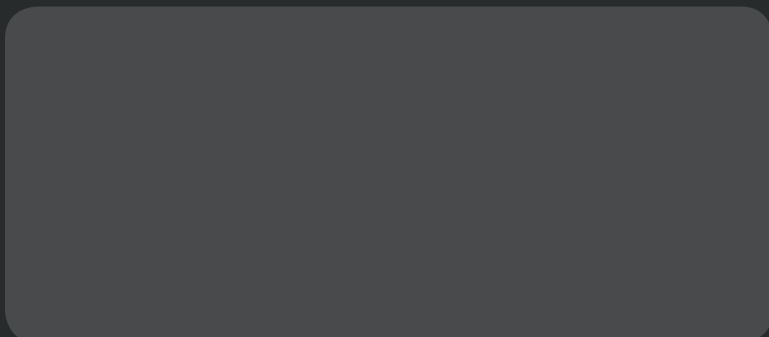




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Oral complications of celiac disease

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Oral complications of celiac disease

Abstract

Celiac disease (CD) is a serious autoimmune disorder that affects approximately one in 100 people worldwide. Ingestion of gluten—a mixture of proteins found in cereal grains, particularly wheat—causes damage to the small intestine of those with the disease. Left untreated, celiac disease can lead to other autoimmune disorders. In addition, celiac disease has oral manifestations, including enamel defects, increased caries, aphthous ulcers, delayed dental development, and cancers of the mouth, esophagus, and pharynx. Dental professionals need to be aware of the oral symptoms of this disease in order to make appropriate recommendations and possible referrals for diagnosis.

Educational Objectives

At the conclusion of this educational activity, participants will achieve the following:

- Describe the systemic and oral effects of celiac disease
- Identify products that are safe in clinical and home use for celiac patients
- Become aware of possible new treatments for celiac disease
- Refer patients for diagnosis if celiac disease is suspected



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What is celiac disease?

Celiac disease is an autoimmune disease in which genetically predisposed individuals cannot tolerate the ingestion of gluten. Gluten, a protein found in wheat, rye, and barley, causes damage to the villi—small, fingerlike projections that line the wall of the small intestine—of celiac patients.¹ Damage to the villi prevents the small intestine from absorbing nutrients properly.¹ This in turn can lead to many other health issues, both systemic and oral.¹

Celiac disease is hereditary. People who have a first-degree relative with celiac have a one in 10 chance of also having the disease.¹ First-degree relatives include parents, siblings, and children.¹

At present, the only treatment for celiac disease is lifelong adherence to a strict gluten-free diet. However, new treatments and ways to prevent celiac damage are being studied.

Patients with celiac disease often have more than one autoimmune condition. Table 1 demonstrates how early diagnosis helps prevent further autoimmune diseases.¹ Table 2 lists the prevalence of associated conditions in celiac patients.¹

What is gluten?

Gluten is “a tenacious elastic protein substance especially of wheat flour that gives cohesiveness to dough”²—the “glue” that holds food together. It is most commonly found in wheat but is also found in barley and rye.³ Some common foods that contain gluten are breads, baked goods, soups, pasta, cereals, salad dressings, malt, food coloring, sauces, gravies, and beer.³ It can also be found in some less obvious places such as processed meats, potato chips, restaurant scrambled eggs and omelets, vegetarian meat alternatives, pickles, and bouillon cubes,^{4,5} as well as nonfood sources,

such as supplements and vitamins, lipstick and other beauty products, drugs, and possibly even dental products.⁶

Prevalence of celiac disease

A 2012 study by Rubio-Tapia et al. estimates the prevalence of celiac disease in the United States to be similar to that of several European countries, about one in 141, or 0.71%.⁷ However, the study concluded that the majority of celiac cases are undiagnosed, so the number could actually be higher. This study also concluded that celiac disease was rare among minority groups.

A 2016 study by Lebwohl stated that the overall prevalence of CD in the United States was 0.79%.⁸ According to the author, “The prevalence was highest in non-Hispanic whites (1.08%) and was much lower in Mexican-Americans (0.23%), other Hispanics (0.38%), and non-Hispanic blacks (0.22%).”⁸

According to a 2009 study by Rubio-Tapia et al., “The prevalence of CD appears to have increased dramatically in the United States during the past 50 years. [. . .] This study suggests that the prevalence of CD has dramatically increased more than fourfold in the United States during the past 50 years,

consistent with the finding in a recent study from Europe. Reasons for the increased prevalence of CD over time are unknown. However, because human genetic changes in response to environmental challenges are extremely slow, the most likely explanation may be environmental, such as a change in quantity, quality, or processing of cereal. Several major changes in wheat genetics, bread processing, and enzymatic modification of wheat prolamins as a result of industry food processing have occurred in the past 40 years. Changing patterns of early childhood infection may also affect the prevalence of autoimmune diseases (‘hygiene hypothesis’), but the host immune system-microbial interactions are complex and some infections (i.e., rotavirus) may increase the risk of CD autoimmunity in genetically predisposed children. The hygiene hypothesis is likely only a partial explanation for the increasing prevalence because CD is a global health problem that affects both developed and developing countries.”⁹ This study also concluded that undiagnosed celiac disease increased the risk of death nearly fourfold.

The Celiac Disease Foundation puts the number of celiac cases at one in 100 worldwide.¹ The CDF estimates the number of undiagnosed celiac cases in America to be 2.5 million. These undiagnosed people are at serious risk of long-term health problems.¹

Systemic symptoms of celiac disease

Celiac disease causes damage to the small intestine, which can lead to improper absorption of nutrients. There are more than 200 known symptoms. Celiac disease has been called the “clinical chameleon” because of its many symptoms and its diverse presentations in different people.¹⁰

The following are some common symptoms¹¹:

- Abdominal bloating and pain
- Chronic diarrhea
- Constipation
- Weight loss
- Fatigue
- Attention-deficit hyperactivity disorder (ADHD)
- Unexplained iron-deficiency anemia
- Depression
- Anxiety
- Vomiting

TABLE 2: Autoimmune and other conditions associated with celiac disease.¹

Associated condition	Prevalence in celiac disease population
Anemia	12%–69%
Autoimmune hepatitis	2%
Autoimmune thyroid disease	26%
Chronic fatigue syndrome	2%
Dermatitis herpetiformis	25%
Down syndrome	12%
Gluten ataxia	10%–12%
Idiopathic dilated cardiomyopathy	5.7%
Juvenile idiopathic arthritis	1.5%–6.6%
Liver disease	10%
Lymphocytic colitis	15%–27%
Microscopic colitis	4%
Peripheral neuropathy	10%–12%
Primary biliary cirrhosis	3%
Sjogren’s syndrome	3%
Type 1 diabetes	8%–10%
Unexplained infertility	12%

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TABLE 1: Early diagnosis lowers chance for developing another condition.¹

Age of diagnosis	Chance of developing another autoimmune condition
2–4 years	10.5%
4–12 years	16.7%
12–20 years	27%
20-plus years	34%

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- Infertility
- Joint pain

Oral symptoms of celiac disease

Patients who have celiac disease may present with any of the following oral manifestations.

ENAMEL DEFECTS

The etiology of enamel defects in celiac patients is not clearly understood but may be due to hypocalcemia due to malabsorption of nutrients. Other possible etiologies are an autoimmune response against ameloblasts and vitamins A and D deficiency.¹² One study found enamel defects in 55% of celiac patients.¹³ Enamel defects included color; rough surfaces with horizontal grooves and pits; changes in tooth shape; sharp, pointed cusp tips; and unevenly thin and rough incisal edges.¹²

DELAYED DENTAL DEVELOPMENT

Children with undiagnosed celiac disease may have delayed loss of deciduous teeth and delayed eruption of permanent teeth.¹⁴

RECURRENT APHTHOUS STOMATITIS (RAS)

A study by Bramanti et al. concluded that RAS was found in 62% of pediatric celiac patients.¹⁰ The same study found that RAS was found more frequently in patients with “silent” celiac disease (i.e., those who did not report any gastrointestinal symptoms before the diagnosis of celiac disease). Strict avoidance of gluten helps lessen the severity of RAS. It may be advisable for dental health-care workers to refer patients with a history of recurrent aphthous ulcers for a celiac evaluation.

DENTAL CARIES

According to the Celiac Disease Foundation, children with celiac disease have a higher incidence of dental caries. The foundation states, “Electron microscopy of the primary teeth (baby teeth) of celiac disease patients shows a structural change as compared to patients without celiac disease. Additionally, chemical analysis of primary teeth of celiac disease patients shows a decrease in the calcium-phosphorus ratio, which could explain the incorporation of calcium in the tissue structure, making it more soluble.”¹⁴

A study by Avşar and Kalayci also found an increased incidence in children with celiac disease.¹⁵ Their study “clearly showed that children with CD were at an increased risk of dental enamel defects compared with healthy subjects. Enamel defects were associated with an increased caries incidence.”¹⁵ Another study, however, stated that the risk of having dental caries was not higher in celiac patients.¹⁶

BURNING SENSATION OF THE TONGUE

Sensations of burning, tingling, pain, or numbness occur in 14% of celiac patients.¹² This may be due to problems with absorption of vitamin B-12, folate, and iron.¹⁴

INCREASED RISK OF CANCERS OF THE MOUTH, PHARYNX, AND ESOPHAGUS

There is an increased risk of developing cancers of the mouth, pharynx, and esophagus in celiac patients who do not adhere to a strict gluten-free diet.¹⁷ For those who adhere to a strict gluten-free diet for a minimum of five years, the risk is equal to that of nonceliac individuals.¹⁷

ANGULAR CHEILITIS

At the time of diagnosis, 50% of patients do not exhibit digestive symptoms. However, many of these individuals do exhibit oral symptoms, such as angular cheilitis and oral ulcerations.¹⁸ Dental health-care workers should consider the possibility of celiac disease in patients with angular cheilitis. A referral to the patient’s physician may lead to earlier diagnosis of celiac disease in these patients.

GEOGRAPHIC TONGUE AND ATROPHIC GLOSSITIS

Geographic tongue presents with a map-like appearance on the dorsal and lateral surfaces of the tongue. Atrophic glossitis causes the papillae of the tongue to shrink, creating a shiny red appearance. Both conditions may be signs of celiac disease.

Atrophic glossitis may be attributed to anemia and hematinic deficiencies, common in celiac patients. In an analysis of 128 celiac cases, 29.6% had a painful, burning sensation of the tongue, and 8.6% had erythema or atrophy of the tongue.¹⁸

DECREASED SECRETED PROTEINS

(E.G., AMYLASE IGG AND IGM) IN SALIVA

Although celiac disease does not alter the salivary flow rate, it does result in decreased protein secretions.¹⁴ Further research may provide celiac-specific, noninvasive salivary biomarkers for the disease.¹⁹

XEROSTOMIA

Up to 15% of patients with Sjögren’s syndrome also have celiac disease. It is unclear why these two autoimmune diseases often occur together; perhaps they share a common genetic cause, or perhaps gluten triggers both conditions.²⁰ Many celiac patients, with or without Sjögren’s syndrome, complain of dry mouth.

TOOTH WEAR

A study by Aguirre et al. concluded that “enamel defects were observed in 72 (52.5%) of the patients with celiac disease (52 patients had systematic defects) and in 22 (42.3%) of the control patients (9 patients had systematic defects).²¹ Systematic defects were significantly more common in the celiac disease group. In the patients with celiac disease, 72.2% were symmetrical, compared with 40.9% of the defects in the control patients. The incisors were the most frequently affected teeth, with the extent of involvement being significantly greater in the celiac group.”

ORAL LICHEN PLANUS

Oral lichen planus is a chronic inflammatory disease that can involve the buccal mucosa, gingiva, and tongue. Lichen planus may share the same autoimmune etiopathogenic mechanism as celiac disease.²² Oral lesions may appear as lacy white patches or swollen, painful, red patches.²³ There is an increased frequency of celiac disease in patients with oral lichen planus.²⁴

The role of the dental professional

Dental health professionals should be aware of the possible oral manifestations of celiac disease and educate patients on these symptoms when they are noted. Thorough health histories should be taken and updated regularly. Systemic symptoms that might point to celiac disease should be discussed with the patient, especially when in combination with oral symptoms.

It is the responsibility of dental professionals to be aware of any products that they use or recommend that contain gluten. Many professional dental products are certified as gluten-free. Table 3, taken from the Celiac Foundation website, celiac.org, lists professional products and home-care products that are safe to recommend to patients.¹⁴

A study by Verma et al. concluded that “gluten contamination is currently not an issue in a wide array of cosmetic and oral hygiene products that are commonly in the market.”²⁷ Dental professionals should check with manufacturers if there are any questions concerning any professional or over-the-counter products that are used or recommended for celiac patients.

Dental professionals should also be aware of the oral symptoms of celiac disease. If a patient presents with any of the oral conditions discussed, it would be prudent to consider whether undiagnosed celiac may be a possibility and a referral to a physician may be suggested.

Effects of a gluten-free diet on people without gluten sensitivity

Some people without gluten sensitivity have opted to adhere to a gluten-free diet for a variety of reasons. Some people think gluten may be the cause of gastrointestinal problems; others fear adverse health effects, such as autism. However, there is no convincing evidence that there is a correlation between these conditions and gluten. In fact, avoiding gluten without being diagnosed as gluten sensitive or intolerant and without having celiac disease could have negative health effects.²⁸ A proper diagnosis should always be obtained before beginning a gluten-free diet.

On the horizon

A possible new approach to treating celiac disease is being studied by Eva Helmerhorst, PhD, a periodontist at the Boston University Henry M. Goldman School of Dental Medicine. Dr. Helmerhorst is conducting research at the Museum of Science in Boston in hopes of developing new treatments to help people with celiac disease. Her team has discovered that human saliva contains enzymes that might help break down dietary gluten. According to Dr. Helmerhorst, “The ultimate goal is to

develop novel and clinically effective strategies to detoxify immunogenic gluten using therapeutic applications including enzymatic and probiotic approaches.”²⁹

Another possible treatment is a vaccine called Nexvac2. The vaccine reprograms the T-cells that attack the small intestine in celiac patients. This vaccine is being fast-tracked by the US Food and Drug Administration.³⁰

Other areas of research include attempts to detoxify wheat. Francisco Barro, a plant

biotechnologist at the Institute for Sustainable Agriculture in Spain, and his team have found a way to genetically engineer wheat that has considerably less gluten. However, according to Wendy Harwood, a crop geneticist at the John Innes Center in England who is not a part of the Barro study, it will take quite a while for this genetically altered wheat to reach the public. Harwood states, “I don’t think it’s the end of the story. This is just a really important step in maybe producing

TABLE 3: Gluten-free professional and home-care products.¹⁴

Polishing pastes	Acclean Prophy Paste 23% APF (Henry Schein)
	Acclean Zero Prophy Paste (Henry Schein)
	D-Lish Prophy Paste (Young Dental)
	Kolorz Prophy Paste (DMG America)
	Nupro Plus Prophy Paste (Dentsply Professional)
	Nupro Extra Care Prophy Paste (Dentsply Professional)
	Oral-B Prophy Paste (Young Dental)
	Smart Select Selective Polishing Prophy Paste (Young Dental)
	Sparkle Prophy Paste (Crosstex)
	Uni-Pro Prophy Paste (Henry Schein)
Zooby Prophy Paste (Denticator)	
Fluoride foams and gels	Acclean 60 Second Fluoride Gel 1.23% APF (Henry Schein)
	Enamel Pro Nonacidulated Fluoride Gel with ACP (Premier Dental)
	Kolorz Fluoride Foam 1.23% APF Foam (DMG America)
	Kolorz Fluoride Gel 1.23% APF Gel (DMG America)
	Nupro Fluoride Foam 1.23% Aerosol (Dentsply Professional)
	Nupro Fluoride Gel 1.23% APF (Dentsply Professional)
	Zap Fluoride Gel 1.23% APF (Crosstex)
Zooby Fluoride Foam 1.23% (Denticator)	
Fluoride varnishes	D-Lish fluoride varnish (Young Dental)
	Duraflor Halo (Medicom)
	ProFluorid varnish (Voco)
	ProGuard 5% sodium fluoride varnish (Crosstex)
	Sparkle V 5% sodium fluoride varnish with xylitol (Crosstex)
	Zooby 5% sodium fluoride varnish (Denticator)
Other products	Biotene products for dry mouth
	Oraqix topical anesthetic
	Sensodyne ProNamel
	Tom’s of Maine toothpastes
	3M Oral Care products*
	Crest products**
	Colgate products***

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* 3M Oral Care states that “Gluten is not an added component to any of 3M Oral Care products. Only dental materials/products are manufactured in our plants.”

** From the Crest FAQ website page: “Does Crest/Oral-B toothpaste contain gluten or wheat?” The answer is: “No. Crest/Oral-B toothpaste does not contain gluten or wheat, and our oral care plants do not process any gluten products.”²⁵

*** Colgate responded to an email query with the following: “All of Colgate’s oral care products are gluten free as defined by the United States Food and Drug Administration (US FDA). Colgate ensures all ingredients used within our formulas are not derived from gluten sources and that there is no cross-contamination of our ingredients or products with sources of gluten at our suppliers’ or at our own manufacturing facilities. Colgate is committed to its long history of maintaining our high standards for safety, quality, and efficacy for all of our products.”²⁶

something that is going to be incredibly useful.³¹ Some countries, including France and Germany, outlaw genetically modified crops.

Researchers are also looking at the possibility of blocking the inflammatory protein interleukin-15 (IL-15) to reverse symptoms. Bana Jabri, an associate professor of medicine and pathology and codirector of the Digestive Disease Research Core Center at the University of Chicago, states, "IL-15 may be a critical element that drives the loss of tolerance to gluten, and we can now think about pathways to block it and potentially develop therapies for celiac disease."³²

Another approach to preventing or treating celiac disease involves development of medications. Scientists at the Vienna University of Technology claim to have developed a medication that can alleviate or eliminate the effects of gluten in celiac patients. They anticipate that the medication could be available as early as 2021.³³

Conclusion

Dental professionals are likely to see more and more patients with confirmed celiac disease as well as patients with undiagnosed celiac disease. Although most over-the-counter oral hygiene products and most professional dental products appear to be safe for patients who have celiac disease, when in doubt about a particular product, contact the manufacturer.

Be aware of the symptoms of celiac disease, especially oral, and always consider the possibility that a patient may have an undiagnosed case. When in doubt, it is a good idea to refer patients to their physicians for diagnosis. You may help someone live a healthier and more comfortable life ... or even save a life.

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QUESTIONS

1. Celiac disease affects approximately one in how many people worldwide?
 - A. 50
 - B. 100
 - C. 200
 - D. 500
2. Which is *not* an oral manifestation of celiac disease?
 - A. Enamel defects
 - B. Aphthous ulcers
 - C. Black hairy tongue
 - D. Oral cancer
3. Ingestion of gluten causes the most damage to which organ in a celiac patient?
 - A. Brain
 - B. Large intestine
 - C. Small intestine
 - D. Liver
4. Gluten is found in which of the following?
 - A. Wheat
 - B. Rye
 - C. Barley
 - D. All of the above
5. People who have a first degree relative with celiac disease have a one in how many chance of also having the disease?
 - A. 10
 - B. 20
 - C. 30
 - D. 40
6. If a person is diagnosed with celiac disease at age 13, what is his or her chance of developing another autoimmune disease?
 - A. 10.50%
 - B. 16.70%
 - C. 27%
 - D. 34%
7. What is the prevalence of anemia in the celiac disease population?
 - A. 10%–12%
 - B. 12%–69%
 - C. 25%
 - D. 5.70%
8. What is the prevalence of type 1 diabetes in the celiac disease population?
 - A. 8%–10%
 - B. 10%–12%
 - C. 4%
 - D. 15%–27%
9. The prevalence of celiac disease in the United States is highest among which of the following populations?
 - A. Mexican Americans
 - B. Other Hispanics
 - C. Non-Hispanic blacks
 - D. Non-Hispanic whites
10. The prevalence of celiac disease in the United States is lowest among which of the following populations?
 - A. Mexican Americans
 - B. Other Hispanics
 - C. Non-Hispanic blacks
 - D. Non-Hispanic whites
11. A 2009 study by Rubio-Tapia et al. found that the prevalence of celiac disease has increased more than how much in the past 50 years?
 - A. Double
 - B. Triple
 - C. Fourfold
 - D. None of the above
12. Which of the following may be affecting the prevalence of autoimmune diseases, according to the hygiene hypothesis?
 - A. Poor oral hygiene
 - B. Changing patterns of early childhood infection
 - C. Vaccinations
 - D. Bacteria ingested from unclean food
13. How much does undiagnosed celiac disease increase the risk of death?
 - A. Double
 - B. Triple
 - C. Fourfold
 - D. No increase in risk
14. There are more than how many known symptoms of celiac disease?
 - A. 200
 - B. 100
 - C. 50
 - D. 25
15. Which is *not* a common symptom of celiac disease?
 - A. Chronic diarrhea
 - B. ADHD
 - C. Fatigue
 - D. Weight gain
16. What is a possible etiology of enamel defects in celiac patients?
 - A. Hypocalcemia due to malabsorption of nutrients
 - B. Autoimmune response against ameloblasts
 - C. Vitamins A and D deficiency
 - D. All of the above

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QUESTIONS

17. A study by Bramanti et al. concluded that recurrent aphthous stomatitis was found in what percentage of pediatric celiac patients?
- 43%
 - 62%
 - 71%
 - 79%
18. A burning sensation of the tongue may be due to problems with absorption of vitamin:
- B12
 - C
 - K
 - D
19. What percentage of patients with Sjögren's syndrome also have celiac disease?
- More than 20%
 - About 50%
 - Up to 15%
 - Between 15%–30%
20. Oral lichen planus is a chronic inflammatory disease that can involve which of the following?
- Buccal mucosa
 - Gingiva
 - Tongue
 - All of the above
21. Celiac patients who do not adhere to a strict gluten-free diet increase their risk for cancer of the:
- Mouth
 - Esophagus
 - Pharynx
 - All of the above
22. At the time of diagnosis, what percentage of patients do not exhibit digestive symptoms?
- 15%
 - 25%
 - 50%
 - 60%
23. Which condition causes the papillae of the tongue to shrink, creating a shiny red appearance?
- Geographic tongue
 - Atrophic glossitis
 - Hairy tongue
 - Kawasaki disease
24. What percentage of patients with Sjögren's syndrome also have celiac disease?
- 10%
 - 15%
 - 25%
 - 33%
25. Children with undiagnosed celiac disease may have:
- Delayed loss of deciduous teeth
 - Early loss of deciduous teeth
 - Missing permanent teeth
 - Supernumerary teeth
26. What is the prevalence of autoimmune thyroid disease in the celiac population?
- 7%
 - 12%
 - 21%
 - 26%
27. Which statement is false?
- Avoiding gluten without being diagnosed as gluten sensitive/intolerant or having celiac disease could have negative health effects.
 - Depression is a common symptom of celiac disease.
 - Lipsticks may contain gluten.
 - Organic wheat has lower levels of gluten.
28. Dr. Eva Helmerhorst discovered:
- That human saliva contains enzymes that might help break down dietary gluten
 - That T-cells that attack the small intestine in celiac patients can be reprogrammed
 - A way to genetically engineer wheat that has considerably less gluten
 - A way to block the inflammatory protein interleuken-15 (IL-15) to reverse symptoms
29. A possible vaccine for celiac disease is being developed and is called:
- Nexvac2
 - Certiva
 - Decavac
 - Glutavix
30. Researchers are looking at the possibility of blocking which inflammatory protein to reverse symptoms?
- Interleuken-2
 - Interleuken-7
 - Interleuken-15
 - Interleuken-20

Oral complications of celiac disease

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Educational Objectives

- Understand the systemic and oral effects of celiac disease
- Identify products that are safe in clinical and home use for celiac patients
- Become aware of possible new treatments for celiac disease
- Refer patients for diagnosis if celiac disease is suspected

Course Evaluation

- Were the individual course objectives met?
 Objective #1: Yes No Objective #3: Yes No
 Objective #2: Yes No Objective #4: Yes No

Please evaluate this course by responding to the following statements, using a scale of Excellent = 5 to Poor = 0.

- | | | | | | | |
|-----------------------------------------------------------------------------------------------|-------|----|---|---|---|---|
| 2. To what extent were the course objectives accomplished overall? | 5 | 4 | 3 | 2 | 1 | 0 |
| 3. Please rate your personal mastery of the course objectives. | 5 | 4 | 3 | 2 | 1 | 0 |
| 4. How would you rate the objectives and educational methods? | 5 | 4 | 3 | 2 | 1 | 0 |
| 5. How do you rate the author's grasp of the topic? | 5 | 4 | 3 | 2 | 1 | 0 |
| 6. Please rate the instructor's effectiveness. | 5 | 4 | 3 | 2 | 1 | 0 |
| 7. Was the overall administration of the course effective? | 5 | 4 | 3 | 2 | 1 | 0 |
| 8. Please rate the usefulness and clinical applicability of this course. | 5 | 4 | 3 | 2 | 1 | 0 |
| 9. Please rate the usefulness of the supplemental bibliography. | 5 | 4 | 3 | 2 | 1 | 0 |
| 10. Do you feel that the references were adequate? | Yes | No | | | | |
| 11. Would you participate in a similar program on a different topic? | Yes | No | | | | |
| 12. If any of the continuing education questions were unclear or ambiguous, please list them. | _____ | | | | | |
| 13. Was there any subject matter you found confusing? Please describe. | _____ | | | | | |
| 14. How long did it take you to complete this course? | _____ | | | | | |
| 15. What additional continuing dental education topics would you like to see? | _____ | | | | | |

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| 3. (A) (B) (C) (D) | 18. (A) (B) (C) (D) |
| 4. (A) (B) (C) (D) | 19. (A) (B) (C) (D) |
| 5. (A) (B) (C) (D) | 20. (A) (B) (C) (D) |
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| 7. (A) (B) (C) (D) | 22. (A) (B) (C) (D) |
| 8. (A) (B) (C) (D) | 23. (A) (B) (C) (D) |
| 9. (A) (B) (C) (D) | 24. (A) (B) (C) (D) |
| 10. (A) (B) (C) (D) | 25. (A) (B) (C) (D) |
| 11. (A) (B) (C) (D) | 26. (A) (B) (C) (D) |
| 12. (A) (B) (C) (D) | 27. (A) (B) (C) (D) |
| 13. (A) (B) (C) (D) | 28. (A) (B) (C) (D) |
| 14. (A) (B) (C) (D) | 29. (A) (B) (C) (D) |
| 15. (A) (B) (C) (D) | 30. (A) (B) (C) (D) |

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