Caries Process and Prevention Strategies: Demineralization/Remineralization

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Disclaimer: Participants must always be aware of the hazards of using limited knowledge in integrating new techniques or procedures into their practice. Only sound evidence-based dentistry should be used in patient therapy.

Introduction

This is part 5 of a 10-part series entitled Caries Process and Prevention Strategies. 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. The role of acid-reducing bacteria, saliva, and fluoride in tooth hard tissue remineralization will also be explained.

Conflict of Interest Disclosure Statement

• The authors report no conflicts of interest associated with this course.

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Overview
Caries is the chemical dissolution of the hard tooth structures - enamel and dentin - by the acid created as 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 the high acidity that leads to demineralization does caries occur. In this section, 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. The role of acid-reducing bacteria, saliva, and fluoride in tooth hard tissue remineralization will also be explained.

Clinical Significance Snapshots

How does understanding the demineralizing-remineralizing 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, then the account becomes overdrawn. Credits that match or exceed the debits leads to a healthy financial situation. The same applies to calcium ions entering and exiting the tooth. Some loss of calcium inevitably occurs at mealtimes, as the cariogenic bacteria in the biofilm on the surface of the tooth metabolize the sugars in the diet via glycolysis. This creates a low pH or acidic environment that is capable of driving demineralization. Between meals, the saliva brings the pH back to safe levels (above pH 5.5) when the calcium ions can return to the tooth (remineralization). If there is not enough time for sufficient remineralization, then there is an overall loss of calcium from the tooth, the subsurface lesion may develop, bacteria enter the tooth material and the cavitation process commences. To prevent the occurrence of caries in your patients, it is important to include information about foods that lead to demineralization in oral health counseling, and note that saliva needs time between food intakes to restore any loss of calcium by sugar-containing foods and beverages. Foods rich in calcium and that stimulate saliva flow are very beneficial at the end of any meal. Examples would be yogurt, cheese, or milk (super-saturated with calcium) or a sugar-free chewing gum (saliva stimulation).
Why is the use of fluoride agents so prominent in the prevention of dental caries?

Hydroxyapatite crystals in enamel are impure, due to the presence of carbonate ions. Carbonate ions make the carbon-hydroxyapatite weak and much more easily dissolved by acids. Fluoride ions can replace some of the carbonate and hydroxyl ions to create fluorapatite. Fluorapatite is physically much stronger than carbon-hydroxyapatite, and more resistant to acid dissolution. Essentially, fluoride tips the demin/remin balance in favor of remin. Fluoride should be applied daily in low concentration via the use of toothpaste that has proven bioavailability of fluoride (ADA Seal of Acceptance). Additional forms of fluoride application should be considered for patients more at risk of caries due to frequent consumption of sugars or poor saliva flow. These would include fluoride rinses (daily or weekly depending upon strength), and professional application of gels or foams rich in fluoride.

Learning Objectives

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

• Discuss the difference in how tooth enamel and dentin structure are affected by demineralization.
• Explain the role of bacterial acid production in demineralization.
• Understand the relationship between critical pH and demineralization.
• Identify five zones of carious dentin in the advanced lesion.
• Describe how demineralization affects young children, the elderly, and other special populations.
• Be familiar with the factors that promote remineralization.

Glossary

acidogenic – Something that produces acid, such as cariogenic bacteria.

aciduric – Capable of growth in an acidic environment.

buffering agent – Adjusts the pH of any solution such as saliva or plaque fluid and can resist changes in pH. Beneficial in the prevention of dental caries.

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.

cariogenic bacteria – Bacteria present in the oral biofilm of dental plaque that will lead to the occurrence of carious lesions when all other necessary factors are present.

demineralization – The chemical process by which minerals (mainly calcium) are removed from the dental hard tissues - enamel, dentin, and cementum. The chemical process occurs through dissolution by acids or by chelation, and the rate of demineralization will vary due to the degree of supersaturation of the immediate environment of the tooth and the presence of fluoride. In optimal circumstances, the minerals may be replaced through the process of remineralization.

dental plaque – An organized community of many different microorganisms that forms itself into 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 people and can vary from being comprised of totally healthy microorganisms (commensals) to being very harmful (pathogenic), predisposing the patient to dental caries or periodontal diseases. Note: Dental plaque is not food debris, nor does it contain food debris. Dental plaque can only be completely removed by mechanical means such as toothbrushing or prophylaxis. Food debris can be removed by rinsing.

fluorapatite – A crystal structure in tooth mineral (Ca₁₀(PO₄)₆F₂) 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 fluoroapatite) 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.

hydroxyapatite – Crystals of calcium phosphate – (Ca_{10}(PO_{4})_{6}OH_{2}) 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 glyco-proteins 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 biofilm.

remineralization – The chemical process by which minerals (mainly calcium) are replaced into the substance of the dental hard tissues - enamel, dentin and cementum. 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.

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

white spot lesion – One of the early clinical signs of dental caries, before cavitation has occurred. The stage at which the disease can be reversed by remineralization.

Introduction
Tooth enamel demineralization, triggered by an increase in the acidity of bacterial plaque, is the initiation of the caries process. In any discussion of the caries process, particular attention is paid to the enamel - the hard, outermost layer - because it is the primary contact with cariogenic bacteria, and where the demineralization process that can lead to caries first begins. It 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. 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. Saliva and fluoride are two key players in remineralization: Healthy saliva contains ample amounts of the calcium and phosphate ions that can replenish lost minerals in hard tooth structure, and fluoride can be incorporated into the tooth structure to strengthen it. 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, the remineralization process may have little or no influence, or not occur at all; and caries will develop.

Tooth Hard Tissue Structure and Composition

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 is so hard because it is composed primarily of inorganic materials: Roughly 95% of enamel is calcium and phosphate ions combined to make up strong hydroxyapatite crystals. Hydroxyapatite crystals contain calcium
and phosphate ions in the following proportions: Ca_{10}(PO_{4})_{6}OH_{2}. Hydroxyapatite readily incorporates 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 concentrations of these trace minerals change the solubility of enamel. For example, the presence of fluoride in the crystal structure strengthens the structure and decreases solubility, while carbonate incorporation increases solubility. It has been found that hydroxyapatite crystals have more fluoride and less carbonate than crystals in the interior, making the outer surface less soluble than deeper layers of enamel.2,4,5

Enamel Formation
Enamel is formed by epithelial cells called ameloblasts. Just before a tooth erupts from the gums, the ameloblasts are broken down, removing enamel's ability to regenerate or repair itself. This means that when enamel is damaged by injury or decay, it cannot restore itself. When a tooth erupts, it is also not fully mineralized. To completely mineralize the tooth, calcium, phosphorous, and fluoride ions are taken up from saliva to add a layer of 10 µm to 100 µm of enamel over time.2

Dentin
Dentin is a hard, light yellow, porous layer of tissue directly 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. Its organic matter is calcium and phosphate ions that form hydroxyapatite crystals as in enamel, but the crystals are 30 times smaller, making dentin somewhat softer than enamel.4

Unlike enamel, dentin is living tissue with the ability for constant growth and repair. This is made possible by the presence of odontoblasts, which are cells on the outer layer of the pulp whose biological function is the creation of new dentin. Tiny dentinal tubules that run between the cementoenamel junction (the interface of crown enamel and the tooth root cementum) and the pulp layer beneath it assist in this regeneration process. Odontoblast processes in the pulp layer reach into the tubules, creating new dentin and mineralizing it. Nerves also pass through these dentinal tubules allowing dentin to transmit pain, unlike enamel.4

Deminerlization
Bacterial Acid Production
Bacteria aggregate in dental plaque on the outer surface of teeth. Bacteria convert glucose, fructose, and sucrose into acids through a process called glycolysis, which is the main energy generating pathway in all bacteria, including caries-associated Streptococcus mutans. In Figure 1 below, the monosaccharides glucose, galactose, and fructose can 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 metabolizing pyruvate (pyruvic acid) further, to generate yet more energy and more acid byproducts. When excess sugars are available, they favor the lactate dehydrogenase pathway to produce lactic acid. This causes the pH in the immediate environment of the tooth to decrease rapidly, making saliva and the interbacterial fluid in dental plaque more acidic.\(^7\)

How quickly acid is produced is due in part to the microbial composition of dental plaque: In general, the more acidogenic, aciduric bacteria, such as *Streptococcus mutans*, are present in plaque, the faster acid is produced. The rate of acid production is also dependent on the speed with which plaque bacteria are able to metabolize the dietary carbohydrate. While sucrose is metabolized quickly, prompting a rapid decrease in pH, a large molecule such as starch diffuses into plaque more slowly because it would need to be broken down before it can be assimilated by plaque microbes.\(^7,8\) The rate of acid production is also influenced by the density of plaque. Less dense bacterial plaque, which can be penetrated by buffering saliva and oxygen, produces less acid than very dense plaque, which cannot be accessed by saliva and oxygen.\(^7,8,10\)

When sugars are not available - typically between meals - bacteria use their energy reserves and form formic and acetic acids in the process. These are weaker acids that are not associated with damage to tooth structure.\(^7\)

**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 environment makes hydroxyapatite less soluble.\(^1,11-13\) In a healthy oral environment that is not undergoing an acid challenge due to dietary-, gastric-, or medicinal-related acids, plaque fluid and saliva are supersaturated with calcium, phosphate, and hydroxyl ions, preventing dissolution of tooth enamel. (Despite this supersaturation, however, hydroxyapatite crystals do not continuously grow on the tooth surface. This is because saliva contains protein inhibitors of hydroxyapatite crystal growth, such as statherin, as well as proline-rich proteins that coat the enamel surface and prevent seeding by exposed crystals.)\(^1\)

If an acid challenge causes plaque fluid and saliva to become increasingly more acidic, calcium, phosphate, and hydroxyl ions combine with hydrogen, removing these ions from the solution.

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![Figure 1. Glycolytic pathway of *Streptococcus mutans*, from monosaccharides to acid.](image)

The solution, therefore, becomes undersaturated with respect to hydroxyapatite, and tooth hard structure dissolves. The more undersaturated plaque fluid and saliva is, the greater the amount of dissolution.\textsuperscript{1,13} In general, the solubility of dental hard tissues increases by a factor of 10 with a drop of each single pH unit. Dissolution continues until saturation is established once again.

Because dental plaque is in close proximity to the tooth, and generally prevents access of saliva to enamel, more attention is paid to the level of supersaturation in the interbacterial fluid in dental plaque. This fluid loses its supersaturation very quickly in response to an exposure to sucrose, and becomes more unsaturated as the concentration of sucrose increases. Frequent sucrose exposures that cause the pH of dental plaque fluid to cycle up and down repeatedly and quickly have been found to deplete calcium and phosphate reservoirs in plaque. This promotes pH-induced undersaturation, which increases the cariogenic potential of plaque fluid. This is why the frequency of sugar intake is considered more harmful than total sugar intake when it comes to caries.\textsuperscript{8,14}

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 cease to be saturated with calcium and phosphate, thereby permitting hydroxyapatite to dissolve. 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 of the enamel and into dentin, where carbonated hydroxyapatite crystals are more susceptible to dissolution. The calcium and phosphate ions that are lost from the tooth diffuse out into dental plaque fluid and saliva. If the acid attack is chronic and prolonged, progressively greater amounts of calcium and phosphate minerals diffuse out of the tooth, causing the crystalline structure of the tooth to shrink in size, while pores enlarge. Eventually, a carious lesion develops; its rate of development is a function of the degree of undersaturation of fluid in its environment and rates of diffusion of ions into and out of enamel.\textsuperscript{1,15}

Development of the Carious Lesion
The initial stages of the carious lesion are characterized by a partial dissolution of the tissue, leaving a 2-μm to 50-μm thick mineralized surface layer and a subsurface lesion with a mineral loss of 30% to 50% extending into enamel and dentin. In a clinical examination, the lesion will appear chalky white and softened. In practice, the goal is to stop the process at the white spot lesion stage, when intervention can still be nonsurgical.

If the lesion advances, the outer enamel layer can eventually become cavitated. At this point the lesion is not reversible and requires operative intervention. Besides observing an obvious hole in the tooth during a clinical examination, the dental professional might also notice that an advanced lesion will feel “sticky” or soft when gently touched with a dental probe.

Demineralization in Special Populations

Young Children Early Childhood Caries
Early childhood caries (ECC) affects primary maxillary anterior teeth (Figure 2). It occurs when sugared liquids (including milk) lay against the anterior region of the mouth for prolonged periods, such as when a child is allowed to fall asleep with a bottle or while nursing. This is why ECC is also often termed nursing bottle caries, baby bottle caries, or nursing caries.
According to the epidemiological data presented in the most recent National Health and Nutrition Examination Survey (NHANES), ECC affects 1% of children by the age of 12 to 24 months, and 5% by 35 months. The condition is more prevalent in poor people, and in people of minority races, with as many as 80% of children under 5 in the Native American population having ECC.\(^1\)

**Older People Root Caries**

With age, the gingival tissues recede below the edge of the enamel, exposing the dentin or cementum. These layers are much more soluble than enamel, and, therefore, more susceptible to acid attack.\(^1\) This is why root caries are more prevalent in geriatric patients.\(^16\) In this population, decreased salivary flow due to age or medications, and a change in diet to softer foods, can make root caries difficult to manage. Table 1 summarizes the differences between enamel caries and root caries.

**Other Special Populations**

There are conditions that can affect the formation of enamel, and thus increase the risk of demineralization. These include the genetic disorder amelogenesis imperfecta, in which enamel is never completely mineralized and flakes off easily, exposing softer dentin to cariogenic bacteria. Other conditions are linked with increased enamel demineralization, such as gastroesophageal reflux disease (GERD) and the eating disorder bulimia, because stomach acid keeps the oral cavity highly acidic. Other special needs patients include those with an inability to remove plaque because of a mental or physical limitation, and patients with xerostomia (dry mouth) due to certain medications, cancer therapies, or conditions such as Sjögren’s Syndrome.\(^1\)

**Base Production Promotes Remineralization**

A key step in the remineralization process is the recovery of plaque pH to a level that is higher than critical pH. The factors that affect this include the buffering capacity of saliva, whether fermentable carbohydrate remains in the mouth, and the diffusion of acids from plaque into saliva or teeth. It is also influenced by the production of bases in plaque. Ammonia from the deamination of amino acids and breakdown of urea in saliva are examples of reactions that make plaque pH less acidic. These bases are important to neutralize acid when carbohydrate intake is moderate.\(^17\) The rise in pH to a less acidic level may also be assisted by the removal of acids by bacteria. For example, the bacterial genus *Veillonella* use lactate as a substrate, metabolizing it to less acidic products, such as propionic acid and acetic acid (Figure 3).\(^7\)

**Remineralization**

When plaque pH rises above 5.5, remineralization can start to occur. Above this pH, interbacterial plaque fluid and saliva return to being saturated, and then supersaturated, with respect to hydroxyapatite.
Remineralization of dental lesions requires the presence of partially demineralized crystals that can grow to their original size when they are exposed to fluid that is supersaturated with respect to hydroxyapatite minerals. Because the carious lesion contains partially demineralized crystals, it is possible for it to become remineralized. Considerable remineralization of the surface of caries lesions has been observed. However, due to slow diffusion, it is difficult to maintain a high level of supersaturation in deeper layers of enamel, so remineralization of the lesion body can be quite slow, if it occurs at all. The surface layer of the lesion that has been remineralized, therefore, prevents the lesion body from being further demineralized, but it also inhibits its remineralization.

**Crystal Growth During Remineralization**

The process by which demineralized crystals grow to become remineralized is quite complicated. During a period of supersaturation, crystal growth is possible as

### Table 1. Differences Between Enamel Caries and Root Caries.

<table>
<thead>
<tr>
<th></th>
<th>Enamel Caries</th>
<th>Root Caries</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intact tissue mineral content (by volume):</td>
<td>85% to 87%</td>
<td>45%</td>
</tr>
<tr>
<td>Etiology:</td>
<td>Plaque</td>
<td>Plaque and recession</td>
</tr>
<tr>
<td>Result of acid attack:</td>
<td>Acid dissolves subsurface; white spot lesion</td>
<td>Acid dissolves surface; subsurface sticky or tacky</td>
</tr>
<tr>
<td>Physical changes:</td>
<td>Complete dissolution = cavitation</td>
<td>Complete dissolution = contour changes</td>
</tr>
<tr>
<td>Remineralization potential:</td>
<td>Possible if outer area is intact</td>
<td>Mineral content can be increased if collagen layer still present</td>
</tr>
</tbody>
</table>

**Figure 3.** How *Veillonella* reduces caries risk by reducing plaque pH acidogenicity.  

**Video 3.** Remineralization and Fluoride.  
[Click on image to view video online.](#)

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demineralized crystals seed new crystals from solution. But crystal growth is susceptible to poisoning by foreign substances, and hydroxyapatite growth inhibitors present in saliva can interfere with the process. Therefore, newly precipitated crystals are usually very small and contain many defects, such as missing ions, which make it more soluble. Crystals that are predominantly bathed in a large volume of solution saturated with respect to hydroxyapatite will tend to perfect themselves, as they become remineralized. The soluble parts will re-form and crystals will grow to reach their maximum natural size in a process called Ostwald ripening.\textsuperscript{1}\textsuperscript{18}

**White Lesions**

In a clinical examination, a remineralized carious lesion will initially appear as a white scar under a shiny, hard surface. This is because the surface layer of the lesion is remineralized, but the lesion body is not, as explained previously. The fate of white lesions is worth noting.

**Other Key Factors that Promote Remineralization**

**Saliva**

Because of its water content and flow rate, saliva physically cleanses the oral cavity of food and debris, removing sources that promote acidity, as well as dilutes and removes organic acids from dental plaque. Saliva also contains a number of electrolytes and organic molecules that minimize decreases in local pH, creating an environment that favors remineralization. For example, sodium bicarbonate and phosphates, along with other salivary components, act as buffers or neutralizing agents in saliva.\textsuperscript{19,21} In addition, one salivary protein called sialin tends to raise salivary pH to neutral levels.\textsuperscript{21} Saliva is also supersaturated with calcium and phosphate ions, increasing the likelihood of remineralization.\textsuperscript{19,21}

**Fluoride**

This mineral primarily exerts its well-known anti-caries effects by reducing demineralization and enhancing remineralization. When fluoride is present in low concentrations in saliva and plaque fluid, fluoride ions are likely to be incorporated into the remineralizing surface of the lesion, making the repaired section higher in fluoride than it originally was. The material formed on the surface of the lesion is more accurately called fluorapatite, a more stable and less soluble material that is protective of the lesion body underneath. It also binds firmly with calcium, making it less likely that calcium ions are pulled out of the tooth and into the solution. When saliva and plaque fluid is supersaturated with respect to fluoride, and when fluorapatite has formed, it has been found that damage to tooth structure does not start occurring at a pH of 5.5, but rather at a more acidic 4.5, emphasizing fluoride’s protective effect. The overall effect is reduced dental demineralization as a result of the protective outer layer of fluorapatite. If fluoride is not available, the oral environment begins to favor demineralization.\textsuperscript{1}

In the United States, fluoride is most commonly delivered systemically via the water supply, or topically in the form of over-the-counter or prescription fluoride dentifrices and mouthwashes. In more serious caries cases, professionally applied fluoride varnishes, gels, foams, or slow-release applications may be necessary.

**Conclusion**

Demineralization and remineralization is a dynamic process of mineral loss from the hard tissue of the tooth and of its repair. These are not distinct processes; rather, both occur to some extent on tooth surfaces at any given time. Which process “wins” is dependent on several factors in the oral environment, such as the frequency of sucrose consumption and the status of saliva, and whether

\textsuperscript{1,18} Video 3. Remineralization and Fluoride. \textit{Click on image to view video online.}
these factors create an environment that favors
demineralization or remineralization. Clearly,
the goal in dental practice is to help the patient
maintain an oral environment that both prevents
demineralization and enhances remineralization
to prevent the formation of caries.

Figure 4. Caries Lesion Initiation and Progression - Demineralization.

Figure 5. Caries Lesion Initiation and Progression - Remineralization.
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/professional-education/ce-courses/ce372/start-test](http://www.dentalcare.com/en-us/professional-education/ce-courses/ce372/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. **How is the biological hydroxyapatite of tooth enamel different than pure hydroxyapatite?**
   a. It readily incorporates trace minerals, such as fluoride and carbonate into its crystal lattice.
   b. It is stronger.
   c. It has the following formula: $\text{Ca}_{10}(\text{PO}_4)_4(\text{OH})_4$
   d. None of the above.

3. **What differentiates dentin from enamel?**
   a. There are no significant differences.
   b. Enamel can repair and regenerate, while dentin cannot.
   c. Unlike enamel, dentin is living tissue with the ability for constant growth and repair, thanks to cells called odontoblasts that create new dentin.
   d. Dentin is harder than enamel.

4. **What acid is *Streptococcus mutans* capable of metabolizing, and in the process, further promoting demineralization?**
   a. lactic acid
   b. acetic acid
   c. pyruvate acid
   d. formic acid

5. **Which factors 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. All of the above.

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. All of the above.
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 and softened spot on the tooth surface.  
   c. Evidence of tooth erosion caused by acid attack.  
   d. Completely demineralized tissue.

10. How does Veillonella bacteria affect the process of demineralization/remineralization?
    a. *Veillonella* use lactate as a substrate, metabolizing it to less acidic products, helping to create an environment that promotes remineralization.  
    b. *Veillonella* increases the acidity of plaque, increasing demineralization.  
    c. *Veillonella* causes xerostomia which increases demineralization.  
    d. *Veillonella* attacks pathogenic bacteria, promoting remineralization.

11. 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

12. 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 process in which small, imperfect hydroxyapatite crystals re-form and grow to reach their maximum size in the presence of a large volume of saturated oral solution.  
    d. It is the name given to the regeneration of dentin.

13. What is the initial clinical appearance of a remineralized carious lesion?
    a. It appears as a black cavitation.  
    b. It appears as a white scar with a shiny, hard 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.

14. Which of the following is a remineralization-promoting characteristic of saliva?
    a. Saliva promotes acidity that promotes hydroxyapatite crystal growth.  
    b. Saliva does not promote remineralization.  
    c. Saliva is supersaturated with calcium and phosphate ions.  
    d. None of the above.

15. 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
References
About the Authors

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Dr. Higham is a Professor of Oral Biology in the Department of Health Services Research and School of Dentistry, University of Liverpool, United Kingdom. She is Director of Postgraduate Research in her University Research Institute and is the National Institute of Health Research, Comprehensive Research Network Oral and Dental Specialty Research Group Lead for North West Coast and National Industry Lead.

Dr. Higham has a background in microbiology and biochemistry, a PhD focused on dental plaque metabolism from the University of Liverpool, Chartered Biologist status and a member of the Royal Society of Biology. She was appointed as a Research Fellow in the Department of Clinical Dental Sciences at the University of Liverpool and later promoted to Senior Lecturer and then to Professor.

Dr. Higham has supervised more than 40 postgraduate students and has published more than 370 book chapters, peer-reviewed papers and peer reviewed abstracts. Her main research interests are in the use of in vitro and in situ models and clinical trials to study dental diseases, together with the development of optical technologies for the quantification of mineral loss/gain in vivo. She has been involved in University teaching at all undergraduate and postgraduate levels for over 30 years. Dr. Higham has been a scientific advisor for the European organization for caries research (ORCA) for many years and is a dentistry panel member for the Research Excellence Framework (REF) in the UK. She has been elected as Vice-President of the Cariology Group of the International Association of Dental Research (IADR) and will serve as President in 2020.

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Chris graduated with a degree in Microbiology at the University of Liverpool in 1994 and then went on to study for a PhD in Chemical Engineering at The University of Birmingham. This somewhat unconventional entry into dental research came via biofilm modeling which led to his appointment at the Eastman Dental Institute – University College London as a research fellow between 2000 and 2005.

In 2005, Chris was appointed as Lecturer in Oral Biology at the University of Liverpool where his experience of biofilm modeling complimented the research group themes of caries and plaque-related disease. Chris developed a biological model of dental caries which acquires enamel lesions in less than two weeks and continued his interests in imaging by studying the natural fluorescence of dental plaque. More recently, he has revisited photodynamic therapy by looking at the lethal photosensitization of periodontal pathogens by means of their intrinsic porphyrins.

Chris served on the British Society for Oral and Dental Research (BSODR) Oral Microbiology and Immunology Group (OMIG) management committee from 2008 to 2011 and then again for a second term from 2015 to 2018. Chris was also elected onto the management board of the BSODR in 2017. He is also on the editorial board of the Journal of Medical Microbiology.

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Dr. Valappil is a lecturer in dental sciences in the School of Dentistry at the University of Liverpool, United Kingdom. He is a deputy Director of Postgraduate Research in his University Research Institute. Dr. Valappil is a microbiologist with special interests in bacteriology and biomaterials. Following his PhD, Dr. Valappil worked at Imperial College London and the University of Westminster on developing tissue engineering composites. He then worked on controlled antibacterial agent delivery systems and bacterial biofilms at Eastman Dental Institute, University College London. Since moving to Liverpool, Dr. Valappil focused his research in the development of novel antibacterial materials for dental applications in treating periodontitis and caries. Dr. Valappil has published over 100 book chapters, peer-reviewed papers and peer reviewed abstracts. Dr. Valappil is an associate editor of BMC Oral Health and Review Editorial Board Member of the journal Frontiers in Antimicrobials, Resistance and Chemotherapy. He is a peer reviewer for over 40 scientific journals and act as grant reviewer for national and international research councils including Medical Research Council, UK; Chilean Science Agency, CONICYT and Italian Cystic Fibrosis Research Foundation.

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Phil is currently Senior Lecturer and Honorary Consultant in Restorative Dentistry at Liverpool University Dental Hospital and he has been an NHS Consultant since 1998. He has been actively involved in teaching, research and clinical service, and is lead clinician for restorative care of CLP patients in Liverpool and North West (West) Region. He has also gained experience in managing clefts from time spent at Oslo. He has published widely including authoring/co-author of 3 textbooks and has been supervisor, mentor and advisor for a number of postgraduate students and trainees. He is a reviewer for Journal of Dental Research, Journal of Dentistry, British Dental Journal, Dental Materials, Journal of The European Journal of Prosthodontics and Restorative Dentistry, and Dental Update. He is also part of a team from Liverpool that has been commended in the recent Medical Futures Innovation awards and is currently President of the British Society of Prosthodontics.

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