Earn **3 CE credits**
This course was written for dentists, dental hygienists, and assistants.

The Impact of Salivary Diagnostics

A Peer-Reviewed Publication
Written by Paul D. Slowey, PhD, and Richard H. Nagelberg, DDS

© Alexander Traksel | Dreamstime.com

Abstract

Salivary diagnostic technology offers a number of advantages over other testing methods. Some of these advantages include non-invasiveness, an unlimited supply, cost-effectiveness, and patient comfort, among others. Saliva testing can provide early diagnosis of a variety of diseases and conditions, thereby reducing morbidity and mortality. A particularly promising area of research is the identification of salivary biomarkers for a variety of cancers such as lung, breast, and oral cancers. Salivary testing is currently available for the identification of periodontal pathogens. Other research to identify a variety of biomarkers of periodontal disease is ongoing.

Educational Objectives

At the conclusion of this educational activity, participants will be able to:

1. Discuss the advantages of salivary diagnostics
2. Discuss the potential impact of salivary diagnostics on a variety of systemic diseases and conditions
3. Describe how saliva testing is currently used by the dental profession
4. Implement saliva testing in the dental practice to enhance patient care

Author Profile

Paul D Slowey PhD, CEO is the Founder of Oasis Diagnostics® Corporation, a pioneer in the area of oral fluid diagnostics, founded in 2002. Dr Slowey holds a PhD in Organic Chemistry from the University of Newcastle (UK). He has over 32 years of experience in the clinical diagnostic and pharmaceutical industries.

Richard H. Nagelberg, DDS has been practicing general dentistry in suburban Philadelphia for 34 years. He is an advisory board member, speaker, columnist, key opinion leader and clinical consultant for several dental companies and organizations as well as a recipient of Dentistry Today's Top Clinicians in CE, 2009-2016.

Author Disclosure

Dr. Slowey has a financial interest in the Corporate Sponsor for this course.

INSTANT EXAM CODE 15124

Go Green, Go Online to take your course

PennWell®

dental CE digest®

ineedCE.com
The Academy of Dental Therapeutics and Stomatology®

ADA C·E·R·P® | Continuing Education Recognition Program

Academy of General Dentistry™

PACE
Program Approval for Continuing Education

Educational Objectives

At the conclusion of this educational activity, participants will be able to:

1. Discuss the advantages of salivary diagnostics
2. Discuss the potential impact of salivary diagnostics on a variety of systemic diseases and conditions
3. Describe how saliva testing is currently used by the dental profession
4. Implement saliva testing in the dental practice to enhance patient care

Abstract

Salivary diagnostic technology offers a number of advantages over other testing methods. Some of these advantages include non-invasiveness, an unlimited supply, cost-effectiveness, and patient comfort, among others. Saliva testing can provide early diagnosis of a variety of diseases and conditions, thereby reducing morbidity and mortality. A particularly promising area of research is the identification of salivary biomarkers for a variety of cancers such as lung, breast, and oral cancers. Salivary testing is currently available for the identification of periodontal pathogens. Other research to identify a variety of biomarkers of periodontal disease is ongoing.

Historically, there have been a number of factors that have led to a slower than expected uptake in salivary diagnostics, and several barriers to widespread implementation of salivary diagnostics still exist. These include a lack in standardization of methods used to harvest saliva samples; a requirement for normalization of methods used to interrogate salivary biomarkers; a current lack of understanding of changes in salivary composition due to age; the impact of diurnal and circadian variation in molecules in saliva; and salivary constituent composition based on diet and fluid intake, among many others.[32] In the past, funding for specific projects targeting salivary biomarkers has also been difficult to find, providing less incentive for diagnostic and biotechnology companies to pursue options looking at saliva.

Discussion

One of the hallmarks of health care is the critical importance of early disease detection. For example, blood tests are commonly used to detect and monitor a wide variety of diseases and conditions. Diagnostic tests typically utilize various biological fluids including whole blood, serum, plasma, cerebrospinal fluid, peritoneal fluid, drainage fluid, and urine, among others.[25] Biomarkers indicative of many diseases are present in the serum in relatively strong concentrations compared to levels in oral fluid specimens. Until recently, identification of the minute concentrations of biomarkers in oral fluid was beyond the detection capabilities of available laboratory technologies. This is not surprising, as disease biomarkers in serum are commonly present in the microgram range (i.e., one millionth of a gram).

[25] In oral fluids, on the other hand, analytes may be present in concentrations of one billionth to one trillionth of a gram (i.e., nanograms and picograms). Recently the advent of new, more sensitive technologies such as next generation sequencing, mass spectrometry, and homogeneous immunoassays, and even quantitative lateral flow technologies for point of care applications, allows adequate detection and quantification of these lower level biomarkers.[39]

Saliva mirrors bodily health and well-being since most of the biomolecules that are present in blood or urine are also present in saliva.[25] Yet utilizing saliva as a diagnostic medium provides a number of advantages over serum, such as non-invasive collection, a virtually unlimited supply, cost effectiveness, and patient comfort. In addition, salivary collection does not require highly-trained professionals such as phlebotomists. Rapid screening of large populations is also readily facilitated using salivary diagnostic methods. When required, sample transportation is also far more cost effective, and saliva also eliminates certain cultural "taboos" associated with blood collection prevalent in some cultures.[26]

Saliva is comprised of multiple secretions from the parotid, submandibular, sublingual, and other minor glands. It contains a variety of biomolecules, including DNA, RNA, proteins, metabolites, and microbes. Biomarker assays can be developed that target changes in the salivary concentration of these biomolecules, which can then be used to identify early stages of oral and systemic diseases, monitor disease prognosis, stratify risk, and evaluate response to treatment.[1,2,3]

In order for biomarkers of systemic diseases to appear in the saliva, an action or some type of impact is needed that affects the salivary glands. More specifically, this would be a disease or condition somewhere in the body other than the oral cavity that would exert an effect on the salivary glands in order for the biomarkers to make their way into the saliva. The exact mechanism whereby a distal disease produces biomarkers that appear in the saliva has not yet been determined, although a number of mechanisms for transfer to the oral cavity are known, including passive diffusion[26] and through the gingival crevices as an "ultra-filtrate" of blood.[39] Some early mouse model cancer studies also suggest that the production of growth factors in tumor tissues alters mRNA expression in salivary glands, causing biomarkers to appear in saliva.[1,4]

Potential salivary biomarkers are present or have already been identified for a wide variety of diseases. Sjogren's syndrome (SS), for instance, is an autoimmune disorder that typically presents with a reduction in salivary and lacrimal gland secretions, and associated endocrine disturbances. Salivary protein analysis in SS patients is under investigation as an early diagnostic tool. The present methods to diagnose SS are invasive, expensive, and non-conclusive in many cases.[5,6] Biomarkers for cystic fibrosis (CF), another autoimmune condition, are also being investigated, and appear to be related to oxidative and inflammatory processes ongoing in these individuals.[7]

Cardiovascular diseases are the leading cause of death in the United States, and levels of several salivary biomarkers have been identified for cardiovascular disease diagnosis, including C-reactive protein (CRP), NT-pro BNP, and cardiac troponin.[7] In the future, salivary tests will ultimately replace blood tests for the detection of cardiovascular diseases. Studies have demonstrated that salivary levels of CRP correlate with plasma CRP levels obtained from individuals at risk for cardiovascular complications.[27] Similarly, reports confirm that levels of NT-pro BNP correlate well between saliva and serum.[37]

Diagnosis of breast cancer, which is the second leading cause of death and the most common form of cancer in women,[8] currently depends on physical examination and imaging technology. Breast cancer is one of the most widely studied diseases, and early detection is universally regarded as a critical factor for favorable long-term outcomes. The sensitivity and specificity of physical examination and mammography is far from ideal,[9,10] and this highlights the need for methodologies with greater accuracy. The aim of developing a non-invasive, salivary test for early detection of breast cancer is to provide clinicians with a way to identify individuals needing closer monitoring and additional imaging. A secondary but highly important aim is reduction in the number of unnecessary biopsies. The American Cancer Society estimates that a staggering 80% of breast biopsies are unnecessary.[9] Recent studies have confirmed that a number of salivary biomarkers for breast cancer have been discovered with the ability to detect breast cancer with high specificity and sensitivity.[9]

Another area of interest is diabetes mellitus, where specific biomarkers have the potential to provide early detection and improved glycemic control in patients. Earlier work has shown the availability of protein biomarkers for type 2 diabetes in serum samples.[7] More recent research has concluded that these serum markers can also be measured in saliva, and that biomarkers emerge over time as diabetes disease develops.[40] The clinical significance of diabetes biomarker identification is as a disease risk evaluation tool. Salivary biomarkers have the ability to increase the predictive nature of diabetes risk scores and provide an economical strategy for type 2 diabetes screening. Risk factors are predictive over time, so periodic assessment is critically important.[11]

The most common cause of cancer-related death in men and women is lung cancer.[41] Symptoms are frequently absent until the disease has metastasized, leading to a poor prognosis.[1] Early detection offers the potential to reduce morbidity and mortality, yet conventional diagnostic methods are not suitable for large population screening due to the expense involved and a lack of accuracy. One important study identified a panel of five salivary biomarkers, which can differentiate lung cancer patients from cancer-free individuals with 93.75% sensitivity and 82.81% specificity.[31]

A group headed by Dr. David Wong at UCLA has developed an exciting test called EFIRM™ that is based upon a "liquid biopsy" assay that uses saliva as the sample matrix.[38] The EFIRM test detects circulating tumor DNA (ctDNA) in the saliva (or blood) of lung cancer patients through the implementation of an electric field-induced release and measurement (EFIRM) technique. It is currently directed towards patients with non-small cell lung carcinoma (NSCLC) and tyrosine-kinase-inhibitor-sensitizing mutations (exon 19 deletion and exon 21 l858R substitution). The EFIRM test has attracted attention in the popular media and may eventually revolutionize cancer testing,, as the same principles may be applied to other cancers as well.

Salivary diagnostic technology is also widely used in forensics, where samples are obtained from glasses, cigarettes, envelopes, and food products, among many other sources. Dry DNA samples from saliva are relatively stable, enabling the use of the items noted above for analysis. Crime suspect identification and legal actions to determine paternity both utilize salivary evaluation of blood group antigens,[12,13] and a significant number of molecular tests now utilize saliva as a viable option for collection and testing purposes.[14] The applications to home collections and consumer-based testing are on the rise.

Technologies based on salivary diagnostics have been available to the dental profession for years. Salivary testing for oral bacteria, HPV, and genetic susceptibility to periodontal disease are just a few of many examples of specific tests that have been available from a variety of companies for some time.

Oral squamous cell carcinoma (OSCC) is the most common type of cancer in the oral cavity. Approximately 40,000 new cases are diagnosed with 8,000 deaths annually.[15,16,17,18,19] This disease is the sixth most common cancer worldwide, with an average survival rate of 60%.[28] This is largely the result of late stage diagnosis (stages III and IV), frequent relapses,reoccurrence? and secondary tumors. Early detection of OSCC utilizing protein biomarkers in saliva could facilitate identification during the initiation and progression of OSCC, with improved outcomes and survival rates.[20] To date, many protein and mRNA salivary biomarkers have been discovered that can identify OSCC with a high degree of sensitivity and specificity. The most accurate protocol would offer detection of multiple biomarkers, since OSCC is multifactorial and has a heterogenic pathogenesis. In the case of OSCC, it is likely that multiple biomarkers may be necessary to reach the high sensitivity and accuracy required, and that a single biomarker may not be sufficiently adequate for use as a diagnostic tool. Cancerous lesions in the oral cavity are in continuous contact with saliva and this direct contact is one of the major reasons that salivary diagnostics for OSCC are very promising.[15]

Infection with human papilloma virus-16 (HPV-16) is a major risk factor for oropharyngeal squamous cell carcinoma (OPSCC). The prevalence of HPV-positive OPSCC is rising in the western world, with more than 90% of cases being attributed to HPV-16 infection.[21] The current protocol for detecting HPV-16 tumors involves tissue biopsy; however, when tumors

are anatomically hidden, detection can be difficult. Sites that can be difficult to access include the tonsillar crypts and base of the tongue. A non-invasive alternative to biopsy for HPV-16 detection would have a number of advantages.[22] Detection of HPV-16 in oral rinse specimens is presently commercially available using the OraRisk HPV 16/18/HR Assay (OralDNA Labs, Eden Prairie, Minnesota). The applications for HPV-16 detection are not restricted to OPSCC. Applications include HPV status in patients with head and neck squamous cell carcinoma as well as a potential diagnostic aid for HPV infection.

There are presently a number of commercially available salivary diagnostic tests for periodontal bacteria. These tests utilize a salivary sample obtained in the dental office, which is then sent to an offsite testing laboratory. The availability of an accurate salivary marker for periodontitis should be applicable to entire populations regardless of systemic diseases, smoking habits, or number of teeth of the individuals in a given population.[30]

A 2015 study investigated a panel of four periodontal pathogens as biomarkers indicative of periodontitis.[30] Previous studies relied on harvesting bacterial samples from subgingival sites, but collection of more readily available saliva specimens offers a number of benefits. These include the ability of non-dental healthcare professionals or patients themselves to collect the sample, ease of transportation, elimination of pain, and user friendliness, among others. This specific study evaluated the salivary concentrations of *Porphyromonas gingivalis*, *Tannerella forsythia*, *Prevotella intermedia* and *Aggregatibacter actinomycetemcomitans* to determine if these bacteria could serve as adequate biomarkers for the diagnosis of periodontitis. The study also looked at the diagnostic effectiveness of the combination of bacteria and each individual species at the same time. The aim of the study was to find salivary biomarkers that could provide an accurate assessment of periodontal risk. The authors concluded that the combination of *P. gingivalis* and *T. forsythia* had the strongest association with periodontitis when compared to the four bacteria analyzed individually or in combination.[30] Applications for this type of risk assessment test might include home testing, collection at remote sites, and geriatric collection and testing, among others. Chairside bacterial identification tests are also currently under development. In addition, researchers are investigating genetic, microbial, and protein biomarkers[23] with the objective of enabling patient screening, monitoring, and treatment planning. The capability to provide risk determination at the clinical level can potentially reduce or eliminate disease occurrence and provide earlier intervention with improved treatment outcomes.

A different approach utilizing salivary diagnostics for periodontal disease involves identification of biomarkers associated with bone remodeling as an alternative to bacterial identification. Researchers have identified and examined levels of biomolecules associated with biological events occurring during bone remodeling in patients with chronic periodontitis.[24,32] In their study, the protein biomarker was identified, which

was 18-times higher in periodontitis patients than in normal, healthy subjects, with the ability to discriminate between periodontal disease and normal health status. The study authors concluded that their findings, along with those from other studies "suggest that the combined presence of elevated levels of a panel of salivary biomarkers representing the three biological phases (inflammatory, connective tissue destruction and bone remodeling) of periodontal disease may offer the sensitivity and specificity for screening for periodontal disease in non-dental settings as well as potentially providing an understanding of the dynamics of the periodontitis lesion, and to the use of biofluid panels as adjuncts in the diagnostic assessment of periodontal disease in the near future."

A further study from 2014 examined the association between three salivary biomarkers and clinically evident periodontal parameters. The concentrations of three biomarkers, MMP-8, interleukin (IL)-1β, and *P. gingivalis*, were used to calculate a novel risk score called the cumulative risk score (CRS), for each of the 493 enrolled study subjects. The authors concluded that together, the salivary concentrations of the three biomarkers were associated with clinical and radiographic measures of periodontitis more strongly than any of the markers alone, regardless of the coronary artery disease status of the study subjects.[29]

The consensus among various studies appears to indicate the importance of using a variety of biomarkers rather than relying on a single biomarker. Given the progressive nature of many diseases, including periodontal disease, the use of multiple biomarkers (i.e., multiplexing), should provide a greater level of sensitivity and specificity and lead to an enhancement in the accuracy of the results.

Conclusions

Fortunately, over the last five years there has been a dramatic increase in the interest in salivary diagnostics as a result of a few significant factors, including the availability of new technologies, both for saliva collection and testing, standardization of collection protocols, more effective technologies to find relatively small quantities of specific analytes in saliva, as well as more effective downstream technologies to quantify low level analytes in oral specimens. Other contributing factors include greater knowledge of saliva sample preparation, including stabilization of samples, isolation of sub-components of saliva, and more effective means of purifying complex saliva matrices.

The availability of an at-home oral fluid test for HIV allowing members of the general public to test themselves for HIV in the privacy of their own homes[34] has paved the way for multiple other tests using saliva, and the impact over the next 5 to10 years is expected to be exponential. In the areas of drug abuse testing, law enforcement professionals in the near future will be able to detect levels of various drugs in saliva at the roadside in 5 minutes or less and apprehend drivers suspected of driving

under the influence of a number of illicit drugs. Saliva is already in widespread use for the detection of nucleic acids (DNA and RNA) and many hundreds of thousands of people every year have their genome tested by companies such as 23andMe and Ancestry.com in an attempt to identify specific genetic traits or determine where they came from. Neurodegenerative diseases such as Parkinson's and Alzheimer's diseases are being investigated in saliva and work is ongoing to determine tendencies to commit suicide or the incidence of traumatic brain disorder. One other area that will be of direct relevance to the dental community is the investigation of various biomarkers in saliva associated with sleep disorders.

Many of the disease targets under development at this time could end up as chairside or at-home tests as the overall in vitro diagnostic market becomes more "patient-centric". The future of salivary diagnostics is indeed very bright and is forecast to move into many areas of disease detection diagnosis and patient monitoring. This is all very good news for the patient!

Bibliography

1. Zhang Y, Sun J, Lin CC, Abemayor E, Wang MB, Wong DT. The emerging landscape of salivary diagnostics. Periodontol 2000. 2016;70(1):38-52. doi: 10.1111/prd.12099.
2. Denny P, et al. The proteomes of human parotid and submandibular/sublingual gland salivas collected as the ductal secretions. J Proteome Res. 2008;7(5):1994-2006.
3. Spielmann N, Wong DT. Saliva: diagnostics and therapeutic perspectives. Oral Dis. 2011;17(4):345-54.
4. Gao K1, Zhou H, Zhang L, Lee JW, Zhou Q, Hu S, Wolinsky LE, Farrell J, Eibl G, Wong DT. Systemic disease-induced salivary biomarker profiles in mouse models of melanoma and non-small cell lung cancer. PLoS One. 2009;4(6):e5875.
5. Daniels TE. Sjogren's syndrome: clinical spectrum and current diagnostic controversies. Adv Dent Res. 1996;10(1):3-8.
6. Streckfus CF, Bigler LR. Saliva as a diagnostic fluid. Oral Dis. 2002;8(2):69-76.
7. Javaid MA, Ahmed AS, Durand R, Tran SD. Saliva as a diagnostic tool for oral and systemic diseases. J Oral Biol Craniofac Res. 2016;6(1):66-75.
8. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. CA Cancer J Clin. 2007;57(1):43-66.
9. Zhang L, Xiao H, et al. Discovery and preclinical validation of salivary transcriptomic and proteomic biomarkers for the non-invasive detection of breast cancer. PLoS One. 2010;5(12): e15573.
10. Berg WA, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. Radiology. 2004;233:830–849.
11. Srinivasan M, et al. Literature-based discovery of salivary biomarkers for type 2 diabetes mellitus. Biomark Insights. 2015;14(10):39-45.
12. Kamodyová N, Durdiaková J, et al. Prevalence and persistence of male DNA identified in mixed saliva samples after intense kissing. Forensic Sci Int Genet. 2013;7(1):124-128.
13. Sweet D, Hildebrand D. Saliva from cheese bite yields DNA profile of burglar: a case report. Int J Legal Med. 1999;112(3):201-203.
14. Behn J. Salivary Diagnostic Testing. Inside Dentistry. 2011;7(7):104-107.
15. Yakob M, Fuentes L, et al. Salivary biomarkers for detection of oral squamous cell carcinoma—current state and recent advances. Curr Oral Health Rep. 2014;1(2):133–141.
16. Siegel R1, Naishadham D, Jemal A. Cancer statistics, 2013. CA Cancer J Clin. 2013;63(1):11-30.
17. Markopoulos AK. Current aspects on oral squamous cell carcinoma. Open Dent J. 2012;6:126-30.
18. Ferlay J, Shin HR, et al. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. Int J Cancer. 2010;127(12):2893-2917.
19. Parkin DM, Bray F, et al. Global cancer statistics, 2002. CA Cancer J Clin. 2005;55(2):74-108.
20. Ni YH, et al. Potential biomarkers for oral squamous cell carcinoma: proteomics discovery and clinical validation. Proteomics Clin Appl. 2015;9(1-2):86-97.
21. Marur S, D'Souza G, Westra WH, Forastiere AA. HPV-associated head and neck cancer: a virus-related cancer epidemic. Lancet Oncol. 2010;11(8):781–789.
22. Chai RC, Lim Y, et al. A pilot study to compare the detection of HPV-16 biomarkers in salivary oral rinses with tumour p16(INK4a) expression in head and neck squamous cell carcinoma patients. BMC Cancer. 2016;16(1):178.
23. Giannobile WV. Salivary diagnostics for periodontal diseases. J Am Dent Assoc. 2012;143(10 Suppl):6S-11S.
24. Al-Sabbagh M, Alladah A, et al. Bone remodeling-associated salivary biomarker MIP-1α distinguishes periodontal disease from health. J Periodontal Res. 2012;47(3):389-95.
25. Punyadeera C and Slowey PD. Saliva as an emerging biofluid for clinical diagnosis and applications of MEMS/NEMS in salivary diagnostics. In Subramani K., Ahmed W., and Hartsfield JK (Eds.). Nanobiomaterials in Clinical Dentistry. William Andrew. Elsevier 2012. Oxford, UK, p. 454.
26. Slowey PD. "Saliva Collection Devices and Diagnostic Platforms." Chapter 3 in Advances in Salivary Diagnostics. Editor: Streckfus CF, Heidelberg: Springer Press 2015 ISBN 978-3-662-45398-8, p. 34.
27. Out D, et al. Assessing salivary C-reactive protein: longitudinal associations with systemic inflammation and cardiovascular disease risk in women exposed to intimate partner violence. Brain Behav Immun. 2012;26(4):543-51.
28. Yoshizawa JM1, Wong DT. Salivary microRNAs and oral cancer detection. Methods Mol Biol. 2013;936:313-24.
29. Salminen A, et al. Salivary biomarkers of bacterial burden, inflammatory response, and tissue destruction in periodontitis. J Clin Periodontol. 2014 May;41(5):442-50.
30. Salminen A, et al. Quantitative PCR analysis of salivary pathogen burden in periodontitis. Front Cell Infect Microbiol. 2015 Oct 1;5:69.
31. Zhang L, et al. Development of transcriptomic biomarker signature in human saliva to detect lung cancer. Cell Mol Life Sci. 2012 Oct;69(19):3341-50.
32. Kinney JS, Ramseier CA, Giannobile WV. Oral fluid-based biomarkers of alveolar bone loss in periodontitis. Ann N Y Acad Sci. 2007;1098:230-51.
33. Kauffman L. Novel Thinking for Dentistry. Decisions in Dentistry. 2016;2(3):13-16.
34. Slowey PD. "Commercial Saliva Collection Tools". Journal of the California Dental Association. 2013;(41): 97-105.
35. Schafer CA, et al. Saliva diagnostics: utilizing oral fluids to determine health status. Monogr Oral Sci. 2014;24:88-98.
36. Lee YH, et al. Salivary transcriptomic biomarkers for detection of ovarian cancer: for serous papillary adenocarcinoma. J Mol Med (Berl). 2012;90(4):427-34.
37. Foo JYY, Wan Y, Kostner K, Arivalagan A, Atherton J, Cooper-White J, Dimeski G and Punyadeera C NT-ProBNP. Levels in Saliva and Its Clinical Relevance to Heart Failure PLoS ONE 7(10): e48452. doi:10.1371/journal.pone.0048452.
38. Tu M, Wei F, Yang J, Wong D. Detection of exosomal biomarker by electric field-induced release and measurement (EFIRM). J Vis Exp. 2015;23 (95):52439.
39. Hu J, Cui X, Gong Y, Xu X, Gao B, Wen T, Lu TJ, Xu F. Portable microfluidic and smartphone-based devices for monitoring of cardiovascular diseases at the point of care. Biotechnol Adv. 2016 May-Jun;34(3):305-20.
40. Chee CS, Chang KM, Loke MF, Angela Loo VP, Subrayan V. Association of potential salivary biomarkers with diabetic retinopathy and its severity in type-2 diabetes mellitus: a proteomic analysis by mass spectrometry. PeerJ. 2016 May 12;4:e2022.
41. https://www.cdc.gov/cancer/lung/statistics. Accessed 6/24/16.

Author Profile

Paul D Slowey PhD, CEO is the Founder of Oasis Diagnostics® Corporation, a pioneer in the area of oral fluid diagnostics, founded in 2002. Dr Slowey holds a PhD in Organic Chemistry from the University of Newcastle (UK). He has over 32 years of experience in the clinical diagnostic and pharmaceutical industries.

Richard H. Nagelberg, DDS has been practicing general dentistry in suburban Philadelphia for 34 years. He is an advisory board member, speaker, columnist, key opinion leader and clinical consultant for several dental companies and organizations as well as a recipient of Dentistry Today's Top Clinicians in CE, 2009-2016.

Author Disclosure

Online Completion   INSTANT EXAM CODE 15124

Use this page to review the questions and answers. Return to www.ineedce.com and sign in. If you have not previously purchased the program select it from the "Online Courses" listing and complete the online purchase. Once purchased the exam will be added to your Archives page where a Take Exam link will be provided. Click on the "Take Exam" link, complete all the program questions and submit your answers. An immediate grade report will be provided and upon receiving a passing grade your "Verification Form" will be provided immediately for viewing and/or printing. Verification Forms can be viewed and/or printed anytime in the future by returning to the site, sign in and return to your Archives Page.

Questions

1. Which of the following statements is correct?
   a. Biomarkers of disease in serum are commonly found in picogram quantities.
   b. In oral fluid, analytes are commonly present in microgram quantities.
   c. In oral fluid, analytes can be in nanogram quantities.
   d. None of the above

2. Diagnostic tests utilizing biological fluids obtain samples from:
   a. Blood
   b. Cerebrospinal fluid
   c. Peritoneal fluid
   d. All of the above

3. Which of the following are advantages of using salivary testing compared to serum?
   a. Invasive nature of salivary testing.
   b. Virtually unlimited supply of saliva.
   c. Blood testing is more cost effective than salivary testing.
   d. Salivary testing is less comfortable for patients than blood testing.

4. Saliva is comprised of secretions from the:
   a. Parotid
   b. Submandibular
   c. Minor salivary glands
   d. All of the above

5. Which of the following statements is true regarding salivary biomarkers?
   a. The exact mechanism whereby a distal disease produces biomarkers that appear in the saliva has not yet been determined.
   b. The exact mechanism whereby a distal disease produces biomarkers that appear in the saliva has been determined.
   c. Some type of impact on the salivary glands is unnecessary for biomarkers of systemic diseases to appear in the saliva.
   d. Biomarkers automatically appear in the saliva.

6. Salivary biomarkers are under development for which of the following conditions?
   a. Sjogren's syndrome
   b. Cystic fibrosis
   c. Diabetes mellitus
   d. All of the above

7. Current methods to diagnose Sjogren's syndrome are:
   a. Invasive
   b. Inexpensive
   c. Highly accurate
   d. Non-invasive

8. Biomolecules normally contained in saliva include all of the following except:
   a. DNA and RNA
   b. Proteins
   c. Gastric enzymes
   d. Metabolites

9. The consensus among researchers appears to indicate the importance of using:
   a. A single biomarker
   b. A variety of biomarkers
   c. Three or more biomarkers
   d. No consensus exists at this time

10. Salivary diagnostic approaches to the identification of periodontal disease include:
    a. Genetic biomarkers
    b. Protein biomarkers
    c. Bone remodeling biomarkers
    d. All of the above

11. A 2014 study by Salminen et al concluded that:
    a. Concentrations of CRS, (MMP)-8 and (IL)-1β were the best markers to predict the presence of periodontal disease.
    b. Concentrations of P. gingivalis, (IL)-1β, and CRP were the best markers to predict the presence of periodontal disease.
    c. Concentrations of (MMP)-8, interleukin (IL)-1β, and P. gingivalis were the best markers to predict the presence of periodontal disease.
    d. Concentrations of P. gingivalis and (IL)-1β were the best markers to predict the presence of periodontal disease.

12. The ability to provide chairside periodontal bacterial identification could potentially:
    a. Increase periodontal disease occurrence.
    b. Improve periodontal treatment outcomes.
    c. Decrease the longevity of favorable therapeutic results.
    d. Reduce the efficacy of biofilm control devices.

13. Which of the following statements is correct regarding oral squamous cell carcinoma (OSCC)?
    a. OSCC is the most common type of oral cancer.
    b. OSCC incidence is decreasing.
    c. OSCC is unrelated to the presence of human papilloma virus.
    d. Approximately 80,000 new cases of OSCC are diagnosed annually in the US.

14. Which of the following is correct regarding human papilloma virus-16 (HPV-16) and oropharyngeal squamous cell carcinoma (OPSCC)?
    a. The prevalence of HPV-positive OPSCC is rising, with less than 60 % of cases being attributed to HPV-16 infection.
    b. The prevalence of HPV-positive OPSCC is rising, with more than 90 % of cases being attributed to HPV-16 infection.
    c. The prevalence of HPV-positive OPSCC is decreasing, with more than 90 % of cases being attributed to HPV-16 infection.
    d. The prevalence of HPV-positive OPSCC is rising, with less than 80 % of cases being attributed to HPV-16 infection.

15. Which of the following is accurate regarding oral cancer detection?

    a. The current protocol for detecting HPV-16 oral tumors involves biopsy.
    b. When tumors are anatomically hidden, detection can be difficult.
    c. A non-invasive alternative to biopsy for oral cancer detection would not be advantageous.
    d. Both a and b.

16. Which of the following is true regarding oral cancer?
    a. The survival rate of OSCC is 50%.
    b. OSCC is the fifth most common cancer worldwide.
    c. Eight thousand deaths annually are attributable to oral cancer.
    d. None of the above.

17. The most common cause of cancer –related death in men and women is:
    a. Oral cancer.
    b. Lung cancer in men only.
    c. Lung cancer in women only.
    c. Lung cancer for both men and women.

18. Biomarkers for diabetes mellitus:
    a. Have the potential to improve glycemic control.
    b. Will likely need to be evaluated only once.
    c. Will likely need to be evaluated periodically over time.
    d. Both a and c.

19. Which of the following is true regarding salivary testing for cardiovascular diseases?
    a. Biomarkers of cardiovascular disease have been identified including C-reactive protein (CRP) and cardiac troponin.
    b. Biomarkers of cardiovascular disease have been identified including CRP and MMP-8.
    c. Biomarkers of cardiovascular disease have been identified including cardiac troponin and (IL)-1β.
    d. Biomarkers of cardiovascular disease have been identified including CRS and cardiac troponin.

20. Commercially available salivary tests presently include:
    a. Periodontal pathogens
    b. HPV
    c. Lung cancer
    d. Both a and b

21. Which of the following is accurate regarding utilization of forensic salivary testing?
    a. Dry salivary samples are not sufficiently stable for sampling.
    b. Paternity can only be determined by blood testing.
    c. Saliva samples can be obtained from used envelopes.
    d. Saliva samples cannot be obtained from food products.

22. A 2012 study by Al-Sabbagh et al:
    a. Examined bone remodeling as an indicator of presence of periodontal pathogens.
    b. Found that the MIP-1α biomarker level was 18 times higher in disease vs. health.
    c. Concluded that salivary tests for bone modeling alone are adequate for periodontal disease risk assessment.
    d. Found that the MIP-1α biomarker level was 28 times higher in disease vs. health.

23. A 2015 study of periodontal pathogens by Salminen et al concluded that:
a. T. forsythia and P. intermedia were the best indicators of periodontitis.
b. T. forsythia and P. gingivalis were the best indicators of periodontitis.
c. P. intermedia and P. gingivalis were the best indicators of periodontitis.
d. P. gingivalis and A. actinomycetemcomitans were the best indicators of periodontitis.

24. Which of the following is true regarding chairside salivary testing for periodontitis?
a. The objective is to enable patient screening, monitoring and treatment planning.
b. Researchers are investigating genetic, microbial and protein biomarkers.
c. Researchers are investigating only genetic and protein biomarkers.
d. Both a and b.

25. Which of the following is true regarding commercially available salivary diagnostic tests for periodontal bacteria?
a. Patients with systemic diseases cannot be tested.
b. Salivary samples are obtained and evaluated in the dental office.
c. Patients who smoke are not candidates for testing.
d. None of the above

26. Salivary testing for the presence of diabetes:
a. Is presently available for type 1 DM.
b. Is presently available for type 2 DM.
c. Is presently available for both types 1 and 2 DM.
d. Is not presently available.

26. The EFIRM™ liquid biopsy technique is an acronym for:
a. Electric field-induced release and measurement.
b. Electric field-induced release and monitoring.
c. Electric field-induced removal and measurement.
d. Electric field-induced removal and monitoring.

27. Which of the following is accurate regarding salivary diagnostic testing?
a. Transportation of salivary samples is more expensive than blood samples.
b. Blood sampling is appropriate for all cultures.
c. Rapid screening of large populations is enhanced with salivary diagnostics.
d. Salivary samples are less stable than blood samples.

28. Biomarkers of disease that are present in saliva may be derived from:
a. Passive diffusion.
b. Active diffusion.
c. As an ultra-filtrate of saliva.
d. As an ultra-filtrate of gingival crevicular fluid.

29. Biomarkers for cystic fibrosis (CF) appear to be related to:
a. Oxidative processes in individuals with CF.
b. Inflammatory processes in individuals with CF.
c. Both a and b.
d. Neither a or b

30. Which of the following is accurate regarding breast cancer detection?
a. The sensitivity and specificity of physical examination and mammography is less than ideal.
b. A goal of finding salivary tests for breast cancer detection is to reduce the number of biopsies.
c. Early detection is universally regarded as a critical factor for long term favorable outcomes.
d. All of the above

Notes

The Impact of Salivary Diagnostics

Name: _____ Title: _____ Specialty: _____

Address: _____ E-mail: _____

City: _____ State: _____ ZIP: _____ Country: _____

Telephone: Home ( ) _____ Office ( ) _____

Lic. Renewal Date: _____ AGD Member ID: _____

Requirements for successful completion of the course and to obtain dental continuing education credits: 1) Read the entire course. 2) Complete all information above. 3) Complete answer sheets in either pen or pencil. 4) Mark only one answer for each question. 5) A score of 70% on this test will earn you 3 CE credits. 6) Complete the Course Evaluation below. 7) Make check payable to PennWell Corp. **For Questions Call 800-633-1681**

Educational Objectives

1. Discuss the advantages of salivary diagnostics

2. Discuss the potential impact of salivary diagnostics on a variety of systemic diseases and conditions

3. Describe how saliva testing is currently used by the dental profession

4. Implement saliva testing in the dental practice to enhance patient care

Course Evaluation

1. Were the individual course objectives met?

Objective #1: Yes No   Objective #2: Yes No

Objective #3: 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 webliography. 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?

_____

If not taking online, mail completed answer sheet to

PennWell Corp.
Attn: Dental Division,
1421 S. Sheridan Rd., Tulsa, OK, 74112
or fax to: 918-831-9804

For IMMEDIATE results,
go to www.ineedce.com to take tests online.
Answer sheets can be faxed with credit card payment to
918-831-9804.

☐ Payment of $59.00 is enclosed.
(Checks and credit cards are accepted.)

If paying by credit card, please complete the following: ☐ MC ☐ Visa ☐ AmEx ☐ Discover

Acct. Number: _____

Exp. Date: _____

Charges on your statement will show up as PennWell

1. Ⓐ Ⓑ Ⓒ Ⓓ	16. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ	17. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ	18. Ⓐ Ⓑ Ⓒ Ⓓ
4. Ⓐ Ⓑ Ⓒ Ⓓ	19. Ⓐ Ⓑ Ⓒ Ⓓ
5. Ⓐ Ⓑ Ⓒ Ⓓ	20. Ⓐ Ⓑ Ⓒ Ⓓ
6. Ⓐ Ⓑ Ⓒ Ⓓ	21. Ⓐ Ⓑ Ⓒ Ⓓ
7. Ⓐ Ⓑ Ⓒ Ⓓ	22. Ⓐ Ⓑ Ⓒ Ⓓ
8. Ⓐ Ⓑ Ⓒ Ⓓ	23. Ⓐ Ⓑ Ⓒ Ⓓ
9. Ⓐ Ⓑ Ⓒ Ⓓ	24. Ⓐ Ⓑ Ⓒ Ⓓ
10. Ⓐ Ⓑ Ⓒ Ⓓ	25. Ⓐ Ⓑ Ⓒ Ⓓ
11. Ⓐ Ⓑ Ⓒ Ⓓ	26. Ⓐ Ⓑ Ⓒ Ⓓ
12. Ⓐ Ⓑ Ⓒ Ⓓ	27. Ⓐ Ⓑ Ⓒ Ⓓ
13. Ⓐ Ⓑ Ⓒ Ⓓ	28. Ⓐ Ⓑ Ⓒ Ⓓ
14. Ⓐ Ⓑ Ⓒ Ⓓ	29. Ⓐ Ⓑ Ⓒ Ⓓ
15. Ⓐ Ⓑ Ⓒ Ⓓ	30. Ⓐ Ⓑ Ⓒ Ⓓ

AGD Code 734

PLEASE PHOTOCOPY ANSWER SHEET FOR ADDITIONAL PARTICIPANTS.

ISD1609DIG