Genetics and Its Implications for Clinical Dental Practice and Education

Report of Panel 3 of the Macy Study

A major study initiative, "New Models of Dental Education," funded by the Josiah Macy, Jr. Foundation, convened three panels of distinguished experts to examine issues related to the dental curriculum. This report is from Panel 3, held February 25–26, 2007, on the subject of genetics and its implications for clinical practice. Staffing the panel were Allan J. Formicola (The Macy Study), Richard W. Valachovic (American Dental Education Association), and Jacqueline E. Chmar (American Dental Education Association). There were nine panelists:

- Lynn Johnson, Ph.D., Director of Dental Informatics, University of Michigan School of Dentistry (co-chair)
- *Robert J. Genco, D.D.S., Ph.D., SUNY Distinguished Professor of Oral Biology and Microbiology, Schools of Dental Medicine, and Medicine and Biomedical Sciences; Director of the Buffalo Periodontal Disease Research Center, State University of New York at Buffalo (co-chair)
- Caroline Damsky, Ph.D., Professor, University of California, San Francisco
- N. Karl Haden, Ph.D., President, Academy for Academic Leadership
- Suzanne Hart, Ph.D., Staff Scientist, Office of the Director, National Human Genome Research Institute, National Institutes of Health
- Thomas C. Hart, D.D.S., Ph.D., Clinical Director, National Institute of Dental and Craniofacial Research, National Institutes of Health
- Charles F. Shuler, D.M.D., Ph.D., Dean, University of British Columbia Faculty of Dentistry
- *Lawrence A. Tabak, D.D.S., Ph.D., Director, National Institute of Dental and Craniofacial Research, National Institutes of Health
- *Lisa A. Tedesco, Ph.D., Vice-Provost for Academic Affairs–Graduate Studies and Dean of the Graduate School, Emory University

*Although unable to attend the meeting due to weather, these members of the panel provided input to the final report.

Opportunities provided by the human genome project to understand the genetic aspects of disease and to generate novel approaches to prevent, diagnose, and manage diseases have created new imperatives for basic science and clinical education in dentistry. New knowledge has emerged in our scientific understanding of the role of genetics for diagnosing diseases and for treatments and prevention. To ensure meaningful application of genomic discoveries for preventing disease and improving clinical outcomes, the role of a professional workforce armed with leading edge knowledge is key to contemporary practice and education. Of equal importance is growing evidence of the dentist's role in recognizing not only dental and oral disorders but also systemic indicators of genetic disorders, making the dentist integral to the overall health and well-being of patients. New and challenging social, ethical, and legal implications are associated with the use of genetic information in the treatment and prevention of disease. As part of the Macy study, this expert panel was asked to provide analysis and recommendations for the contemporary dental curriculum, pedagogy, directions for clinical education, student assessment, and faculty development in dental education.

The panel examined how changes in the definition of dental practice can begin with changes to the dental school curriculum and clinical education. The goal is to provide curriculum and clinical training so that dental practitioners can precisely and consistently evaluate oral, dental, and craniofacial diseases using an understanding of the genetic basis of oral diseases and related systemic conditions and, when appropriate, seek clinical collaborations to address patient conditions and treatments.

Why Teach Genetics?

The contribution of hereditary factors to caries, periodontal disease, oral cancer, absent or malformed teeth, and other common oral disorders is becoming increasingly evident in dentistry, as are the implications of systematic genetic disease on oral health care. Dentists should be prepared to discuss genetic factors as well as genetic tests for susceptibility to common oral health concerns and structural oral-facial

anomalies and the impact of genetic disorders on oral health care. An improved understanding of genetic susceptibility, lifestyle, and oral health risk factors allows a family's dentist to offer effective preventive and treatment strategies for oral diseases.

A rough draft of the human genome was published in February 2001.[1] Now, as information from the Human Genome Project is being put to practical use, it becomes increasingly important for dental practitioners to understand human genetics and to carefully select and apply genetic information to diagnosis and treatment of patients. It is predicted that knowing the molecular biology of bone, periodontal structures, salivary gland, and tooth development will lead to innovative treatment approaches that will differ greatly from dentistry's current surgically based techniques. Tissue engineering is already making significant strides in cell manipulation and in developing tissue such as skin, bones, and cartilage. Similarly, advances in drug delivery, gene therapy, and biopharmaceuticals will create additional new therapeutic methods that are vastly different from those currently used.[2]

Of the approximately 5,500 known inherited diseases in humans, more than 700 involve craniofacial malformations.[3] Congenital defects occur in almost 7 percent of live births in the United States; three-quarters of those include oral-dental-craniofacial defects.[3] Additionally, there is mounting evidence that many complex disorders, such as diabetes and hypertension, as well as caries and periodontal disease, are the result of gene-environment interactions. Differential diagnosis of developmental anomalies relies on the ability of the clinician to recognize and differentiate between normal and dysmorphic physical characteristics. Twelve of the twenty-six categories of malformations used for diagnostic purposes, according to *Smith's Recognizable Patterns of Human Malformation,*[4] involve features of the head or neck. Several are limited to oral structures such as hypodontia, microdontia, micrognathia, and cleft lip/palate.

Not all genetic anomalies are evident at birth. Dental professionals have a unique opportunity to observe the development of preadolescent and adolescent patients during periods when important growth and development changes occur. After preadolescents have completed their vaccinations (by age three), they are often seen infrequently by their physician unless specific health concerns arise. In contrast, many children are seen for routine dental care on a biannual basis regardless of their health status. Because dentists concentrate their diagnostic expertise on the face and mouth, they can be the most skilled to observe anomalies suggestive of major developmental malformations. Dentists who are able to recognize genetic disorders can also provide a valuable service to their patients by proper referral to a medical geneticist and/or genetic counselor.

Dental practitioners are well aware of the environmental and behavioral risk factors that contribute to poor oral health.[5,6] They routinely counsel patients about the risks of tobacco and alcohol usage, poor diet, and traumatic injuries to the head and mouth. As information about the genetic makeup of individuals increases, additional genetic susceptibility or resistance factors will be identified that influence the severity of periodontal and other oral diseases. Once these factors are identified, tests can be performed to identify those at risk, permitting practitioners to educate patients about the importance of their behaviors and tailor preventive strategies to individual patients.[7,8]

> "Education is about the future, not the past, and we are now entering the era in which genetics and genomics will play a vital role in both oral health research and dental practice."
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> *—Collins F, Tabak L. A call for increased education in genetics for dental health professionals. J Dent Educ 2004;68(8):807–8.*

For dentists, other challenges will emerge in the management and use of information generated by the Human Genome Project. Currently, dentists see patients with genetic dental defects such as X-linked amelogenesis imperfecta.[9] In the future, dentists may need to identify the specific gene defect in order to provide the best possible treatment.[10]

Dental professionals will need to anticipate how genetic information might be used in ways that are unethical or detrimental to an individual or groups of people. Because information about genetics and genetic research is reported almost daily in newspapers and magazines and on radio and television, a patient might hear of a new discovery before the provider has read about it in a scientific journal. Oral health professionals need to be prepared to answer patients' questions and know where to refer a patient for additional information

or counseling. This requires a basic understanding of the genetics of human disease, knowledge of the types of genetic testing available, and sensitivity to a family's concerns.

This report answers two questions regarding genetics education in dentistry:

- What knowledge, skills, and attitudes are required for oral health professionals to properly care for patients with genetic conditions?
- What educational strategies are needed to prepare dental students to provide care for patients with genetic conditions?

A summary of the panel's discussion of each question follows.

Knowledge, Skills, and Attitudes Required for Oral Health Professionals to Care for Patients with Genetic Conditions

The panel's recommended competencies are based on recommendations from the Association of American Medical Colleges regarding genetics education[11] and are written from the perspective that knowledge about genetics and genetic disease will change rapidly.

The list of competencies is exhaustive. The panel recognizes that few schools will implement the entire list. The competencies are written in a flexible manner to accommodate future knowledge and to allow schools to implement those that fit their curriculum.

What Knowledge Is Required

Biomedical and clinical sciences associated with genetics are changing constantly and rapidly. Professionals need a foundation of knowledge about genetic principles and must have the ability to apply these principles to patient care and in interactions with other health care professionals who are part of a patient's health care team. "Foundation knowledge" includes knowing the structure and function of the genome in the cell and applying genetic information to patient care.

Dental graduates should demonstrate foundational knowledge of fundamental genetic principles, including the following.

Principles of genetic transmission:

- modes of single gene inheritance
- chromosomes and chromosomal abnormalities
- multifactorial inheritance and the role of genetic factors in common disease
- concepts of penetrance, expressivity, pleiotropism, genetic heterogeneity, mosiacism, and new mutation
- phenomena of imprinting and anticipation

Molecular biology of the human genome:

- structure and roles of major macromolecules involved in information transfer from DNA to protein
- structure, function, and regulation of genes
- organization of the human genome
- nature and types of genetic variation, mutations, and polymorphisms
- mechanisms of replication and repair of genetic information
- structure and function of chromosomes and roles in meiosis and mitosis
- basis for genotype-phenotype correlations
- role of genetic factors in dental disease and health

Principles of population genetics:

- gene frequency and Hardy-Weinberg equilibrium
- mutation and selection
- polymorphism, single nucleotide polymorphisms (SNPs), haplotypes, and haplotype mapping
- genetic drift and founder effect
- consanguinity/inbreeding
- concepts of genetic linkage and association
- genome-wide association studies

Working knowledge of genetic terminology

Applications of genetics to patient care:

- role of genetic factors in determining rare and common disorders
- importance of somatic genetic change in disorders such as cancer
- use of population screening for disease risk or carrier status
- use of cytogenetic, biochemical, and molecular genetic tests in diagnosis
- use of microarrays, expression analysis, etc. in prognosis and therapy
- role of genetics in determining response of an individual to environmental factors or pharmacological agents
- major strategies in prevention and management of monogenic and chromosomal disorders
- role of genetics in modification of risk for common multifactorial disorders

- role of genetics in personalized preventive and therapeutic strategies

What Skills Are Required

Skills that are important to dental professionals include the ability to take and update a family history, recognize signs of genetic disease and include this information in the differential diagnosis, and prescribe and interpret the results of genetic tests.

Dental graduates should thus demonstrate the following skills:

- take a family history, recognize patterns of inheritance, and carry out basic genetic risk calculations;
- perform a head and neck examination with special attention to signs of major genetic disorders;
- consider genetic conditions as a contributor in a differential diagnosis and modify treatment to accommodate genetic conditions;
- recognize when to refer a patient for genetic screening, testing, and counseling;
- interpret results of genetic tests and explain them to patients and family members;
- explain and obtain informed consent for genetic testing (HIPAA);
- access and critically assess appropriate literature to determine the appropriateness of a referral, prescription, and treatment or of a genetic test;
- include a genetics/development component in differential diagnosis; and
- work collaboratively with other members of the genetics health care team.

What Attitudes Are Required

Genetics contributes to all diseases, including dental disease. Clinicians need to appreciate the emerging uses of genetics in prevention, diagnosis, and treatment of dental conditions. They need to understand the current limits of knowledge and that it will be necessary to continue to update knowledge and skill sets as information about genetics expands during their professional careers. Graduates need to understand the ethical, legal, and social implications, for patients and their families, of genetic information. Currently, genetic testing is becoming more widely accepted; however, it is often conducted without focused diagnostic goals.

Dental graduates should thus understand the following attitudes:

- the possibility that there is a genetic etiology for every patient;
- the potential for genetics to contribute to the development of new approaches to prevention, diagnosis, and treatment of disease;
- the potential for genetics to expand understanding of the basic pathophysiology of all human, including dental, disease;
- the possibility of using a genetic approach to provide personalized health care;
- current limitations in the existing knowledge base;
- that the principles for use of genetic information in decision making are largely the same as for other areas of medicine;
- the rapidity of the advancing front of knowledge;
- that genetic information may have treatment implications not only for an individual patient, but also for a family and, in some cases, for an entire community;
- the potentially disconcerting nature of genetic information, particularly as it relates to interpretation of predictive tests;
- the need to reduce public fear and misinformation about genetics;
- the diversity in public understanding of genetic information and evaluation of information sources; and
- the need for continued learning and receptivity to advances in knowledge and changes in practice.

Educational Strategies to Prepare Dentists to Care for Patients with Genetic Conditions

The past two decades saw an increased interest in teaching decision-making skills to dental students.[12] However, currently, practitioners are rarely trained in the complex decision-making skills of diagnosis and treatment planning associated with the genetics, genome technology, and ethical, legal, and social implications that will continue to arise as we gain more information about the role of genetic factors in genetically related oral disease and anomalies. A survey of the literature reveals that the need for developing decision-making skills as part of the preparation of oral health professionals is widely recognized by oral health educators.[13,14] Recognizing that the dense curriculum in dental education hinders

schools from instituting one or more courses dedicated to genetics,[15] this panel suggests increasing prerequisites and eliminating outdated content—among other curriculum changes—to make room for a spiral approach to the genetics curriculum (Figure 1).

The Spiral Curriculum Model shows genetics principles being taught and assessed in one or more foundational courses, shown as Platform Knowledge Courses on the diagram. Subsequent discipline-based courses (represented as cylinders) reinforce genetics content (represented as spirals) in varying didactic experiences, while integration courses and/or experiences blend genetics concepts with the instruction of clinical decision making. A

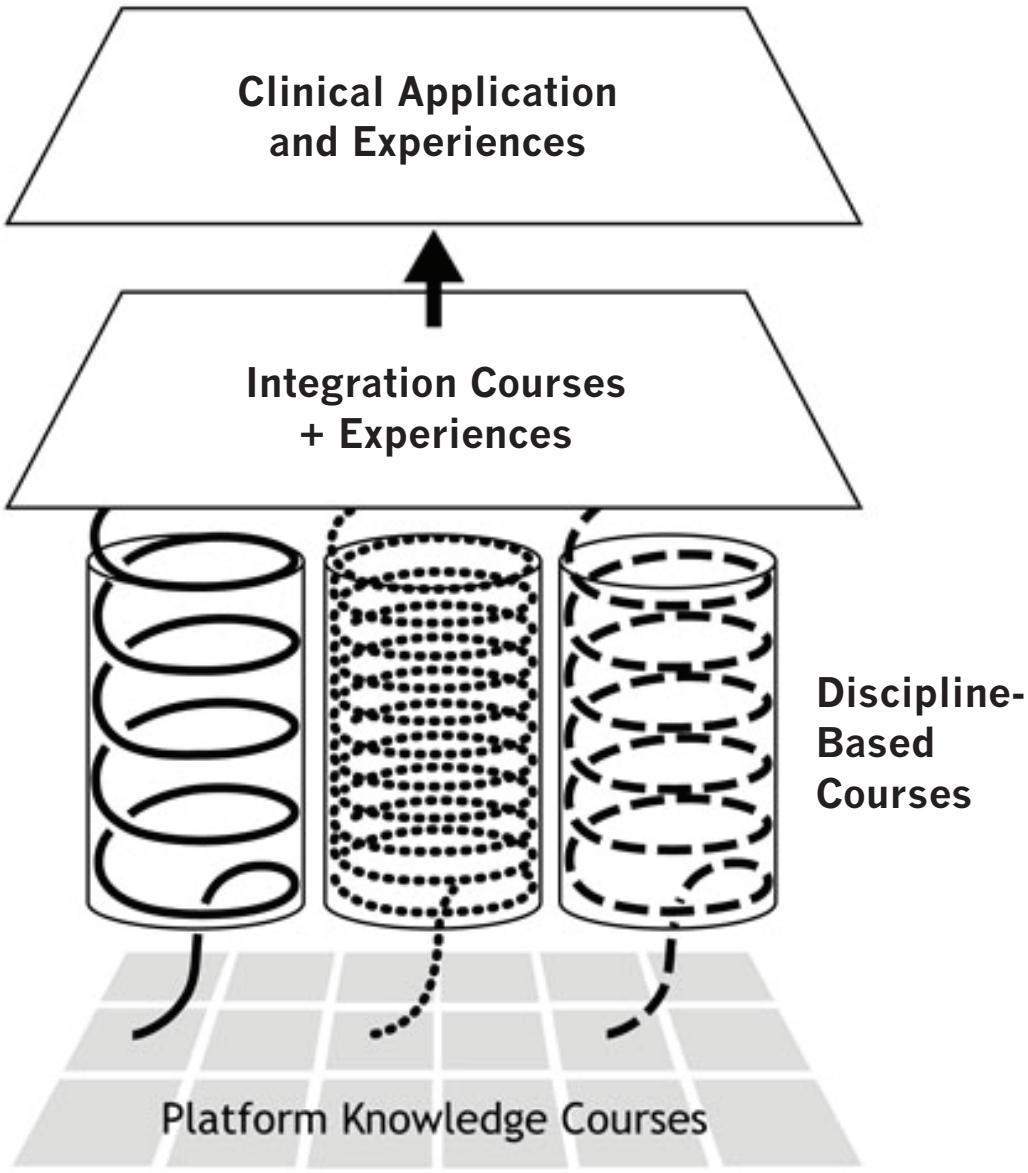

Figure 1. Spiral curriculum model for genetics education in dentistry

similar model for integration of all the basic science content in the dental curriculum would reinforce the relevance of this material and linkage to patient care. Finally and most importantly, genetics principles are applied to patients through actual clinical experiences. Throughout the entire spiral curriculum, various teaching and learning strategies instruct and strengthen clinical decision-making skills related to genetics. Concurrently, students are taught to use the numerous and varied genetics resources to help them make evidence-based decisions. Upon graduation, new dental professionals will be prepared to incorporate new genetics knowledge, apply diagnoses and treatment techniques, and address unanticipated issues surrounding the genetics care of dental patients.

Cell differentiation and proliferation and the relationship to genetic concepts, such as gene expression and gene transcription, are a few of the genetic concepts that could be taught in foundational courses. These concepts might be reinforced in a discipline course, such as in a discussion of periodontal treatment planning, using genetic information integrated with other facts. Students would integrate genetics concepts in discussing a problem-based learning case of a diabetic patient, for example, who is experiencing severe periodontal disease and other diabetic complications with genetic components. As a requirement of completing the case, students would be asked to discuss the reason behind the patient's complex disease pattern. Finally, students would apply these concepts to an actual patient who has diabetes, a disorder they will inevitably encounter in practice.

The instructional issues and strategies associated at each point in this spiral curriculum are described below.

Platform Knowledge Courses

The panel recognizes that the lack of trained geneticists in most dental schools is an obstacle to including genetics in foundational courses. However, dental schools in university medical centers often have access to faculty in other schools or institutions within the academic medical center who have expertise in genetics and are willing to share it. Thus, the panel proposes that dental schools form collaborations in which schools that have genetics expertise share it with schools that do not. The instruction could be done via videoconferencing, online courses, and other forms of distance and collaborative education.

It needs to be recognized that a school's lack of expertise in genetics does not mean that the course would be taught completely by a faculty member at another institution. Local facilitation will be required. This may require that facilitators be trained in strategies for successfully supporting student learning using distance and/or collaborative learning. Local facilitation serves the second purpose of building a base of genetic expertise and faculty familiarity with genetics resources within the local institution, as well as building relationships with other dental educators who are experts in genetics. Thus, if a patient-based genetic question arises, the local genetics facilitator will be better equipped to resolve the question or ask a more knowledgeable question of a genetics expert.

Integration Courses and Experiences

Among the numerous methodologies for teaching decision-making skills to health care providers,[16,17] many researchers consider case studies to be the most effective.[18,19] Case studies model the interaction students will encounter with patients and can be used effectively in traditional settings such as lectures and seminars.[19]

In health care education, computer-based patient simulations have been proven to be among the most effective forms of case-based instruction.[20-23] The 1990s saw dental education begin to implement and research case-based strategies of problem-based learning,[24-26] standardized patient instructors,[27,28] and computer-based patient simulations.[29] In the past decade, paper-based portfolios have given way to electronic portfolios (also known as e-portfolios). E-portfolios document students' accomplishments during their academic career, including knowledge acquisition, technical skills, and critical thinking, as well as clinical decision making applied to patient care.[30] E-portfolios go beyond tracking progress; they also include students' reflections about their work and their patients and thus track changes in attitude that reflect growing professionalism.

In the clinical teaching setting, it is often difficult to match the skill level of the student with the special problems of available patients. Case-based strategies provide a supplemental learning experience that can be sequenced and tailored to the particular educational needs of the individual student. Case-based instruction permits students to master required skills in less time and with fewer "live" patient encounters.[31,32] Research shows that interactive case

studies shorten the time required for learning and that the learned skills are retained longer than in less interactive forms of instruction.[33]

Research also demonstrates that to acquire the decision-making skills necessary to assess and treat a complex patient, students and practitioners require properly sequenced experiences with numerous and varied patients.[29] This panel proposes that institutions use case-based strategies to effectively implement a genetics curriculum that presents a properly sequenced series of patient experiences to enable dental students to gather and evaluate a complex array of genetic and patient information and to use this information to recommend rational and appropriative treatment.

Clinical Application and Experiences

It is critical that concepts and principles of genetics move from being classroom content to being knowledge that is applied in the care of patients. Like all other patient information, it is important that genetic information be in the patient files. Reports containing genetic information can be placed inside a patient's paper file or "attached" to his or her electronic record.

A patient's genetic information needs to be core information gathered on each patient, just like radiographs or periodontal charts. During the preparation of this report, however, research revealed not a single electronic patient record system that contained fields for genetic information. The only way a pedigree chart would become part of the patient's electronic record was for a paper chart to be scanned and a PDF attached to the chart. The interpretation of the chart and its impact on patient care could only be included in the "notes" section, where it might not receive the attention it deserves. Just as there are "medical alerts," there need to be "genetic alerts." Thus, this panel calls for companies that produce electronic patient information systems to, at a minimum, add the following capabilities to their systems: a pedigree chart, genetic conditions to differential diagnosis lists, genetic tests, and genetic counselors and other genetic specialists to referrals lists. Panel members feel it is critical for students to consider a genetic component to their differential diagnosis and the treatment recommendations that would result. This information would then be perceived as important to patient care and not just classroom material.

Faculty Development

The vast majority of dental faculty members have had limited education and experiences regarding genetics and the oral health care of patients with genetic conditions. Even if electronic record systems contained fields for genetic information, most faculty would be limited in their ability to guide students. Thus, faculty development programs to educate faculty to appreciate the relevance of genetics in health care are required. Faculty do not need to become geneticists, but they do need to consider the role of genetics in dental care. For example, a patient's gingival overgrowth might have a genetic basis. Only a genetic test could determine this, which would affect the patient's treatment.

Recommendations

A number of factors would help ease the adoption of genetics into the curriculum of dental schools and, subsequently, into the practice of oral health providers. This panel, recognizing that change needs to occur in steps, makes the following short-, medium-, and long-term recommendations. The initial focus is on changes in dental education, followed by recommendations for practitioners.

Short-term (the next five years) recommendations for dental education:

1. Require the genetics competencies, listed above, of all graduates.
2. Electronic health records should add family histories to their functionality, and schools should require that family histories be taken of all patients.
3. Teach the genetic basis to the diagnosis of oral conditions and the genetically based diagnostic tests that are available for single gene disorders and chromosomal abnormalities.
4. Teach the methodologies, integration, and results of genetic studies on complex diseases such as diabetes mellitus, cardiovascular disease, and periodontal disease.
5. Use genetic resources in patient evaluation.
6. Be aware of the insurance options for patients with inherited diseases.
7. Include genetics concepts as an accreditation standard and on national board exams.

Medium-term (five to ten years) recommendations for practitioners:

1. National organizations should issue a "quality of care index" for taking and interpreting a family history.

2. National organizations should develop "quality of care indices" for genetics-based prevention, diagnostic tests, and treatment; genetic counselor referrals; and ethical, legal, and social issues related to genetics.
3. Practitioners should routinely use genetic resources to obtain current information and incorporate that information into patient care.
4. Practitioners should understand that there are genetic diagnoses for some oral conditions.

Long-term (more than ten years) recommendations for practitioners:

1. Practitioners should routinely develop their differential diagnosis, understanding that there is a genetic basis for some oral and system conditions.
2. Genetic tests should be routinely used for risk assessment.
3. Practitioners should look to biomarkers for diagnosis, progression, and treatment of disease (e.g., oral cancer).

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