Commentary

Scientific Investments Continue to Fuel Improvements in Oral Health (May 2000–Present)

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The release of *Oral Health in America: A Report of the Surgeon General* in May 2000 raised national, state, and local awareness, for the first time ever, of the impact of oral disease in America. The report emphasized oral health's link to general health and well-being, and called for a national effort among individuals, communities, and health care providers to improve oral health among all Americans. One of the objectives from the Surgeon General's Report On Oral Health was to "advance the science base and translate into practice." Our objective here is to address how the science base has progressed in 3 main areas that have significant potential to impact oral health: sequencing of the human genome, tissue engineering, and saliva diagnostics. A secondary objective is to comment on progress in our understanding of dental caries and its impact on young children.

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In 2003, scientists completed the sequencing of the human genome, which comprised 3 billion base pairs (nucleotides) and 21 000 genes. This major initiative was made possible by advances in technology that are now accelerating our progress toward understanding the causes of oral diseases, including heritable craniofacial malformation syndromes, oral cancer, periodontal disease, and dental caries.[1] An estimated 1 out of every 33 children in America is born with a birth defect every year. Of these, defects affecting the craniofacial complex are among the most common, representing approximately a third of all birth defects. This includes almost 7000 children born with orofacial clefting, such as cleft lip and palate—one of the most common birth defects. The oral health implications are particularly important for this group of children because of the involvement of dental, oral, and craniofacial tissues in these syndromes. In addition, children with these conditions may experience developmental delays or require special feeding regimens that put them at risk for early childhood caries once the primary dentition erupts.

By the year 2000, the gene mutations associated with 21 of these heritable craniofacial syndromes had been discovered; by 2007, the molecular cause of an additional 17 craniofacial syndromes had been found. This research has revealed the complexity of craniofacial developmental processes. For example, it now appears that even the most common of craniofacial malformations—orofacial clefting—may involve as many as 7 gene variants. There may also be an interaction with other known etiologic factors, such as deficiency of folic acid during pregnancy.

Oral cancer is the sixth most common cancer in the general population and has one of the highest rates of mortality. Early diagnosis can save lives. Visual assessment to detect changes in the appearance of oral mucosal tissues is effective for those patients with leukoplakia or erythroplakia. However, in some cases, normal-appearing oral mucosa has been shown to have dysplastic cells and early oral squamous-cell carcinoma. Several new technologies have been developed to help diagnose oral cancers early, but to date, none yet has the necessary specificity, sensitivity, or practicality to be used routinely in the clinical setting. Advances in molecular biology have contributed significantly to the understanding of the initiation and progression of oral cancer. These range from cytogenetic and epigenetic alterations to mutations in specific tumor suppressor genes. Alcohol and tobacco are well recognized as risk factors for oral cancer, but more recently, human papillomavirus has also been established as a risk factor for head and neck cancer, independent of other risk factors. The current understanding of risk factors combined with molecular technologies has the potential to inform both diagnosis and treatment of oral cancers in the future.[2,3]

Although caries has traditionally been thought to be completely preventable, there is now evidence from genetic studies to show that genes play a role in individual susceptibility or resistance to caries.[4,5] Some genes are involved in enamel development and mineralization; others determine the flow rate, buffering capacity, and antimicrobial activities of saliva; still others contribute to taste preferences and immune responses to oral pathogens. It is anticipated that a better understanding of the genetics of this disease will lead to improved risk assessment and more targeted preventive interventions in the future.

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Currently underway is a genomewide search for markers associated with either caries resistance or susceptibility using extensive samples obtained from investigators across the United States. Results are expected in a few years.

BIOMIMICRY TO DESIGN AND FABRICATE DENTAL TISSUES

Biomimetics, or biomimicry, is an emerging field for the design and fabrication of cells, tissues, and organs based on sound bioengineering principles. One of the more significant scientific discoveries of the last decade is that multipotential mesenchymal stem cells can be cultured from the pulp tissue of primary teeth. In these studies, cells isolated from exfoliated primary teeth were capable of differentiating into osteoblasts, chondrocytes, and adipocytes. Subsequent studies with permanent exfoliated teeth found similar capabilities. With such accessible stem cells, the opportunities for a number of clinical applications now exist that were only speculative in the past. Therapies such as autologous stem-cell transplantation and tissue engineering are just two of the possibilities that are being applied to regenerative medicine and dentistry.

Advances in cell, molecular, and developmental biology, tissue engineering, and bioengineering have made possible the design and fabrication of bone, cartilage, cementum, dentin, muscle, salivary glands, and teeth. In many ways, the engineering of a tooth is similar to that of organ culture. One primary difference is that the tooth must be formed within bone and requires specific cells (the periodontal ligament) to be present between the root and adjacent alveolar bone in order for there to be attachment and proper function of the tooth. This problem has been successfully addressed in a number of research laboratories around the country and is close to being ready for translation into the clinical setting. For example, mesenchymal stem cells within a 3-dimensional scaffold were conditioned to fabricate a tooth root with complementary periodontal ligament integrated with adjacent bone.[6]

SALIVA AS AN INFORMATIVE DIAGNOSTIC FLUID

In the health care area, accurate diagnosis is an essential first step in providing care for patients. Traditionally, this has involved invasive procedures such as radiographs or blood tests. Recently, saliva has become a desirable and effective diagnostic fluid because it is readily available, can be collected noninvasively, and contains proteins, mRNA, microbes, and other analytes that can be used for diagnostic purposes. The accessibility of this fluid and the desirability of chairside diagnostic tests and advances in bioengineering have resulted in the development of microelectronic devices termed *lab on a chip* that are capable of measuring a variety of substances commonly found in saliva. These devices permit point of contact diagnosis of both medical and dental conditions.[7]

EARLY CHILDHOOD CARIES

With such significant advances in basic sciences and technology, it is concerning that we are not seeing concomitant improvement in the oral health of young children. As documented in this issue, efforts at prevention of dental caries (Tinanoff and Reisine[8]), caries risk assessment, and early detection of caries lesions (Milgrom and Zero[9]) have been disappointing at best. The multifactorial nature of dental caries necessitates a comprehensive approach to prevention and/or management. Behavior plays a major role in oral health, and children are reliant on parents to provide guidance in behaviors that promote good oral health. Education regarding the consequences of dental caries in young children does not always translate into motivation to provide children with a healthy diet, ensure good oral hygiene with appropriate use of fluoride toothpaste, and be proactive about seeking care. Poverty and limited access to care (Edelstein and Chinn)[10] further complicate efforts to eradicate this disease.

Disparities exist in all areas of health, including oral health. In response to this, the National Institutes of Health has funded a number of Centers for Research to Reduce Disparities in Oral Health. The 5 centers that were funded have contributed to our understanding of caries in underserved populations, but to date, they have not resulted in significant improvements in oral health for those most at risk. In the last few years, the National Institute for Dental and Craniofacial Research has funded practice-based research networks with the goal of performing clinical trials in multiple practices around the country. These studies have the potential to improve our understanding of oral diseases and techniques that are effective in improving oral health behaviors.

Conclusions

Since the Surgeon General's Report of May 2000, there have been unprecedented advances in basic science and technology related to oral diseases. For these advances to be translated into clinical practice, it is necessary for well-designed clinical trials to be performed with ample numbers of patients to provide strong evidence of both efficacy and safety. This should be the goal of future research funding in oral health.

Meanwhile, comprehensive health care that includes oral, mental, and vision health care and the essential scientific workforce will require significant improvements in coordination and integration among oral health, public health, and medical and behavioral health care systems; alignments between payment and educational systems that focus on prevention rather than treatment at the expense of prevention and health promotion; increased scientific evidence to inform health policy decisions and plans; and reduction or removal of regulatory barriers that inhibit or prevent alternative models of comprehensive health care.[11] Major revisions in health care professional and biomedical sciences education are required to hasten improved health for all people.

The framework for action in the Surgeon General's Report involved changing perceptions of the public, policy makers, and health providers concerning oral health. These continue to be valid recommendations for the future. In addition, dental and medical education should focus on early identification of caries risk and recognition of dental caries as a disease that needs to be managed comprehensively, including modifying behaviors to promote oral health. Medical practitioners in particular need more oral health knowledge to apply emerging oral science and identify other oral diseases in children and adults. Parents need to be empowered to make healthy decisions for themselves and their children. Policy makers need to approve programs to support improved access to care and clinical trials to identify the most effective preventive interventions. The consequences of oral diseases are significant, especially for children. Surprisingly, the general public continues to be unaware of this silent epidemic that continues to effect 1 out of 4 children under 5 years of age. The most important call to action should be to spread the word about this devastating, mostly preventable disease.

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