# The National Institute of Dental and Craniofacial Research

## Research for the practicing dentist

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## ABSTRACT

**Background and Overview.** Established in 1948, the National Institute of Dental and Craniofacial Research (NIDCR) has helped transform dentistry into a profession that is based firmly in prevention and technological innovation. This article introduces the new NIDCR initiative in general dentistry practice-based research. It also highlights research supported by the NIDCR and its implications for dental practice in restorative dentistry, oral and systemic disease, stem cell research, salivary diagnostics, gene transfer therapy and pain.

**Clinical Implications.** The NIDCR supports research that will help guide the practitioner in the delivery of patient care and have a direct impact on the practice of dentistry.


**Key Words.** National Institute of Dental and Craniofacial Research; dental practitioner; oral health research.

In 1948, largely through the efforts of the American Dental Association, legislation was signed into law by President Harry S. Truman that established what now is called the National Institute of Dental and Craniofacial Research (NICDR) (Figure 1). As one of 27 Institutes and Centers at the National Institutes of Health (NIH) and with a fiscal year 2004 budget of $382 million (Figure 2, page 730), the NIDCR seeks to improve oral, dental and craniofacial health through research, research training and the dissemination of health information. To accomplish its mission, the NIDCR performs and supports basic and clinical research; conducts and supports training of investigators; coordinates relevant research in the broader research community; and promotes the timely transfer of research knowledge and its health implications to the public, health professionals, researchers and policy makers.

**The NIDCR supports research that will help guide the practitioner in the delivery of patient care.**

In the past 57 years, the NIDCR has helped to transform dentistry from a profession that in the 1940s dealt primarily with extractions, dentures and caries to one that today is firmly based in prevention and technological innovation. Indeed, NIDCR-supported research has helped to advance several mainstays of prevention and modern dental care, such as water fluoridation, dental sealants, composite restorations, acid-etch bonding and periodontal therapy.

While some practitioners might be put off by talk of genes and protein arrays, they do so to some extent at their own professional peril. For it is increasingly possible to see the broad outlines of molecular-based dentistry that will dominate the 21st century and transform dental practice. For instance, it is easy to imagine that one day dentists routinely will use office procedures to measure the genes expressed by the plaque biofilm that, in turn, will guide them in selecting appropriate antibacterial therapy to match a specific bacterial genetic profile to prevent or treat the major oral infectious diseases of caries and periodontal disease. It is likely that restorations will play a less prominent role in dental practice, because earlier detection of decay will enable dentists to apply remineralizing agents to teeth to reverse the carious process and restore teeth to health without surgical intervention (Figure 3, page 730). And it is possible that the dentist of the future will use postnatal stem cells to regenerate lost dental or periodontal structures.

The purpose of this article is to update the dental practitioner on

research currently being supported by the NIDCR that has the potential to influence dental practice in the near future. We also will provide a glimpse of possible advances to follow.

**Figure 1. June 24, 1948: President Harry S. Truman (seated) signs the bill establishing the National Institute of Dental Research. Standing, from left: Dr. C. Willard Camalier, director of the Washington office of the American Dental Association; Rep. Walter E. Brehm, R-Ohio, author of the bill; Dr. H.B. Washburn, ADA president; Dr. Bruce D. Forsyth, chief dental officer, U.S. Public Health Service; Dr. Carl O. Flagstad, chairman, ADA Committee on Legislation; Dr. Daniel F. Lynch, past president, District of Columbia Dental Society; and Dr. H. Trendley Dean, dental director, National Institutes of Health. Photo courtesy of the National Institute of Dental and Craniofacial Research.**

## CLINICAL RESEARCH: A PRIORITY FOR THE NIDCR

The NIDCR recently embarked on a new program to accelerate clinical research that will have an impact on the general practice of dentistry and will inform public health policy. This program involves many new initiatives, including a call for proposals and funding to establish general dentistry practice-based research networks; centers and research to eliminate disparities in the oral health of people in the United States; and research in oral cancer, orofacial pain, special-needs populations, health literacy and obesity. This program also involves shifting the NIDCR's emphasis on small, single-center clinical trials to large, multicenter Phase III clinical trials that are more in concert with the standards of the general medical community. As new initiatives become available under this new program of clinical research, they are posted in the NIH Guide for Grants and Contracts ("grants.nih.gov/grants/guide/index.html") and on the NIDCR Web site ("www.nidcr.nih.gov"). We invite oral health practitioners to visit this site and become more familiar with the research conducted by the NIDCR.

**General dentistry practice-based research networks.** The NIDCR recently committed $75 million over the next seven years to establish three practice-based research networks (PBRNs) in general dentistry that will answer questions raised by dental practitioners in the everyday practice of dentistry. These networks will be centered in the east at New York University in New York City, in the south at the University of Alabama at Birmingham and the University of Florida, Gainesville, and in the west at the University of Washington, Seattle, and Oregon Health & Science University in Portland. Several state dental associations have indicated their support for these networks.

The overall objective of the PBRN initiative is to accelerate the development and conduct of clinical trials and other clinical studies of important issues concerning oral health care related to general dental practice. The PBRNs will perform relatively short-term clinical studies, with emphasis on comparing the effectiveness of various oral health treatments, preventive regimens and dental materials. The primary objective of each study carried out by the PBRNs will be to strengthen the knowledge base for clinical decision making by testing particular clinical approaches and evaluating the effectiveness of strategies for the prevention, management and treatment of oral diseases and conditions. Secondary objectives of the PBRNs will be to con-

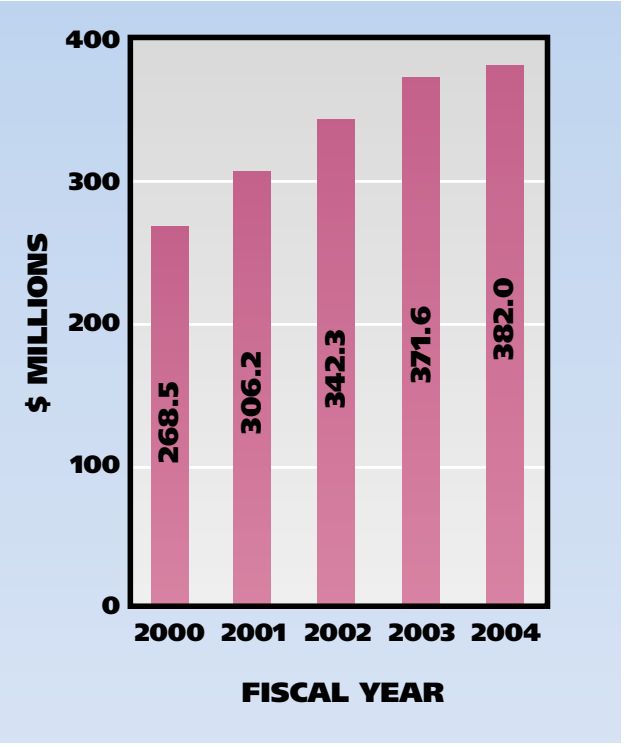


**Figure 2. Funding for the National Institute of Dental and Craniofacial Research.**

duct anonymous chart reviews, as allowed by the Health Insurance Portability and Accountability Act, to provide data on disease and treatment trends and to obtain estimates of the prevalence of less common conditions.

PBRNs can generate important and timely information to guide the delivery of health care and improve patient outcomes. Many of the unique questions faced by dental health practitioners on a daily basis can be addressed most appropriately in dental practice settings in the context of the oral health care delivery system. Indeed, the 2001 American Dental Association Future of Dentistry report specifically noted that national clinical research networks should be established to link treatment approaches and outcomes in private practice settings.[1] By connecting practitioners with experienced clinical investigators, PBRNs can enhance the clinical research agenda of the NIDCR and produce findings that are immediately relevant to practitioners and their patients. PBRNs can support a variety of clinical studies with clear and easily defined outcome measures, and they typically draw on the experience and insight of practicing clinicians to help identify and frame research questions. Because research is conducted in the

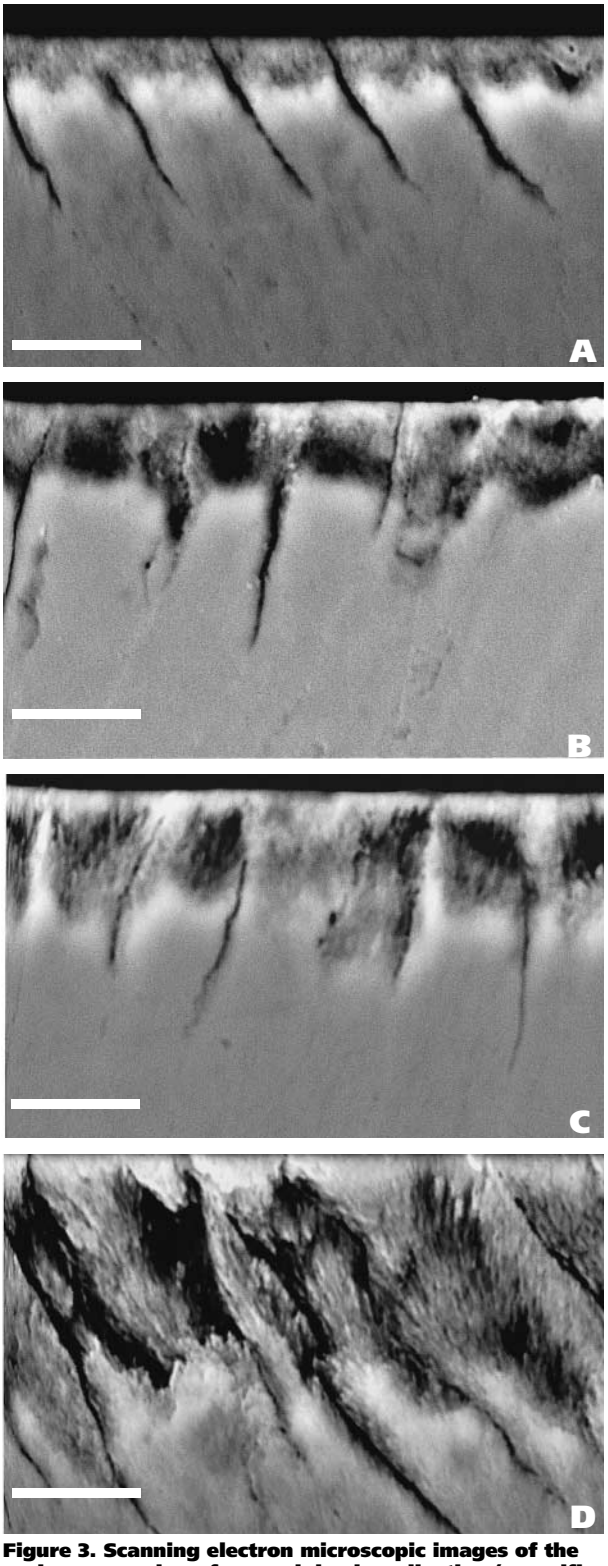


**Figure 3. Scanning electron microscopic images of the early progression of enamel demineralization (magnification × 5000). Horizontal bar indicates 5 micrometers. A. At four hours. B. At eight hours. C. At 12 hours. D. At 16 hours. Photos reproduced with permission of Drs. Masatoshi Ando and George Stookey, Indiana University, Bloomington.**

real-world environment of dental practice, practitioners are more likely to accept and adopt the results readily and translate them into daily practice. Moreover, PBRNs use the existing personnel and infrastructure of established dental practices, and this permits certain types of clinical studies to be conducted in a cost-effective manner.

**Research in restorative dentistry.** The NIDCR has supported research in restorative dentistry throughout its existence.[2] For example, early work at the then National Institute of Dental Research by Drs. Harold Stanley and Herbert Swerdlow documented the reactions of the dental pulp to the newly discovered high-speed turbine handpiece.[2] The NIDCR supported the research of Dr. Michael Buonocore at the Eastman Dental Center, Rochester, N.Y., which led to the acid-etching technique that revolutionized operative dentistry by introducing adhesive bonding. For many years, the NIDCR also supported the work of Dr. Rafael Bowen at the ADA Foundation's Paffenbarger Research Center (formerly the ADA unit of the National Bureau of Standards), where he synthesized bis-phenol-A-diglycidyldimethacrylate, a substance that is found in many composite restorations.

*Composites.* NIDCR support for research in restorative dentistry continues to this day. For example, it is clear that use of composite restorations in dental practice is increasing. However, composites have limitations; resins are prone to polymerization shrinkage that can lead to stress on bonded interfaces with the tooth, microleakage and recurrent decay. Furthermore, extended chair time often is required for large restorations because of the slow cure rate and the layered application that is required. Research currently supported by the NIDCR is addressing many of these issues, including strengthening of the resin-filler interaction and use of nanostructured particles and resin monomers for increased durability. Additionally, biocomputational approaches are being used to design new materials in modeling studies of the dentin-resin interface and to develop combinations of resin, primer and filler for optimal stress tolerance.

*The dentin-enamel junction.* Insight into the unique biomechanical properties of the dentino-enamel junction (DEJ) and the mechanism of biomineralization of enamel are two areas of basic research supported by the NIDCR that may provide a glimpse into the future of restorative dentistry. Using interfacial fracture mechanics to quantify the fractures in the DEJ region, Imbeni and colleagues[3] estimated that the DEJ fracture toughness was about five to 10 times higher than that of enamel, but approximately 75 percent lower than that of dentin. They found that dentin located immediately subjacent to the DEJ, rather than the DEJ itself, prevented cracks in enamel from traversing the DEJ interface and causing catastrophic tooth fractures.[3] Another recent example of basic research found that the self-assembly of amelogenin nanospheres into linear arrays may serve as a scaffold during early enamel mineralization.[4] These studies provide insight into factors that may be critical in the design of biomimetic dental materials that could be used by the dentist of the future.

**Investigators found no overall association between amalgam exposure and clinically evident peripheral neuropathy.**

*Amalgam safety.* Despite lack of any direct evidence of harm, there are long-standing concerns regarding the safety of mercury-containing dental amalgam and controversy about its continued use in dental practice. Very recently, the NIDCR and the U.S. Air Force collaborated in the ongoing Air Force Health Study (AFHS) of Vietnam-era veterans.[5] The study included an assessment of exposure to dental amalgam fillings to investigate possible associations between amalgam exposure and neurological abnormalities. In this study of 1,663 dentate AFHS participants, the investigators found no overall association between amalgam exposure and clinically evident peripheral neuropathy. The findings did not support the hypothesis that exposure to amalgam produces adverse, clinically evident neurological effects.[5] The NIDCR also is supporting two large prospective, randomized, single-blinded safety trials designed to detect even subtle adverse health effects associated with amalgam.[6] The trials include more than 500 children and will identify whether any neurological, behavioral or cognitive adverse effects occur during five to seven years of follow-up. An independent data and safety monitoring board is following both trials closely to ensure the continued safety of the volunteer participants and that scientific and ethical standards are maintained.

## CLINICAL RESEARCH ON ORAL AND SYSTEMIC DISEASE: IMPACT ON DENTAL PRACTICE

Dentists have always maintained that good oral health is essential for good general health. But—largely through the research supported by the NIDCR—specific evidence is beginning to emerge that oral disease may have profound systemic effects on organ systems elsewhere in the body. Many NIDCR-supported studies have linked periodontal disease to adverse pregnancy outcomes, cardiovascular disease, diabetes and pulmonary disease.

**Adverse pregnancy outcomes.** Defined as birth at earlier than 37 weeks' gestation, preterm birth accounts for about 12 percent of all U.S. births[7] but is responsible for three-quarters of neonatal mortality and one-half of long-term neurologic impairments in children.[8] Moreover, the rate of preterm birth continues to rise in the United States and has increased 16 percent since 1990.[7] Despite the numerous methods of prevention and treatment that have been proposed, the incidence of preterm birth has changed little during the past 40 years.[8] As first reported by Offenbacher and colleagues[9] in 1996, periodontal disease may be a risk factor for preterm birth and low birth weight. Many other observational studies have confirmed this finding, although there is evidence that it may not be a risk factor in all populations.[10] There is also preliminary evidence that periodontal treatment during pregnancy may reduce the incidence of preterm birth.[11-14] Investigators have proposed several biologic mechanisms involving the effect of various inflammatory cytokines and periodontal bacteria to explain the possible relationship between periodontal disease and preterm birth/low birth weight.[15-20] However, there is conflicting evidence to support any one mechanism, and the precise way in which periodontal disease may have an adverse effect on pregnancy outcomes is unclear.[21]

*Research implications for dental practice.* To date, there is no evidence that periodontal disease causes adverse pregnancy outcomes, nor are there sufficient data to conclude that periodontal treatment during pregnancy will reduce the incidence of preterm birth or low birth weight. To answer this critical question, the NIDCR has invested more than $20 million to support two large multicenter clinical trials. These trials are known as Obstetrics and Periodontal Therapy (OPT) and Maternal Oral Therapy to Reduce Obstetric Risk (MOTOR), and, together, they are in the process of enrolling more than 2,600 pregnant women at seven locations in the United States (Figure 4). The results of the OPT trial should be available in about one year. The results of these trials will provide sound evidence as to whether periodontal care can reduce the incidence of adverse pregnancy outcomes that have an enormous burden in terms of infant mortality and morbidity and economic cost. As such, this NIDCR-supported research has the potential to dramatically change the dental and periodontal treatment of women during pregnancy.

**Cardiovascular disease.** Atherosclerosis now is understood to be a disease characterized by inflammation that results in a host of complications, including ischemia, acute coronary syndromes (unstable angina pectoris and myocardial infarction) and stroke.[22] Similar to adverse pregnancy outcomes, evidence has been accumulating that periodontal disease may be a risk factor in cardiovascular diseases and stroke.[23,24] Some studies have questioned this relationship, mainly owing to the possible common effect of cigarette smoking on both diseases.[25-27] Perhaps the most direct evidence of such a relationship is an NIDCR-supported study called Oral Infections and Vascular Disease Epidemiology Study (INVEST) that recently was published in the medical literature.[28] This study of 1,056 older people showed that the presence of pathogenic periodontal bacteria in dental plaque was associated with increased thickness of the carotid artery wall, as measured by high-resolution B-mode ultrasound scan (Figure 5, page 734). Significantly, the association was found even after adjustments were made for conventional risk factors for cardiovascular disease. A follow-up study in the same population reported that radiographic evidence of severe periodontal bone loss was associated with a nearly fourfold increase in the risk of the presence of carotid artery plaque that can lead to stroke.[29] Moreover, there was a dose-response effect between severe periodontal bone loss and carotid plaque thickness that was even more pronounced in never-smokers.[29] The association between periodontal and cardiovascular diseases continues to be a major area of research interest for the NIDCR. The results of these studies could have a major role in defining the future practice of dentistry and its integration with health care in general.

*Research implications for dental practice.* As

**Figure 4. A volunteer patient participating in the Obstetrics and Periodontal Therapy clinical trial funded by the National Institute of Dental and Craniofacial Research to determine if periodontal therapy reduces the incidence of preterm birth.**

with adverse pregnancy outcomes, there is no direct evidence that periodontal disease causes cardiovascular disease, heart attack or stroke. There also is no direct evidence that periodontal treatment has any effect on these diseases. However, given the complexity of studying the possible relationship between periodontal and cardiovascular disease, the NIDCR is supporting a multicenter study called Periodontitis and Vascular Events (PAVE) to determine the feasibility of conducting a clinical trial to investigate whether periodontal treatment has any effect on these diseases. While the potential results are years away, if periodontal treatment is shown to have an effect on cardiovascular disease, which is a leading cause of death in the United States, this finding could have profound effects on preventive dentistry and medicine, as well as public health policy.

**Diabetes.** Diabetes has long been associated with periodontal disease, and new epidemiologic evidence has strengthened this association. For example, evidence from an 11-year prospective study of 628 subjects supported by the NIDCR indicated that periodontal disease was a strong predictor of cardiorenal mortality and diabetic nephropathy in Pima Indians with type 2 diabetes.[30] Another study reported clinical and epidemiologic evidence to support considering periodontal infection a risk factor for poor glycemic control in people with type 2 diabetes.[31] Therefore, there is some evidence to support the hypothesis that not only may diabetes cause increased severity of periodontal disease, but also that treatment of periodontal disease may influence diabetic control by decreasing insulin requirements.[32] The NIDCR is supporting research to evaluate the feasibility of conducting

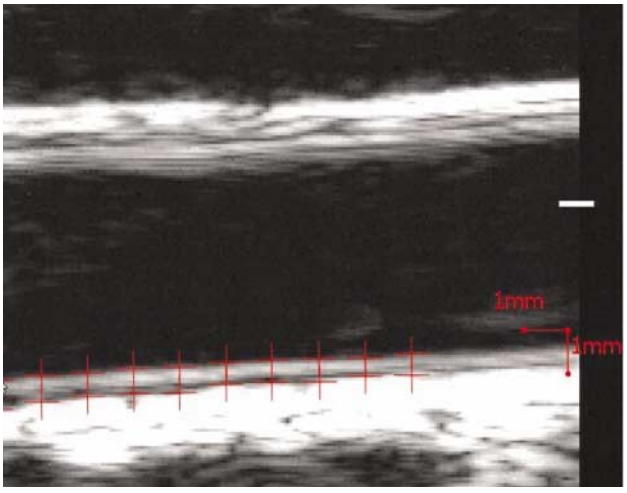


**Figure 5. B-mode ultrasound measurement of the carotid artery (intima-media thickness). A thicker wall is associated with future vascular events. Photo reproduced courtesy of Dr. Moise Desvarieux, Columbia University, New York City, and University of Minnesota, Minneapolis.**

a large multicenter trial to test this hypothesis.

*Research implications for dental practice.* Based on current data from clinical research supported by the NIDCR, it is clear that people with diabetes are more likely to have periodontal disease, particularly if their diabetes is poorly controlled or is of type 2.[33-38] This should alert practicing dentists to the increased risk of periodontal disease in their patients with diabetes and the need for increased surveillance and procedures to prevent periodontal disease in these patients. Moreover, if future NIDCR-supported research indicates that diabetic control is improved with periodontal therapy, it will mean that dentists will have an integral role in achieving and maintaining glycemic control in these patients and will need to work closely with physicians in the care of patients with diabetes.

**Pulmonary disease.** Emerging evidence suggests that various respiratory infections may be associated with periodontal disease,[39,40] and reports indicate that potential respiratory pathogens that cause pneumonia colonize the mouths of patients at high risk of developing respiratory disease, such as those in intensive care units.[41-43] Moreover, preliminary studies indicate that oral hygiene using either mechanical cleaning or antiseptic rinses can reduce the rate of respiratory infections in institutionalized patients.[41,44,45] The NIDCR is supporting a study to determine the feasibility of conducting a full-scale clinical trial to determine if oral hygiene procedures can reduce the pulmonary disease in patients at high risk of developing such disease.

*Research implications for dental practice.* If respiratory infections or chronic obstructive pulmonary disease can be prevented by simple procedures such as mechanical cleaning or use of antiseptic mouthrinses, this could have a major effect on the preventive care that is provided by dentists and other health care workers for patients who may be at risk of developing pulmonary disease because of ventilator use or confinement to intensive care units.

## BASIC RESEARCH: THE PATH TO THE FUTURE OF CLINICAL PRACTICE

The NIDCR has always been a strong supporter of basic and translational research, and exciting new research findings in these areas may well revolutionize the way dentists practice in the future. Some examples include research on tissue engineering and the biologic mechanisms for regenerating dental structures, genetic control of various oral diseases and conditions, production of drugs by the salivary glands, the use of saliva for screening and diagnosis, and postnatal recovery of stem cells from exfoliated deciduous teeth. Each of these may well lead to breakthrough discoveries that could change the practice of dentistry.

**Stem cell research: dental and craniofacial regeneration.** Postnatal stem cells have the capacity to form many different tissue types. Further study of the isolation, nature and differentiation potential of stem cells likely will have a positive impact on our understanding of human development and the potential use of these cells for cellular therapeutics in craniofacial and dental regeneration. Research conducted at the NIDCR has raised the possibility of regenerating periodontal tissues—including periodontal ligament, cementum and bone—that have been lost because of periodontitis. This research found that stem cells could be isolated from surgically extracted third molars and that these cells have the potential to generate cementum or periodontal ligamentlike tissue and might hold promise as a therapeutic approach for reconstruction of tissues destroyed by periodontal disease.[46] Another exciting development is the discovery that multipotent stem cells can be obtained from exfoliated deciduous teeth.[47] These stem cells from human exfoliated deciduous teeth (SHED) were identified to be a population of highly proliferative, clonogenic cells capable of differentiating

into a variety of cell types, including neural cells, adipocytes and odontoblasts. Thus, for the very first time, NIDCR researchers showed that a naturally exfoliated human organ contains a population of stem cells that are completely different from previously identified stem cells. SHED not only are derived from a very accessible tissue resource but also are capable of providing enough cells for potential clinical application.

*Research implications for dental practice.* If stem cells from the periodontal ligament, extracted third molars or multipotent SHED cells can be used to regenerate periodontal structures, the dentist of the future may participate in a dental stem cell bank of autologous stem cells that are maintained for people to regenerate, if necessary, lost periodontal or perhaps other craniofacial tissues that are lost or damaged by disease or trauma. Perhaps this technology even could be used to regenerate and replace teeth that are lost to oral disease.

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**Saliva and salivary gland research.** *Saliva as a diagnostic fluid.* NIDCR researchers are exploring the role that saliva and the salivary glands may have in future dental and medical practice. As we enter the era of molecular medicine, increasing use of salivary diagnostics will help catalyze a shift from disease diagnosis to health surveillance. Saliva is a noninvasive medium from which a wide range of hormones, pharmaceuticals and antibodies can be measured as a convenient source of host and microbial DNA.[48]

*"Lab on a chip."* C-reactive protein (CRP) is widely accepted as a serum marker of inflammation. Research has indicated that increased levels of CRP can predict cardiovascular disease,[49] and researchers have recommended that strategies to lower cardiovascular risk with statins should include monitoring CRP as well as cholesterol levels.[50] In this regard, a "lab on a chip" recently was used to measure CRP in saliva. This method uses an electronic sensor array platform to perform chemical and immunological reactions using microspheres in an ultrasensitive silicon microchip.[51] This "lab on a chip" measures CRP in saliva with much more sensitivity than is possible using standard laboratory assays of serum. Moreover, preliminary data indicate that salivary measurement of CRP using this method is able to discriminate with an accuracy of 86 to 93 percent between people with periodontal health and those with disease.[51]

*Detection of oral cancer.* Since morbidity and mortality rates due to oral cavity and oropharyngeal squamous cell carcinoma (OSCC) have improved little in the past 30 years, early detection or prevention of this disease is likely to be most effective in arresting the disease. Scientists whose work is funded by the NIDCR recently reported that the cytokines interleukin (IL)-8 in saliva and IL-6 in serum hold promise as biomarkers for OSCC.[52] Since a saliva-based test could be a cost-effective adjunctive tool in the diagnosis and follow-up of patients with OSCC, the researchers next evaluated the diagnostic value of this new approach by evaluating gene expression in the saliva of 32 patients with OSCC and 32 healthy control subjects.[53] They found that 1,679 genes were expressed at significantly different levels in the saliva of patients with cancer compared with the control subjects. Furthermore, seven cancer-related biomarkers exhibited at least a 3.5-fold elevation in salivary levels of subjects with OSCC compared with salivary levels of control subjects. Combinations of these biomarkers had a 91 percent accuracy (sensitivity and specificity) in distinguishing patients with OSCC from control subjects. Importantly, this research demonstrated that it may be possible to use salivary diagnostics for early detection of oral cancer.

*Salivary glands as pharmaceutical "factories."* NIDCR researchers are investigating whether the salivary glands can be used to deliver various pharmacological agents to the blood and saliva by means of gene transfer.[54-58] A major application of this emerging biotechnology will be for gene therapeutics or the use of a gene as a drug. For example, the salivary glands may be induced to increase salivary production in patients with xerostomia or perhaps even induced to produce insulin in patients with diabetes. Increased secretion of saliva recently was induced in animals that had radiation-induced xerostomia without significant general adverse events,[58] and if this can be achieved in humans, it would be a major breakthrough in oral health research.

*Research implications for dental practice.* It is likely that genetic and biochemical analyses can be used in salivary diagnostics for detection and monitoring of a variety of systemic diseases. It also is inevitable that salivary assays one day will be used by dentists for the screening or diagnosis of oral diseases, such as periodontal disease and oral cancer, or even to assess the ongoing activity of systemic diseases that have a link to oral disease. Moreover, if functional salivary gland gene transfer can be accomplished safely in humans, it will mean that dentists one day may be treating oral diseases using gene therapy of the salivary glands to prompt the salivary glands to deliver a controlled and constant dosage of immunopharmaceutical agents to the mouth or even the bloodstream.

**Research on pain.** The NIDCR has long been recognized as a leader in supporting research on pain. For example, recent findings of basic scientists supported by the NIDCR may yield important insight into why women experience painful temporomandibular joint (TMJ) disorders (TMD) more often than men.[59] Using animals, researchers found that induced TMJ inflammation or chronic systemic estrogen treatment increased excitability of TMJ afferent neurons. Moreover, the effects of induced inflammation and estrogen were additive in terms of neuron excitability. This finding may help explain the profound sex differences observed in TMD and suggest novel ways to control TMD pain by blocking estrogen receptors in the TMJ. Another NIDCR-supported study recently showed that the administration of a potent chemical agonist, resiniferatoxin (RTX), results in selective deletion of nociceptive neurons that express high levels of a specific receptor (TRPV1). This "molecular neurosurgery" leaves other adjacent neurons unaffected.[60] The net result is that pain resulting from inflammation, hyperalgesia or cancer may be eliminated by administration of RTX without the accompanying negative side effects of opioid sedation or other nonselective chemical or surgical neuroablative interventions.

## SUMMARY

Research supported by the NIDCR promises to have a dramatic impact on the future practice of dentistry. The NIDCR has embarked on a bold new program of clinical research that involves partnering with dentists in PBRNs to answer questions that they face in the everyday practice of dentistry. Moreover, the NIDCR is investing in clinical and basic research in many areas that may well revolutionize the practice of dentistry as we know it. Examples include research in restorative dentistry and new dental materials; studies of the relationship between oral disease and systemic disease; stem cell research to regenerate periodontal, dental and craniofacial tissues that have been lost to disease or trauma; salivary research that will lead to new diagnostic tests; and gene transfer therapy that may prompt the salivary glands to produce hormones, antibodies or other biological agents to prevent or treat oral and systemic diseases. With so much research activity under way, the future looks bright for dentistry and the nation's oral health in the 21st century. ■

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