

# Expanding the Boundaries: Enhancing Dentistry's Contribution to Overall Health and Well-Being of Children

**Harold C. Slavkin, D.D.S.**

*Abstract:* The Surgeon General's Report, *Oral Health in America*, is the first comprehensive assessment of oral, dental, and craniofacial health in the history of our nation. The intent of this report is to alert all Americans to the full meaning of oral health and its importance to general health and well-being across the life span. Moreover, the report has been released at a time of enormous changes in human history as well as opportunities. The convergence of public health policies, "quality of life" expectations, global informatics, a new century of biotechnology, the advent of nanotechnology, the completion of the human genome project, changes in the management of health care, and the acknowledgment of enormous health disparities heralds a call to action. These changes affect children and their caregivers and the elderly. They also affect the social, economic, and health issues associated with special patients, including those with developmental disabilities. This paper highlights dentistry's future and how oral health is broadening the impact on patient and community health and dental practice, with a focus on children's oral health. The paper provides recommendations and suggests a call to action.

Dr. Slavkin is Dean of the School of Dentistry, University of Southern California. Direct correspondence to him at Office of the Dean, Room 203, School of Dentistry, University of Southern California, 925 West 34<sup>th</sup> Street, Los Angeles, CA 90089-0641; 213-740-2811 phone; 213-740-1509 fax; Slavkin@hsc.usc.edu.

*Key words:* oral health, children, health policy, science, genetics, craniofacial

All members of the oral health professional team are faced with two significant questions. First, how should we deal with the enormous growth in scientific and technological knowledge? Second, how should we translate new knowledge into evidence-based health promotion, risk assessment and disease prevention, diagnostics, treatments, therapeutics, and the everyday management of patients? The Fourth Washington Dental Service Distinguished Professorship Symposium was designed to consider how new knowledge and derived biotechnology are changing the face of clinical dentistry. It further considers these scientific and technological advances in the larger social context of changing health care management, demographics, patterns of disease, information technology, health disparities, and quality of life expectations.

Today, science and technology are rapidly advancing. If we reflect on the past 100 years, we note that most of our citizens enjoy longer and better lives than ever before. Remarkable public health advances in personal hygiene, sanitation, water and air safety measures, nutrition, and immunization (e.g., rubella, typhoid, tetanus, diphtheria, polio) contributed to increasing the human life span during the past cen-

tury. Today, most of our nation's more than 281 million people expect and receive outstanding oral health care. The introduction of water fluoridation almost fifty years ago has contributed to reducing the burden of dental caries. Today, more people retain more teeth for longer periods than ever before in human history. In tandem, we continue to struggle with the challenge to allocate human and financial resources effectively to reduce the major causes of disease and disorders, and to decrease health disparities associated with socioeconomic and ethnic status, and special populations. Ironically, almost one-third of our nation's population presents striking oral health disparities. This paradox has major social, economic, and political implications for our democracy.

This article will highlight the health of America's children and their caregivers. First, the paper presents a snapshot of the health of America's children that reveals opportunities for oral health promotion and disease prevention during preconception, prenatal, neonatal, and postnatal development to reduce the burdens of oral, dental, and craniofacial diseases and disorders and improve general health. Second, the paper highlights a few examples of scientific research discoveries from the oral microbial, dental

and craniofacial human genome projects, biomimetics, and biomaterials that have the potential to reduce the burden of disease and disabilities and lead to evidence-based treatments and therapeutics to improve the well-being of children and their caregivers.

---

## The Health of America's Children

Many aspects of oral health care for children and their caregivers were highlighted in the Surgeon General's Report on *Oral Health in America*,<sup>1</sup> *The Face of a Child: Surgeon General's Conference on Children and Oral Health*, June 12-13, 2000, Washington, D.C. ([www.nidcr.nih.gov/sgr/children/children.htm](http://www.nidcr.nih.gov/sgr/children/children.htm)), and *Healthy People 2010*.<sup>2</sup> These comprehensive national studies and their scientific evidence-based recommendations provide enormous opportunities for oral health care in the twenty-first century.

The developing human being is a complex organism that results from an exquisite interplay of biological, behavioral, and environmental factors. The interactions among these factors need to be considered within the context of developmental, environmental, and social changes that occur over time. By understanding multiple interrelationships, (such as those between the developing brain, face, sensory organs [vision, hearing, taste, smell, touch], dentition, skeleton and other tissues, organs, and systems), we can consider effective developmentally appropriate approaches to promote total health and prevent disease using the oral cavity as an important and innovative diagnostic and treatment model.<sup>1,2</sup>

The health of America's children reveals many different issues during prenatal, neonatal, and postnatal development.<sup>1</sup> At this time in history, our nation of almost 281 million people has 4.2 million live births each year. More than 7 percent of these babies are born premature, weighing less than 5.5 pounds.<sup>3</sup> Another 4 percent of these babies, more than 150,000 babies each year, are born with birth defects such as cleft lip and palate, spina bifida, heart and limb deformities, mental retardation, and severe malocclusion.<sup>1,3</sup> And almost 1 percent (8.9 babies per 1,000 live births) will die in the first year of life, primarily from infectious microbial pathogens.<sup>3</sup>

Our nation has about 57 million children and adolescents. The majority of America's children present a health profile that has significantly improved during the past five decades: 1) age-specific mortality rates have declined except for violent deaths among adolescents; 2) lead poisoning, anemia, and dental caries have all declined; 3) perinatal HIV infection has declined; and 4) immunization rates have improved. However, almost 25 percent (14 million) of these children live below the poverty line, and these children have not benefited from these promising trends.<sup>1-3</sup>

In the 1990s, the proportion of America's children (especially subgroups of Hispanic, African American, and American Indian) living below poverty level doubled.<sup>3</sup> Oral, visual, speech, and hearing health are too often neglected in poor children. Immunization rates for poor children are less than 40 percent.<sup>3</sup> Lead poisoning, malnutrition, and nutrient deficiencies have increased among America's children, especially among America's poor.<sup>3</sup> Disparities in children's oral health and access to care are evident in children from low-income, minority populations and those with special health care needs.<sup>1,78</sup>

Risk factors such as diet, lack of needed health professional services, and exposure to environmental hazards (such as tobacco products, alcohol, lead, and lack of housing) contribute to the overall health status of our children.<sup>3</sup> Each year an estimated 2 million people in the United States lack access to a conventional dwelling or residence; families with children constitute 38 percent of the homeless population and present unmet oral health needs. Half of all children under five and about 85 percent of females twelve to nineteen years of age do not meet the 1989 Recommended Dietary Allowance (RDA) for calcium; even fewer of these children reach the government's new guidelines, the Dietary Reference Intakes (DRIs) established in 1997.<sup>3</sup> Calcium is critical in building enamel and dentin mass, as well as bone mass in order to support physical functions throughout life.

Prenatal and postnatal dietary deficiencies place the developing human being at risk for a variety of diseases and conditions, including dental caries, the most common chronic disease of children. Early childhood dental caries (ECC), or "baby-bottle tooth decay," is caused by the colonization of *Streptococcus mutans* and several other types of bacteria within biofilms on the surfaces of teeth coupled to

prolonged exposure to sugars. Between 5 percent and 10 percent of all preschool children present ECC. Fifty-five percent of all preschool-age children and 50 percent of all school-age children do not have private dental insurance.<sup>1,2</sup> New reports indicate that 8.8 percent of middle school (grades six through eight) and 32.8 percent of high school (grades nine through twelve) children smoke cigarettes or cigars or use smokeless chewing tobacco.<sup>1,2</sup> It is projected that 5 million children alive today will eventually die as a result of tobacco products.

One direct challenge for oral health professionals is to address infants, toddlers, children, adolescents, and adults with special needs—those individuals whose oral health care is complicated by a physical or mental condition<sup>4,5</sup> or social disadvantage. The federal Maternal and Child Health Bureau defines children and adolescents with special health care needs (CSHCN) as “those who have or are at increased risk for chronic physical, developmental, behavioral, or emotional conditions and who also require health and related services of a type or amount beyond that required by children generally.”

A developing child, from conception to high school graduation, is not independent of his or her caregivers and the community institutions and mores to which he or she is exposed. Social policies and programs, as well as parental education, income, and social values, all contribute to a child’s health and well-being.

---

## Positive Effects of Science Discoveries at All Developmental Stages

Improving the science of developmental biology and behavior, improving the dissemination of scientific evidence to the health professions, policymakers, and the larger public, improving health outcomes, quality of health care, and access to health care remain major opportunities to improve the health of America’s children in the twenty-first century.<sup>6</sup>

To understand the patterns and principles of normal and abnormal development, as well as the diseases and disorders of children and adolescents, is a formidable and complex undertaking. The patterns and principles of development begin prior to conception.<sup>7</sup> The well-being (social, economic, and bio-behavioral) of the mother, father, and subsequent

caregivers and the child’s environment are major determinants.<sup>1-3,7</sup> Prior to conception, genetic and/or environmental factors begin to shape the development of the forming human being. During early development in utero, genetic as well as environmental factors (e.g., biological, physical or chemical teratogens, nutrient and micronutrient deficiencies, maternal oral health) further influence embryonic and fetal development. The neonatal, infant, preschool, child, and adolescent stages of life each contain exquisite requirements for well-being that further encompass physical, intellectual, and emotional factors. (The reader is encouraged to explore the vast and expanding scientific websites as well as the print literature that analyzes human development from conception through adolescence and beyond.<sup>1-3,6,10-12</sup>)

## Risk Factors, a Probabilistic Approach

The past few years have witnessed the emergence of a developing consensus among health and education policy experts, parents, teachers, clinicians, and researchers concerning the biological, environmental, and behavioral *risk factors* in the etiology of childhood illness, prevention of disease, and the promotion of health and well-being.<sup>8</sup> The examples of scientific discoveries highlighted below demonstrate how *risk assessment* can effectively promote oral health and the overall well-being of America’s children and their caregivers.<sup>1,2</sup>

At the dawn of the twenty-first century, the major diseases and disorders that compromise the human condition are linked to risk factors that include poverty, unhealthy food choices and/or malnutrition, poor water supply, sanitation, personal hygiene, unsafe sexual behavior, tobacco use, illicit drug use, alcohol consumption, occupational hazards, hypertension and stress management, physical inactivity, and air quality. Many of these are risk factors for oral and craniofacial disease. Our challenge is to foster health promotion and disease prevention strategies that can maintain and improve life expectancy and the quality of life for all people. The existence of *common* risk factors raises the possibility of interdisciplinary and interprofessional initiatives for targeted populations addressing interrelated conditions (e.g., diabetes, heart disease, and periodontal disease).<sup>9</sup>

One critical element to understanding and adopting risk assessment is related to our acceptance

of this probabilistic perspective. During the past century, our dental education and clinical practices held to a deterministic or “cause and effect” explanation for oral diseases and disorders. However, through scientific research and advances in technology we now appreciate that most human diseases and disorders are multifactorial (e.g., periodontal diseases, temporomandibular joint disorders, autoimmune diseases, cardiovascular diseases, pulmonary diseases, cerebrovascular diseases). Genetic, behavioral, and environmental risk factors change the probability of health outcomes. For example, in periodontal diseases we readily note that there are multiple risk factors for the disease that include age, gender, ethnicity, socioeconomic status (education and accumulated wealth), stress, tobacco consumption, medications, existing health conditions (e.g., diabetes, osteoporosis, rheumatoid arthritis, cardiovascular diseases), genetic polymorphisms or variations, and oral pathogens (e.g., virus, bacteria, or yeast microbes).

## Preconception

The health of the developing organism is thus determined by the interaction of risk factors, many of which are present preconceptually. Critical among biologic factors are the several thousand structural and/or regulatory genes required for the development and maintenance of oral, dental, and craniofacial cells, tissues, and structures. Genetic polymorphisms or variance within these multiple genes can alter response and result in disease or disorders that affect the developing organism at all subsequent stages. The recent scientific progress from the human genome project has yielded enormous new knowledge for oral health professionals. The human genetic blueprint consists of 35,000 to 45,000 structural and regulatory genes or alleles packaged within forty-six chromosomes that reside in each somatic cell found in a human being.<sup>13</sup> The haploid human genome consists of 2.9 billion nucleotide or base pairs (A, adenosine; T, thymidine; C, cytosine; and G, guanosine) within DNA that are distributed among twenty-three distinct chromosomes (twenty-two autosomes and one sex chromosome, either X or Y).<sup>2</sup> Within the vast array of bases are the encoded 35,000 to 45,000 regulatory or structural genes and the necessary elements that control the regulation of genes throughout the life span of the organism.<sup>7</sup> In addition to the genomic information found within the nucleus of each human reproductive cell (sperm in testes and ova in ova-

ries), genes are also encoded within DNA (deoxyribonucleic acid) uniquely found within the maternally derived mitochondrial genome (mitDNA). In February 2001, the completion of the human genome project (95 percent completion of the nucleic acid sequence, mapping, and annotations with 99.6 percent accuracy) were published from two competing research groups: Craig Venter and his team in *Science*,<sup>13</sup> and Francis Collins and the international consortium led by the National Institutes of Health in *Nature*.<sup>14</sup>

At conception, each partner contributes twenty-three chromosomes towards the creation of the new individual organism. The fidelity of the processes of maternal and paternal meiosis and subsequent fertilization, embryogenesis, fetal development, and birth are profoundly influenced by maternal and paternal age, diet and health status, and combinations of multiple gene-gene and gene-environment interactions over time.<sup>15-17</sup> Alterations (mutations) or misspellings of the genetic code within any one or combination of the 35,000 to 45,000 genes can result in inherited genetic diseases or disorders.<sup>13,14</sup>

Of the more than 5,000 presently known inherited diseases in humans, there are just over 1,200 genetic defects known to produce oral, dental, and craniofacial diseases and disorders.<sup>18</sup> These genetic defects may be identified as chromosomal anomalies such as trisomy 21 or Down syndrome, fragile X syndrome, or trisomy 18. Genetic defects may also be individual inherited mutations within discrete genes transmitted from maternal and/or paternal lineages in a normal complement of forty-six chromosomes. Today, we know of 360 such inherited genetic diseases or disorders that involve the oral, dental, and craniofacial features such as X-linked anhydrotic ectodermal dysplasia,<sup>19-21</sup> the hemifacial microsomia seen in Treacher Collins or Pierre Robin syndrome,<sup>22</sup> tooth, eye, and facial anomalies seen in Rieger syndrome,<sup>23</sup> X-linked amelogenesis imperfecta caused by mutations in the amelogenin gene,<sup>24</sup> autosomal amelogenesis imperfecta caused by mutations in the tuftelin gene on chromosome 1,<sup>25</sup> osteogenesis imperfecta caused by mutations in the alpha1 collagen gene,<sup>26</sup> dentinogenesis imperfecta caused by a mutation in the dentin matrix gene on chromosome 4 (dentin sialoprotein, dentin phosphoprotein and dentin matrix proteins),<sup>27</sup> conditions of congenitally missing teeth in PAX9<sup>28</sup> or MSX1 mutations, or mutations in fibroblast growth factor receptor genes (FGFR) and various syndromes that

include craniosynostosis<sup>29-31</sup> (see details in the “Genetics of Dental and Craniofacial Diseases and Disorders” at the website [www.nidcr.nih.gov](http://www.nidcr.nih.gov) and other websites in Table 1).

Many significant genetic mutations may not present clinical manifestations at birth, but rather may be expressed during subsequent stages of child development. One curious example is a mutation found in the cathepsin C gene that has recently been discovered to be the cause of Papillon-Levere syndrome (PLS).<sup>32,33</sup> In this rare disease, children often lose all of their primary teeth by age four, and all of their permanent teeth by age fourteen as a result of an abnormal inflammatory response to oral infections. The condition also involves the palms of the hands and soles of the feet. The reader is encouraged to access the Online Mendelian Inheritance in Man website maintained by the National Library of Medicine, National Institutes of Health (see <http://ncbi.nlm.nih.gov/omim> and other websites in Table 1).

In addition to inherited genetic diseases and disorders, genetic mutations (additions, deletions, rearrangements) can occur in response to drugs or substances that possess the biological activity of teratogens, mutagens, or carcinogens during embryonic development. For example, nuclear radiation exposures during early stages of pregnancy can produce multiple genetic mutations or misspellings that may result in the progression of neoplastic diseases such as leukemia.

## Prenatal

During embryonic and fetal development, there are remarkable associations between the diet and health of the mother and the fidelity of the biological processes required for the normal formation of cells, tissues, organs, and systems. Maternal exposure to teratogens such as *physical* (x-rays), *chemical* (lipophilic or fat-soluble drugs or substances such as vitamin A, alcohol, or chemotherapy agents used for cancer treatments) and/or *biological* (maternal diabetes, viral or bacterial infections, protein/calories malnutrition, other nutrient deficiencies such as folic acid) insults are the most common causes of human birth defects that affect the craniofacial, dental, and oral structures.<sup>34-36</sup> For example, vitamin A (Accutane) used for maternal cystic acne during the first trimester has been found to cause severe craniofacial, dental, and limb anomalies.<sup>36</sup> Maternal alcohol consumption during pregnancy is known to cause craniofacial and dental malformations, includ-

---

### Table 1. Children's oral health and genomic information and databases

The reader is encouraged to access the expanding web-based children and maternal oral health as well as human and microbial genomic databases using the Internet:

National Maternal & Child Oral Health Resource Center  
<http://www.mchoralhealth.org/>

American Academy of Pediatric Dentistry  
<http://aapd.org/>

American Cleft Palate-Craniofacial Association  
[www.cleftline.org](http://www.cleftline.org)

Human Genome News  
<http://www.ornl.gov/hgmis/archive/news.html>

National Coalition of Health Professional Education in Genetics  
<http://www.nchpeg.org>

American Society of Human Genetics  
<http://www.faseb.org/genetics/ashg/ashgmenu.htm>

Ethical, legal, and social implications of genome research on privacy/confidentiality  
<http://www.ornl.gov/hgmis/elsi/elsi.html>

Craniofacial, Dental, and Oral Genetic Diseases and Disorders <http://www.nidr.nih.gov/cranio/index.html>

Human Genome Map compiled by the National Center for Biotechnology Information  
<http://www.ncbi.nlm.nih.gov/genemap/>

Online Mendelian Inheritance in Man (OMIM database)  
<http://www.ncbi.nlm.nih.gov/omim/>

GenBank, current status of human and microbial genomics  
<http://www.ncbi.nlm.nih.gov/Genbank/GenbankOverview.html>

#### Organizations

National Center for Education in Maternal and Child Health  
Georgetown University  
2000 15<sup>th</sup> Street North, Suite 701  
Arlington, VA 22201-2617  
<http://www.ncemch.org>

National Institute of Dental and Craniofacial Research  
Information Office  
National Institutes of Health  
Bethesda, MD 20892  
1-301-496-4261  
<http://www.nidr.nih.gov>

National Human Genome Research Institute  
Information Office  
National Institutes of Health  
Bethesda, MD 20892  
<http://www.nhgri.nih.gov>

Special Care Dentistry  
(formerly the Federation of Special Care Organizations in Dentistry)  
211 East Chicago Ave., 5<sup>th</sup> Floor  
Chicago, IL 60611  
<http://www.foscod.org>

---

ing cleft lip and palate, growth retardation, and central nervous impairment (neurological, cognitive, and behavioral). Fetal alcohol syndrome (FAS) is the direct result of the mother's consumption of beverage alcohol during her pregnancy.<sup>35</sup> Estimates of prevalence range from 0.6 to three cases per 1,000 live births in most populations, but some communities show a prevalence as high as nine cases per 1,000.<sup>36</sup> Maternal protein/calorie malnutrition or severe nutrient deficiencies are known to cause immune deficiencies and craniofacial and skeletal malformations in newborn infants.<sup>34-36</sup>

The geometric design of the human brain and cranial nerve connections to sight, sound, taste, smell, and touch are formed during the first trimester of development.<sup>37</sup> Tooth development (when, where, number, shape, and size) is initiated during the third month of embryonic development, and enamel formation begins by the fifth month.<sup>37-39</sup> The development of the primary dentition, the formation of the dental tissue extracellular matrices, and the subsequent biomineralization processes required to form the enamel and dentin bioceramics are strictly controlled by genes and gene-environment interactions.<sup>37-39</sup> Altered gene expression may result in missing or abnormally shaped teeth, tooth structure, and the related maxillary and mandibular bones as well as salivary gland and tongue formations.<sup>37-40</sup>

During the fetal period of human gestation, biological processes that deliver sufficient oxygen and nutrients to the forming central nervous system and skeletal system are well established. This is also a critical period when environmental risk factors such as tobacco products and alcohol can compromise neurological and neuromuscular development.<sup>36</sup>

## Perinatal/Neonatal

Recently, evidence has accumulated indicating that maternal oral infections are a major risk factor associated with prematurity and low-birthweight (less than 2,500 grams) babies.<sup>41,42</sup> Additional studies indicate that maternal tobacco consumption is also a risk factor for premature births.<sup>36</sup> The new genetic knowledge bases have recently provided significant advances in neonatal diagnosis, treatments, and therapeutics. For example, oral buccal epithelial cells can readily be used for gene-based diagnostics. A few cells are sufficient to isolate and amplify human genomic DNA that can be sequenced and analyzed for specific mutations. The cost, time, and miniaturization of these techniques enable clinical applications

in the very near future. Along with these new technologies, important ethical, legal, and social issues arise, especially for infants and children who cannot participate in decisionmaking, yet whose lives may be profoundly altered by the results of such tests.

## Infant/Toddler (zero to two years)

During infancy and toddler stages of human development, diet and sensory stimulation are particularly significant for normal physical and intellectual development. This is also a period when the infant is particularly susceptible to nutrient and micronutrient deficiencies or excesses (glucose, fructose, proteins, calories, calcium, selenium, zinc, magnesium, fluoride), a period critical for continued tooth and skeletal formations.<sup>43,44</sup> Protein/calorie malnutrition during this period is devastating to the infant and results in deficiencies in brain structure/function, immunity, and cardiovascular, pulmonary, skeletal, and continued dental tissue formation.<sup>43,44</sup>

This is also a vulnerable period for the transmission of oral bacteria from mother or other caregivers to the developing infant.<sup>45-48</sup> And this is often the time when excess sugar-containing fluids are introduced into the daily diet of infants and toddlers through bottle feeding that can produce rampant dental caries.<sup>2,3</sup> Severe caries can result in failure to thrive, significant systemic sequelae, emergency room visits, surgeries, and other avoidable health care costs.

In terms of very early dental caries, for example, emerging scientific evidence is providing new concepts and approaches to health promotion and disease prevention. The primary teeth begin to erupt into the oral cavity by six months of age during infancy, and tooth eruption continues through the toddler period of development. Oral hygiene and fluoridation of drinking water are cost-effective health approaches to reduce the prevalence of dental caries.<sup>1,2</sup> Recently, new studies provide another complementary strategy to prevent disease. One of these lines of evidence involves the use of noninvasive optical imaging for the early "precavitation" detection of dental caries. Complementary to such early detection is the utilization of remineralization techniques—such as fluoride varnishes—that have been shown to be an effective method to eliminate or inhibit the caries process. This approach can be applied to the primary as well as permanent dentition.<sup>1,2</sup>

Infants, toddlers, and young children are also vulnerable to injuries that affect the oral and craniofacial regions (including child abuse injuries). There is an important role for oral health professionals in the identification and proper referral of such children and families.

## Preschool and School-Age Children (three to eleven years)

During child and adolescent development, diet, exercise, personal and professional oral hygiene, and a host of social, behavioral, and economic factors shape the well-being of the child.<sup>1,2</sup> During this period, continued fluoridation of drinking water, personal and professional oral hygiene, and the utilization of dental sealants and/or fluoride varnishes that cover the surfaces of posterior or molar teeth are cost-effective approaches to prevent disease.<sup>1,2</sup> These interventions are especially important for children at high risk for dental caries, such as those from low socioeconomic or minority families and those with special health care needs. Another strategy is the use of passive immunization by the child eating foods termed “plantibodies” that contain immunoglobulin-A antibodies specifically directed against surface antigens of *Streptococcus mutans*.<sup>49,50</sup> Preliminary clinical trials indicate that this form of passive immunization eliminates or reduces bacterial colonization on tooth surfaces and thereby reduces biofilms formation. As more microbial genomes are completed, more gene-based drug development will become available to target at-risk children for many infectious diseases, including dental caries.

## Adolescents (twelve to nineteen years)

A number of behavioral and environmental insults challenge the health and well-being of adolescents, including automobile accidents, sports injuries, tobacco and alcohol consumption, dietary and exercise deficiencies, oral infections, sexually transmitted diseases, child abuse, and pregnancy.<sup>1-3,6</sup> Adolescent children often present cystic acne conditions. Isotretinoin (Accutane; 13-*cis*-retinoic acid) is commonly used for the treatment of severe acne. In 1985, Dr. Edward Lammer and his colleagues were the first to report on retinoic acid embryopathy, reporting that retinoic acid treatment, when directed to reproductive adolescent females, may result in malformations

of the craniofacial, cardiac, thymic, and central nervous system tissues.<sup>51</sup> These findings indicate the importance for all health professionals (physicians, dentists, nurses, dental hygienists, pharmacists) as well as parents and the community to communicate emerging scientific discoveries and to promote health and risk factors for disease prevention. For teens with craniofacial conditions, adolescence is a time of heightened awareness of oral and craniofacial appearance. Advances in biomaterials, orthodontics, implantology, and osseous integration can help improve the quality of life of these youths.

## Caregivers

Prior to pregnancy, men and women have a number of opportunities to make “healthy choices” to reduce the burden of birth defects such as neural tube defects, cleft lip and palate, and cardiovascular defects. During pregnancy, especially during the first trimester, additional opportunities are available to promote health and reduce disease through healthy choices that eliminate or manage oral infection,<sup>1-2,41-42</sup> eliminate alcohol and tobacco consumption,<sup>35,36</sup> utilize multivitamin supplements,<sup>52-56</sup> maintain a healthy diet, and exercise as appropriate.<sup>1-2,8</sup> Later, parents will need information about appropriate infant nutrition and feeding techniques and means to promote oral health and access to oral health care.

The “parenting” that provides guidance and nurturing of infants and children has significantly changed during the past three decades. Today, a child’s “caregiver” is often a single parent, usually female, but may also be an older brother or sister, an aunt or uncle, grandparent or grandparents, foster care provider, or state or local child support agency. The socioeconomic status, health, and well-being of the caregiver(s) has a profound effect upon styles of parenting,<sup>3,8</sup> “content” and “modeling” of developmentally appropriate health promotion, and disease prevention. Although the focus of this paper has been on the developmental phases in the life of a child towards reducing oral health disparities in children, including those with special health care needs, it is becoming increasingly evident that the health and well-being of the caregiver is a major determinant of children’s health outcomes. Race and ethnicity appear to influence health beliefs and perceptions of health. Beliefs and perceptions, in turn, can determine when or whether an individual seeks treatment.<sup>57-61</sup> Perceptions of oral health, particularly of those conditions that an individual believes to be

“normal,” can be influenced by age, race, ethnicity, education, general health, and utilization of the health care system.<sup>62</sup>

---

## Translating Scientific Discovery into Clinical Practice

The past few years have witnessed remarkable advances in biomedical research. How we see, what we see, our models of thought, the speed and efficiency of communication, and how we are beginning to understand the biological revolution have all been influenced by advances in science and technology. Bioimaging and structural biology allow us to visualize the human condition from the macro to the nanometer (one billionth of a meter) levels of biological organization. The human genome provides a “parts list” of each of the 35,000 to 45,000 structural and regulatory genes that are required to fabricate a human being from zygote to mature adult. Gene and stem cell biology offer incredible opportunities for treatment of diseases. The strategy of these scientific advances has been based upon creating a knowledge base of biology, and involves “mining” or “extract” concepts and principles that translate into new diagnostics, treatments, and therapeutics. Moreover, the emergence of biotechnology translates into innovations in oral, dental and craniofacial diagnostics, treatments, therapeutics including biomaterials, and biomarkers for the molecular epidemiology of oral diseases and disorders. The reader is encouraged to assess the emerging literature related to scientific advances in translating discovery into oral health care.<sup>63-73</sup>

### Diagnosis

How will we formulate a diagnosis? What “tools” will we use? How can we achieve early detection? Advances in science and technology lead us to appreciate that the mouth is a portal to the body and mirrors many conditions of the body. Many systemic diseases and disorders manifest themselves in the mouth. Diagnosis, therefore, will soon utilize biomarkers for systemic health status, disease and the progression of disease, and the reversal of the disease progression from treatments and/or therapeutics. Principles from internal and oral medicine will

become routine tools for all oral health professionals. Biomarkers will be identified and then used to measure oral microbes (virus, bacteria, yeast) as well as human oral fluids such as saliva and crevicular fluids. Biofilms and the microbial ecosystem will be a target for sophisticated diagnostics and therapeutic strategies. Host immunoglobulins, hormones, enzymes, antimicrobial molecules, and many other informative molecules will become routine in dental diagnosis procedures. Isolated oral buccal epithelial cells will be used as samples for genotyping to identify genes for susceptibility to diseases. The oral epithelial cell sample for human genomics offers unique opportunities for “chip” clinical biochemistry. In addition, digital radiography and other forms of imaging such as functional high-resolution MRI (magnetic resonance imaging) will enhance our ability to “see” significant physiological and pathophysiological changes associated with diseases. Innovations of imaging will also enhance the diagnosis of pediatric and adolescent growth and development and further herald innovations in dental orthopedic therapy.

### Treatments and Therapeutics

Dentistry will rapidly evolve from dependency upon mechanical and surgical responses to disease towards “bio” solutions. For example, early detection of enamel demineralization vis-à-vis early dental caries can lead to treatment with remineralization technology. Colonization of *Streptococcus mutans* in biofilms on enamel surfaces can be inhibited using gene-mediated therapeutics such as monoclonal antibodies directed against adhesion and/or quorum sensing molecules. Further, gene-based treatments and therapeutics will revolutionize how we “treat” diseases and disorders such as periodontal diseases, oral cancers, oral mucosal lesions, temporomandibular joint diseases, oral candidiasis, xerostomia, and chronic pain. Tissue regeneration as well as tissue replacements will become a dominant feature of dental orthopedics and prosthodontics. Implantology will predictably evolve to become tooth regeneration and tooth replacement. Endodontics will use innovative biomaterials for soft- and hard-tissue therapy. Orthodontics will use imaging, computer-assisted predictions of growth and development, and a number of virtual interventions for orthodontics therapy. Oral and maxillofacial surgery as well as periodontal surgery will increasingly use gene-based controls of wound healing, repair, and tissue regeneration. Combinations of growth factors and other tissue regula-

tory molecules will become routine tools of modern dentistry (see Table 2).

---

## Burden of Oral Disease

Oral, dental, and craniofacial diseases and disorders are among the most common health problems affecting people in the United States during a life span.<sup>1,2</sup> The burden of disease ranges from birth defects such as cleft lip and palate, which occurs in every 1 in 525 to 714 births, multiple types of craniosynostosis that occurs in 1 in 2,000 births, to injuries/trauma of the head and face that result in nearly 20 million emergency room visits per year, and devastating head and neck cancers, accounting for 9,000 deaths and more than 42,000 new cases per year.<sup>1,2</sup> The treatment of more than 1.2 million cancer patients each year (e.g., breast, colon, prostate) can result in severe complications in 425,000 patients each year such as painful mouth ulcers, mucositis, loss of salivary gland functions with xerostomia, fungal infections, impaired taste and smell, and rampant dental caries. Oral, dental, and craniofacial complications are also associated with a number of viral infections (AIDS, herpes facialis, herpes zoster, Epstein-Barr, human papilloma), as well as diabetes, osteoarthritis, osteoporosis, and a number of neuropathies such as trigeminal neuralgia and Bell's palsy.<sup>74,75</sup>

Dental caries or tooth decay is the most common chronic infectious disease of children. The microbial opportunistic infection that results in dental caries is experienced by about 50 percent of elementary-aged school children. Almost 94 percent of adults have experienced this microbial infection at some point. Periodontal disease microbial infections

occur in 90 percent of individuals older than thirteen years and may be associated with a number of systemic diseases and disorders, including diabetes, low-birthweight premature babies, cardiovascular disease, and many respiratory conditions.<sup>1-2,11,42,45-49,73-77</sup>

It is evident that in the United States the burden of oral diseases and disorders falls disproportionately among ethnic minorities, individuals from lower social economic classes, women, and children.<sup>1-3,11-12</sup> Nearly 50 million Americans present extreme oral health disparities.<sup>1-3</sup> Some of the most extreme disparities in oral health and access to care may be associated with special populations.

---

## Summary

Ironically, the scale and impact of oral diseases and disorders on children and their caregivers still are challenges for the twenty-first century.<sup>78,79</sup> The health care of our poorest children has for many years been bitterly deficient when compared with the provision made for children in other industrial nations; oral health has been particularly insufficient for inner-city children and poor rural children suffering the most extreme forms of neglect.<sup>80</sup> We have the potential to deliver to every American the highest-quality comprehensive health care, including mental, vision, and oral health care.<sup>78,79</sup> Advances in the human genome, microbial genomes, developmental biology, gerontology, biotechnology, information technology, and new oral health-quality improvement techniques, as well as patients' desire to be active partners in their health care can all serve as major drivers to enhance health for all people. Our goals for the dental profession (dentists, dental hygienists, dental assistants, dental technicians, and oral, dental, and craniofacial product and service manufacturers) need to include: 1) automatic and affordable oral health insurance coverage for all; 2) access to oral health care for all; 3) patient-, family-, and community-responsive oral health care; 4) scientific evidence-driven oral health care; and 5) commitment to quality improvement. The recommendations by this author in Table 3 are suggested to address the needs of all children and their caregivers. It is time for action. Federal and state policies with implementation coupled to partnerships between public and private sectors are urgently needed to enhance the health and well-being of all Americans.

---

### Table 2. Prospects for gene-based diagnostics, treatments, and therapeutics

Gene-Based Diagnostics (viral, bacterial and yeast infection, host immunity, vaccines, host response, host susceptibility, microbial virulence, detection of recreational drugs and substances)

Gene-Based Treatments and Therapeutics (antimicrobial therapy, delivery of insulin for diabetes, production of saliva in severe xerostomia, growth factors for soft and hard tissue repair and regeneration, chemotherapy for oral cancers, biomaterials for dental tissue regeneration [enamel, dentin, and cementum], tooth regeneration, management of chronic pain)

**Table 3. Recommendations for the oral health professional team (dentists, dental hygienists, dental technicians, dental assistants, speech therapists, physical therapists, physicians, nurses, pharmacists) to improve the oral health of all children and their caregivers**

1. Oral health promotion and disease prevention should be integrated into the curriculum for all health professional students, including dentistry, medicine, nursing, and pharmacy as well as the social and behavioral sciences.
2. All women of reproductive age should take multivitamins supplemented with folic acid prior to and during pregnancy.
3. A national campaign on health determinants for women should emphasize tobacco cessation, alcohol reduction or elimination, healthy food choices, the benefits of fluoridated drinking water, the benefits of calcium in the diet of children and adolescents, and the values of physical exercise. A comprehensive and unifying theme is needed that can address a pluralistic and culturally diverse democracy.
4. All pregnant women should receive comprehensive prenatal care, including oral health care and anticipatory guidance about infant oral health issues.
5. Mothers, fathers, and other caregivers of infants and toddlers should be informed about immunizations, oral and general hygiene, transmission of oral and other pathogens, and healthy food and beverage choices.
6. All preschool programs should include oral health determinants.
7. All school-based programs should inform parents and children about how to optimize health and reduce the burden of oral disease.
8. National standards for health promotion and disease prevention that are developmentally appropriate for grades preK-12 should be designed.
9. Clinical competencies for all health professionals should include human development, human genetics, bioethics of clinical genetics, oral-dental-craniofacial dysmorphogenesis, child abuse and orofacial trauma, antimicrobial resistance, oral health disparities, immunization, head and neck cancer, diabetes, heart disease, autoimmune diseases viral infections such as HIV/AIDS, mental disorders, chronic facial neuropathies, and cerebrovascular diseases and disorders.
10. Public/private coalitions that promote health promotion, risk assessment and disease prevention, and research investments need to be created and sustained among all agencies of the federal and state governments as well as nonprofit foundations/agencies and private industry.
11. The health needs of the nation's population, especially those of individuals with special needs and disabilities, must be addressed by adequately supporting a continuum of biomedical, behavioral and health services research, community-based prevention strategies, health services for vulnerable and medically/dentally underserved populations, and health professions training.
12. Cross-disciplinary training programs among medicine, dentistry, pharmacy, and nursing should focus on children's health promotion and disease prevention.
13. Culturally and scientifically competent health professionals need to be educated and trained to meet the depth and breadth of these health and well-being issues.

## REFERENCES

1. U.S. Department of Health and Human Services. Oral health in America: a report of the Surgeon General. Rockville, MD: U.S. Department of Health and Human Services, National Institute of Dental and Craniofacial Research, National Institutes of Health, 2000.
2. U.S. Department of Health and Human Services. Healthy people 2010. Rockville, MD: U.S. Department of Health and Human Services, U.S. Public Health Service, 2000.
3. Pamuk E, Makuc D, Heck K, Reuben C, Lochner K. Socioeconomic status and health chartbook: health, United States, 1998. Hyattsville, MD: National Center for Health Statistics, 1998.
4. Davies R, Bedi R, Scully C. ABC of oral health: oral health care for patients with special needs. *British Medical Journal* 2000;321:495-8.
5. McPherson M, et al. A definition of children with special health care needs. *Pediatrics* 1998;102:137-40.
6. Isaacs SL, Knickman JR, eds. To improve health and health care 2000. San Francisco: Jossey-Bass Publishers, 1999.
7. Slavkin HC. Regulation of embryogenesis. In: Polin R, Fox R, eds. Fetal and neonatal physiology. 2<sup>nd</sup> ed. Philadelphia: W.B. Saunders Co., 1998:37-46.
8. Anderson NB. Levels of analysis in health science: a framework for integrating sociobehavioral and biomedical research. *Ann New York Acad Sci* 1998;840:563-76.
9. Sheiham A, Watt RG. The common risk factor approach: a rational basis for promoting oral health. *Community Dent Oral Epidemiol* 2000;28:399-406.
10. Morrill WA. Overview of service delivery to children. *The Future of Children* 1992;2:32-43.
11. U.S. Department of Health and Human Services. Women of color health data book. Rockville, MD: National Institutes of Health, 1998.
12. Redford M, Jeffcoat M, Silverton S. Oral health. In: Agenda for research on women's health for the 21<sup>st</sup> century: a report of the task force on the NIH women's health research agenda for the 21<sup>st</sup> Century, Vol. 2. Rockville, MD: U.S. Department of Health and Human Services, 1999.
13. Venter JC, Adams MD, Myers EW. The sequence of the human genome. *Science* 2001;291:1304-10.
14. International Human Genome Sequencing Consortium. Initial sequencing and analysis of the human genome. *Nature* 2001;409:860-5.
15. Chambers D, ed. DNA, the double helix: perspective and prospective at forty years. New York: New York Academy of Sciences, 1995.
16. Collins FS, McKusick VA. Implications of the Human Genome Project for medical science. *JAMA* 2001;285:540-5.
17. Jamison JL, ed. Principles of molecular medicine. Totowa, NJ: Humana Press, 1998.

18. Slavkin HC. The human genome, implications for oral health and disease, and dental education. *J Dent Educ* 2001;5:463-79.
19. Zonana J, et al. X-linked hypohydrotic ectodermal dysplasia: localization within the region Xq11-12, by linkage analysis and implications for carrier detection and prenatal diagnosis. *Am J Hum Genet* 1996;43:75-80.
20. Kere J, et al. X-linked anhydrotic (hypohydrotic) ectodermal dysplasia is caused by mutation in a novel transmembrane protein. *Nature Genetics* 1996;3:409-15.
21. Slavkin HC, Shum L, Nuckolls GH. Ectodermal dysplasia: a synthesis between evolutionary, development and molecular biology and human clinical genetics. In: CM Chuong, ed. *Molecular basis of epithelial appendage morphogenesis*. New York: Landes Science Publishers, 1999:15-37.
22. The Treacher Collins Syndrome Collaborative Group. Positional cloning of a gene involved in the pathogenesis of Treacher Collins syndrome. *Nature Genetics* 1996;12:130-5.
23. Semina EV, et al. Cloning and characterization of a novel *bicoid*-related homeobox transcription factor gene, RIEG, involved in Rieger syndrome. *Nature Genetics* 1996;14:392-6.
24. Backman B. Inherited enamel defects. In: Chadwick DJ, Cardew G eds. *Dental enamel*. London: John Wiley & Sons, 1997:175-96.
25. Deutsch D, Dafni L, Palmon A, Hekmati M, Young MF, Fisher LW. Tuftelin: enamel mineralization and amelogenesis imperfecta. In: Chadwick DJ, Cardew G, eds. *Dental enamel*. London: John Wiley & Sons, 1997:135-47.
26. Luder HU, Steinman B. Teeth in osteogenesis imperfecta: a mirror of genetic collagen defects. In: Cohen Jr. MM, Baum BJ, eds. *Studies in stomatology and craniofacial biology*. Amsterdam: IOS Press, 1995:209-28.
27. MacDougall M, Simmons D, Luan X, Nydegger J, Feng J, Gu TT. Dentin phosphoprotein and dentin sialoprotein are cleavage products expressed from a single transcript coded by a gene on human chromosome 4. *J Biol Chem* 1997;272:835-40.
28. Stockton DW, Das P, Goldenberg M, D'Souza RN, Patel PI. Mutation of PAX9 is associated with oligodontia. *Nature Genetics* 2000;24(1):18-23.
29. Nuckolls GH, Shum L, Slavkin HC. Progress towards understanding craniofacial malformations. *Cleft Palate Craniofacial J* 1999;36:12-8.
30. Cohen Jr. MM, MacLean RD, eds. *Craniosynostosis*. New York: Oxford University Press, 2000.
31. Cohen Jr. MM. Fibroblast growth factor receptor mutations. In: Cohen Jr. MM, ed. *Craniosynostosis*. New York: Oxford University Press, 2000:77-94.
32. Zhang Y, et al. Evidence of a founder effect for four cathepsin C gene mutations in Papillon-Lefevre syndrome. *J Med Genet* 2001;38:96-100.
33. Hart TC, Shapira L. Papillon-Lefevre syndrome. *Periodontol* 2000 1994;6:88.
34. Slavkin HC. *Developmental craniofacial biology*. Philadelphia: Lea Febiger Publishers, 1979.
35. Sadler TW. *Langman's medical embryology*, 6<sup>th</sup> ed. Baltimore: Williams & Wilkins, 1990.
36. Goldman AS. Pathophysiology of congenital malformations. In: *Fetal and neonatal physiology*, 2<sup>nd</sup> ed. Philadelphia: W.B. Saunders Co., 1998:47-57.
37. Gorlin RJ, Slavkin HC. Embryology of the face. In: Tewfik TL, Der Kaloustian VM, eds. *Congenital anomalies of the ear, nose and throat*. London: Oxford University Press, 1997:287-96.
38. Shum L, Takahashi K, Takahashi I, Nagata M, Tanaka O, Semba O, Tan DP, Nuckolls GH, Slavkin HC. Embryogenesis and the classification of craniofacial dysmorphogenesis. In: Fonseca R, ed. *Oral and maxillofacial surgery*. Vol. 6. Philadelphia: W. B. Saunders Co., 2000:149-94.
39. Slavkin HC. Molecular determinants of andontia. In: Cohen Jr. M, Baum B, eds. *Studies in stomatology & craniofacial biology*. Amsterdam: IOS Press, 1997:397-405.
40. Sperber GH. *Craniofacial development*. Hamilton, Ontario: BC Decker, Inc., 2001.
41. Offenbacher S, et al. Potential pathogenic mechanisms of periodontitis associated pregnancy complications. *Ann Periodontol* 1998;3(1):233.
42. Dasanayake AP. Poor periodontal health of the pregnant woman as a risk for low birth weight. *Ann Periodontol* 1998;3:206-10.
43. Sparks JW. Infant growth in the first year of life. In: *Fetal and neonatal physiology*, 2<sup>nd</sup> ed. Philadelphia: W. B. Saunders Co., 1998:291-4.
44. Pereira GR, Georgieff MK. Nutritional assessment. In: *Fetal and neonatal physiology*, 2<sup>nd</sup> edition, Philadelphia: W. B. Saunders Co., 1998:383-93.
45. Slavkin HC. First encounters: transmission of infectious oral diseases from mother to child. *J Amer Dent Assoc* 1997;128:773-5.
46. Caufield PW, Dasanayake P, Li Y, Pan Y, Hsu J, Hardin JM. Natural history of *Streptococcus sanguinis* in the oral cavity of infants: evidence for a discrete window of infectivity. *Infection & Immunity* 2000;68:4018-23.
47. Petit MDA, et al. Transmission of *Actinobacillus actinomycetemcomitans* in families of adult periodontitis patients. *J Periodontal Res* 1993;28:335-45.
48. Von Troil-Linden F, et al. Periodontitis patient and the spouse: periodontal bacteria before and after treatment. *J Clin Periodontol* 1007;2:893-8.
49. Slavkin HC. Changing patterns of disease and mucosal immunity. *J Am Dent Assoc* 1999;130:735-8.
50. Ma JK, et al. Characterization of a recombinant plant monoclonal secretory antibody and preventive immunotherapy in humans. *Nat Med* 1008;4:601-6.
51. Lammer EJ, et al. Retinoic acid embryopathy. *N Engl Jour Med* 1985;313:837-40.
52. Scott JM, Weir DG, Molloy A, McPartlin J, Daly L, Kirke P. Folic acid metabolism and mechanisms of neural tube defects. *Ciba Found Symp* 1994;181:180-5.
53. Hall J, Solehdin F. Folic acid for the prevention of congenital anomalies. *Eur Jour Pediatr* 1998;157(6):445-50.
54. Hoag SW, Ramachandruni H, Shangraw RF. Failure of prescription prenatal vitamin products to meet USP standards for folic acid dissolution. *J Am Pharm Assoc (Wash)* 1997;37(4):397-400.

55. James SJ, et al. Abnormal folate metabolism and mutation in the methylenetetrahydrofolate reductase gene may be maternal risk factors for Down Syndrome. *Am Jour Clin Nutr* 1999;70(4):495-500.
56. Knowledge and use of folic acid by women of childbearing age—United States. *Morb Mortal Wkly Rep* 1997;46(31):721-5.
57. Kuthy RA, Odom JG, Salsberry PJ, Nickel JL, Polivka BJ. Dental utilization by low-income mothers. *J Public Health Den* 1998;58:44-50.
58. Gazmararian JA, et al. Health literacy among Medicare enrollees in a managed care organization. *JAMA* 1999;281:545-51.
59. Williams DR, Collins C. US socioeconomic and racial differences in health: patterns and explanations. *Ann Rev Sociology* 1995;21:349-86.
60. Vargas CM, Crall JJ, Schneider DA. Sociodemographic distribution of pediatric dental caries: NHANES III. *J Am Dent Assoc* 1998;129:1229-38.
61. Williams MV, et al. Inadequate functional health literacy among patients at two public hospitals. *JAMA* 1995;274:1677-82.
62. Slavkin HC. Diabetes, clinical dentistry and changing paradigms. *J Am Dent Assoc* 1997;128:638-44.
63. McCarthy JJ, Hilfiker R. The use of single-nucleotide polymorphism maps in pharmacogenomics. *Nature Biotechnology* 2000;18:505.
64. Bumol TF, Watanabe AM. Genetic information, genomic technologies and the future of drug discovery. *JAMA* 2001;285:551.
65. Slavkin HC. Entering the era of molecular dentistry. *J Am Dent Assoc* 1999;130:413.
66. Genco RJ, Scannapieco FA, Slavkin HC. Oral reports. *The Sciences* 2000;Nov./Dec.:25.
67. Hart TC, Kornman KS. Genetic factors in the pathogenesis of periodontitis. *Periodontol* 2000 1997;14:202.
68. Slavkin HC. Toward increased sensitivity and specificity in the treatment of neoplastic disease. *J Am Dent Assoc* 1998;129:473.
69. Leethanakul C, et al. Distinct pattern of expression of differentiation and growth-related genes in squamous cell carcinomas of the head and neck revealed by the use of laser capture microdissection and cDNA arrays. *Oncogene* 2000;19:3220.
70. Baum BJ, O'Connell BC. The impact of gene therapy on dentistry. *J Am Dent Assoc* 1992;126:179.
71. Baum BJ, et al. The mouth is a gateway to the body: gene therapy in the 21<sup>st</sup> century dental practice. *CDA Journal* 1998;26:455.
72. Slavkin HC. Possibilities of growth modification: nature versus nurture. In: MacNamara Jr, JA, ed. *Growth modification: what works, what doesn't*. Ann Arbor: University of Michigan Press, 2000.
73. Hamilton J. Dental implications of the human genome project. *CDA Journal* 2001;29:35.
74. Slavkin HC, Baum BJ. Relationship of dental and oral pathology to systemic illness. *JAMA* 2000;284:1215.
75. Cohen DW, Slavkin HC. Periodontal disease and systemic disease. In: Rose LF, Genco RJ, Cohen DW, Mealey BI, eds. *Periodontal medicine*. St. Louis: BC Decker, Inc., 2000:11-33.
76. Slavkin HC. Health promotion made easy—give a gift! *J Am Dent Assoc* 2000;131:87-92.
77. Slavkin HC. Infection and immunity. *J Am Dent Assoc* 1996;127:1792-6.
78. Mouradian WE, Wehr E, Crall JJ. Disparities in children's oral health and access to dental care. *JAMA* 2000;284:2625.
79. Allukian M. The neglected epidemic and the Surgeon General's Report: a call to action. *Am Jour Public Health* 2000;90:843.
80. Mouradian WE, ed. *Children our future: ethics, health policy, medical/dental care for children*. Seattle: Washington State Department of Health, 1999.