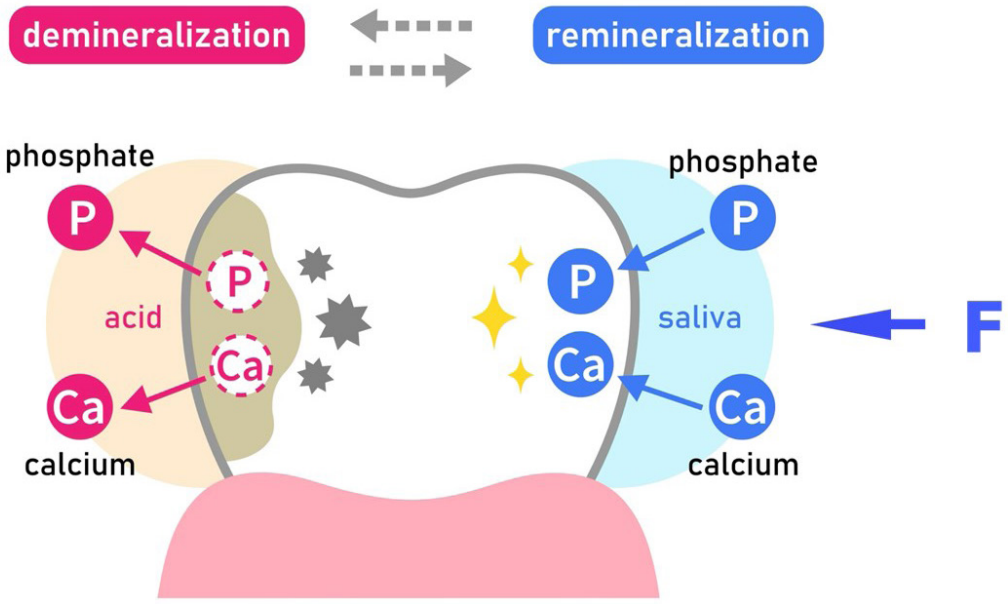

Figure 3. The dem-rem cycles are dynamic and delicate, tipping either way several times a day.

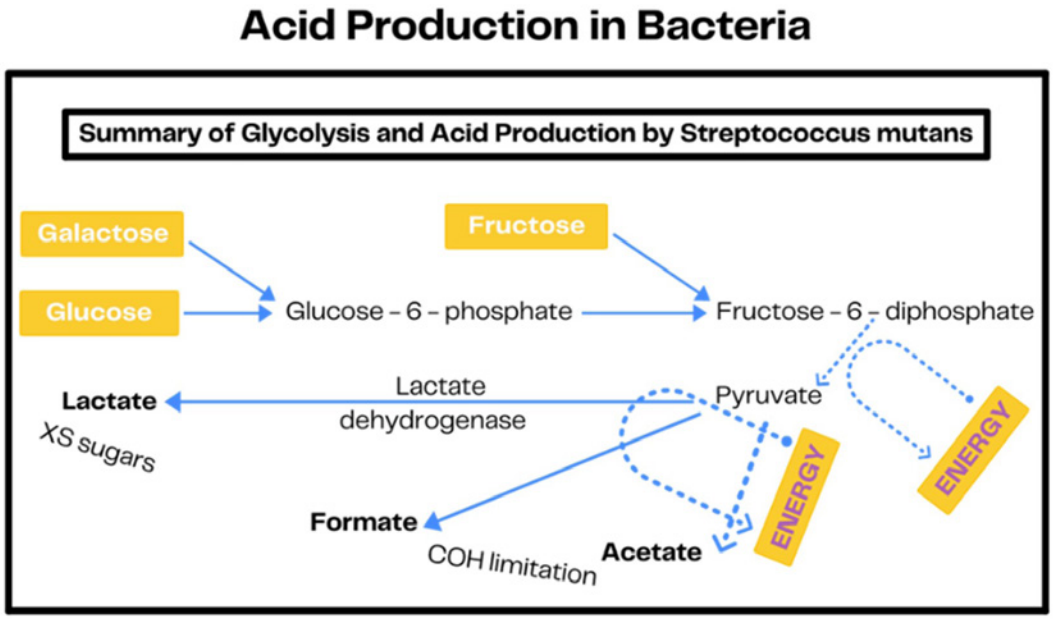

Figure 4. Glycolytic pathway of Streptococcus mutans, from monosaccharides to acid. *Adapted from: Marsh PD, Lewis MAO, Rogers H, et al. Oral Microbiology. 6th ed. 2016; Edinburgh: Churchill Livingstone Elsevier.*

leading to a rapid decrease in pH, while larger molecules like **starch** diffuse more slowly into plaque. These large molecules must first be broken down into simpler sugars before they can be assimilated by plaque microbes.[10,11] In addition to carbohydrate metabolism, the rate of acid production is influenced by the density of plaque. Less dense plaque, which can be penetrated by buffering saliva and oxygen, produces less acid than very dense plaque, which is more resistant to the penetration of saliva and oxygen.[10,12,13]

When sugars are not available - typically between meals - bacteria use their energy reserves to produce formic and acetic acids, which are weaker acids compared to lactic acid. These acids are less likely to damage tooth structure, as they do not significantly lower the pH to the critical threshold needed for enamel demineralization.

Acid and Hydroxyapatite Solubility

The solubility of hydroxyapatite is greatly affected by the pH of oral fluids. In general, a more acidic environment causes hydroxyapatite to become more soluble, while a less acidic (more neutral or basic) environment makes hydroxyapatite less soluble.[14,15-17] In a healthy oral environment not exposed to acid challenges, such as those caused by dietary, gastric, or medicinal acids, both plaque fluid and saliva are typically supersaturated with calcium, phosphate, and hydroxyl ions. This supersaturation helps prevent the dissolution of tooth enamel. However, despite this favorable ionic environment, hydroxyapatite crystals do not continually grow on the enamel surface. This is due to the presence of specific salivary proteins, such as statherin and proline-rich proteins, which inhibit hydroxyapatite crystal growth. These proteins coat the enamel surface and prevent crystal seeding, thus maintaining a balanced mineral state.[14]

If an acid challenge causes plaque fluid and saliva to become more acidic, hydrogen ions bind with calcium, phosphate, and hydroxyl ions, effectively removing these ions from the solution. As a result, the solution, becomes undersaturated with respect to hydroxyapatite, leading to the dissolution of dental hard tissues. The greater the degree of undersaturation, the more extensive the demineralization. In general, the solubility of dental hard tissues increases by a factor of 10 with each one-unit drop of pH. Dissolution continues until the solution becomes saturated again.

Because dental plaque is in close proximity to the tooth, and generally prevents access of saliva to enamel, greater attention is given to the level of supersaturation within the interbacterial fluid in dental plaque. This fluid rapidly loses its supersaturation following exposure to sucrose, and becomes increasingly unsaturated as sucrose concentration rises. Frequent sucrose exposures cause repeated and rapid fluctuations in plaque fluid pH, which have been shown to deplete calcium and phosphate reservoirs within the plaque. This depletion promotes pH-induced undersaturation, which increases the cariogenic potential of plaque fluid. Consequently, the frequency of sugar intake is considered more harmful to dental health than the total sugar amount of sugar consumed.[11,18]

The Role of Critical pH

Critical pH is the term given to the highest pH at which there is a net loss of minerals from tooth enamel. This is the pH at which saliva and plaque fluid are no longer saturated with calcium and phosphate, allowing hydroxyapatite to begin dissolving. Critical pH is generally accepted to be 5.5, but it can be a little higher or lower depending on individual factors. During the demineralization process, acid diffuses between the rods and reaches deeper areas into the enamel and dentin, where carbonated hydroxyapatite crystals are more susceptible to dissolution. The calcium and phosphate ions released from the tooth diffuse into dental plaque fluid and saliva. If the acid exposure is frequent and prolonged, increasing amounts of these minerals are lost, leading to a reduction in the size of the crystals and enlargement of enamel pores. Eventually, a carious lesion may develop. The rate at which it forms depends on the extent of fluid undersaturation in the surrounding environment and the rate at which ions diffuse into and out of the enamel.[14,19]

Development of the Carious Lesion

The initial stages of the carious lesion are characterized by partial demineralization of enamel, resulting in a subsurface lesion beneath a relatively intact surface layer approximately 2-50 µm thick. This lesion typically shows a mineral loss of 30% to 50% may extend into the underlying enamel and even into dentin. Clinically, the lesion will appear as a chalky white, opaque area with a roughened surface, commonly referred to as a **white spot lesion**.

If the demineralization continues unchecked, the surface layer may eventually collapse, resulting in cavitation. Once cavitated, the lesion becomes irreversible and requires restorative treatment. Clinically, advanced lesions into dentin may present as visible holes in the enamel and often feel "sticky" or soft when gently probed, indicating structural breakdown of the tooth.

Demineralization in Special Populations

To favor remineralization over demineralization, it is essential to address both sides of the mineral balance. Fluoride remains the most effective agent for enhancing remineralization,

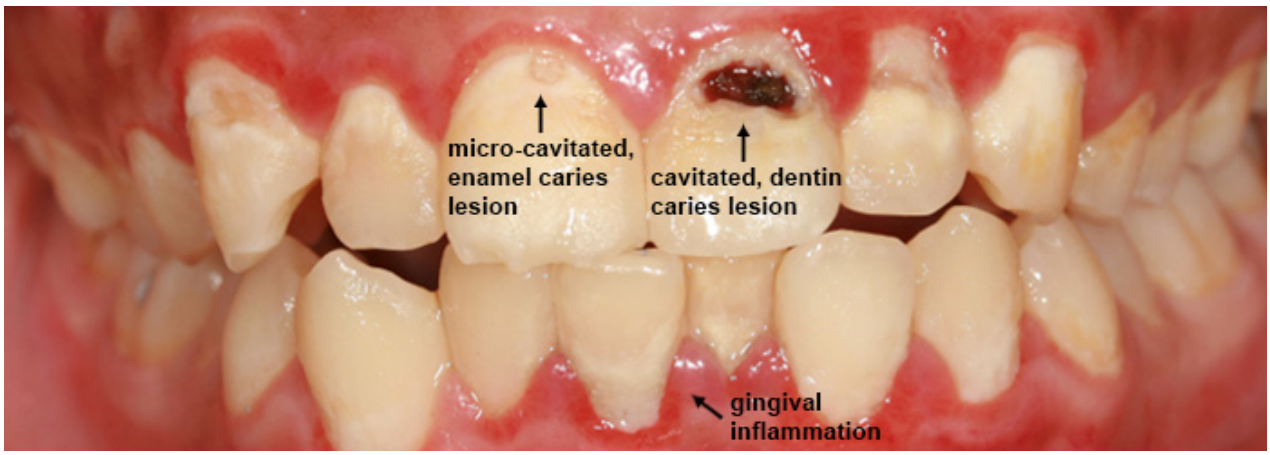

Figure 5. Examples of caries lesions at different stages in a patient at high-risk for caries. Note heavy plaque accumulation and gingival inflammation.

as it significantly accelerates the process. Its high electronegativity allows it to attract calcium and other cations, facilitating the formation and precipitation of apatite crystals, particularly fluorapatite, which is more resistant to acid dissolution. This property makes fluoride a critical component in preventing caries and promoting enamel repair.

At the same time, efforts must be made to reduce demineralization, which is triggered by acid production following meals, snacks, or the consumption of sugary beverages like coffee with sugar or soft drinks. The two most effective strategies for reducing demineralization are:

1. Limiting the frequency of acid challenges, such as reducing how often sugary snacks and drinks are consumed throughout the day.

2. Improving oral hygiene, which lowers the overall cariogenic potential of dental plaque. Older plaque biofilms generate significantly more acid - by a logarithmic factor - compared to younger plaque (e.g., less than 12 hours old). Therefore, regular brushing (at least twice daily, and especially at bedtime), flossing, and routine plaque control are essential in minimizing demineralization and maximizing the opportunity for remineralization.

Young Children Early Childhood Caries

Early childhood caries (ECC) is a highly prevalent and aggressive form of dental decay (Figure 6). ECC typically develops when cariogenic liquids - such as those containing free sugars, including milk or formula - remain in prolonged contact with teeth, especially during sleep. This often occurs when infants or toddlers are put to bed with a bottle or breastfed on demand throughout the night without appropriate oral hygiene. For this reason, ECC has historically been referred to as "nursing caries," "baby bottle tooth decay," or "bottle mouth," though the term early childhood caries is now preferred to reflect the multifactorial nature of the disease. This is why ECC is also often termed nursing bottle caries, baby bottle caries, or nursing caries.

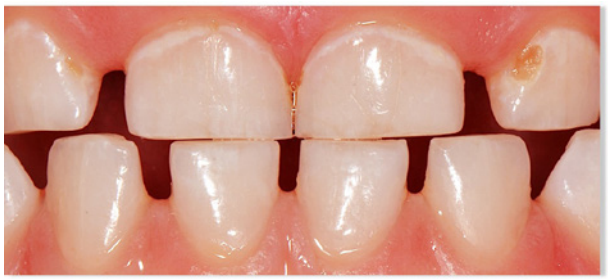

Figure 6. Early Childhood Caries
Provided by and used with permission from: Dr. Marcelle Nascimento, DDS, MS, PhD.

According to the most recent data from the National Health and Nutrition Examination Survey (NHANES), ECC affects 1% of US children by the age of 12 to 24 months of age, with prevalence rising to about 5% by 35 months. ECC disproportionately affects children from low-income families and underrepresented minority populations. In particular, Native American and Alaska Native children continue to experience the highest burden, with studies reporting ECC prevalence as high as 80% in children under 5 years of age.[20]

Root Caries

As individuals age, gingival recession often occurs, exposing root surfaces composed of dentin and cementum. These tissues are significantly more susceptible to acid dissolution than enamel due to their lower mineral content. As a result, root caries lesions are more prevalent in older adults, especially those with periodontal attachment loss. In this population, several risk factors contribute to the development and progression of root caries. Decreased salivary flow, commonly due to polypharmacy and age-related changes in salivary gland function, compromises the natural protective mechanisms of the oral cavity. Many medications—particularly antihypertensives, antidepressants, and anticholinergics—are known to induce xerostomia, which reduces oral clearance and buffering capacity. Additionally, dietary changes such as increased consumption of soft, carbohydrate-rich foods, along with challenges in maintaining adequate oral hygiene due to cognitive or physical limitations, further exacerbate the risk.

Recent evidence also suggests that root caries is associated with frailty, cognitive decline, and institutionalization in older populations, and managing these lesions requires tailored preventive and restorative strategies. Non-invasive interventions such as high-fluoride toothpaste, silver diamine fluoride application, and regular professional cleanings have shown efficacy in arresting root caries and should be part of individualized care plans for older adults.

Other Special Populations, Systemic Conditions and Salivary Function in Dental Caries

Certain medical conditions and special health care needs can increase susceptibility to enamel demineralization and development of dental caries. One such condition is *amelogenesis imperfecta*, a genetic disorder that disrupts normal enamel formation. In affected individuals, enamel may be hypoplastic, hypocalcified, or hypomature, resulting in a structurally weak surface that flakes or wears away easily, exposing underlying dentin to cariogenic bacteria and accelerating caries progression.

Other individuals at increased risk include those with physical, developmental, or cognitive disabilities that impair their ability to perform adequate oral hygiene. Patients with neuromuscular disorders, intellectual disabilities, or limited dexterity may struggle with plaque removal, placing them at heightened risk for caries and periodontal disease.

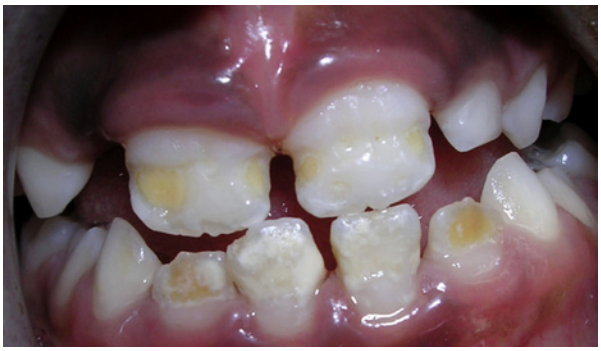

Figure 7. Amelogenesis Imperfecta
Image from: Know the Amelogenesis Imperfecta, a disorder that affects the development of tooth enamel — Steemit

Xerostomia (dry mouth), whether caused by systemic diseases such as *Sjögren's Syndrome*, use of several medications, or cancer treatments (e.g., radiation to the head and neck), is another major contributor to caries risk. Saliva plays a vital role in buffering acids, clearing food debris, and supporting remineralization. Reduced salivary flow significantly impairs these protective functions, increasing the vulnerability of teeth to the caries process. Any medical condition, or treatment, that reduces salivary flow significantly increases the risk of caries.

One of the most dramatic examples is head and neck cancer treated with radiation therapy, particularly when the parotid or other major salivary glands are within the radiation field. Radiation damages salivary gland tissue, leading to long-term or permanent xerostomia. As a result, patients may experience severe and rapid onset of caries, sometimes developing in one month what might typically occur over two years in a healthy individual.

Other systemic conditions such as diabetes mellitus or chronic kidney disease can also contribute to altered salivary flow or composition. Additionally, xerostomia is frequently reported in patients taking medications, and it is well established that a large proportion of commonly prescribed drugs, such as antihypertensives, antidepressants, antipsychotics, and antihistamines, have salivary reduction as a side effect. Thus, individuals taking multiple medications, particularly older adults, are at significantly increased risk for caries due to reduced salivary protection.

Preventive care for these populations often requires individualized strategies, including the use of high-fluoride products, saliva substitutes or stimulants, dietary counseling, and more frequent dental visits. Therefore, proactive caries prevention and salivary management strategies are essential in these populations.

Plaque pH Modulating Agents

The dynamic equilibrium between demineralization and remineralization of

tooth enamel is crucial for maintaining dental health. While acid production by cariogenic bacteria leads to enamel demineralization, the generation of alkaline substances within dental plaque can neutralize these acids, thereby promoting remineralization. Recent research highlights the critical role of alkali production, particularly via the arginine deiminase system (ADS) in certain oral bacteria, in maintaining plaque pH balance and reducing caries risk.[21-23] By metabolizing arginine into ammonia, these bacteria raise plaque pH, counteracting acid from carbohydrate fermentation and promoting remineralization over demineralization. Higher ADS activity is associated with lower caries incidence, while reduced alkali production correlates with greater caries risk.[21,22] Clinical studies support the use of arginine-containing oral care products to enhance ADS activity, increase ammonia production, and foster a less cariogenic oral environment, making this a promising strategy for caries prevention and management.[23]

Xylitol, a naturally occurring sugar alcohol, has been widely studied for its ability to reduce dental caries through multiple mechanisms, including its impact on plaque pH. Unlike fermentable sugars, xylitol is not metabolized by cariogenic bacteria such as *Streptococcus* mutans, leading to reduced acid production in the dental biofilm. Moreover, xylitol may inhibit the growth and adhesion of *S. mutans*, which contributes to a healthier oral microbiome. A 2024 systematic review indicates that xylitol consumption, particularly in the form of chewing gum or lozenges, can increase plaque and salivary pH by stimulating saliva flow and reducing bacterial acidogenicity.[24] These effects support remineralization and help maintain a neutral to slightly alkaline environment, making xylitol an effective adjunct in caries prevention strategies.

Clinical investigations have revealed that individuals with higher salivary and plaque ADS activity tend to have a lower incidence of dental caries. Conversely, reduced alkali-generating capacity in oral biofilms is associated with increased caries risk. These findings suggest that enhancing alkali production in dental plaque could be a viable strategy for caries prevention.

Stannous fluoride (SnF_2), commonly used in fluoride dentifrices, has shown potential not only for its well-established anticaries and antimicrobial properties but also for its effect on plaque pH. The stannous ion (Sn^{2+}) may inhibit acidogenic bacterial enzymes and reduce bacterial acid production, helping to stabilize plaque pH levels.[25] In some formulations, stannous fluoride is combined with sodium fluoride to enhance both remineralization and antimicrobial activity. Studies have also suggested that stannous-containing fluoride toothpaste may help create a less acidic environment in the plaque matrix, thereby supporting a shift toward a less cariogenic biofilm.[26,27] While more targeted studies are needed to isolate its alkalinizing effects, current data supports its role in reducing the cariogenic potential of dental plaque alongside its benefits for gingival health and enamel protection.

The inclusion of pH-modulating agents in oral care products, such as stannous fluoride and arginine, represents a strategic approach to caries prevention beyond mechanical plaque removal and remineralization. These agents may help support plaque pH homeostasis, inhibit acidogenic bacteria, and foster a biofilm less favorable to caries development. Continued research is essential to further understand their synergistic effects and optimize their use in clinical care.

Remineralization and Fluoride

When the pH of dental plaque rises above the critical threshold, typically around 5.5, the oral environment shifts from favoring demineralization to enabling remineralization. At this point, the interbacterial plaque fluid and saliva become saturated, and eventually supersaturated, with calcium, phosphate, and hydroxyl ions. This supersaturation is essential for the deposition of minerals back into demineralized enamel and dentin.

Remineralization of early carious lesions depends on the presence of partially demineralized enamel crystals that that serve as scaffolds for mineral redeposition. These residual crystals can grow back toward their original size when exposed to fluids supersaturated with respect to hydroxyapatite or fluorapatite. Because incipient carious lesions (such as white spot lesions) retain

a crystalline framework, remineralization is not only possible, it can be substantial, particularly at the lesion surface. Studies have shown that considerable remineralization can occur in the outer layer of carious lesions. However, due to limited permeability and slower diffusion, the lesion body (subsurface zone) remineralizes at a much slower rate - if it occurs at all. This creates a paradox: while the remineralized surface layer helps protect the lesion from further acid attack, it also forms a diffusion barrier, limiting further ion penetration and thus inhibiting full remineralization of the deeper lesion body.

The Role of Fluoride in Remineralization

Fluoride plays a central role in enhancing the remineralization process. It promotes the formation of fluorapatite, a more acid-resistant and stable mineral phase, by incorporating fluoride ions into the enamel crystal lattice during the remineralization process. Fluoride also facilitates the precipitation of calcium and phosphate by lowering the solubility of enamel and shifting the demineralization-remineralization equilibrium in favor of mineral gain.

Additionally, fluoride enhances remineralization even at low concentrations by:

- Attracting calcium ions to the enamel surface
- Inhibiting bacterial metabolism and acid production
- Forming a calcium fluoride-like reservoir on the tooth surface, which can release fluoride in response to future acid challenges

Topical fluoride sources such as toothpaste, gels, varnishes, and fluoridated water are critical in providing a continual supply of fluoride ions that help drive the remineralization process.

In conclusion, remineralization is a naturally occurring process that depends on pH, ion availability, and lesion accessibility. Fluoride is an essential adjunct that enhances this process, especially in early caries lesions. However, the structural barrier posed by the outer remineralized layer means that complete restoration of deeper enamel may be limited, underscoring the importance of early intervention and prevention.

Figure 8. Caries Lesion Initiation and Progression - Remineralization

Crystal Growth During Remineralization

The process crystal growth during remineralization is complex and influenced by both the oral environment and the characteristics of the lesion. During periods when plaque fluid and saliva are supersaturated with respect to hydroxyapatite, demineralized enamel crystals can act as nucleation sites, allowing new mineral to precipitate from solution. These existing, partially demineralized crystals "seed" new crystal growth. However, this process can be disrupted by the presence of various inhibitors in the oral cavity. Saliva contains proteins such as statherin and proline-rich proteins that regulate crystal growth to prevent unwanted mineral precipitation. These natural inhibitors can also interfere with the regrowth of enamel crystals during remineralization. As a result, newly formed crystals tend to be small, contain numerous structural defects (such as missing ions), and are more soluble than mature, well-formed crystals.

Despite these challenges, when crystals are consistently exposed to a large volume of solution that remains supersaturated with respect to hydroxyapatite, a slow refinement process known as *Ostwald ripening* can occur. During this process, smaller, less stable crystals dissolve, and the released ions contribute to the growth and perfection of larger, more stable crystals. This leads to the gradual formation of fewer but larger, more stable, and less soluble crystals, enhancing the structural integrity of remineralized enamel. This natural healing mechanism underscores the importance of maintaining prolonged periods of supersaturation in the oral environment - achievable through fluoride exposure, adequate salivary flow, and reduction of acid challenges - to support optimal crystal maturation and long-term enamel resistance.

White Lesions

During a clinical examination, an early remineralized carious lesion often appears as a white, opaque area beneath a smooth, shiny, and hard enamel surface - sometimes described as a "white scar." This appearance is due to partial remineralization of the surface layer, while the subsurface lesion body remains porous and less mineralized, as discussed previously.The clinical significance of white lesions lies in their potential outcomes. With appropriate intervention—such as improved oral hygiene, fluoride use, dietary modifications, and regular professional monitoring; these lesions can arrest or even show signs of further remineralization. However, without these protective measures, the lesion may progress, particularly if exposed to frequent acid challenges, eventually leading to surface breakdown and cavitation.

Understanding and recognizing white spot lesions as a reversible stage of caries is critical, as it represents a window of opportunity for non-invasive management and preservation of tooth structure.

Other Key Factors that Promote Remineralization

Saliva

Saliva plays a vital protective role in maintaining oral health and supporting the balance between demineralization and remineralization. Due to its high-water content and continuous flow, saliva physically cleanses the oral cavity by washing away food particles and debris that could otherwise serve as substrates for acid-producing bacteria. Additionally, it helps dilute and remove organic acids from dental plaque, thereby reducing the cariogenic potential of the oral environment.

Saliva contains a complex mixture of electrolytes and organic molecules that help stabilize pH levels. Components such as sodium bicarbonate and phosphate function as buffering agents, neutralizing acids and minimizing pH drops after carbohydrate

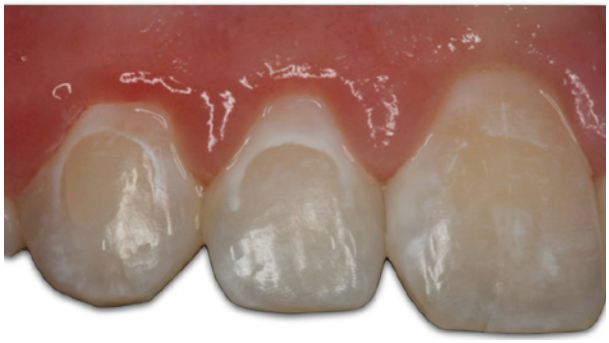

Figure 9. Inactive, remineralized white spot lesion on anterior permanent teeth. Remineralization occurred by improved oral hygiene and fluoride exposure after removal of orthodontic devices.

intake. Among the organic molecules, sialin, a salivary peptide, plays an important role in raising salivary pH, helping to restore neutral conditions conducive to remineralization.

Furthermore, saliva is naturally supersaturated with calcium and phosphate ions, which facilitates the redeposition of minerals into partially demineralized enamel, promoting enamel repair. This combination of mechanical cleansing, acid buffering, and ion delivery underscores saliva's essential role in protecting against dental caries and supporting enamel remineralization.

Fluoride

Fluoride is a key agent in caries prevention, primarily due to its ability to inhibit demineralization and enhance remineralization of enamel. When present in low concentrations in saliva and plaque fluid, fluoride ions are incorporated into demineralized enamel surfaces during the remineralization process. This leads to the formation of fluorapatite - a more acid-resistant and less soluble crystalline form of apatite compared to hydroxyapatite, which naturally constitutes enamel.

The newly formed fluorapatite-enriched layer is not only more stable but also better able to protect the underlying lesion body from future acid attacks. Fluoride also strengthens enamel by binding with calcium ions, reducing the likelihood that calcium will be lost from the tooth during acidic challenges.

A significant benefit of fluorapatite is its ability to lower the critical pH for enamel dissolution. While demineralization of hydroxyapatite typically begins at a pH of around 5.5, fluorapatite resists acid dissolution until the pH drops closer to 4.5. This shift underscores fluoride's protective role in maintaining enamel integrity in acidic conditions.

If fluoride is lacking in the oral environment, especially in the presence of frequent acid exposure from fermentable carbohydrates, the balance shifts toward demineralization and the risk for caries increases.

In the United States, fluoride is most commonly delivered through:

- Systemic sources, such as fluoridated community water supplies, and
- Topical sources, including over-the-counter or prescription fluoride toothpastes and mouthrinses.

For patients at higher risk of caries, professionally applied fluoride products - such as varnishes, gels, foams, or slow-release fluoride devices - may be recommended to provide enhanced protection and sustained therapeutic effects.

Conclusion

Demineralization and remineralization represent a continuous and dynamic cycle of mineral loss and repair affecting the hard tissues of the tooth. These are not distinct processes; rather, both occur simultaneously on the tooth surface throughout the day. The net outcome - whether a lesion progresses or is halted - depends on several key factors in the oral environment, including the frequency of sucrose exposure, the composition and activity of dental plaque, the availability and composition of saliva, and the presence of protective agents like fluoride. When conditions favor remineralization, such as infrequent sugar intake, good salivary flow, and exposure to fluoride, lost minerals can be redeposited, helping to halt or reverse early caries development. Conversely, frequent acid challenges and compromised salivary function tip the balance toward demineralization, increasing the risk of caries progression.

The primary objective in dental practice is to support and maintain an oral environment that minimizes demineralization while promoting effective remineralization. Doing so not only prevents the initiation of carious lesions but also preserves tooth structure and promotes long-term oral health.

Course Test Preview

To receive Continuing Education credit for this course, you must complete the online test. Please go to: *www.dentalcare.com/en-us/ce-courses/ce714/start-test*

1. Which of the following is true about enamel?

A. It has a blood and nerve supply.
B. It contains no pores.
C. It is comprised mostly of inorganic materials: 95% of it is calcium and phosphate ions combined to make up strong hydroxyapatite crystals.
D. Water makes up 12% of its composition.

2. Which of the following is true about enamel?

A. It has a blood and nerve supply.
B. It contain no pores.
C. Its hydroxyapatite crystals are highly organized.
D. Water makes up 12% of its composition.

3. What differentiates dentin from enamel?

A. There are no significant differences.
B. Unlike enamel, dentin is a living tissue with the ability for constant growth and repair, thanks to cells called odontoblasts that create new dentin.
C. Enamel can repair and regenerate, while dentin cannot.
D. Dentin is harder than enamel.

4. Which acid resulting from bacterial metabolism of sugar can significantly lower the pH in the immediate environment of the tooth?

A. lactic acid
B. acetic acid
C. pyruvate acid
D. formic acid

5. Which of the following does NOT affect the rate at which acid is produced in plaque?

A. The microbial composition of the dental plaque.
B. The density of plaque.
C. The speed at which bacteria are able to metabolize the dietary carbohydrate.
D. The number of cavities present.

6. What prevents hydroxyapatite from continuously growing out of control?

A. Hydroxyapatite crystal growth-inhibitors in saliva.
B. p-rich proteins in saliva that coat enamel to prevent seeding by exposed crystals.
C. Fluoride prevents seeding by exposed crystals.
D. A and B

7. What is the effect of sucrose on interdental plaque ion stores?

A. Frequent sucrose exposure depletes calcium and phosphate reservoirs in plaque.
B. Sucrose increases calcium stores in interdental plaque.
C. Sucrose increases fluoride stores in interdental plaque.
D. Sucrose has little impact on calcium and phosphate reservoirs in plaque.

8. At what pH does tooth enamel begin to demineralize?

A. 8.3
B. 7.5
C. 5.5
D. 3.2

9. What is the clinical appearance of the initial stage of a carious lesion?

A. A large cavitation that extends into the dentin.
B. A chalky white opaque area with a roughened surface.
C. Evidence of tooth erosion caused by acid attack.
D. Completely demineralized tissue.

10. Which of the following is true about the remineralization of a carious lesion?

A. Deeper layers of enamel remineralize first and more fully.
B. Surface layers of enamel remineralize last and completely.
C. The lesion body in deeper layers of enamel does not remineralize because slow diffusion doesn't allow supersaturation in deeper layers.
D. B and C

11. What is Ostwald ripening?

A. It is the name given to the maturing of bacteria in interdental plaque.
B. It is the name given to the maturing of dental enamel.
C. It is the name given to the regeneration of dentin.
D. It is the name given to the process where smaller, less stable crystals dissolve, and the released ions contribute to the growth and perfection of larger, more stable crystals.

12. What is the initial clinical appearance of a remineralized carious lesion?

A. It appears as a black cavitation.
B. It appears as a white opaque area beneath a smooth, shiny and hard enamel surface.
C. It appears as a brown spot that feels soft and sticky with dental probing.
D. It appears as a white chalky soft spot that flakes with dental probing.

13. Which of the following is a remineralization-promoting characteristic of saliva?

A. Saliva stimulates odontoblasts to promote enamel remineralization.
B. Saliva does not promote remineralization.
C. Saliva is supersaturated with calcium and phosphate ions.
D. Saliva is slightly acidic, which helps to stimulate the remineralization process.

14. Which of the following is true about fluorapatite?

A. It is not very stable, making it more prone to demineralization.
B. It binds with calcium, making it less likely that calcium ions are pulled out of the tooth and into the solution.
C. It can change the critical pH level to 4.5.
D. B and C

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About the Author

Marcelle M. Nascimento, DDS, MS, PhD

Dr. Marcelle Nascimento is a Professor of Restorative Dentistry, serving as the Director of Cariology and Assistant Dean for Clinical Research at the University at Buffalo (UB) School of Dental Medicine since May 2024. Holding DDS, MS, and PhD degrees in Cariology from the University of Campinas, Brazil, Dr. Nascimento has been actively engaged in the teaching of Cariology and Operative Dentistry in the U.S. since 2007. Prior to joining UB, she served as Professor with tenure and Director of the Dental Clinical Research Unit at the University of Florida (UF) College of Dentistry (2007-2024). Committed to providing exceptional education to predoctoral and graduate students, Dr. Nascimento possesses a wealth of experience in developing pre-clinical and clinical courses and fostering an engaging learning environment in dental education.

Dr. Nascimento has been funded by NIH/NIDCR and industry to conduct clinical and translational science research in Cariology and Oral Microbiology. She is a member of the Executive Board of Directors of the American Academy of Cariology (AAC) and is serving as the AAC president for the 2024-2025 term. She has served as the president of the Cariology Research group of the International Association for Dental Research (IADR), and as chair and councilor of the American Dental Education Association (ADEA) Cariology section. In addition, Dr. Nascimento has served as Chair of Seal Subcommittee and member of the American Dental Association (ADA) Council on Scientific Affairs. With an established record of research funding, and highly cited, peer-reviewed publications in renowned dental journals, Dr. Nascimento has attained national and international eminence owing to her scholarly and scientific contributions to the fields of Cariology, Oral Microbiology and Operative Dentistry.

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