Caries Process and Prevention Strategies: The Host

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Continuing Education Units: 1 hour


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.

This is part 3 of a 10-part series entitled Caries Process and Prevention Strategies. It has been established that a host must be present for caries to develop. In this course, three host factors – the tooth, saliva, and the oral cavity’s immune response – are introduced, and their roles in the caries process are explained.

Conflict of Interest Disclosure Statement

• The author reports no conflicts of interest associated with this work.

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Overview

It has been established that a host must be present for caries to develop. Here, three host factors - the tooth, saliva, and the oral cavity’s immune response - are introduced, and their roles in the caries process are explained.

Clinical Significance Snapshots

In managing patients at risk of dental caries, how should I approach managing ‘host’ factors involved in the caries process?

The two tissues of the host affected by dental caries are the enamel and the dentin. In young persons, enamel is the main tissue that is affected, as no dentin is exposed directly to the oral cavity. Later in life, when gingival recession has exposed the roots of the teeth, dentin becomes exposed to the oral cavity. So, as a first line of defense, it is important to protect the enamel and try to prevent gingival recession.

First, saliva bathes all tissues exposed to the oral cavity. In health, there is an adequate flow (quantity) of this fluid that helps flush away cariogenic foods, and the fluid is saturated with respect to calcium, which reduces demineralization and encourages remineralization (quality). The effects of medication are the most common problem that leads to a lack of saliva. Many prescription and OTC medicines, and some recreational drugs, reduce the flow of saliva and cause Xerostomia or dry mouth. In cases of dry mouth, caries and erosion are highly prevalent. It is important that the dental professional checks for adequate quantity and quality of saliva, and consults with the patient’s physician if necessary.

Second, the hard tissues should be protected by a plentiful exposure to fluoride. Brushing twice daily with a fluoride toothpaste is clinically proven to reduce dental caries by more than 50%. Fluoride can also be applied in the office or at home by the use of rinses, gels, and similar products. The roots can be protected from risk of root caries by preventing gingival recession first and foremost, and by practicing safe and gentle oral hygiene methods. If roots are exposed, they can also be treated with fluoride compounds, and the patient should be advised of the increased risk of dental caries and the need for thorough oral hygiene of the exposed root surfaces.

Learning Objectives

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

- Discuss tooth structure.
- Describe how the mineral composition and structure of enamel relates to caries.
- Be familiar with the concept of enamel maturation.
- Explain what saliva is and how it is produced.
- Identify the major salivary glands.
- Explain the nerve control of saliva secretion.
- List the physical, chemical, and antibacterial properties of saliva.
- Describe the host’s immune response in the dental caries process.
Course Contents

- Glossary
- Introduction
- The Tooth
  - Enamel Structure and Composition
  - Dentin Structure and Composition
    - Pulp Chamber
    - Cementum
- Saliva
  - Anatomy of Salivary Glands
  - Innervation of Salivary Glands
  - Host-Protective Properties of Saliva
- Immune Response
  - Secretory Immunoglobulin A (IgA)
  - Immunoglobulin G (IgG)
- Conclusion
- Course Test Preview
- References
- About the Author

Glossary

**ameloblasts** – The cells in the embryonic tooth germ that produce enamel. Once tooth formation is complete, the ameloblasts are unable to produce further enamel. Therefore, if enamel is lost or damaged by caries, tooth wear, or trauma, it cannot be repaired or replaced.

**cariogenic** – The ability to cause dental caries. A cariogenic diet contains sugars. Some bacteria in dental plaque (S. mutans) are cariogenic. The mere presence of cariogenic sugars or cariogenic bacteria are not enough to cause the initiation of the caries process. Many other factors play a role, and taken together they may or may not contribute to the process that leads to dental caries.

**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.

**fluorapatite** – A crystal structure in tooth mineral (Ca_{10} (PO_{4})_{6} F_{2}) resulting from the replacement of hydroxyl ions (OH-) in the hydroxyapatite structure with fluoride ions (F-). Fluorapatite (also commonly referred to as fluoroapatite, fluoroapatite or fluoroapatite) is stronger and more acid resistant than hydroxyapatite.

**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. 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.

**parasympathetic nerves** – The part of the nervous system that controls and regulates various organs and glands unconsciously, such as the secretion of salivary and lachrymal fluids.

**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, the presence of fluoride, and adequate buffering.

**sympathetic nerves** – The part of the nervous system that controls the stress and flight-or-fight response. It controls the force of contraction and rate of the heartbeat, and dilates the pupils and the bronchioles.

Introduction

Caries cannot develop without the presence of a host, which comprises tooth structure, the saliva that surrounds a tooth, and the immune responses of saliva and plasma in the oral cavity. In 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 demineralization first begins. It is also the only tissue of the tooth that does not have the ability to grow or repair itself after maturation. Saliva is also important to consider in the caries process because it has protective properties that can reduce caries risk: It neutralizes pH in the vicinity of the tooth,
assists in remineralization, acts as an antibacterial agent, and plays a role in the immune responses to cariogenic oral bacteria.

The Tooth
The four major tissues of the teeth are enamel, dentin, dental pulp, and cementum (Figure 1). Each of these is defined and further explained next.

Enamel Structure and Composition
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. It can vary in thickness and hardness on each tooth, from tooth to tooth and from person to person. It can also vary in color (typically from yellowish to grayish white) depending on variations in the thickness, quality of its mineral structure and surface stains. Enamel has no blood or nerve supply within it. It is enamel’s hardness that enables teeth to withstand blunt, heavy masticatory forces. Enamel is so hard because it is composed primarily of inorganic materials: Roughly 95% to 98% of it is calcium and phosphate ions that make up strong hydroxyapatite crystals. Yet, these are not pure crystals, because they are carbonated and contain trace minerals such as strontium, magnesium, lead, and fluoride. These factors make “biological hydroxyapatite” more soluble than pure hydroxyapatite.

Approximately 1% to 2% of enamel is made up of organic materials, particularly enamel-specific proteins called enamelines, which have a high affinity for binding hydroxyapatite crystals. Water makes up the remainder of enamel, accounting for about 4% of its composition.

The inorganic, organic, and water components of enamel are highly organized: Millions of carbonated hydroxyapatite crystals are arranged in long, thin structures called rods that are 4 µm to 8 µm in diameter. It is estimated that the number of rods in a tooth ranges from 5 million in the lower lateral incisor to 12 million in the upper first molar. In general, rods extend at right angles from the dento-enamel junction (the junction between enamel and the layer below it called dentin) to the tooth surface. Surrounding each rod is a rod sheath made up of a protein matrix of enamelines. The area in between rods is called interrod enamel, or interrod cement.

While it has the same crystal composition, crystal orientation is different, distinguishing rods from interrod enamel. Minute spaces exist where crystals do not form between rods. Typically called pores, they contribute to enamel’s permeability, which allows
fluid movement and diffusion to occur, but they also cause variations in density and hardness in the tooth, which can create spots that are more prone to demineralization – the loss of calcium and phosphate ions – when oral pH becomes too acidic and drops below 5.5. In demineralization, the crystalline structure shrinks in size, while pores enlarge.\(^3,4\)

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 be restored beyond the normal course of remineralization. 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.\(^3\)

There are conditions that can affect the formation of enamel and thus increase the risk of caries. These include the genetic disorder amelogenesis imperfecta, in which enamel is never completely mineralized and flakes off easily, exposing softer dentin to cariogenic bacteria.\(^4\) Other conditions are linked with increased enamel demineralization, such as gastroesophageal reflux disease (GERD) and celiac disease.\(^5,6\)

Dentin Structure and Composition

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.\(^1\)

Another way in which dentin is different than enamel is that it is living tissue with the ability for constant growth and repair. 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. Cell 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.\(^1\)

Pulp Chamber

The dental pulp is the soft tissue of the tooth. The chamber containing the dental pulp that underlies, and is connected to, the dentin layer is called the pulp chamber. It contains the coronal pulp within the crown that is continuous with the radicular pulp within the root. Pulp contains odontoblasts, cells whose biological function is the creation of dentin.\(^7\) It also contains neurons, vascular tissues, fibroblasts and macrophages. (It was long thought that pulp contained lymphatic vessels but a 2010 immunohistochemical staining study found that, under normal conditions, dental pulp does not contain true lymphatic vessels.)\(^8\) One area of note is the apical foramen at the end of the radicular pulp. Blood vessels, nerves, and connective tissue pass through this area to reach the interior of the tooth.

Cementum

This is a thin, light yellow layer of bonelike tissue that covers the roots of the teeth. Its main function is to anchor teeth to the bony walls of the tooth sockets in the periodontium by attaching to the periodontal ligament. The cementum is composed of approximately 55% organic material and 45% inorganic material, mainly calcium salts. It joins the enamel at the cervix of the tooth at the cementoenamel junction. In most teeth, the cementum overlaps the enamel for a short distance; in some, enamel meets the cementum in a sharp line; and in a few teeth, there is a gap between the enamel and the cementum, exposing a narrow area of root dentin. Such areas may be very sensitive to thermal, chemical, or mechanical stimuli. Cementum is formed continuously to make up for the loss of tissue due to wear, and to allow for the attachment of new fibers of the periodontal ligament to the surface of the root.\(^9\)

Saliva

Saliva is a mixture of mucous and serous fluid, the term given to bodily fluids that are pale yellow, transparent, and benign in nature. This mixture is formed by the salivary glands, whose structure and function are explained in more detail below.
Anatomy of Salivary Glands

These are made up of an ancinus (a berry-shaped cluster of excretory cells) and ductal systems. Saliva is formed in the ancini with the serous (watery) secretion formed by serous cells, and the mucous (viscous) secretion formed by the mucous cells. There are three major bilateral salivary glands: the parotid, the sublingual and the submandibular (Figures 2a & 2b).

The parotid is the largest pair of glands, occupying the parotid facial space, an area posterior to the mandibular ramus, and anterior and inferior to the ear. It secretes saliva through the Stensen’s ducts into the oral cavity to facilitate mastication and swallowing. The submandibular are a pair of glands located beneath the lower jaws. Even though they are smaller than the parotid, they produce 70% of saliva, secreted via the Wharton’s ducts. These two glands produce “true” saliva – the combination of serous fluid and mucous. They also have ancini connected to intercalated ducts (essentially, transitional tissue) which then connect to striated ducts that have the capacity to modify the mineral content of saliva. On the other hand, the third major set of glands – the sublingual glands which are located beneath the tongue – secretes mainly mucous, and does not have striated ducts, releasing its mucous directly from ancini via excretory ducts.

In the oral cavity, there are also over 600 minor salivary glands. These are found in all parts of the oral mucosa, except for the gingival tissue and the anterior hard palate. Each gland is usually a number of ancini connected in a tiny lobule, and they may have their own excretory duct, or they may share one with another minor gland. Their secretion is mainly mucous and they work to keep the whole oral cavity coated with this fluid.

Innervation of Salivary Glands

The salivary glands are innervated by the parasympathetic and sympathetic branches of the autonomic nervous system.

Parasympathetic stimulation favors serous (watery) secretion and occurs via cranial nerves, with the glossopharyngeal nerve innervating the parotid, and the facial nerve innervating the submandibular and the sublingual glands. These release acetylcholine and substance P, neurotransmitters that bind to receptors on acinar and ductal cells of the salivary glands.

Direct sympathetic stimulation favors viscous (mucoid) secretion and takes place via preganglionic nerves in the thoracic segment of the spinal cord which synapse with postganglionic neurons. These release the neurotransmitter norepinephrine that binds to receptors on the salivary gland acinar and ductal cells. There is also indirect sympathetic stimulation of the salivary glands via innervation of the blood vessels that supply the glands.

With both types of stimulation, the binding of neurotransmitters to salivary gland receptors leads to increases in intracellular calcium and alterations in membrane permeability, and a corresponding increase of saliva, as organic molecules, electrolytes, water and mucous are excreted into the acinar lumen.

Host-Protective Properties of Saliva

It has been established that saliva plays a crucial role in reducing caries risk. This is due in large part to saliva’s physical, chemical and antibacterial properties.

Physical Protective Qualities

Due to its water content and flow rate, saliva physically cleanses the oral cavity of food and debris. Unstimulated flow rates are approximately 0.3 to 0.4 ml/min, while stimulated flows are approximately 1.5 to 2 ml/min, although there are wide variations between

Video 1. Saliva

Click here to view this video on dentalcare.com.
bicarbonate and phosphates, along with other salivary components, act as buffers or neutralizing agents in saliva. In addition, one salivary protein called sialin tends to raise salivary pH to neutral levels.

**Chemical Protective Qualities**

Saliva 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 hydroxyapatite, fluorapatite, and calcium and phosphate ions compared to the carbonated hydroxyapatite in enamel. This supersaturation...
is maintained by the proline-rich proteins and statherhins in saliva, and it increases the likelihood of remineralization via the incorporation of calcium and phosphate into enamel.\textsuperscript{8,10}

**Antibacterial Properties**
Saliva contains several proteins with different types of antibacterial properties: The **mucins** are sulfated glycoproteins that trap, aggregate, and clear bacteria. The enzymes called **amylases** break down food particles that stick to teeth, reducing the bacterial build-up that can lead to decay.

Lysozyme is a cationic protein that lyses (damages) the cell walls of bacteria, rendering them inactive. **Lactoferrin** is an iron-binding glycoprotein that deprives bacteria of energy-generating iron so that they cannot survive. **Peroxidase enzyme** is a protein that forms free radical compounds in bacterial cells which cause them to self-destruct.\textsuperscript{14} Immunoglobulins are antigen-binding proteins that block the adherence of bacteria to the tooth surface and/or promote the clearance of bacteria from tooth structure.

**Immune Response**
Saliva plays a pivotal role in the health of the mouth and contributes to host defense mechanisms through physio-chemical barriers, non-specific (innate immunity) factors, and specific (adaptive immunity) factors. Of key importance are the specific factors, which include the immunoglobulins that increase in number when there is exposure to cariogenic bacteria.

**Secretary Immunoglobulin A (IgA)**
This is the dominant immunoglobulin in the healthy mouth.\textsuperscript{15} IgA is produced by gland-associated immunocytes that are scattered in anciini and in clusters adjacent to salivary ducts. IgA is composed of two molecules of heavy and light chains, a secretory component that protects the immunoglobulin from being degraded by proteolytic enzymes, and a J chain. This is a unique joining chain not found in any other immunoglobulin that connects the two IgA molecules into a dimeric structure.\textsuperscript{16}

IgA can agglutinate oral bacteria, such as *S. mutans*, modulate enzyme activity, and inhibit the adherence of bacteria to the buccal epithelium and to enamel.\textsuperscript{15,17} It does well at interfering with the initial colonization of caries-associated microflora on the tooth surface, but being a salivary protein, it does not always have access to bacteria that are deeper in periodontal pockets. IgA is also a poor activator of the complement system, the biochemical cascade that helps antibodies physically clear pathogens. It is also a poor opsonizer that does not reliably make bacterial cells susceptible to phagocytosis.

**Immunoglobulin G (IgG)**
This type is almost entirely derived from gingival crevicular fluid, now more commonly called gingival fluid. This is a blood exudate (a protein-rich fluid that has escaped from blood vessels) that emerges from the crevice between the gingiva and the tooth. It contains immunoglobulins such as IgG, which can be produced by plasma in periodontal pockets. An increase in gingival fluid and IgG to a variety of oral microbial agents, including *S. mutans*, has been seen in response to periodontal irritation and inflammation. Yet, IgG to oral microbial agents are also present in the healthy mouth, suggesting that it prevents early stages of plaque development from worsening.\textsuperscript{18} Compared to IgA, IgG is strong in complement-activating and opsonizing that can lead to antibody-mediated phagocytosis. In the absence of inflammation, the naturally low levels of complement would reduce IgG, and may play a role in modulating oral microflora.

**Conclusion**
A primary factor in the development of caries is the presence of a host. A number of host-related subfactors can influence the caries...
process. These include tooth structure, the physical, chemical, and antibacterial properties of the saliva that surrounds the tooth, and the immunity conferred by the immunoglobins in the host environment, the mouth. Understanding tooth anatomy and the composition of all the tooth tissues, the protective role of saliva, and the two main different types of immune responses by secretory Immunoglobulin A and Immunoglobulin G will help dental professionals reduce caries risk in their patients.
Course Test Preview

To receive Continuing Education credit for this course, you must complete the online test. Please go to:


1. Which of the following is not a major tissue of teeth?
   a. Enamel
   b. Hydroxyapatite crystals
   c. Pulp
   d. Cementum

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. When a tooth erupts, it is not fully mineralized. Which ions are taken up from saliva to complete mineralization?
   a. Calcium
   b. Phosphorous
   c. Fluoride
   d. All of the above.

4. What are the main differences between dentin and enamel?
   a. Dentin has more organic matter, dentin is softer, and dentin is living tissue that can grow and repair.
   b. Dentin has more organic matter, dentin’s hydroxyapatite crystals are smaller, and enamel can be repaired and regenerated.
   c. There are no significant differences.
   d. Enamel contains tubules that connect it to pulp, dentin is harder, and enamel has more inorganic matter.

5. Which of the following is true about pulp?
   a. It is formed by epithelial cells called ameloblasts.
   b. One of its main roles is the creation of dentin.
   c. It is devoid of blood vessels and nerves.
   d. It is directly connected to enamel via tubules.

6. What is the main role of cementum?
   a. To protect against tooth sensitivity.
   b. To create dentin.
   c. To anchor teeth to the body walls of tooth sockets.
   d. None of the above.

7. Which of the following are major salivary glands?
   a. Parotid
   b. Submandibular
   c. Wharton’s ducts
   d. A and B
8. Which of the following traits differentiates the sublingual salivary glands from the parotid and submandibular glands?
   a. The sublingual glands secrete mostly mucous and have excretory ducts.
   b. The sublingual glands secrete mostly serous fluid and have excretory ducts.
   c. The sublingual glands produce thicker saliva and have intercalated ducts.
   d. There is no difference between sublingual glands and parotid and submandibular glands.

9. Salivary glands are innervated by the parasympathetic and the sympathetic branches of the autonomic nervous system. Which of the following pairings is correct for nerve control and secretion?
   a. Parasympathetic stimulation favors mucoid secretion.
   b. Parasympathetic stimulation favors serous secretion.
   c. Direct sympathetic stimulation favors serous secretion.
   d. Indirect sympathetic stimulation favors serous secretion.

10. Which of the following represents the physical role of saliva?
    a. Cleanses the oral cavity.
    b. Dilutes and removes organic acids from dental plaque.
    c. Aids in digestion.
    d. A and B

11. In humans, major and minor salivary glands secrete approximately what volume of saliva each day?
    a. 5 liters
    b. 2 liters
    c. 1 liters
    d. .01 liters

12. Which of the following act as pH neutralizing agents in saliva?
    a. Sodium bicarbonate, phosphates, and sialin
    b. Statherins, phosphates, and calcium
    c. Sodium bicarbonate, hydroxyapatite, sialin
    d. All of the above.

13. Which of the following is an antibacterial property of saliva?
    a. Mucins that trap, aggregate, and clear bacteria.
    b. Lysozyme that deprives bacteria of iron.
    c. Lactoferrin that activates bacterial clumping.
    d. Salivary peroxide that triggers hydrogen peroxides.

14. The increase of which of the following results from an exposure to cariogenic bacteria?
    a. Plasma cells
    b. Antigens
    c. Immunoglobulin
    d. Opsonizes

15. Which of the following correctly describes secretory immunoglobin A (slgA)?
    a. slgA is produced in salivary ducts and primarily inhibits adherence of bacteria.
    b. slgA is produced in gingival fluid and triggers phagocytosis.
    c. slgA is produced only in gingival fluid and inhibits adherence of bacteria.
    d. slgA is made of three molecules of light and heavy chains.
References
About the Author

Susan Higham, BSC, PhD, CBIol, MSB
Dr. Higham is a Professor of Oral Biology, Department of Health Services Research and School of Dentistry, University of Liverpool, United Kingdom and is Director of postgraduate research in her University Research Institute.

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 membership in the Institute of Biology. She was appointed a research fellow in the Department of Clinical Dental Sciences at the University of Liverpool, where she was promoted later to senior lecturer and then to a professor.

Dr. Higham has supervised 24 Doctoral students and 10 Master’s degree candidates and has published more than 300 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 is a scientific advisor for the European Organisation for Caries Research (ORCA) and is a dentistry panel member for the Research Excellence Framework (REF 2014) in the UK.

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