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Oral Diagnostics for the Geriatric Populations: Current Status and Future Prospects

Yolanda Ann Slaughter, DDS, MPH[a],
Daniel Malamud, PhD[b,*]

[a]*Department of Preventative and Restorative Sciences, School of Dental Medicine, University of Pennsylvania, 240 South 40th Street, Philadelphia, PA 19104, USA*
[b]*Department of Biochemistry, School of Dental Medicine, University of Pennsylvania, 240 South 40th Street, Philadelphia, PA 19104, USA*

Because it is a noninvasive technique, there is growing interest in replacing blood with oral-based methods of diagnostics. Oral diagnostics may be used for diagnosis and therapeutic drug monitoring of both oral diseases (eg, caries, periodontal disease, oral lesions, oral cancer) and systemic diseases (eg, infectious diseases, including HIV and AIDS, autoimmune diseases, cancer, and endocrine disorders). Two general approaches to oral diagnostic analyses exist: (1) an oral sample may be collected and sent to a central site for analytic testing or (2) the sampling and analysis may be performed on site, a process referred to as point-of-care diagnostics. For hospitalized patients, laboratory analysis of blood or urine samples is routine; for mobile outpatients and functionally dependent or homebound individuals, point-of-care diagnostics would be a major advance. The benefits of oral sampling as opposed to blood testing include safety (little or no contact with blood), cost-effectiveness, and increased patient compliance, particularly in compromised subjects, such as infants, children, and geriatric subjects. Indeed, whether because of dehydration, sclerosed veins, or limited tolerance to the procedure [1], geriatric patients demonstrate unique difficulties in blood draws.

A number of reviews of saliva-based and other oral-based diagnostics have recently appeared [2–8]; however, none of these has focused on

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* Corresponding author.
E-mail address: malamud@pobox.upenn.edu (D. Malamud).

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applications for the geriatric populations. In the present review and commentary, the authors address both existing techniques and oral-based diagnostics that will be applicable to the aging population in the future. They also highlight those techniques that are uniquely suited to point-of-care applications.

It is well known that most molecules found in blood or plasma also can be detected by sampling the oral cavity. The accuracy of any diagnostic test is defined by its sensitivity, specificity, predictive value, and efficiency [9]. The major issues in developing a successful oral diagnostic test are the sensitivity of the assay and the relationship of the oral level of the analyte to the reference blood levels. Sensitivity is an issue because most molecules in saliva are present at lower levels than those found in blood. Fortunately, advances in amplification and detection technologies now permit analyses at the low concentrations of analyte found in oral samples. The relationship of the oral level to the plasma level, the saliva/plasma (S/P) ratio [10], is relevant when quantitative values are required from the diagnostic test. For a qualitative assay—for example, the presence or absence of antibodies to HIV—the only issue is sensitivity. The oral test must be sensitive enough to detect the lower levels of antibodies found in the oral cavity, but because the HIV diagnosis is "yes or no," the exact amount of antibody present is not required. In contrast, for therapeutic drug monitoring or determining blood alcohol concentration with salivary samples, the S/P ratio must be constant over a range of plasma concentrations if the diagnostic test is to be useful.

Fluids from the oral cavity that can be used for analysis include whole saliva, parotid saliva, submandibular saliva, minor salivary gland secretions, gingival crevicular fluid (GCF), and oral mucosal transudate. A description of these fluids and a summary of methods for their collection have been published in the Guidelines for Saliva Nomenclature and Collection section of the *Annals of the New York Academy of Sciences* [3]. In addition, oral tests may use buccal epithelial cells as a source of DNA [11], oral/pharyngeal swabs for identification of a number of infectious pathogens, a cytobrush for oral cancer detection [12], and volatiles to assess malodor or gastrointestinal dysfunction [13,14]. A new approach to saliva collection that might be particularly useful to homebound or institutionalized geriatric populations is self-collection with the Oracol sponge device (Malvern Medical Developments, Worcestershire, United Kingdom). This device, along with a questionnaire, was mailed to 14,800 individuals in an epidemiologic survey designed to monitor antibodies to infections [15]. Returned samples were successfully tested for antibodies to a number of viral pathogens.

The decision about which type of oral sample to collect will largely depend on the biologic question being asked. In quantitative diagnostics, one can often predict whether the S/P ratio will be constant based on the characteristics of the molecule being analyzed. This is because the mechanism whereby a molecule enters the oral cavity is the major determinant of the S/P ratio. For example, some molecules enter the oral cavity by direct diffusion from the blood, whereas others enter by active transport following tissue damage or by blood contamination of saliva. Unconjugated steroid hormones, such as dehydroepiandrosterone (DHEA), freely cross cell membranes, and thus salivary levels correlate closely with blood levels. However, the conjugated form of this hormone, dehyroepiandrosterone sulfate (DHEAS), does not freely diffuse into saliva. Some reports have demonstrated that DHEA measurements have an acceptable S/P ratio, whereas other reports note that the addition of sulfate impairs the lipid solubility of DHEA and thus the value of the salivary measurement as an index of blood levels of DHEAS [16].

A second factor to consider in the case of steroid hormones is that blood contains both free and protein-bound steroid hormone, whereas saliva contains only free hormone. In blood tests one either measures total hormone (bound plus free) or separates the two forms before assay. In contrast, salivary measurements of steroid hormones only detect free hormone. This limitation could be a positive attribute, because the free hormone concentration is often more relevant to biologic effects. Similar considerations may apply to therapeutic drug monitoring, because blood may contain both free and bound forms of the drug, whereas saliva will typically only contain free drug. The factors that affect the transport of a molecule from blood to saliva include molecular weight, pH, surface charge, hydrophobicity, and protein binding [17]. Some large molecules (eg, albumin) enter saliva as a result of tissue damage, leakage, or blood contamination. Blood contamination can be assessed by monitoring a known marker, such as hemoglobin [18] or transferrin [19]. It is then possible either to discard the contaminated samples or correct for leakage from blood.

Oral diagnostics: lifespan developmental ideas

As the population continues to age and to benefit from advances in managing chronic illnesses, a growing number of persons will fit the paradigm of successful aging [20–23]. This phenomenon will be seen dramatically in the aging baby boomers. The desire to maintain quality of life and good functionality over the lifespan sets the stage for use of oral diagnostics, which may have particular relevance to risk assessment and monitoring of disease onset and severity among various older adult cohorts. As the population continues to change in size and diversity [24], there will necessarily also be changes in the demand for health care delivery among the young-old (65 to 75 years), the old-old (75 to 85 years), and the oldest-old (>85 years) [25–28]. Because increasing functional disabilities affect an individual's ability to seek medical and dental services [29], health care providers should be developing collaborations to provide both oral and general health care, using novel methods that permit multiple tests from easily obtained samples [30]. Health care of the elderly from head to foot is complex and relies on a host of specialists—for example, the physician, dentist, nurse, social worker, physical therapist, and nutritionist. Homebound and institutionalized elders have good access to medical health care delivery. However, they are often unaware of oral health needs and of the relationship between oral health and general health. The authors believe that the development of new diagnostics for oral and systemic health will enhance communication between dental and medical health care providers and integrate oral health into the overall health care of the individual.

Overview of lifespan developmental issues

Functionally independent older adults

These persons are characterized as living in the community and requiring little to no assistance in their activities of daily living (ADL) [31]. This group constitutes the vast majority (85%) of the older adult population [32] and will increase dramatically as the baby boomers become ‘‘senior boomers’’ [20]. The senior boomers tend to place a high value on health, in part owing to their ability to pay for these services [20]. The senior boomers are characterized as using medical and dental services on a regular basis and as being accustomed to the advances of modern medicine and dentistry [27]. They are expected to continue using health services as they did when they were younger [27]. Because this group is aware of preventive medicine, its members are likely to perceive oral testing as beneficial to their health. Moreover, the senior boomers are expected to engage in behaviors that maintain their health, and oral-based testing may be a strategy for successful aging. Specific testing might assess caries activity, periodontal status, steroid hormone levels that affect postmenopausal bone loss, and possible onset of cancer, diabetes mellitus, or coronary heart disease [22,33–35].

Frail older adults

These persons reside in the community and require assistance in their ADL because of chronic physical, medical, or emotional problems [31]. This group includes homebound older adults, who constitute 10% of the older adult population [32]. The current dental care delivery system is least equipped to meet the needs of these homebound elders [36]. This deficiency is due in part to a dearth of dental providers who have geriatrics training and are willing to provide mobile services, and in part to barriers imposed by Medicare/Medicaid, which excludes dental services to the elderly [24,32,36]. Point-of-care diagnostics could identify systemic conditions or emotional problems that characterize the functional status of this population. The homebound population and its caregivers highly value point-of-care medical services that accommodate their desire to avoid institutionalization [36]. Therefore, the use of oral tests to monitor chronic illnesses that influence the elders’ ability to remain at home would be particularly favorable to the caregiver. The medical providers have access to the homebound elders and have developed trusting relationships with the patients and caregivers. The initiation of oral health promotion by the visiting medical provider, by means of oral diagnostic testing, may motivate the homebound elder and the caregiver to view oral health as integral to maintaining general health. In the future, oral tests may include monitoring for nutritional deficiencies, which plays an important role in promoting medical and dental health care. Vitamin and nutrient deficiencies lead to oral signs and symptoms; they also influence resistance to disease and the ability to repair damaged tissues. Common systemic illnesses that affect frail elders, such as diabetes, chronic obstructive pulmonary disease, osteoporosis, and atherosclerotic cardiovascular disease, are well known to be associated with malnutrition [37]. Although point-of-care diagnostics for malnutrition do not yet exist, this is clearly an area for future development.

Functionally dependent older adults

These persons reside in nursing homes and constitute 5% of the older adult population [32]. This population is so impaired by a combination of physical, mental, or emotional problems that its members are unable to maintain their independence [31]. Unlike the frail homebound elders, elderly nursing home residents have well-documented dental care needs, with oral hygiene poor and chronic oral infections prevalent [31,32,36,38,39]. These elders require total assistance with their personal hygiene, and oral hygiene is not a major concern of the overworked, underpaid, and non–dentally educated staff who are responsible for up to 90% of their daily care [38,39]. This barrier to dental care delivery has serious implications for the quality of life and potential for successful aging of residents in long-term care facilities. As in the frail homebound population, the use of oral diagnostics by the nursing staff to identify and monitor disease severity in these patients may reduce the risk of acute exacerbations. A greater benefit to the oral hygiene of nursing home residents is seen when nursing aids receive encouragement from other members of the nursing staff, as opposed to instruction by a dentist or hygienist [38]. In this context, oral diagnostics may be a useful approach to educating and motivating nursing aides to consider daily oral health care essential to overall care. Poor oral hygiene and chronic oral infections have been shown to be associated with aspiration pneumonia and bronchopulmonary infections [40,41]. Specific tests applicable to long-term care residents include evaluation of oral and respiratory infections so that they can be treated either prophylactically or therapeutically.

Demand for dental and medical care: cohort differences in dental care need

The graying of America means that people are living longer; however, demographic transition trends among birth cohorts provide a more specific explanation of the process of population aging. Trends in oral disease patterns have resulted in a dramatic decline in total tooth loss with increasing age; more elders are retaining their natural teeth [42]. In the younger generation of elders, this factor is coupled with positive expectations about retaining and maintaining teeth and maintaining good general health over the lifespan. The oldest generation of elders, by contrast, tends to have ageist views about the possibility of retaining teeth and maintaining good general health. These different attitudes of different older populations present a challenge to the dental profession in meeting their care needs [20,25,43,44].

A clear understanding of the patient's desires and needs is key to the clinical decision-making process and is essential for providing care based on rational health assessments of the growing elder population. Perceived need is the most common reason cited by elders for not seeking medical or dental care services [45]. Therefore, this section's discussion of new diagnostic techniques is guided by an awareness of the different perceptions of health care need and attitudes toward health among different generations of the elderly.

Oldest-old (>85 years)

This cohort has the distinction of being the fastest-growing segment of the elderly population, and its health care needs are also increasing dramatically [27–29]. Historically, most people in this age cohort were totally edentate, and tooth loss was considered an inevitable part of growing old [27]. This attitude was due to a lack of money and to a philosophy of dentistry that was not directed toward saving teeth. The typical dental practice was to have teeth extracted in response to symptoms of tooth pain, so many of the aged over 85 wear complete dentures [27]. Patients in this cohort are more likely to suffer from the effects of chronic diseases, of taking multiple drug regimens to treat these problems, and of not seeking dental services, particularly when they are edentulous. Although root caries and periodontal disease are not as prevalent in this cohort [46–48], other age-prevalent changes relevant to oral diagnostic procedures might be used to promote successful aging in collaboration with medical health care providers [49]. Particular interest is focused on elders who lack dental services and who have Alzheimer's disease, stroke, Parkinson's disease, or oral-motor dysfunction disabilities that impair the ability to perform oral self-care behaviors [50–52]. These persons are more susceptible to the adverse health effects of oral pathogens, salivary dysfunction, and adverse drug interactions [53]. Additionally, oral lesions are common among older adults using dental prosthesis [28]. Health care providers have access to this population, in which noninvasive tests may be particularly beneficial because of its tendency toward inadequate oral hygiene due to combativeness or tremors. Risk assessment on the part of the medical provider may facilitate increasing referrals to the dentist to promote overall health.

Specific tests for this population include therapeutic drug monitoring and health assessments applicable to long-term care residents and the frail homebound.

Old-old (≥75 years)

Most people in this cohort have retained more natural teeth and total tooth loss is less common than in the previous cohort [27,28]. These elders use dental services on a more regular basis than the oldest cohort and have benefited from the philosophy of dentistry that focused more on restorative care [28,29]. This cohort is better educated and more financially secure and has experienced more dental contact for preventive services. Although the presence of teeth is reported to be highly correlated to perceived need in this age group—more so than income or education—the expectation of having complete dentures as a normal part of growing old still prevails in this cohort, as in the oldest one [28]. By contrast with the oldest cohort, the trend toward tooth retention, resulting in increased rates of root caries and periodontal disease, is an issue in this one [28,42,47,48]. Dental health is not generally perceived as important by this cohort, so many have unmet oral health issues that can adversely affect chronic conditions and quality of life. Given that people in this cohort have experienced more frequent dental contacts for reasons other than tooth extraction, and that they routinely sent their children to the dentist [28,29], they may be more amenable to changing their demand for dental care when the change is initiated by the medical provider as a means to preserve their health. Like the oldest cohort, these elders are affected by age-prevalent changes and normative age changes that can benefit from oral diagnostic testing.

Young-old (>65 years)

Most people in this cohort are characterized as retaining more natural teeth and having had more regular dental contacts than previous generations. This so-called "new elderly" had the advantages of more education, more consumable income, and the technological advances of modern dentistry [26,28]. The baby boomers constitute a growing proportion of this cohort. Because they are more aware of the benefits of maintaining good medical and dental health, they may hold the most promise for using new diagnostic methods to track medical and dental conditions. The political and social movements experienced by this cohort were fueled by the desire to take action to advance the public well-being. Likewise, the new elderly will likely continue to access dental and medical services, and they will demand continued technological advances in medicine and dentistry to help them achieve successful aging [20,26,28]. Hence, the use of new oral-based tests by this cohort may help persuade third-party insurers to compensate providers for this service. Additionally, the fact that medical providers can easily use oral diagnostic testing may have an impact on policy makers. More emphasis will be directed toward increasing awareness of the importance of oral health to overall health to compress morbidity and decrease medical costs.

The aforementioned cohorts include subsets of persons identified as being low income, members of minority groups, or persons with special needs. These vulnerable elders (including the frail homebound and nursing home residents) have less than ideal access to dental care services compared with their counterparts in the general population [30,54–57]. The opportunity exists for dental providers to build community partnerships on a local level with aging networks that target these underserved groups, such as senior centers, residential care centers, and mental health centers. Oral diagnostics could be incorporated into these community-based programs and provide point-of-care services in a familiar setting. This approach could increase awareness of the relationships between oral and systemic health among the community-dwelling vulnerable elders and could increase the standard of care in residential facilities for special needs elders. Thus, oral diagnostics may serve to decrease health disparities among underserved groups. Other conditions of importance to low-income elders include diagnostics for toxic materials, including heavy metals, because these elders often live in areas that are more exposed to environmental hazards.

Specific applications of oral-based diagnostic tests

Caries

Because a number of factors contribute to caries formation, including host genetic factors, presence of bacterial pathogens, and nutrition, tests that monitor these three factors may prove useful in predicting caries activity. Classic microbial sampling and culture techniques for dental pathogens are widely used. A sample is collected on a swab or paper point and sent in appropriate transfer media to a microbiologic test site. Samples are cultured for approximately 48 hours, and typically the results are sent directly to the clinician to help guide treatment planning. These types of assays can be used for both cariogenic and periodontal organisms, although there is some question about the impact of such testing on subsequent treatment options. A simpler diagnostic system uses test strips to identify either *Streptococcus mutans* or *Lactobacilli* (Dentocult strips, Orion Diagnostica, Finland). The strips are exposed to the oral tissue and then incubated for 48 hours; a colorometric analysis is used to identify the presence of *S mutans* or *Lactobacilli*. Perhaps more relevant to point-of-care diagnostics, several investigators are developing polymerase chain-reaction and microarray-based assays that may be used to identify oral pathogens rapidly [58,59]. The approach uses a miniaturized detection system, sometimes referred to as lab-on-a-chip, which would amplify the signal and give a positive or negative result on site. Rapid test results lead to prompt dental and medical decision-making.

An alternative approach to predicting caries susceptibility is to monitor oral pH or buffer capacity. Because demineralization of the tooth is accelerated in an acid environment, salivary pH and the ability of saliva to buffer bacterial acid production are likely to be related to caries activity. Subjects with high buffer capacity have an increased ability to resist caries formation. Buffer capacity can be assessed quickly with Dentobuff strips (Orion Diagnostica, Finland); this assessment may be useful for identifying individuals who need to be monitored more closely or given additional nutritional counseling and other preventive measures.

Saliva also contains a large number of proteins that help control bacterial colonization, by influencing the balance between bacterial clearance from the oral cavity and adherence to oral tissues [60]. Several recent reviews address this topic [61,62]. Ideally, one would have a single marker that correlates with actual or potential caries activity. One such possibility is suggested by research from the Denny laboratory [63]. Their studies suggest a relationship between the *S mutans* titer in the oral cavity and the concentration of MG2, the low molecular weight mucin present in whole and submandibular saliva [64]. In a study of 24 subjects aged 65 to 82, elevated titers of *S mutans* were associated with decreased levels of MG2. Previous reports from this group had demonstrated that mucin concentration decreases with aging [65]. A rapid test for MG2 in the oral cavity that is amenable to point-of-care diagnosis appears to be feasible and could facilitate identification of elder individuals who are at an increased risk for caries formation.

Periodontal diseases

Advances in the diagnosis of periodontal diseases have focused on new microbiologic methods for detecting periodontal pathogens and on various techniques to monitor the host response to gingival inflammation. As noted earlier for caries diagnostic tests, traditional methods of identifying periodontal pathogens rely on oral sampling followed by bacterial culturing at remote laboratory sites. Newer approaches are using a variety of molecular approaches, which could be adapted to point-of-care diagnostics. In terms of assessing the host responses to periodontal disease, both saliva and GCF tests have been used. Although GCF testing may be valuable, it requires a dental professional to obtain the sample, whereas saliva-based tests could be performed by relatives, care-givers, or even by the functionally independent individual. Analytes that may be useful for monitoring periodontal diseases have recently been reviewed [66–68] and include lactoferrin, collagenase, lysozyme, prostaglandin E2 (PGE2), proinflammatory cytokines, and markers of cell death such as aspartate aminotransferase. To date, no single marker appears to correlate specifically with the presence or extent of periodontal disease, but a constellation of markers may prove to be useful. Another issue raised by oral-based testing for both caries and periodontal disease is the need to educate and encourage the dental professional to support these tests. Some of the geriatric cohorts described earlier may provide this incentive and facilitate controlled clinical trials.

Antibodies/infectious diseases

One of the most successful applications of oral-based diagnostics is the use of an oral sample (saliva or mucosal transudate) to detect antibodies to HIV and a wide range of other infectious agents [69–71]. In general, ductal saliva contains mostly secretory IgA (sIgA), whereas whole saliva and mucosal transudates contain both IgA and IgG antibodies. Crevicular fluid generally has the highest level of immunoglobulins, but difficulties in collection of GCF limit its usefulness. Notably, salivary levels of IgA appear to increase with age [72], suggesting that detection may be easier in a geriatric population. Numerous studies have reported the use of oral fluids for detection of antibodies to a wide range of bacterial, viral, and fungal pathogens, and it is reasonable to predict that if the fluids are a useful source of these antibodies, any antibody can be detected. Because levels of antibody in oral samples are lower than those in blood, more sensitive assays are required. A second generation of sensitive immunoassays using polymerase chain reaction or time-resolved fluorescence may prove particularly valuable for use with oral specimens [73].

Saliva and other oral fluids can also be used to detect antibodies associated with autoimmune diseases. In Sjögren syndrome, for example, there are numerous reports of studies tracking anti–SS-A (anti-Ro) and anti–SS-B (anti-La) antibodies (see [74] for a recent review). In addition, autoantibodies against M3 muscarinic acetylcholine receptors are closely correlated with decreased salivary flow and salivary lysozyme levels [75], suggesting that this may be another useful marker for diagnosing Sjögren syndrome. It has also been reported that salivary antimitochondrial antibodies are associated with primary biliary cirrhosis [76], a disease with increasing prevalence in postmenopausal women.

Therapeutic drug monitoring

One of the major concerns of health care workers managing geriatric clients is therapeutic drug monitoring. One issue in this area is adherence to the prescribed drug regimen: patients may forget, lose track of, or purposely "overdose" on their prescription drugs ("if a little is good, more must be better"). In some cases, the consequences are insignificant, but in many cases the therapeutic window is small, and serious adverse events can result from too little or too much of the prescribed drug.

A large body of literature addresses the use of oral samples for detecting and quantizing the drugs of abuse (eg, ethanol, opiates, cannabis, cocaine, amphetamine) as a noninvasive point-of-care diagnostic [77–79]. In general, these studies have demonstrated that oral testing is as accurate as blood or urine testing, and it is possible to distinguish drugs of abuse from legal drugs (eg, codeine or benzodiazepines). The therapeutics most widely studied with oral tests include anticonvulsants (phenytoin, carbamazepine, and phenobarbital), cotinine as a measure of tobacco smoke exposure, theophylline, and lithium. Although all these drugs demonstrated acceptable S/P ratios, there appears to be no incentive to develop these as marketable tests, probably because of the perceived modest market size for such diagnostics.

More recently, oral samples have been used to monitor the hormone melatonin [80], the epilepsy drug lamotrigine [81], schizophrenia therapeutics such as clozapine [82], and the anti-HIV drug nevirapine [83]. In all these cases, oral drug levels were correlated with blood or urine levels; however, none of these has been developed as a commercial test. In cases where the patient is hospitalized and blood is routinely collected, there is no incentive to use an oral test for the drug. However, the geriatric population may be an ideal cohort for oral diagnostics, creating an impetus for commercial development.

Cancer

A large body of information exists on saliva-based diagnostics for oral cancer. These studies include antibodies to the common tumor suppressor p53, associated with squamous cell carcinoma of the oral cavity [84,85]. Extraction of DNA from saliva revealed mutations in p53 that were much higher in samples from oral squamous cell carcinoma (5/8, 62%) than in healthy salivary samples (5/27, 18%), suggesting that specific mutations could be used as a molecular marker [86]. In addition, microsatellite analysis using salivary DNA has been used for molecular analysis of tumorigenesis in head and neck carcinoma [87]. Although these changes can be detected by isolating DNA from saliva samples, brushing of the lesion may increase the sensitivity of these assays [88]. Streckfus et al [89] have reported that a number of tumor markers (CA15-3, c-erb-2, EGF receptor, and p53) can be detected in the saliva of women with breast cancer. If confirmed, these findings would provide great impetus for the development of screening tests for breast and perhaps other tumors. The cancer markers just described are compatible with point-of-care diagnostics.

A summary of lifespan developmental stages and age cohorts, as related to relevant oral diagnostics, is presented in Tables 1 and 2.

Future possibilities for oral-based diagnostics

In a number of cases, oral-based tests have demonstrated that a particular analyte can be monitored, but approved commercial tests are not yet available—this is the case, for instance, with monitoring steroid hormone levels. Reports also exist of defensin-1 in saliva associated with oral

Table 1
Oral diagnostics: lifespan developmental stages related to functional status

Functional status	Characteristics	Health care need	Oral diagnostics
Functionally independent older adults	Community-residing; no assistance with ADL	Increasing medical and dental care need with aging baby boomers	Diabetes mellitus, coronary heart disease, cancer, caries/periodontal tests, therapeutic drug monitoring
Frail older adults	Community-residing; assistance with ADL; include homebound	Dental care needs unknown; value point-of-care medical services	Nutritional deficiencies, autoimmune diseases, infectious diseases, dementia, Parkinson's
Functionally dependent older adults	Nursing home residents	Poor oral hygiene and chronic oral infections	Oral and respiratory infections, cancer

inflammation [90] and oral carcinoma [91], C-reactive protein associated with periodontal disease [92], and salivary endothelin associated with chronic heart failure [93]. In addition, there are factors for which oral testing would clearly be useful, but no test yet exists, such as prostate-specific antigen (PSA), vitamin and other micronutrients, and markers for arteriosclerosis, Alzheimer's disease, and Parkinson's disease. One of the potential advantages of point-of-care oral-based diagnostics is the capacity to monitor changes over time, instead of relying on a single determination. For example, it appears that the rate of change in PSA levels may be more

Table 2
Oral diagnostics: lifespan developmental stages related to age cohort

Age cohort	Health care need	Demand for health care	Oral diagnostics
Oldest-old (85 y and older)	Susceptible to health effects from oral pathogens, salivary dysfunction, drug interactions	Increased medical use; little dental contact; most edentate	Therapeutic drug monitoring, autoimmune diseases, nutritional deficiencies, infectious diseases
Old-old (75 y and older)		Increased medical use; more regular dental contact; total tooth loss less common	
Young-old (65 y and older)	Modeling successful aging; more knowledgeable about benefits of maintaining medical and dental health	Regular medical and dental contact; retained more natural teeth	Caries activity, periodontal status, steroid hormone levels, cancer, autoimmune diseases

important in predicting prostate cancer than a single reading. Such might also be the case for markers of inflammation, coronary heart disease, and arteriosclerosis. As more oral tests become approved and as health care providers and health management organizations recognize the potential for such tests, it is likely that efforts will be directed to the identification of markers that can monitor or predict disease.

The National Institutes for Dental and Craniofacial Research have issued a request for applications to identify and develop new oral-based diagnostics (Development of Technologies for Saliva/Oral Fluid Based Diagnostics RFA: RFA-DE-02-002) and have funded seven research projects. Some of these are likely to result in novel detection systems that include point-of-care diagnostics.

With the characterization of the saliva proteome, also supported by NIDCR (The Salivary Proteome: Catalogue Of Salivary Secretory Components RFA: RFA-DE-04-007), a complete catalogue of all salivary proteins will be available, facilitating future studies to correlate specific proteins with specific stages in the aging process. Likewise, the determination and cataloging of all the metabolic small molecules in the oral cavity, referred to as the metabolome, will provide a benchmark for determining specific alterations in these molecules throughout the aging process. It is possible to envision an in-dwelling sensor with capabilities for continuously transmitting data on the levels of proteins, small molecules, and hormones in the oral cavity. Indeed, a number of companies are currently developing biochips that could carry out this type of measurement.

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