Nutrition and Oral Health

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- Complete the questions at the end of the course.
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Faculty Disclosure
Contributing faculty, Mark J. Szarejko, DDS, FAGD, has disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

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The division planner and director have disclosed no relevant financial relationship with any product manufacturer or service provider mentioned.

Audience
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A complete Works Cited list begins on page 23.

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Course Objective

The purpose of this course is to provide clinicians with a better understanding of the impact of nutrition on dental health and care.

Learning Objectives

Upon completion of this course, you should be able to:

1. List the common proteins, carbohydrates, and lipids that are essential for proper function of the structures of the oral and maxillofacial complex.
2. Review the water-soluble and fat-soluble vitamins and their role in optimal oral health.
3. Identify the minerals that have the most importance for the teeth, gingival, oral mucosa, and the osseous structures of the oral and maxillofacial complex.
4. Describe the impact of certain digestive disorders on oral health.
5. Outline the oral and systemic impact of bariatric surgery.
6. Discuss the oral issues that may arise in patients with eating disorders.

Sections marked with this symbol include evidence-based practice recommendations. The level of evidence and/or strength of recommendation, as provided by the evidence-based source, are also included so you may determine the validity or relevance of the information. These sections may be used in conjunction with the course material for better application to your daily practice.

INTRODUCTION

Dental professionals practice a variety of treatment modalities in an effort to optimize the oral health of each patient. Prevention of dental caries and periodontal disease remains the usual goal. The restoration and preservation of teeth involves a multitude of interventions and prophylactic approaches. Without adequate and proper nutrition, the health of the hard and soft tissues of the oral cavity may be compromised and even the best efforts of the patient and dental professionals may not be enough to ensure optimal oral health.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The American Dental Association encourages dentists to routinely counsel their patients about the oral health benefits of maintaining a well-balanced diet.

(https://www.ada.org/en/advocacy/current-policies/diet-and-nutrition. Last accessed October 19, 2020.)

Level of Evidence: Expert Opinion/Consensus Statement

This course will provide an overview of how nutrition influences oral health. The specific functions that proteins, carbohydrates, lipids, vitamins, and minerals exert in oral health will be discussed, as will the consequences of their depletion. In addition, common medical and psychologic conditions affecting nutrition and oral health will be explored.

ESSENTIAL NUTRIENTS

PROTEINS

Approximately 50% of the dry weight of a typical human cell is protein [1]. Proteins assume numerous roles in the maintenance of homeostasis of the body as enzymes, contractile filaments of muscles, hormones, transporters, structural components, and a myriad of other substances. All proteins are composed of carbon, hydrogen, oxygen, and nitrogen. Additionally, some contain sulfur and/or phosphorus. Amino acids are composed of varying amounts of these basic elements and are the building blocks of all proteins. An adequate intake of protein is an essential component for optimal oral health at all stages of life.

The sequence of amino acids determines the composition of a given protein. The hard and soft tissues of the oral cavity rely on varying types and amounts of protein compounds for their development, maturation, and replenishment. Collagen is the most abundant protein in the body. It is a fibrous protein, the molecules of which are condensed into helical formation to form a strong, rope-like structure that is insoluble in water [2]. Glycine, proline, and hydroxyproline are the major amino acid constituents of the collagen helical chain. The functional qualities of collagen make it ideal for the provision of mechanical support and tensile strength for oral tissues. There are several different types of collagen, each with a different functional.

There main types of collagen are I through V, each serving different functions. Type I collagen is the predominant protein in the structures of the oral cavity. The connective tissue in the gingiva is composed of type I and III collagen in a 5:1 ratio. Type III collagen predominates in granulation tissue that is the matrix for wound healing [3]. In the oral mucosa, type I and type III collagen are the main constituents of the upper connective tissues layer (lamina propria), while type I predominates in the deeper layers of the connective tissue stroma [4]. The amount of collagen in the layers of the tooth structure itself varies. Enamel is composed of 97% inorganic matrix; in the remaining 3% of organic matrix, type VII collagen has been identified surrounding the enamel rods at the dentin-enamel junction and may confer a higher resistance to fracture [5]. Type I collagen is the predominant protein in the dentin matrix and in the primary extracellular matrix of dental cementum [6]. Type I collagen is also the major collagenous constituent of the dental pulp, the periodontal ligament, and

the alveolar bone. Small amounts of type III collagen are found in the dental pulp and the alveolar bone; about 20% of total collagen found in the periodontal ligament is type III [3].

Because collagen is a protein, a protein-deficient diet can lead to an inadequate quantity and/or quality of collagen, with a direct impact on the structures of the oral cavity. These patients may develop degeneration of the connective tissue of the oral mucosa and gingiva, atrophy of the lingual papilla, alteration in the formation of dentin and cementum, and impaired development of the osseous structures of the oral and maxillofacial complex [7]. Connective tissue problems in the gingiva decrease its ability to withstand masticatory forces and can attenuate its attachment to the tooth, increasing the potential for periodontal disease. Alterations in the formation of the dentin can have adverse effects on the bonding to enamel and can lead to enamel that is more prone to fracture. The attachment of the periodontal ligament from the bone to the cementum can be compromised if there are deficiencies in the formation of the bone and/or cementum [2].

Functional movements in the oral cavity are the result of coordinated muscular action, which is dependent on actin and myosin (contractile proteins). The muscles that function to provide an appropriate opening and closing axis for mastication and that control movements of the tongue rely on actin and myosin—and adequate intake of protein is required for these substances to be present. Prolonged protein deficiency can therefore compromise the ability of the muscles of the oral and maxillofacial complex to function properly.

CARBOHYDRATES

Carbohydrates are molecules that contain carbon, hydrogen, and oxygen, with the hydrogen and oxygen atoms in the same 2:1 ratio as water. Carbohydrates are classified according to size, with a monosaccharide being one sugar, a disaccharide being two sugars, and a polysaccharide being a polymer of simple sugars. The storage form of carbohydrates in plants is starch, but in animal tissues, it is glycogen stored mostly in the liver and skeletal muscles.

Dietary carbohydrates can be used as an energy source by all animal cells or stored as an energy reserve. There has been significant negative attention given to dietary carbohydrates in the lay media, and low-carbohydrate diets have been promoted as weight-loss approaches. Further, fermentable carbohydrates are a potential source of dental caries. This may give the impression that carbohydrates are not essential to oral health, but this is untrue.

Glucose, sometimes referred to as "blood sugar," is the principal carbohydrate in human circulation and will be the carbohydrate discussed in this course. Glucose is a monosaccharide and is the main carbohydrate used by the cells to produce adenosine triphosphate (ATP), the organic molecule that stores and releases chemical energy for utilization by all cells of the body. While most body cells can metabolize fat and proteins to produce glucose during periods of carbohydrate deprivation, fasting, or starvation, the brain and the red blood cells (erythrocytes) cannot and solely rely on dietary or stored glucose as their energy source.

Two hormones regulate blood glucose levels: insulin and glucagon. Insulin is produced by the beta cells of the pancreas and promotes glucose uptake into tissue cells, which lowers blood glucose levels. Glucagon is produced by the alpha cells of the pancreas and raises blood glucose levels by decreasing conversion to glycogen and stimulating the formation of glucose from non-carbohydrate molecules, such as amino acids (a process referred to as gluconeogenesis). Chronic elevated levels of blood glucose (hyperglycemia) manifest as type 1 or type 2 diabetes, both of which can have adverse consequences upon oral health. Some of the most common oral manifestations of diabetes include xerostomia, increased susceptibility to oral bacterial and fungal infections, delayed healing of surgical sites, and periodontal disease that progresses rapidly and is refractory to conventional treatment options [8].

While no oral lesions are directly pathognomonic of decreased blood glucose levels (hypoglycemia), the oral mucosa requires consistent blood glucose levels to meet the metabolic demands of the rapidly dividing cells of its outer layer. The ability of erythrocytes to provide oxygen adequate for the metabolic needs of epithelial, muscle, nerve, and osseous cells can be compromised when glucose levels are decreased. Impaired erythrocyte function can also lead to anemia, which may manifest as pallor of the oral mucosa. Long-term restriction of carbohydrate intake can force the body to metabolize stored fat as an energy source (ketosis), with the potential to interrupt the acid-base balance of the body [9]. Because life-sustaining metabolic reactions occur in a limited pH range, a sustained state of nutritional ketosis can have an adverse multisystem effect.

LIPIDS

Lipids are most commonly referred to as fats or fatty acids. Because diets low in fat and cholesterol are promoted as healthy, the role of lipids in maintaining a healthy body and oral tissues is often overlooked.

Lipids are water-insoluble molecules composed of carbon, hydrogen, and oxygen. Lipids include triglycerides, phospholipids, sterols, fats, and lipoproteins. The plasma membrane of all human cells is a lipid bilayer that is composed mostly of phospholipids, cholesterol, and glycolipids into which proteins are embedded [2]. The composition of the plasma membrane is critical, as it is the selectivity of this membrane that allows for the ingress of hormone and medication molecules that will exert a specific effect upon a specific tissue, organ, and/or system. Membrane permeability to ions such as sodium, calcium, and potassium is critical for the conduction of neural impulses and the contractility of cardiac and skeletal muscle fibers.

Adrenocortical and gonadal hormones require cholesterol for their synthesis. Many patients may be prescribed a diet low in cholesterol and saturated fat in order to decrease the risk of developing or worsening cardiovascular disease. In general, even these diets provide enough cholesterol and fat to support the body's functions.

As a class, lipids have minor implications for oral health. However, some animal studies have suggested that lipid molecules are a component of a protective layer on teeth that impedes the formation of a bacteria-laden biofilm. It is hypothesized that this layer may decrease the risk of smooth-surface caries [10]. Other studies have suggested that low levels of omega-3 fatty acids may correlate with an increased risk of periodontitis [10]. However, dental clinicians should not make recommendations to increase fat intake based on these limited studies given the prevailing evidence that implicates the various dietary lipids as risk factors in the development of cardiovascular disease.

VITAMINS

Vitamins are organic compounds essential to at least one chemical reaction or process in the body. Vitamins also generally cannot be synthesized by the human body at all or are synthesized in quantities that are insufficient to meet the full needs of the body. Vitamins that can be stored in the body are considered fat-soluble, while those that cannot are considered water-soluble. Vitamins A, D, E, and K are fat-soluble vitamins, while the B-complex vitamins and vitamin C are water-soluble. Vitamins are not an energy source but are coenzymes or portions of coenzymes that enable chemical reactions to occur.

Fat-Soluble Vitamins

Fat-soluble vitamins have several important roles in the maintenance of optimal oral health. These vitamins must bind to ingested lipids for absorption from the digestive tract, so any disease or medication that interferes with fat absorption can decrease the bioavailability of these nutrients and undermine a patient's systemic and oral health. Dental clinicians should take a holistic approach that includes adequate nutrition as an important component in the maintenance of their patient's oral health.

Vitamin A

Vitamin A is required for the proper functioning of the visual system and for the development and maintenance of epithelial cellular integrity; it also contributes to the proper function of the immune and reproductive systems [11]. Systemic deficiencies in vitamin A can cause retinal disorders such as night blindness and hyperkeratosis [12]. Deficiencies can also influence the development of teeth via impact on the cells that form the enamel (ameloblasts) and the dentin (odontoblasts). Sustained deficiency of vitamin A prior to the eruption of teeth can lead to enamel hypoplasia, defects in the formation of the enamel matrix, and incomplete calcification of the enamel and dentin. Odontoblasts can depart from their parallel linear arrangement and cause the degeneration and atrophy of ameloblasts. The regular spacing of teeth and the stimulation of osteoblasts (progenitor bone-forming cells) also depend on adequate intake of vitamin A [11].

Vitamin A deficiency beginning in utero and continuing to the early teenage years can negatively impact the development of enamel and dentin. Calcification of the deciduous teeth occurs first on the maxillary and mandibular central incisors at about 14 weeks' gestation, while the initial calcification of the deciduous molars ranges from 15 to 23 weeks' gestation. The initial calcification of the permanent maxillary and mandibular first molars occurs about the time of birth, while those of the maxillary and mandibular third molars ("wisdom teeth") can range from 7 to 10 years [13]. As such, maternal vitamin A deficiency during pregnancy has the potential to adversely affect the formation of offsprings' enamel and dentin. Childhood deficiencies may likewise result in irregularities in permanent teeth; a vitamin A deficiency that develops in early adolescence or later would have minimal or no impact or oral health.

Abnormalities in the formation of enamel and dentin can result in several problems. The enamel of deciduous teeth is thinner than that of the corresponding permanent teeth, and surface deformities in the enamel make these teeth more difficult to clean and more prone to decay. The normally smooth surface of enamel can become pitted and mottled and develop a "chalky" appearance. Surface irregularities promote the retention of plaque and increase the potential for the development of dental caries.

Restoring the carious lesions of teeth with abnormal formation of enamel and dentin can be a challenge, as can minimizing the development of recurrent carious lesions. Conventional composite (resin-based) restorations rely on a strong bond with the enamel for their retention. Enamel that is abnormally formed will have compromised bond strength with composite restorations, and these teeth are more prone to debonding, leakage, and recurrent caries. In these cases, it may be necessary to extend cavity preparations beyond the usual conservative boundaries in order to locate and include enamel that is properly formed [14]. This additional involvement of tooth structure may require the use of more involved, longer-term restorations, such as stainless steel crowns on posterior deciduous teeth, polycarbonate crowns on anterior deciduous teeth, and ceramic or metallic (e.g., gold, semi-precious metal) restorations on permanent teeth. Given the potential difficulty in restoring carious deciduous teeth with abnormally formed enamel, clinicians may consider referral to a pedodontist. Adolescents and adults with enamel defects may require more frequent recall appointments given the heightened potential for carious lesions. Any patient with these issues should be provided with specific oral hygiene instructions

regarding the use of fluoride-containing mouth rinses or gels placed in custom trays.

Excesses of vitamin A deficiency during pregnancy have been linked to facial deformities and other birth defects [10]. Pregnant women should consult with their obstetrician to determine the safest vitamin intake levels for her and her fetus.

Vitamin D

Vitamin D is unique among the vitamins in that it can be synthesized by the human body in reasonable quantities provided that there is adequate access to sunlight and that the skin, liver, and kidneys are functioning. It also has characteristics of a hormone, as its physiologic activity requires interaction with a receptor [1]. In humans, the two most important forms are vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol).

Normally, vitamin D is primarily stimulated by ultraviolet radiation, or sunlight, on the skin and then by hydroxylation in the liver and kidney. Vitamin D then acts to increase intestinal absorption of calcium and promote bone formation. Deficiency of vitamin D in children causes rickets, and adult deficiency results in osteomalacia [2]. Rickets is characterized by deficient mineralization at the growth plate, while osteomalacia is the result of impaired mineralization of the bone matrix (osteoid) [15]. Lateral bowing of the tibia and the femur is a common presentation of both conditions when they occur in younger patients. In older patients, osteomalacia increases the risk of fracture. Because it is not practical for many individuals to get adequate levels of vitamin D from exposure to sunlight, increasing vitamin D levels through diet and supplementation should be encouraged [2]. However, few foods naturally contain vitamin D. The flesh of fatty fish (such as trout, salmon, tuna, and mackerel) and fish liver oils are among the best sources. Beef liver, cheese, and egg yolks have small amounts of vitamin D, primarily in the form of vitamin D3 and its metabolite 25(OH)D3. In addition, in the United States, almost all of the milk supply is fortified with about 3 mcg/cup (120 IU), usually in the form of vitamin D3 [16].

Osteomalacia is a special concern for dental patients who require oral surgery. The pressure exerted during the elevation and forcep delivery of a tooth may exceed the limits of weakened bone, with an increased potential for fracture. Before any dental care is provided, clinicians should assess their ability to provide the care with an atraumatic technique that minimizes pressure on the supporting alveolar bone. Referral to an oral surgeon should be considered for patients with osteomalacia.

Smaller-than-normal molars and delayed eruption of teeth can also be manifestations of vitamin D deficiency [11]. Hypoplasia of the enamel can also develop in individuals with vitamin D deficiency and can be more diffuse than hypoplasia that develops from vitamin A deficiency [17]. The individual's age and the duration of the deficiency determine the teeth involved. Problems with increased retention of plaque, risk of caries, and the challenges of restoring teeth with enamel abnormalities are similar to those discussed related to vitamin A deficiency.

Vitamin E

Vitamin E is not a single molecule but a group of eight molecules that possess similar activity and that are divided into two major classes: the tocopherols and the tocotrienols. The tocopherols are more abundant in nature, with alpha-tocopherol being the most prevalent form and the focus of this section [1].

As a key extracellular antioxidant, vitamin E stabilizes the cell membrane by terminating the free radical reaction that precipitates cellular damage [18]. Free radicals have unpaired electrons available to bond with cellular chemical constituents, making them highly reactive. Most free radical activity occurs in the mitochondria, the cellular organelle that produces ATP [2]. Protracted free radical damage and the subsequent decreased energy production can impair cellular reproduction and renewal, especially in cells of the oral epithelium, which have a rapid turnover and the need for sustained replenishment.

Vitamin E deficiency is rare, because it is widely distributed in foods, including vegetable oils, nuts, seeds, green leafy vegetables, and fortified breakfast cereals. However, muscular and neurologic problems can develop in patients with inadequate levels of vitamin E [11].

No lesions are considered pathognomonic of vitamin E deficiency. However, high doses of vitamin E may increase the risk of bleeding [19]. This is a concern for dental patients for whom invasive treatment, such as oral or periodontal surgery, has been planned. The combination of excessive doses of vitamin E with antiplatelet medications (e.g., aspirin, clopidogrel) or anticoagulant medications (e.g., warfarin) can decrease the ability to obtain hemostasis during and after invasive dental procedures. In patients taking warfarin, hemorrhage may be treated with vitamin K injection, but newer anticoagulant medications (e.g., dabigatran, rivaroxaban, apixaban) do not have a reversal agents [20]. It is incumbent that vitamins and nutritional supplements are included with the patient's medical history, as patients can be unaware of their potential adverse drug interactions.

Vitamin K

Vitamin K exists in three main forms. Phylloquinone occurs naturally in green plants; menaquinone is produced by bacteria in the intestine; and menadione is the synthetic version used in animal feed [21]. In humans, the most significant role of vitamin K is its role in coagulation. It serves as a catalyst for the synthesis of blood-clotting factors, especially in the maintenance of clotting factor II (prothrombin). The conversion of prothrombin to thrombin transforms the soluble clotting factor I (fibrinogen) to the insoluble polymer fibrin, which forms the cross-linked fibrin mesh at the foundation of a blood clot. Deficiencies in vitamin K are rare, given its availability in food and endogenous production by intestinal bacteria. However, deficiency can occur if intestinal absorption is impaired due chronic gastrointestinal disease and/or resection or long-term use of broad-spectrum antibiotics. Vitamin K deficiency can lead to issues with occult bleeding and hemorrhage during and after invasive dental procedures. Conversely, excessive vitamin K intake can impair the action of warfarin [22]. This can increase risk for an adverse cardiovascular or cerebrovascular event among patients who require anticoagulation therapy.

Vitamin K is also important for the formation of the proteins osteocalcin and periostin, which are integral to bone metabolism [12]. Low bone density can result in the development of osteoporosis, which is associated with increased risk of fracture. Decreased bone density of the maxillary or mandibular arch predisposes patients to fracture during extractions or from minimal force. Decreased bone density can also preclude the placement of implants.

Water-Soluble Vitamins

Water-soluble vitamins are absorbed with water from the digestive tract, with an insignificant fraction stored in the lean tissue of the body. Ingested amounts that are not utilized by the body within approximately one hour of absorption are excreted in the urine [2]. Vitamins B and C are water-soluble, and each has an important role in oral and systemic health.

Vitamin B1 (Thiamine)

Thiamine plays a critical role in energy metabolism necessary for the growth, development, and function of cells [23]. As discussed, the rapid turnover of cells of the oral mucosa and epithelium relies on a consistent source of energy, and thiamine is an essential component of these reactions. Therefore, oral manifestations of a thiamine deficiency include prolonged healing and the diminished renewal of the surface layer of the oral mucosa and epithelium, which can result in tissue sloughing and surface ulcerations.

Perhaps the most serious systemic complication of a thiamine deficiency is beriberi, a disease characterized by peripheral neuropathy and wasting. It can cause irreversible neuromuscular disorders as well as defects in memory. Some cases of beriberi

can progress to congestive heart failure and death [24]. A more common and serious manifestation of a thiamine deficiency is Wernicke-Korsakoff syndrome, which is up to 10 times more common in those with chronic alcoholism but can also affect patients with gastrointestinal disorders (e.g., hyperemesis gravidarum), hematologic malignancies, substance use disorders, or HIV/AIDS [25]. The syndrome consists of two phases. The first phase is acute and life-threatening and features a characteristic peripheral neuropathy. Approximately 20% of patients will die without treatment; those who survive develop Korsakoff psychosis [26]. Korsakoff psychosis features severe short-term memory loss, disorientation, and confusion between real and imagined memories (confabulation) [24].

The oral signs of a thiamine deficiency are not pathognomonic nor are they as severe as the systemic manifestations. However, dental professionals who treat patients with thiamine deficiency should be aware of potential drug-drug interactions and may need medical clearance prior to the initiation of dental treatment.

Vitamin B2 (Riboflavin)

Riboflavin is a component of coenzymes used in multiple metabolic pathways, including the regulation of cellular metabolism and the metabolism of carbohydrates, amino acids, and fats [27; 28]. Riboflavin deficiency is rare in the United States, as it is fortified in many grains and cereals. Other possible food sources include eggs, organ meats, lean meats, milk, and green vegetables.

Riboflavin deficiency can result in both oral and systemic effects. Oral manifestations include angular cheilitis, an erythematous (red) tongue, and a burning/tingling oral sensation [29]. Angular cheilitis is a mixed fungal and bacterial infection that features bilateral involvement of the commissures of the lips. When riboflavin deficiency is the etiologic factor, angular cheilitis resolves when adequate intake is restored. Systemic manifestations of riboflavin deficiency include weakness, dermatitis, anemia, fatigue, personality changes, and cognitive dysfunction [30]. Developmental defects caused by riboflavin deficiency during pregnancy can have systemic and oral/maxillofacial manifestations in offspring, including cleft lip and palate abnormalities, congenital heart defects, and impaired growth [27].

Vitamin B3 (Niacin)

Niacin (also known as nicotinic acid) is a critical coenzyme in ATP production. Additionally, niacin has a role in oxidative reactions, DNA metabolism and repair, cellular signaling, and antioxidant protection [30].

Although uncommon in developed countries, when present (usually as a result of food scarcity) niacin deficiency may result in pellagra. Pellagra features a triad of clinical manifestations: a localized pigmented rash (dermatitis), gastroenteritis (diarrhea), and neurologic deficits (dementia) [31]. Dietary supplementation with niacin will reverse the condition. Other systemic manifestations of niacin deficiency include alopecia, muscle weakness, peripheral neuropathy, altered gait, depression, anxiety, and psychiatric symptoms [32].

Oral manifestations of niacin deficiency can involve several structures. Loss of the filiform and fungiform papilla of the tongue changes its appearance to be smooth and shiny. The oral mucosa can become erythematous, and the gingival tissues may resemble that of ulcerative gingivitis [11]. Pain can emanate from any of the affected tissues and can interfere with the patient's ability to eat, speak, and swallow. The ability to maintain oral hygiene may also be compromised. Fortunately, niacin supplementation will reverse these effects. Liquid nutritional supplementation, topical and/or systemic analgesics, and a bland diet may be required until the oral tissues are restored to health. The pain associated with these manifestations usually precludes elective dental treatment. Patients who present with oral and/or systemic signs and symptoms should be referred to their physician for further evaluation.

Vitamin B5 (Pantothenic Acid)

Pantothenic acid is a constituent of coenzyme A, which plays a significant role in oxidative metabolism and the provision of energy for the body. Coenzyme A also is involved in the synthesis of cholesterol, phospholipids, amino and fatty acids, and several neurotransmitters and steroid hormones [32].

Vitamin B5 deficiency is rare, as it is available in meat and poultry, fish, mushrooms, and whole grains and is synthesized by bacteria in the gastrointestinal tract. When a vitamin B5 deficiency does occur, systemic manifestations include peripheral neuropathy, dermatitis, diarrhea, encephalopathy, behavioral changes, and demyelination of axon (nerve) sheaths [30]. There are no oral lesions or developmental anomalies that are uniquely pathognomonic of vitamin B5 deficiency. However, coenzyme A cannot function without pantothenic acid, so a deficiency decreases cellular renewal of the oral epithelium and the oral mucosa are replenished. Prolonged healing of oral surgery sites, tissue sloughing, and oral ulcerations could develop with a protracted deficiency of this vitamin.

Vitamin B6 (Pyridoxine)

Pyridoxine is the precursor to pyridoxal, which is involved in the metabolism of proteins, carbohydrates, and fats. Pyridoxal also facilitates the release of glycogen stored in the muscles and liver and is a component in the synthesis of neurotransmitters such as dopamine, serotonin, and gamma aminobutyric acid (GABA) [19]. Deficiency of vitamin B6 alone is uncommon and usually occurs in conjunction with a deficiency of other B-complex vitamins. When such a deficiency occurs, systemic manifestations include anemia, fatigue, muscular twitching, irritability, depression, dementia, and convulsions [32].

Oral manifestations of a vitamin B6 deficiency typically involve the tongue. An initial sensation of burning of the tongue is followed by a reddening and hypertrophy of the filiform papilla. Pain and edema of the tongue may also develop. Angular cheilosis can also occur [11]. Diagnosis of a vitamin B6 deficiency cannot be made by based on the presence of systemic and/or oral manifestations alone. Dental patients with any such presentation should be referred for further evaluation.

Vitamin B7 (Biotin)

Biotin is essential for the metabolism of carbohydrates, fatty acids, and the amino acid leucine [1]. Deficiency is rare, as this nutrient is available in multiple food sources (e.g., organ meats, eggs, fish, meat, seeds, nuts, sweet potatoes) and generally occurs as a deficiency with the other B-complex vitamins. Oral and systemic manifestations can occur but are not diagnostic. Systemic manifestations of a biotin deficiency can include peripheral neuropathy, pallor, fatigue, elevated cholesterol, eczematous rash, depression, lethargy, hallucinations, and seizures [30]. Oral manifestations include pallor of the tongue and a segmented atrophy of the lingual papilla that resembles benign migratory glossitis, also known as geographic tongue. This pattern can be limited to the lateral borders of the tongue or can be generalized to include the entire dorsum [33]. The exact cause of benign migratory glossitis has not been identified, and this temporary pathologic state is usually self-resolving. In patients with biotin deficiency, loss of the lingual papilla will resolve when adequate biotin levels are achieved.

Vitamin B9 (Folic Acid or Folate)

Vitamin B9 is known as both folic acid (the synthetic form that is found in dietary supplements) and folate (the naturally occurring form found in foods). Vitamin B9 is required for the synthesis of several coenzymes involved in metabolic processes essential in the production of DNA and RNA, especially in cells and tissues that are dividing rapidly. It also works in concert with vitamin B12 in the formation of red blood cells (erythrocytes) and supporting the function of iron in the body [33]. A deficiency of vitamin B9 can have serious adverse systemic effects. Megaloblastic anemia, characterized by larger-than-normal erythrocytes, can develop secondary to vitamin B9 deficiency and can lead to peripheral neuropathy, gastroin-

testinal problems, lethargy, altered taste perception, weakness, decreased appetite, and weight loss [34]. A deficiency during pregnancy can lead to neural birth defects, most prominently spina bifida. Spina bifida can lead to lifelong problems, including paralysis, learning disabilities, depression, memory impairment, and urinary and bowel dysfunction [33].

Oral manifestations of vitamin B9 deficiency are the result of compromised DNA and RNA, which decreases the production of new cells. This can cause protracted surgical site healing and tissue surface ulcerations. Vitamin B9 is also important in the production of white blood cells, a major component of the immune system [19]. This immune system dysfunction can result in the development of opportunistic oral infections and periodontal disease.

Vitamin B12 (Cyanocobalamin)

Vitamin B12 serves as a coenzyme for fat and carbohydrate metabolism and protein synthesis and is integral component in the production of red blood cells. The absorption of vitamin B12 from the gastrointestinal tract requires that it binds to intrinsic factor, a substance produced by the parietal cells of the stomach mucosa. Vitamin B12 is absorbed in the distal small bowel (terminal ileum), and persons with disease of the terminal ileus (e.g., Crohn disease, Whipple disease, celiac disease) are at risk for malabsorption of vitamin B12 and other nutrients. The primary natural sources of dietary vitamin B12 are animal products, including fish and shellfish, beef, poultry, pork, eggs, and dairy products [2]. However, fortified cereals also usually contain 100% of the recommended daily value of vitamin B12. Strict vegetarians and particularly vegans (who consume no animal products) are at an increased risk of insufficient intake of vitamin B12, and these patients may benefit from vitamin B12-fortified foods, oral vitamin B12 supplements, or vitamin B12 injections [1].

The most severe systemic complication of vitamin B12 deficiency is pernicious anemia. It is characterized by a decrease in red blood cells resulting from impaired intestinal absorption of vitamin B12, caused by autoimmunity against intrinsic factor or gastric parietal cells (which produce intrinsic factor). Intrinsic factor is necessary for the absorption of vitamin B12, and decreased production of intrinsic factor leads to reduced absorption of vitamin B12 [33].

Oral manifestations of a vitamin B12 deficiency are variable and can include angular cheilosis, oral ulcerations, hemorrhagic gingivitis, and detachment of the periodontal fibers [35]. The tongue may be painful and eventually lose its filiform and fungiform papillae, which can distort the patient's sense of taste [11]. The tongue may also develop a glossy, red surface that is prone to ulceration and can be very sensitive to temperature extremes and spicy foods. If these signs and symptoms are noted in the course of providing dental care, the patient should be referred for prompt medical evaluation.

Vitamin C (Ascorbic Acid)

Among all of the vitamins discussed in this course, the history of vitamin C is perhaps the most interesting. In the 18th century, scurvy was excessively common among sailors of the British Navy [1]. Scurvy is a disease caused by a vitamin C deficiency, with symptoms that include connective tissue defects (including gingivitis, loosening of teeth, rashes, internal bleeding, delayed wound healing), dermatitis, depression, and fatigue. Limes were found to be protective against scurvy, and in 1933, vitamin C was identified as the substance responsible for this action.

Vitamin C is involved in the synthesis of collagen, hormones, and amino acids. It is critical for the synthesis of connective tissues and for iron absorption and storage [19]. Vitamin C deficiency can have profound adverse effects on oral health, as it can impair collagen production and quality. A deficiency often firsts manifests as edematous, hemorrhagic, and painful gingival tissues [12].

The strength and resilience of the gingival tissues and the oral mucosa are impaired with a decreased production of collagen. These tissues are more prone to injury and take longer to heal after a traumatic incident or invasive dental procedure. Collagen deficiency can also impair the structure of the oral mucosa and its ability to support partial or complete dentures. The periodontal ligament and alveolar bone may display decreased ability to support the teeth in their sockets, leading to an increase in mobility and tooth loss.

Further compromise of the oral structure may occur as the intercellular cement in the connective tissues bone and dentin become defective [36]. Capillary integrity is weakened and vascular permeability is increased, with extravasation of blood into the interstitial hard and soft tissues. The lining of the gingival sulcular epithelium is also weakened; this compromises the epithelial attachment and results in apical migration of the periodontal attachment, a deepened periodontal pocket, and tooth loss [10].

Vitamin C deficiency during pregnancy or during childhood or adolescence may cause atrophy of the ameloblasts and odontobalsts [37]. The age at which the deficiency occurs and the duration of the deficiency will determine the degree of enamel and dentin malformation and the impact on oral health. The enamel of deciduous teeth is relatively thin, and any malformation of this layer can increase the potential for rapidly advancing caries. Although the enamel of permanent teeth is proportionately much thicker, malformation nonetheless increases the potential for plaque retention, caries, and periodontal disease.

MINERALS

Minerals are inorganic compounds found in nature that combine with other elements and organic compounds to contribute to a myriad of physiologic reactions. These substances are not a direct source of energy but are incorporated into various structures and tissues that sustain life.

Most minerals exist in their ionized form in the interstitial fluids and are bound to organic compounds to form hormones, proteins, and phospholipids. The body requires moderate amounts of 7 minerals and trace amounts of about 12 others. This section will discuss the minerals that have the most direct impact on oral health without regard to their relative amounts within the body.

Fluorine (Fluoride)

Fluoride is the ionized form of fluorine and is the mineral most associated with oral health and the reduction of carious lesions in children and adults. The Centers for Disease Control and Prevention (CDC) has named community water fluoridation one of the 10 great public health achievements of the 20th century, given the substantial decline in carious lesions since the program began in 1962 [38]. Today, approximately 75% of people in the United States are served by fluoridated community water systems [38].

Fluoride exerts an anticaries effect by forming fluoroapatite and inhibiting bacterial growth and adhesion, thereby strengthening enamel and cementum [12]. Developing teeth incorporate fluoride via foods, fluoride supplements, and water absorbed from the gastrointestinal tract. However, ingested fluorides are no longer useful after the development of the teeth is complete (usually by the middle to late teenage years) [39]. At this stage, the benefits of fluoride are limited to topical application via dentifrices, gels/pastes, varnishes, and mouth rinses [40]. Residual fluoride in the saliva and the dental plaque decrease the risk of caries by encouraging the remineralization of tooth surfaces [41]. Some restorative materials (e.g., glass ionomers) contain fluoride and release it slowly, thus decreasing the potential for recurrent caries at the tooth-restoration junction [42]. The benefits of fluoride are balanced by the potential risks [41].

There are levels at which chronic fluoride ingestion can be associated with adverse effects. The maximum allowable concentration of fluoride in community water systems, also known as the maximum contaminant level (MCL), is 4.0 mg/liter [43]. This

level is nearly six times the recommended level for community water systems. Ingestion of fluoride at the MCL for a long period of time can lead to the development of dental and skeletal fluorosis [44]. The most common adverse effect associated with the long-term ingestion of fluoride in excess of 2 mg/liter is dental fluorosis [45]. Mild forms of dental fluorosis feature small white spots or streaks in the dental enamel (i.e., mottled enamel). Severe forms of dental fluorosis feature brown or black pits in the enamel. These are not carious lesions but may require composite restorations, as surface pitting will enhance the retention of plaque and increase the potential for the development of caries. In more severe cases, all the enamel may be damaged [46]. A study published by the Centers for Disease Control and Prevention found that approximately 23% of the U.S. population between 6 and 49 years of age had some form of dental fluorosis; 16.0% had very mild fluorosis, 4.8% had mild fluorosis, 2.0% had moderate fluorosis, and less than 1% had severe fluorosis [47]. An additional 16.5% were classified as having questionable or possible dental fluorosis. This same study found that the rates of dental fluorosis among adolescents (12 to 15 years of age) significantly increased between 1986–1987 and 1999–2004. Skeletal fluorosis is characterized by pain and stiffness in major joints and an increased risk for fractures. This condition is extremely rare in the United States.

EVIDENCE-BASED PRACTICE RECOMMENDATION

The U.S. Preventive Services Task Force recommends people at risk of developing dental caries receive 2.26% fluoride varnish or 1.23% fluoride (acidulated phosphate fluoride) gel, or a prescription-strength, home-use 0.5% fluoride gel or paste or 0.09% fluoride mouthrinse for those 6 years of age or older.

(https://ebd.ada.org/en/evidence/guidelines/topical-fluoride. Last accessed October 19, 2020.)

Strength of Recommendation: In Favor (for patients 6 to 18 years of age)/Expert Opinion For (for patients older than 18 years of age)

Calcium

Calcium is the most abundant mineral in the human body and accounts for about 40% of its mineral composition; approximately 99% of this calcium is sequestered in the bones and teeth [1]. Calcium plays a role in the formation of teeth and bone, muscle contraction, coagulation, cardiac rhythm maintenance, and enzyme reactions.

Calcium metabolism is under hormonal control; parathyroid hormone raises serum calcium levels while calcitonin lowers levels. Approximately 65% of bone mass is inorganic hydroxyapatites (mineral salts), most of which is composed of highly condensed calcium phosphate crystals [2]. The enamel layer of teeth consists of a 96% inorganic matrix, with about 25% of this matrix composed of calcium [48]. Ameloblasts release both calcium and phosphate, so deficiencies in calcium during tooth development stages (including in utero) can cause incomplete tooth calcification, dental malformation, and increased caries risk after tooth eruption [10].

Calcium deficiency can decrease the density of alveolar bone, compromising its ability to support and retain teeth. Patients with nutritional deficiencies of calcium and vitamin D also are at increased risk of osteoporosis. When the extraskeletal calcium level is inadequate, bone tissues are resorbed in an attempt to maintain equilibrium. To prevent excessive skeletal calcium loss, an adequate amount of calcium, as well as vitamin D, must be ingested.

Men 50 to 70 years of age should obtain at least 1,000 mg/day of elemental calcium; women 51 years of age and older and men 71 years of age and older require 1,200 mg/day of elemental calcium [49]. National nutrition surveys have revealed that many individuals in the United States consume less than half of the recommended daily amount of calcium in their diet [49]. Dietary supplements may be necessary. Intakes in excess of 1,200–1,500 mg per day provide limited benefit and may increase the risk of developing kidney stones or cardiovascular disease [49]. The upper safe limit for total calcium intake is 2,500 mg/day [50; 51].

Calcium supplements are especially necessary in more fragile, older patients; however, the problem of reduced calcium absorption is more acute in older persons. This may be overcome by increasing overall calcium intake and maintaining adequate levels of vitamin D [50]. The best way to increase calcium intake is through diet (e.g., consumption of dairy products), because supplements are not always absorbed well. To increase absorption, supplements should be taken with meals [50]. For patients on acid-reducing medications, calcium citrate should be used because calcium carbonate requires an acidic environment.

While calcium deficiencies can cause problems with oral and systemic health, the use of supplements is not without adverse consequences. Calcium supplements can decrease the absorption of iron, zinc, and magnesium, deficiencies of which can lead to renal insufficiency, neuropsychiatric problems, and xerostomia [22].

Zinc

Zinc is an essential trace mineral that serves as a cofactor in many enzyme-controlled processes, functions as an antioxidant, and reduces bacterial toxins [12]. Zinc is necessary for new tissue formation and immune system (particularly antibody) function, actions that are essential to the prevention of oral infections and periodontal disease [10]. Zinc has been added to oral health products to help control plaque and calculus formation and to reduce halitosis. It has the ability to persist for several hours in the saliva and plaque. Low levels of zinc are anticariogenic, as it can inhibit enamel demineralization and promote remineralization [52]. Zinc deficiencies can cause prolonged healing of surgical sites, delayed replenishment of the gingival and mucosal surface layers, and compromised immune function.

Concern about zinc levels has generally focused on systemic complications from excessive ingestion rather than a deficiency. Aside from nutritional supplements, the most common source of excess zinc is denture adhesive pastes, powders, or pads. Many patients who use partial or complete dentures use an adhesive to provide additional retention for eating and speaking. While properly fabricated prostheses should require no or little adhesive, over time the mucosa and underlying bone atrophy, which can compromise retention and function. Ideally, the existing prostheses should be relined or replaced to reflect the patient's current oral topography. However, the cost can be prohibitive for some, leading to a reliance on adhesive. The cumulative ingestion of zinc from denture adhesives and dietary sources can result in a systemic excess, with the competitive inhibition of copper absorption the primary concern. Zinc and copper use similar metabolic pathways for absorption from the gastrointestinal tract. Therefore, an increase in zinc in the digestive tract will decrease the amount of copper absorbed; when this is sustained, a copper deficiency (hypocupremia) can develop [53]. Symptoms of hypocupremia develop gradually and can include anemia, gait and balance problems, and paresthesias in the extremities [54]. Patients with excessive zinc are often older and may attribute these issues to conditions common with aging. It is therefore essential for dental professionals to educate their patients about the potential systemic complications of sustained ingestion of zinc-containing denture adhesives. Zinc-free denture adhesives have been developed and are the preferred formulations, when possible.

Phosphorus

Phosphorus is the second most abundant mineral in the body, and approximately 85% of phosphorus is located in bone [1]. It is found in smaller amounts in tissues throughout the body and is a major component of ATP. It is essential for bone and tooth formation, maintenance of the body's acid-base balance (necessary for RNA and DNA synthesis),

and for energy production and storage. Phosphate is the common inorganic form of phosphorus and consists of one phosphorus atom bonded with four oxygen atoms. This negatively charged ion (anion) is capable of bonding with a positively charged ion (cation), such as calcium.

Calcium phosphate is a major constituent of both teeth and bone, so phosphorus deficiency during dental development can adversely affect the formation of the inorganic matrices of both enamel and dentin. Malformation of the enamel surface can predispose it to the retention of plaque and the associated increased potential caries and periodontal disease. This effect of phosphorus deficiency ceases to be an issue after early adolescence, when dental development is complete [48].

Bone is dynamic tissue that undergoes changes throughout life. Phosphorus deficiency at any stage of life can interfere with the subtle but constant process of bone remodeling. The formation of new bone in the matrix of an extraction site can be compromised in patients with phosphorus deficiency. Similarly, the repair and the replacement of the alveolar bone that supports the teeth can be adversely affected.

Deficiencies of phosphorus are rare, as this mineral found in many foods, including dairy products, meats and poultry, fish, eggs, nuts, legumes, vegetables, and grains. However, conditions such as diabetes, malnutrition/anorexia, and alcohol use disorder can decrease phosphorus levels in the body. Certain gastrointestinal conditions, such as Crohn disease and celiac disease, can compromise a patient's ability to absorb phosphorus and other nutrients. Symptoms of a phosphorus deficiency are not pathognomonic but include anxiety, fragile bones, fatigue, irregular breathing, numbness, and weight change [55]. Referral to a physician is advisable when phosphorus deficiency is suspected.

DIGESTIVE DISORDERS

CELIAC DISEASE

Celiac disease is a global health concern, impacting 1% to 3% of the global population and requiring a multidisciplinary approach to care and treatment [56; 57]. Research estimates that as many as 1 in 133 Americans, or approximately 1% of the U.S. population, has celiac disease [58].

Celiac disease is defined as "an immune-mediated systemic disorder elicited by gluten and related prolamins in genetically susceptible individuals and characterized by the presence of a variable combination of gluten-dependent clinical manifestations and celiac disease-specific antibodies" [57]. Celiac disease, also known as gluten intolerance, gluten-sensitive enteropathy, nontropical sprue, and celiac sprue, is an immune-mediated response to gluten (e.g., wheat, rye, barley) in genetically predisposed individuals [59]. When an individual with celiac disease consumes gluten, it damages the small intestines and results in difficulty absorbing nutrients from foods. As previously noted, approximately 1 in 133 individuals in the United States (or about 1%) have celiac disease. The risk is greater (i.e., 1 in 22) in individuals with a first-degree relative with celiac disease [60].

Gluten is the general term used for storage proteins considered antigenic in celiac disease. Gluten is a complex macromolecule that is largely indigestible and, under normal circumstances, left partly unabsorbed by the gastrointestinal tract [61]. The gluten in wheat, rye, and barley is toxic to the intestinal epithelial cells of genetically susceptible individuals [62]. Specifically, the alcohol-soluble protein fraction (prolamins) of gliadin in wheat (secalin in rye, hordein in barley) is responsible for initiating the intestinal damage typical of celiac disease [63]. Exactly how gliadin is able to cross the intestinal epithelial barrier is not clear.

Celiac disease originates as a result of a combined action that involves both adaptive and innate immunity [61; 64]. Four presentations are recognized [61; 64]:

- Typical: gastrointestinal signs and symptoms
- Atypical (extraintestinal): Minimal or absent gastrointestinal signs/symptoms, but a number of other manifestations
- Silent: Damaged small intestinal mucosa and no symptoms, but disease can be detected by serology
- Latent: Individual possesses genetic compatibility and may show positive autoimmune serology but normal mucosa, with or without symptoms

A strict, lifelong gluten-free diet and supportive nutritional care (for iron, calcium, and vitamin deficiencies) is the only recommended treatment for celiac disease [65; 66; 67; 68]. Adherence to a gluten-free dietary pattern involves all foods containing or derived from wheat, barley, and rye. This may result in a diet that is low in carbohydrates, iron, folate, niacin, zinc, and fiber. Individuals with celiac disease often suffer from malabsorption and can develop vitamin and mineral deficiencies despite adequate intake. Age-specific gluten-free vitamin and mineral supplements are an important addition to the diets of persons with celiac disease [69]. Iron supplements are recommended for iron-deficiency anemia, and folic acid and vitamin B12 should be taken to avoid anemia due to folate or B12 deficiencies. Vitamin K is necessary for individuals with abnormal prothrombin times. Calcium and vitamin D supplements should be encouraged for individuals with low blood calcium levels or osteoporosis.

Although celiac disease is commonly associated with pathology of the small intestine, almost any body system can be affected, including the oral cavity. Oral manifestations will depend on the age of celiac disease onset. Children with celiac disease may exhibit delayed eruption of teeth, enamel hypoplasia defects in primary and permanent teeth, angular cheilitis, and recurrent aphthous stomatitis [11]. Defects caused by enamel hypoplasia are more common in the permanent dentition and are the result of malabsorption of calcium and immunologic factors associated with celiac disease [1]. Enamel defects occur in a chronologic and symmetrical fashion in each of the four quadrants, with the incisors and molars most often affected [18]. Delayed eruption of the primary teeth can cause problems with eating and the development of appropriate speech patterns. This may also become a cosmetic concern. Approaches to restoration of enamel defects in the primary dentition are commensurate with the degree of malformation. The enamel layer of primary teeth is thin, and even small defects in enamel formation can expose the underlying dentin and cause sensitivity. Restorative options include conservative composite restorations for small-to-moderate defects but may require polycarbonate crowns for anterior teeth and stainless steel crowns for posterior teeth when larger defects involve the incisal edges of posterior teeth and the occlusal surfaces of posterior teeth. Enamel formation defects in the permanent teeth of patients with celiac disease vary. The surfaces of these teeth may be intact but discolored with white, opaque, brown, or yellow spots. Surface pitting of the enamel can vary in depth and distribution. Larger surface irregularities predispose the patients to staining and the retention of bacterial plaque. This usually requires composite restoration to achieve an optimal enamel surface contour. Cosmetic bleaching, porcelain veneers, and all-ceramic crowns are options for teeth with moderate-to-severe staining and/or extensive pitting.

Children with celiac disease who have problems with the delayed eruption of primary and/or permanent teeth may require the dual care of a pedodontist or an orthodontist. While there are no specific contraindications for dental treatment in patients with celiac disease, the malabsorption of nutrients can affect dental care decisions, as discussed. Consultation with the patient's physician may be required prior to dental treatment if

the patient with has nutritional deficiencies that impact systemic health and compromise his/her ability to withstand dental treatment.

CROHN DISEASE

Inflammatory bowel disease is a broad term that describes conditions characterized by chronic inflammation of the gastrointestinal tract. The two most common inflammatory bowel diseases are ulcerative colitis and Crohn disease. Inflammation affects the entire digestive tract (including the oral cavity) in Crohn disease and only the colon in ulcerative colitis. In 2015, an estimated 3 million adults in the United States reported being diagnosed with either Crohn disease or ulcerative colitis [70].

Although Crohn disease can involve any portion of the lining mucosa and submucosa of the gastrointestinal tract, the distal portion of the small intestine, the ileum, the proximal colon, and the rectum are most often involved. Systemic signs and symptoms include diarrhea, fatigue, weight loss, and generalized abdominal pain. Diagnosis of Crohn disease is made by colonoscopy, ileoscopy, and biopsy at the junction of the ileum and colon.

The initial signs of Crohn disease can include specific and nonspecific oral manifestations. Oral changes that are considered specific and pathognomonic of Crohn disease include mucosal tags (similar to skin tags), "cobblestoning" of the buccal mucosa, deep linear ulcerations, and oral granulomatosis (mainly affecting the lips). Nonspecific changes can include xerostomia, aphthous stomatitis, mucogingivitis, and inflammation of the salivary glands and ducts [21].

There is no cure for Crohn disease; however, there are typically sporadic periods of remission. Medical treatment typically involves the use of medications to control inflammation and to suppress the immune response. Surgical treatment may be needed when gastrointestinal inflammation is not controlled by pharmacotherapy and can include partial or total removal of the affected area of the colon.

Medications prescribed to treat Crohn disease can have effects on the oral tissues or may interact with medications used in the provision of dental care. Azathioprine and mercaptopurine (also known as 6-mercaptopurine) were the first two immunosuppressive agents widely used to treat Crohn disease. Both medications can cause a drug-induced thrombocytopenia (i.e., low platelet count), which can lead to significant bleeding during and after oral or periodontal surgery and root planing and curettage. Methotrexate, another immunosuppressant drug, can cause ulcerative stomatitis, gingivitis, glossitis, and mucositis. These side effects usually appear within three to seven days and resolve within two weeks [22]. When a nonsteroidal anti-inflammatory drug (NSAID) is used to control pain associated with dental treatment concurrent with methotrexate, severe bone marrow suppression can occur, with a subsequent significant decrease of erythrocytes, leukocytes, and the platelets [12]. Decreased production and circulation of erythrocytes impairs oxygenation of all body tissues. Fatigue and pallor of the skin and mucosa ensue when the metabolic demands exceed the oxygen supply which is available. Decreased leukocyte production is associated with impaired immunity. In addition, decreased production of platelets compromises a patient's ability to attain hemostasis during and after invasive dental treatment. If possible, NSAIDs should be avoided in patients currently taking methotrexate. A complete blood count with differential should be ordered if there is any concern regarding a potential interaction.

The optimal time for dental treatment for patients with Crohn disease is during periods of remission, although their occurrence and the duration are not predictable. It is important to tailor treatment to the unique oral and physical condition of the patient. Dental professionals should appreciate that acute exacerbations of Crohn disease can occur without warning and may require the patient to cancel an appointment at the last minute.

BARIATRIC SURGERY: ORAL HEALTH IMPLICATIONS

Obesity is a well-recognized problem in the United States, affecting 39.8% of adults and 18.5% of youth [70]. Health problems related to obesity, including diabetes, heart disease, arthritis, and certain cancers, produce significant disability. More than 100,000 deaths each year are directly related to obesity [71]. Many of the health problems related to obesity can be ameliorated or eliminated with weight loss and exercise. Because weight loss through diet and exercise is difficult and studies suggest that obese patients tend to regain lost weight, interest in bariatric (weight-loss) surgery has been increasing. In spite of its well-established benefits, however, bariatric surgery is not without risk.

According to a statistical report from the Agency for Healthcare Research and Quality (AHRQ), the annual number of bariatric surgeries in the United States increased from 13,386 to 121,055 between 1998 and 2004, a change of more than 800% [72]. According to the American Society for Metabolic and Bariatric Surgery (ASMBS), the number of bariatric surgeries performed in the United States increased from 158,000 in 2011 to 216,000 in 2016, an increase of 27%, with the biggest jump occurring between 2015 and 2016 [73].

Weight loss and metabolic outcomes after bariatric surgery are of similar magnitude in men and women; however, women continue to undergo bariatric surgery more often than men, comprising more than 80% of procedures [74; 75; 76]. Bariatric surgery is a general term for surgical procedures that alter the digestive tract to promote weight loss. The surgery may reduce the size of the stomach or portion off a small area, reconfigure the small intestine, or comprise a combination of such alterations. Procedures that change the size of the stomach are called "restrictive." Those that reconfigure the intestine are "malabsorptive."

By reducing the area of stomach available to hold ingested food, restrictive surgeries decrease the amount of solid food that a person can comfortably eat and promote a sense of satiety. When the stomach outlet is reduced in diameter, these surgeries also slow the flow of ingested nutrients, helping patients to feel full longer. Malabsorptive surgeries reduce the area of the small intestine available to absorb nutrients. Weight-loss surgeries most commonly used in the United States are the laparoscopic sleeve gastrectomy (LSG), or "sleeve," and Roux-en-Y gastric bypass (RYGB), surpassing the historically popular laparoscopic adjustable gastric band (LAGB), or "band." RYGB is a mixed restrictive/malabsorptive procedure, while LSG and LAGB are purely restrictive. Based on data from the University HealthSystem Consortium Clinical Database, gastric bypass made up 66% of bariatric surgeries performed at academic medical centers in 2007, while LAGB accounted for 23% [77]. By 2016, LSG had become the leading procedure performed, accounting for 58.1% of bariatric surgeries, compared with 17.8% in 2011 [73]. In 2016, RYGB comprised 18.7% and LAGB made up only 3.4% [73; 98].

The American College of Physicians recommends considering surgery as an option for patients with body mass index (BMI) of 40 or greater who have obesity-related conditions, such as diabetes, impaired glucose tolerance, hypertension, hyperlipidemia, or obstructive sleep apnea. Patients should have tried and failed "an adequate exercise and diet program," with or without drug treatment [78].

In 2019, the American Association of Clinical Endocrinologists, the Obesity Society, the American Society for Metabolic and Bariatric Surgery (ASMBS), the Obesity Medicine Association, and the American Society of Anesthesiologists released updated guidelines for the perioperative care of the bariatric surgery patient [79; 80; 81; 98]. Their selection criteria include BMI greater than 40 if no comorbidities are present, greater than 35 if there is one or more obesity-associated comorbidity, or greater than 30 with diabetes or metabolic syndrome [80; 81; 98].

NUTRIENT DEFICIENCIES

Vitamin and mineral deficiencies may occur after any bariatric procedure if the patient's diet does not supply adequate nutrition. Due to the altered configuration of the small intestine, patients who undergo RYGB and other surgeries with a malabsorptive element, such as LSG, are particularly at risk of specific deficiencies. Folate, thiamine, riboflavin, niacin, pyridoxine, vitamin C, zinc, and copper are primarily absorbed in the duodenum and jejunum, and iron is primarily absorbed in the duodenum [82]. After RYGB, ingested food does not pass through the duodenum and bypasses a portion of jejunum as well.

Anemia is a common problem following any type of bariatric surgery. In the case of RYGB, direct malabsorption due to lack of contact with the duodenum may be a contributing factor, and other malabsorption surgeries may produce low or absent secretion of gastric acid required to convert iron to its absorbable form. Overall decrease in food intake, combined with a common intolerance of red meat, may also contribute to deficiency [83]. Giving iron with vitamin C can help to provide the acidic environment needed for absorption [84].

Anemia may also be due to deficiencies in vitamin B12 [85; 86]. Although vitamin B12 is absorbed primarily in the ileum, which is intact following many surgeries, decreased gastric acid, decreased exposure to intrinsic factor, and other changes in the digestive process may all contribute to malabsorption [82]. Additional contributors to anemia may include deficiencies in copper, folate, and other vitamins absorbed in the upper portion of the small intestine [86; 87].

Folate deficiency appears to be particularly common in patients who have undergone bariatric surgery, occurring in up to 65% of patients [86]. In addition to reduced absorption, low levels of vitamin B12 may contribute to low folate levels. However, the actual role of surgery in causing folate deficiency is not clear.

Symptomatic thiamine deficiency after bariatric surgery is not usual, but cases of Wernicke-Korsakoff syndrome, a degenerative brain disorder, after both malabsorptive and restrictive procedures have occurred [86]. Patients who have unresolved nausea and vomiting may be particularly at risk.

Vitamin D is absorbed in the ileum and jejunum, suggesting that deficiency of this nutrient would not be severe following RYGB. However, studies of vitamin D deficiency before and after bariatric surgery suggest that suboptimal levels of vitamin D are quite common even before surgery. The ASMBS estimates that as many as 90% of obese patients may have low levels of vitamin D preoperatively [86]. In addition, the ASMBS estimates that up to 100% of post-bariatric surgery patients have a vitamin D deficiency [86].

Calcium is primarily absorbed in the duodenum and proximal jejunum. Low calcium intake and low levels of vitamin D can both contribute to deficiency in whole-body calcium, leading to the many oral, skeletal, and systemic effects [86]. For calcium supplementation, calcium citrate, which does not require high acidity for absorption, may be a better choice than calcium carbonate, particularly in RYGB and LSG patients and others with reduced gastric acid.

Zinc and copper are both absorbed in the duodenum and proximal jejunum. In surgeries in which these structures are bypassed, deficiency is common. In order to address these and other possible deficiencies, it is recommended that postsurgery patients take a high-potency multivitamin/mineral supplement, B12, vitamin D, calcium, iron, and an optional B complex [86]. Supplements for fat-soluble vitamins (A, E, and K), zinc, and copper should also be taken, with the dose dependent on the type of bariatric procedure [86].

Anatomic changes are likely not the only cause of nutritional deficiencies after bariatric surgery. Purely restrictive surgeries, while once thought not to be associated with nutritional deficiencies, may in fact lead to deficiencies due to poor diet and food intolerance. Protein deficiency has been suggested as a concern following bariatric surgery due to malabsorption and/or reduced caloric intake and possible food intolerances. However, protein deficiency does not appear to be common following bariatric surgery, except perhaps in patients whose diets are very low in protein. It may be more of a problem in patients who undergo more significantly malabsorptive procedures.

ORAL EFFECTS

The oral side effects of bariatric surgery vary among patients. As with all patients, oral hygiene habits and adherence to routine dental prophylaxis appointments should be stressed. Aside from nutritional deficiencies, patients may develop gastroesophageal reflux disease (GERD) and chronic vomiting.

GERD has been defined as having troublesome symptoms, impaired quality of life, and/or mucosal damage or complications resulting from reflux of gastric fluid into the esophagus, oropharynx, and/or respiratory tract. Certain bariatric surgery techniques (specifically LAGB and laparoscopic sleeve gastrectomy) are consistently associated with new-onset reflux in patients who did not have GERD prior to surgery or worsening GERD symptoms when reflux is already present. These approaches are not recommended in obese patients with GERD as a first-line option [88; 89].

When gastric contents are introduced into the oral cavity, either due to GERD or vomiting/regurgitation, it has an erosive effect on the teeth. The repeated exposure of the oral mucosa to acidic gastric contents can also result in the development of oral ulcerations, damaged salivary glands, and trauma.

Dietary patterns following bariatric surgery are often characterized by frequent small meals, to adapt to the altered digestive system. It may be difficult for these patients to maintain adequate oral hygiene with necessary increased frequency, which can increase the risk for caries [33].

There have been conflicting studies about the influence of bariatric surgery on periodontal health [35]. However, the potential for adverse oral effects post-surgically should be explored. Patients may be required to adhere to stricter oral hygiene protocols to mitigate these adverse effects.

EATING DISORDERS AND DENTAL HEALTH

Few behavioral or psychologic problems have as direct an adverse effect on nutrition, the teeth, and the oral mucosa as anorexia nervosa and bulimia nervosa. There are classic oral manifestations of these eating disorders that members of the dental staff may discover during the course of routine dental treatment.

The exact etiology of eating disorders is unknown, but a combination of genetic, hormonal, societal, cultural, and attitudinal factors are believed to be involved. Images in mass media that promote a thin body as a vehicle to success and happiness have been implicated in altering a person's perception of his or her appearance [90].

ANOREXIA NERVOSA

Patients with anorexia nervosa have an extreme obsession with their body weight and the restriction of food intake. Women comprise 90% to 95% of anorexia cases, and it is estimated that 1% of all women suffer from anorexia in their lifetime, with the onset usually occurring during the adolescent years [91; 92]. Anorexic patients often view themselves as overweight even though most are 15% or more below ideal weight.

Patients with anorexia go to extreme measures to lose weight and prevent weight gain. The most common mechanism is restricting or halting eating. Other patients may exercise excessively. Some anorexic patients will use laxatives, enemas, or self-induced vomiting as a supplemental means to control their weight. These behaviors can lead to severe acute and chronic medical problems. Patients may appear emaciated but refuse to acknowledge the serious nature of the problem and do not consider the potential medical consequences of the disease.

Women who are anorexic often have irregular menstrual cycles. The skin can become dry and thin and at greater risk for traumatic injury. The restriction of caloric intake can stunt the physical and mental development of children and adolescents, and cognitive damage is possible in all patients. Problems with the cardiovascular system, including hypotension, bradycardia, and cardiac arrhythmias, are very common. Self-induced vomiting and use of laxatives can cause a severe disturbance in the body's mineral and electrolyte balance, and a drastic reduction of the minerals potassium, sodium, and calcium can interfere with the conduction of nerve impulses and the contraction of smooth, skeletal, and cardiac muscle. Failure of multiple organs and systems can lead to death. As part of the disease process, repeated episodes of self-induced vomiting can cause ulceration of the esophageal lining, with the subsequent development of esophageal varicosities and bleeding. Oral effects are generally limited to those caused by extreme starvation and malnutrition.

BULIMIA NERVOSA

Patients with bulimia nervosa tend to lack the emaciated appearance of patients with anorexia nervosa; their body weight and appearance often appear normal. Bulimia nervosa features recurrent binge eating, in which a large quantity of food is consumed in a short time, followed by purging (e.g., self-induced vomiting, use of diuretics, laxatives, or enemas) to compensate for the excessive overeating. During binging episodes, the bulimic patient experiences a loss of control over the quantity and variety of food consumed [93]. The practice of binge eating and purging must continue at least twice a week for three months for a diagnosis of bulimia nervosa to be made [94].

The teeth and the oral mucosa of bulimic patients can undergo damage as the recurrent regurgitation of highly acidic gastric contents can induce pathologic change in both. In addition, the mucosa of the soft palate and the anterior pharyngeal area can be traumatized when fingers or objects are inserted to induce vomiting. Healing of these areas may be prolonged by the physical and chemical assault associated with this repetitious behavior. Ulcerated areas of the oral mucosa may lead to local or regional oral infections. The virulence of infections can be exacerbated when the altered nutritional status of these patients compromises their immune response.

Enamel is the hardest substance in the human body, but the repeated exposure to the hydrochloric acid in regurgitated gastric contents over an extended period of time can lead to a unique pattern of enamel erosion called perimylolysis. Perimylolysis features the loss of enamel on the lingual, occlusal, and incisal surfaces of the teeth. As opposed to attrition, which is the loss of enamel from repetitive tooth-to-tooth contact or abrasion via an external source (e.g., excessive or overly forceful tooth brushing), the gradual dissolution of the enamel matrix in patients with bulimia nervosa leaves a glossy, smooth surface, most commonly on the lingual surfaces of the maxillary anterior teeth [95]. Any lost enamel cannot be regenerated. The underlying matrix of dentin is then exposed; it will wear faster than enamel and is more prone to caries. While enamel is devoid of any neural element, dentin contains dentinal tubules whose odontoblastic processes can perceive thermal stimuli as a source of pain. This can cause patients to neglect oral hygiene and increase the risk of caries and periodontal disease. The irreversible loss of enamel will also cause a change in the occlusion, decreasing the vertical dimension of occlusion. The loss

of tooth structure requires that more complicated and expensive restorative options, such as crowns, be utilized. The loss of enamel support around composite or amalgam restorations can lead to their weakening and ultimate loss. The amount of time necessary for the enamel to be eroded in such fashion can range from six months to two years [96].

Some patients with eating disorders will be treated with antidepressant medications, which can decrease salivary flow and result in xerostomia. The reduction of salivary flow and its lubricating and self-cleansing action for the teeth increases plaque retention and causes a subsequent increased risk in the development of caries and periodontal disease.

The parotid, sublingual, and/or submandibular glands of bulimic patients can experience a unilateral or bilateral enlargement during the progression of the disease, often referred to as "chipmunk facies." The exact etiology of enlargement in the glandular secreting elements (acini) is unknown, although various hypotheses include increased likelihood of infection, increased oral flora, hypersecretion, duct obstruction, or extended trauma. In chronic cases, the hypertrophy is irreversible [97].

The treatment of patients with eating disorders involves physicians, nutritionists, psychologists, and mental health counselors. The acknowledgement of an eating disorder can be the most difficult obstacle to overcome in the treatment of these patients. Because eating disorders can progress to debilitation and death, dental professionals who suspect that a patient may have a disorder should offer compassionate support and refer the patient for treatment.

CONCLUSION

The field of nutritional science is complex and constantly changing. The intent of this course has been to identify the role of nutrition in optimal oral health and to incorporate it as an essential component of the tenets of preventive dentistry. When nutrition is inadequate, the cellular renewal of the oral mucosa and the oral epithelium is compromised, wound healing is protracted, immune function is compromised, and systemic diseases can emerge and further exacerbate oral health issues.

Most dental professionals have limited training in the nutritional sciences and may not appreciate the impact that proper nutrition has on establishing and maintaining oral health. As the continuum between oral health and systemic health becomes more intertwined, dental professionals should consider nutrition an important component of optimal dental care.

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