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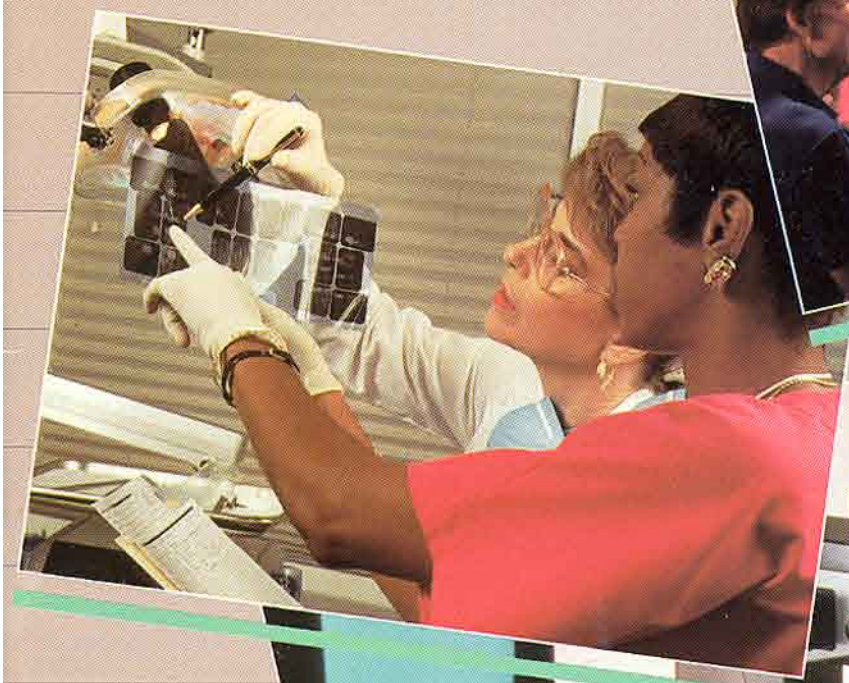
Dentists as Gene Therapists

Oral Cancer

NATIONAL INSTITUTE OF DENTAL RESEARCH

50 Years of Progress in Oral Health



Harold C. Slavkin, DDS

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DEPARTMENTS

FEATURES

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Commitment – A Vanishing Commodity?

Jack F. Conley, DDS

Immediate Past President Eugene Sekiguchi was there when the California Dental Association needed him most. In the wake of the resignation of Kenneth Zakariasen in early October 1997, Gene Sekiguchi took over the reins of the nation's largest state dental association.

For a volunteer to make such a commitment is extraordinary. The wet-fingered dentist from Monterey Park put aside family, dental practice, and the conveniences of a normal regimen to go to Sacramento and do more than be just an interim caretaker. He identified shortcomings in the function of the holding company and worked diligently to improve the working relationships of the various components of the California Dental Association. He brought stability to a staff that had experienced a troubling and traumatic period. And, he was able to demonstrate to other members of the volunteer leadership that he could, with their support, steer CDA successfully through the many challenges of 1998.

It is important that the membership at large, as well as volunteer leaders, recognize his contributions to the well-being of the organization. Current President Ken Lange is also to be congratulated for his role in steering the course during this unique period in the history of CDA. He made some very difficult decisions of the type not routinely expected of the top volunteer leader. The team of Sekiguchi and Lange kept CDA focused and on course.

The strength and commitment in current volunteer and staff leadership has enabled the association to move forward in the absence of a permanent administrative leader. However, we do see troubling indications that the commitment of members to consider volunteer service to the profession is declining. Some readers may recall that the issue of "Vanishing Volunteers" was raised in this space in May 1996. An indication that this is again a factor of some concern became apparent when two weeks prior to a May 1 deadline for nominations, very few nominations for association councils, committees, and other volunteer positions had been received. It is low enough to raise concern that insufficient nominations would be forthcoming for the screening process prior to the deadline.

What is particularly troubling to this writer is not the possible shortfall of volunteers for 1999, but for the future of the CDA leadership process if the trend is not reversed. One factor that seems to explain the shortage of volunteers is the high debt load many younger members carry, forcing them to concentrate more effort in practice-related activity to reduce debt than was necessary by their predecessors. It is reasonable to expect that the entry of some younger dentists into volunteerism will be delayed.

What about many others within the ranks of CDA's more than 14,000 active members who are, or could become, eligible to serve their profession but don't choose to do so? A possible explanation of this attitude was demonstrated in a letter in which a member described his criticism of a variety of membership services and policies. In the letter, he also made a comment that he had been offered the opportunity to serve as a volunteer but didn't have the time. He displayed a mind-set that has been expressed by other members from time to time that says, "I have the right to criticize my profession or the services it offers, but

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I am unwilling to make a commitment to serve and contribute to its progress." We hope that this remains an isolated attitude, held by only a few. Dentistry will grow and achieve the goals important to the membership only if there is a unity of spirit and purpose.

Each year, CDA has approximately 130 volunteer positions out of approximately 200 that must be evaluated and filled through appointment or election by the Board of Trustees or House of Delegates. Our profession depends on committed members, qualified by virtue of their service activities at all levels of the tripartite structure as well as other pertinent dental professional service activities. Individuals who are committed to serve must make their commitment and qualifications known to their colleagues at the component society level who have the responsibility to forward nominations to CDA. While our message here will not influence the screening process this year, we hope to stimulate increased interest and commitment by CDA members to provide service to their profession in the future.

Those who serve will probably never be expected to make the extraordinary commitment demonstrated by our current immediate past president and president. However, the professional leadership development process requires that we bring forth new participants whose service prepares them to be ready to make a commitment of time and effort if the circumstance arises.

It is important that new members, or those who have not previously participated, consider the commitment to participate in the future. This commodity is extremely important to the well-being of the dental professional in the future.

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An Approach to Solving the Problem of Oral Cancer

Raymond J. Melrose, DDS

AUTHOR

Raymond J. Melrose, DDS, is professor and chairman in the Department of Oral and Maxillofacial Pathology at the USC School of Dentistry. He is immediate past president of the American Academy of Oral and Maxillofacial Pathology.

A few weeks ago, the California division of the American Cancer Society released its annual publication "California Cancer Facts and Figures." This document again graphically displays the fact that neither incidence nor death rates from oral and pharyngeal cancer are appreciably declining. This fact is mirrored in national statistics as well. In California, 3,315 new cases of oral/pharyngeal cancer will occur – an average of more than nine per day. It is predicted that 935 people will die the terrible death of this disease – almost 20 per week. Oral/pharyngeal cancer continues to rank in the top 10 in incidence among all cancer types and sites.

As bad as the above may be, a worse statistic is to be found in the fact that at the time of initial diagnosis, a larger percentage of oral cancer patients have metastases to regional nodes than do patients with cancers of the breast, prostate or colon. In my mind, these data suggest that dentistry is failing in its responsibility to detect and diagnose oral/pharyngeal cancer early.

Why blame dentistry and not give medicine a share of the guilt? Dr. Larry Meskin said it well in an editorial in the Journal of the American Dental Association (128:1494-7, 1997) titled "Do It or Lose It." In that piece, Dr. Meskin made the argument that oral (and pharyngeal) cancer is "dentistry's disease." He is absolutely correct. No one knows more about the mouth than dentists. No one can examine it better than we can. No licensed dentist in this state has any reason or excuse to say that he or she does not know how to perform a complete oral cancer detection examination. Continuing education courses on the subject abound. At least one is offered at every CDA Scientific Session. Local dental societies and study groups have ready access to experienced speakers.

The principal risk factors for oral cancer – tobacco use and alcohol abuse – are well-known in the profession. Textbooks and monographs, even the Internet, provide access to information and photos of leukoplakia, specked leukoplakia and erythroplakia, the three most common clinical lesions associated with the disease.

If we know so much about this devastating cancer and have the opportunity to detect it early and to save lives, why are we failing?

There are several reasons – not justifications – that come to mind. First, patients may not present for dental care. Studies have shown that the highest risk patients for oral cancer have associated medical problems that take them to their physicians' offices four to five times

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more frequently than they elect or need to visit the dentist. So, is the solution to try to teach physicians to perform oral examinations and detect the cancers? My experience says emphatically, NO.

Another reason may be that dentists are still not routinely performing a complete oral cancer screening as part of their routine patient examination. For example, a 1993 study that examined oral cancer screening procedures among physicians and dentists reported that although dentists felt better prepared than physicians to identify oral lesions, only 14 percent of dentists performed all aspects of the intraoral examination.

Another reason is that patients know little about oral cancer and, thus, don't know enough to ask for an examination or to inquire if one has been done. In a 1990 study assessing U.S. adults' knowledge of risk factors and signs of oral cancer, tobacco use was the only risk factor most adults identified, and only 25 percent could name even one sign of oral cancer. And remember, even the signs expounded by the American Cancer Society are not those of early disease. Overall, the U.S. adult population is uninformed about oral cancer; and this is not improved by our profession, which is doing too little to educate them about risk factors, prevention, and means of early detection. Even if you do routinely perform an oral cancer screening examination, do you take the time to tell the patient what you are doing and why?

Is it going to take a public relations disaster – such as would occur if a major public figure was to be diagnosed with advanced oral cancer that his or her dentist failed to detect – to sound the clarion call for action? Do we need another AIDS-type black eye?

It seems to me that what is needed to address the problems of an uneducated public and to motivate more in our profession to do the job they are trained to do is a major national public education program on the subject of oral cancer.

The first question would be can it work. As an example of how it might work, I cite the example of cancer of the uterine cervix. Fifty years ago, that disease was a major killer of women. When Dr. George Papanicolaou and others discovered that a simple cytologic smear (Pap test) of cervical surface cells was an excellent early diagnostic tool, one would have thought the problem was ready for solution. It wasn't. Physicians resisted this "new" method. It was different and revolutionary, and they weren't ready to be convinced that it was useful. There was a myriad of reasons, but the bottom line was that the test was not widely adopted. Women's groups, the American Cancer Society, and others launched a public relations effort directed at the county's women. Women began to demand the test, and it wasn't too long before the Pap smear became a standard of care in women's health. As a result, cervical cancer has ceased to be a major killer of women.

The parallel with oral cancer is obvious. The questions are who should develop such a campaign and who should pay for it. I believe the American Dental Association ought to develop and sustain an annual oral cancer awareness month just like they do for children's dental health. I recently proposed the idea to the ADA leadership and was turned down, ostensibly for financial reasons. The American Cancer Society won't do it: it can't afford it, and oral cancer is not one of its primary focus activities. The federal government shouldn't do it; the problems would be too great. Individual states could launch programs, but they would duplicate each other and be cost-inefficient.

Coalitions of state dental associations working with ADA and in concert with organizations such as the Academy of General Dentistry, dental specialty groups, and large organizations such as Oral Health America could come together and agree to take on this challenge. Could come together? MUST come together, or oral cancer will remain a black mark on dentistry's otherwise phenomenal record of solving its health issues.

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Yes, It Can Be a Jungle Out There

By David G. Jones

Endodontist W. Paul Brown, DDS, waits for the uncooperative patient to be anesthetized then performs a root canal on an abscessed tooth. After the procedure is finished, the patient gradually awakens, blinks his eyes a few times, then stands to his full 10-foot height.

The Kodiak bear, a San Francisco Zoo resident, is just one of the many animals Brown has worked on during a 17-year relationship with animal dentistry. General dentist Robert W. Turner, DDS, Brown's daughter Sarah de Sanz, DDS, and endodontist A. Scott Cohen, DDS, form the rest of the team which visits the zoo and Marine World Africa USA in Vallejo six to 10 times a year to work on assorted teeth, fangs, beaks and tusks.

Veterinarians are familiar with the anatomy of many different animals, but most are not trained in dentistry. In a chance encounter in the early years of his practice, one of Brown's patients was a San Francisco Zoo veterinarian.

"I asked him how the zoo managed animals with dental problems," Brown says. "The vet said they were paying a lot of money to have a dentist fly up from L.A. to perform this service. I told him that I would provide the treatment free of charge."

Brown then teamed with Turner, and together they've since worked on koalas, lions, tigers, bears, snow leopards, jaguars, African wild dogs, orangutans, chimpanzees, gorillas, spider and green monkeys, horses, camels, bobcats, elephants, sea lions, killer whales, seals, dolphins and walrus. They've even mended the beaks of a dove and a small turtle.

A second-year endodontics resident at the University of California, San Francisco, de Sanz has worked with her father on animals since she was a second-year dental student at UCSF in 1990. Cohen and de Sanz were classmates in dental school, and he joins the group when needed on endodontic cases.

"The basic anatomy of animal teeth is similar to that of humans, with enamel, dentin, pulp and cementum, but in different shapes and sizes," Cohen says. "We apply dentistry to animals, similar in many respects to human dentistry."

When Brown and Turner began, they had no knowledge of animal dentistry.

"We learned strictly from looking at animal skulls at the Berkeley Hall of Science," Turner recalls. "We took x-rays of teeth and skulls and tried to evaluate the anatomical differences that way. Paul then would work out the file system for root canals, and I'd work out post variations for the inside of the canal."

The large number of anatomical variations among various species required some ingenuity and trial-and-error to develop instruments for use on animals. Large cats and other carnivores, for instance, have specialized teeth, such as long, sharp canines which require special instruments. Most of the equipment is made by a surgical supply company in Burlingame, and a local lab makes the crowns.

"From a restorative standpoint, the most difficult challenge involves making posts that fit into long, curved canals, but are strong enough to withstand the forces large animals put on them," Turner says. "Earlier, I tried to use pre-cast posts, which in many cases either fell out or fractured. I experimented with different materials and wound up using an implant-grade surgical steel post."

Brown also had to go to some lengths to find suitable instruments.

"One of my patients, a Nobel Prize winner in physics, made me a special lentula spiral so I could work on a lion," Brown says. "I also asked for an endodontic file and an orthodontic wire to be precision machined together to make a long, flexible, narrow file for use in the elongated, curved canals in lion, tiger or gorilla canine teeth."

He describes another case where an elephant had cracked the tip of its tusks.

"The Stanford engineering department cast the crowns, and we installed them," Brown says.

Other differences between human and animal dentistry make treatment more difficult. For example, almost all animals undergoing dental treatment must be anesthetized, because they won't remain still for long periods. The roots of many animals' teeth often are deeply buried within thick bone, making extractions more difficult. And custom impression trays are necessary because of the variety of mouth sizes and shapes.

"We couldn't use a full arch impression tray because of the divergence of the teeth," Turner says. "I could put it in but couldn't get it back out after the impression was formed. We finally went to quadrant trays and pieced the arches together, and that worked well."

According to de Sanz, most dental problems animals encounter are trauma-related.

"They fracture their teeth and expose the nerve, requiring endodontic treatment to prevent abscess formation," she says. "If they break their teeth, they would die in the wild as a result, because they can't eat their normal diet."

Sometimes routine, the work can also be exciting, dramatic and dangerous.

"We trust that the vets are doing a good job keeping the animals under anesthesia, but we did have a large male tiger wake up while we were getting a bite registration, and all the vets and technicians jumped on him and held him down until we finished," de Sanz says.

The team has worked on animals for

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movies, and once worked on the Exxon tiger's teeth. Later this month, the father-daughter team will gain even more attention. Brown and de Sanz will be featured on a National Geographic Explorer segment on exotic animal dentistry. It is scheduled for broadcast at 7 p.m. June 21 on TBS.

They Like You, They Really Like You

Dentists are among the most trusted professionals in the United States, according to a poll conducted in the fall of 1997 by CNN, USA Today, and the Gallup Organization.

Dentists ranked fifth in the poll, which has been conducted annually since the early 1980s. The 1997 poll, which ranked 26 professions, showed that 54 percent of American consumers rated the honest and ethical standards of dentists as "high" or "very high."

Pharmacists ranked first with 69 percent of American consumers rating their honesty and ethical standards as "high" or "very high." Clergy ranked second with 59 percent; doctors were third with 56 percent; and college teachers were fourth with 55 percent.

Engineers and police officers tied for sixth with 49 percent; funeral directors had 36 percent; and bankers had 34 percent. Journalists completed the top 10 with 23 percent.

Dentists have finished in the top five every year but one since the poll was first conducted. The only time dentists did not finish in the top five was the year following the David Acer/Kimberly Bergalis case in which there was public concern that dentists could transmit HIV to patients. In that year, dentists finished sixth.

Women Continue to Gain Ground

In the past decade, the number of women joining the profession, enrolling in dental schools and joining the faculty of those institutions has dramatically increased, reports the April issue of AGD Impact.

In 1968, women made up just 1.2 percent of all dentists, and in 1983, just 3 percent. In 1997, 12 percent of all dentists were women; women now account for 36 percent of all dental school students. In fact, women outnumber men at the Dental College at Howard University in Washington, D.C., and make up half – or nearly half – of all students at several other dental schools. That trend may continue as more women who might have once chosen careers in dental hygiene now consider being a dentist a viable option.

"There is a place for women in every aspect of dentistry," says June Warren Lee, DDS, past president of the American Association of Women Dentists. "Years ago women were encouraged to go into pediatric dentistry rather than pursue traditionally male areas. That's not happening today."

But women still have a way to go. Some female dentists say they are not always judged solely on their abilities – a problem not unique to dentistry. And some say a "glass ceiling exists relative to obtaining leadership positions – the overwhelming majority of which are held by men. In California, 3,400 women practice dentistry, about 13 percent of all dentists. CDA has total membership of about 17,550, and of that number, 2,300 are women, also 13 percent. The association is lead by 43 trustees, none of whom is a woman. The association has 15 standing councils and committees, and two are chaired by women.

While most dentists are owners or share ownership of their practices, a greater proportion of owners is more likely to be men than women. Men are also more likely to be solo private practitioners, and women are likely to be in group practices. Studies have shown that women, on average, work slightly fewer weeks per year and slightly fewer hours per week, and that women have been shown to spend slightly more time with each patient.

Strings Can Tangle Research Gifts

University researchers think corporations often place restrictions on research gifts and expect returns that may pose problems for recipients and institutions, according to an article in the April 1 issue of the Journal of the American Medical Association.

Eric G. Campbell, PhD, of Massachusetts General Hospital and Partners Healthcare System, Inc., Boston, and colleagues, surveyed 3,394 life science researchers at the 50 universities that received the most research funding from the National Institutes of Health in 1993. The survey asked if the scientists had received any research-related corporate gifts over the past three years, and if so, how important the gifts were to their research. The authors also wanted to know what, if anything, the recipients thought donors expected in return for their gift.

A significant number of respondents said they believe companies expected something in return for gifts:

- Thirty-two percent reported that the donor wanted pre-publication review of any articles or reports stemming from the use of the gift.
- Nineteen percent indicated a donor expected ownership of all patentable results from research for which a gift was used.
- Thirty percent indicated the company expected testing of their products.

Researchers also found that more than half the recipients reported that donors expected acknowledgment in publications (63 percent); that the gift not be passed to

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a third party (60 percent); and that the gift be used only for the agreed-on purposes (59 percent).

The authors received responses from 2,167 faculty members, or 64 percent of those surveyed. They found that 43 percent of respondents received a research-related gift in the previous three years independent of a grant or contract. Of those who received a gift, 66 percent reported the gift was important to their research. They continue: "The most frequently received gifts were biomaterials (24 percent), discretionary funds (15 percent), research equipment and trips to meetings (11 percent each), support for students (9 percent), and other research-related gifts (3 percent)."

The authors suggest several general guidelines concerning corporate gifts. "First, faculty should become familiar, if they are not already, with their institutional policies that govern gifts vs. grants and contracts. Second, if existing policies regarding gifts are inadequate, academic institutions should develop through faculty new or revised policies that simultaneously encourage the sharing of resources and timely dissemination of results to the academic community and at the same time protect the legitimate interests of donors.

"Third, faculty should not accept any resources from a firm that expects ownership of intellectual property without an institutionally negotiated research grant or contract," the authors write. "Fourth, faculty bear the primary responsibility to avoid using the gift mechanism as a means to bypass existing institutional policies and administrative structures for exchanges that are more appropriately managed under the auspices of a research grant or contract."

The authors conclude that prohibiting or heavily regulating acceptance of gifts is not warranted. But they urge universities to monitor cases where expectations of return clearly pose problems for the recipient or the institution. And they suggest: "At times it may be prudent for faculty members to 'look a gift horse in the mouth.' "

Radiation May Boost Stroke Risk

Patients with oral cancer who receive radiation therapy in the neck are five to six times more likely to have damaged carotid arteries that leave them more vulnerable to a stroke, according to a study published in the April issue of the Journal of Oral and Maxillofacial Surgery.

Each year, oral and maxillofacial surgeons, dentists and physicians diagnose more than 43,000 patients with oral cancer.

The X-rays of 61 male patients who had received radiation of the neck in the previous three years showed that 17 (nearly 30 percent) had calcified plaques obstructing at least one of their carotid arteries, with six showing artery blockage on both sides of the neck. In comparison, only three of the 61 patients in the control group had X-rays that revealed artery blockage.

Radiation oncologists often radiate the neck to kill oral cancer cells that have spread to lymph nodes. Patients receiving that therapy usually have other risk factors – such as tobacco or alcohol abuse or hypertension – that make them more susceptible to other health problems. All of the study group patients had already developed osteoradionecrosis of the mandible, which the study's authors contend should be considered a marker for potential artery complications.

"Our research shows that radiation can damage the carotid arteries lining each side of the neck and may induce atherosclerosis," says Dr. Arthur H. Friedlander, lead author of the study and chief of oral and maxillofacial surgery at the Veterans Affairs Medical Center, Sepulveda, Calif. "After enduring the trauma of fighting cancer, these irradiated patients are now at risk for stroke much earlier in life than those in the control group."

Atherosclerosis, a buildup of cholesterol and calcium in the inner layer of the arteries, kills more people in the United States than any other disease. Its first visible symptom is often a stroke, which affects 550,000 Americans each year and causes more than 150,000 deaths.

To identify whether they are at increased risk of stroke, oral cancer patients should ask their oral and maxillofacial surgeon or dentist to check their X-rays for calcium deposits in the neck. Many of those patients already see oral and maxillofacial surgeons for help in coping with dry mouth syndrome, an uncomfortable side effect of radiation.

Researchers Close in on Cause of Cleft Palate

Scientists at the University of Southern California have identified a genetic circuit that when broken causes cleft palate in newborn mice, according to a story in Dentistry Today.

The critical points of the circuit represent genes and gene products that interact with each other to direct palate formation. The surge that caused the circuit to break in the mice was an environmental assault in the form of steroid hormones given to female mice during pregnancy.

According to the study, which was partly supported by the National Institute of Dental Research, this is the first time that a cause-and-effect scenario for cleft palate has been worked out at the molecular level.

The finding may help define the genetic components of cleft palate in humans and explain the link of risk factors such as stress, smoking and certain medications that are known to elevate the level of steroids in the body.

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"Facial clefting disorders are among the most common human birth defects and occur in almost 1 in 2,000 live births," says Dr. Tina Jaskoll, one of the study's principal investigators. "The defects can range in severity from a relatively minor split uvula at the rear of the mouth to a cleft running the length of the hard and soft tissues forming the roof of the mouth."

The more severe forms require surgery and are often associated with psychological and physical problems, she added.

The investigators believe cleft palate results from a combination of genetic and environmental factors, but attempts to identify those components in human populations have proved inconclusive.

Lower Doses, Less Pain

In the not-too-distant future, patients in pain may be better treated with fewer side effects using lower morphine doses combined with new painkillers already under development, according to a study reported by researchers from the University of California, San Francisco, in the March 26 issue of the journal Nature.

Pain may be perceived by most people as a continuum ranging from irritating to unbearable, but a UCSF research team led by Allan Basbaum, PhD, has made the discovery that – biologically – mild pain and more intense pain are distinct and governed by different signaling molecules. Effective management of intense pain should take those distinctions into account, Basbaum said.

"Pain is not a single phenomenon that can always be attacked with one type of analgesic drug," according to Basbaum.

Yu Qing Cao, a graduate student in Basbaum's lab, conducted key experiments on mice that revealed that two different types of signaling molecules, called neurotransmitters, are involved in mild pain and more intense pain.

For several years, researchers have known that the neurotransmitter glutamate is important is signaling pain. But Cao, along with researchers in the lab of Charles Epstein, MD, developed a "knockout" strain of mice lacking a gene for substance P and neurokinin A, two members of a different class of neurotransmitters called the tachykinins.

By measuring how long it took mice to move away from applied mechanical pressure, or how many seconds they licked skin where hot pepper extract had been applied, Cao determined that the knockout mice were as sensitive to mild pain as normal mice, but that they were much less sensitive to moderate or more intense pain.

The research team concluded that substance P or neurokinin A – or both – are needed to transmit moderate or more intense pain signals in a variety of painful conditions. Although the mutant and normal mice needed the same amount of morphine to relieve mild pain, the mutant mice, which lacked the tachykinins, needed less morphine to experience pain relief under more intense pain conditions.

Pharmaceutical companies have been developing prototype painkillers to block the action of substance P and neurokinin A on receptors on the surfaces of pain-transmitting nerve cells. The recent rodent studies by Basbaum and others are defining and refining scientific understanding of the roles played by those and other molecules in specific pain syndromes. Their findings point to strategies that might be adopted to design more effective drugs to individually target the various molecules.

Embezzlement is Serious but Avoidable

Dentists are among those victimized by embezzlers, but potential victims can protect themselves, reports the April 1998 issue of AGD Impact.

Theft by employees will cost American business $60.8 billion or more in 1998, according to data from the U.S. Department of Justice. Dentists can reduce their losses by watching for danger signs and taking preventive action.

"Any dental office is prone to embezzlement," warns John Sullivan, DDS, JD, a practice management consultant in Wheaton, Ill. The usual target, he said, is a dentist-owner who is extremely busy, quite successful, and over-reliant on one trusted employee.

Practice management experts list six warnings of embezzlement:

- Patients frequently complain about billing errors.
- One or more employees are living beyond their means.
- The office manager is overly protective of day sheets, ledgers, or computer records.
- An employee is volunteering too eagerly to open mail and go to the bank.
- Checking account statements continually fail to balance.

A few precautions can help dentists avoid becoming victims, says William Nicrosi, CPA, of the accounting firm of Williams, Taylor & Associates, PC, in Birmingham, Ala. He recommends keeping the staff in the picture.

"But it has to be done in a positive manner," he says. "Let the staff know you will be changing some procedures to make everyone feel better, to improve the practice, and to strengthen the dental team."

Nicrosi and the ADA offer seven anti-embezzlement tips:

- Pay attention to what's going on in your practice. Review collection records weekly; review financial statements and patient receivables monthly.
- Split up responsibilities. Have one person write deposit slips for checks,

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but have someone else take checks and deposit slips to the bank.
- Sign your checks personally. A signature stamp invites theft.
- Insist that employees take vacations. Embezzlers, fearing discovery, can't afford to be away from the office.
- Ask an expert. Hire an outside accountant to check your financial management system for weaknesses and suggest solutions.
- If you think someone is embezzling, see an accountant and attorney before you confront the employee. If you confront the person, do it privately and write down what is said.
- Finally, lead by example. Avoid using company checks or petty cash for personal items. Encourage your employees' honesty by your own honest performance.

Honors

Dr. Craig S. Yarborough has been named assistant dean for student services at the University of the Pacific School of Dentistry.

UOP has bestowed its 1998 Medallion of Distinction awards upon Dr. Ronald Borer, professor of endodontics and associate dean of clinical services; Dr. Louis Geissberger, immediate past president of the UOP Alumni Association; Arlene Burbank, former director of public relations; and Katherine Dugoni, wife of Arthur Dugoni, DDS, dean of UOP's School of Dentistry.

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Introduction: National Institute of Dental Research Shapes the Future of Dentistry

By David G. Jones

In 1948, just three years after the end of World War II, the transistor was first demonstrated, and the World Health Organization was established. Baseball legend Babe Ruth died at the age of 53. The Berlin airlift began on June 24 in response to a Soviet blockade; and on that same day, halfway around the globe, a fledgling government agency was launched with a small $8 million budget, an investment that today is paying dividends in the oral health of the American people.

As it celebrates its 50th anniversary, the National Institute of Dental Research is a "learning organization." It is dedicated to shaping the future through research, training, evaluation, science transfer, and information programs designed to promote health, prevent disease, develop new and improved diagnostics and therapeutics, and invest in basic research that can power the engine of technology and patient-oriented health progress.

As NIDR nears the turn of the century, it has formulated a strategic plan with three initiatives that address research opportunities, research capacity, and health promotion. These initiatives will help NIDR chart a new course over the next three to five years, allowing the institute to investigate new possibilities for research and service to the NIDR community, which consists of academic, private and federal organizations; professional and patient groups; health care providers; the NIDR staff; and the domestic and global public at large.

The first of the three strategic plan initiatives is the research opportunity initiative, which involves identifying and setting priorities and implementing scientific opportunities to advance each of the six major areas of the NIDR research portfolio: inherited diseases; infectious diseases; neoplastic diseases; chronic disabling diseases and disorders; biomaterials, tissue engineering and biomimetics; and oral health promotion and disease prevention.

"This means that NIDR must be at the leading edge of scientific discovery if it's to be relevant," said Harold C. Slavkin, DDS, the institute's director. "So it's a never-ending undertaking to discover what are the best scientific opportunities. We're in the business of discovering knowledge."

The research capacity initiative encompasses the enhancement and innovative development of human, physical and technological resources essential to the realization of scientific opportunities. These resources provide the critical personnel and infrastructure for the creative conduct of research.

"We can't pursue science without people, so research capacity means do we have a pipeline filled with bright, innovative, and creative young men and women excited about pursuing either basic or translational or patient-oriented research?" Slavkin noted.

The third initiative, health promotion, involves NIDR serving as a national catalyst for promoting science-based activities that will accelerate improvements in craniofacial, oral and dental health.

"Promotion of health and prevention of diseases and disorders remains a major centerpiece of the institute," Slavkin emphasized. "So in the course of research, if we can learn what the determinants of health are and can communicate those to the profession and public at large, more people will stay healthy longer, and as a consequence the national health bill and the heath crisis in families will be lessened."

As the organization's sixth director, Slavkin has since July 1995 led a cadre of 450 highly trained people in the quest for new dental knowledge. With a multitude of responsibilities, Slavkin says his job's most important part is to be a cheerleader for dental science, dental education, and the practice of clinical dentistry.

"How to communicate that on all levels of society, whether with federal policy-makers; at the state level; or with various nonprofits, universities, and patient advocacy groups is extremely important. Being optimistic and seeing the possibilities and inspiring people is clearly the vast majority of my value," said the CDA member, who came to the institute after heading the Center for Craniofacial Molecular Biology at USC's School of Dentistry.

The fruits of NIDR's many programs affect every dentist's practice on a daily basis. It's a world far removed from that day in 1948 when President Harry Truman brought the institute to life.

"If you think of what was on the plate of a dentist in 1948, it was tooth extraction, silver amalgam, and building dentures," Slavkin said. "We have many dentists today who never think of a full-denture solution for patients because of science, patient-oriented research, and new dental industries springing up; and that's an unbelievable achievement in less than 50 years. Many of my brothers and sisters tend to take this for granted, and think that it's always been that way. This may remind them that the American people's investment in dental science has paid off for the public and the profession."

As Slavkin nears the completion of his third year on the job, he realizes what he cherishes the most.

"I love working and learning with highly creative people, and the Institutes of Health is loaded with people like that. I've always been around terrific people, but here there is such a density of them, it's constantly inspiring."

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NIDR: 50 years of Scientific Progress

By Harold C. Slavkin, DDS

ABSTRACT The National Institute of Dental Research turns 50 this month. During those 50 years, scientific research has resulted in amazing progress in reducing the prevalence and severity of tooth decay, periodontal diseases, and tooth loss. With these successes in mind, NIDR looks to more progress in such areas as the design and fabrication of biomaterials for replacement of teeth, early detection of caries lesions, and innovative remineralization strategies to optimize and preserve the health of dental tissues.

AUTHOR

Harold C. Slavkin, DDS, is the director of the National Institute of Dental Research.

American dentistry is the finest in the world. During the last half of this remarkable 20th century, our nation increased its investment in science with the goal of improving the health of the American people. The investment has paid off and continues to pay off as we prepare for the next millennium.

Just reflect on 1940's life expectancy; patterns of morbidity and mortality; and prevalence and severity of tooth decay, periodontal diseases, and tooth loss. Life expectancy was 55. Viral and bacterial infectious diseases were major determinants for morbidity and mortality. Tooth decay was rampant. Most people expected to be edentulous by the time they reached 45.

Access the NIDR home page on the Internet.

What a difference advances in science and technology have made to the oral health of the American people and to the effectiveness of today's clinical dentistry and medicine as the National Institute of Dental Research closes in on its 50th anniversary this June 24. Life expectancy is approaching 80. Remarkable progress has been made in the prevention and management of many infectious diseases. The etiology and pathogenesis of dental caries and periodontal diseases are now understood in the context of infectious microorganisms and host immunity; the selective use of antimicrobial drugs and routine professional prophylaxis strategies; and a number of health promotion measures including

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fluoridation, dental sealants, and personal oral hygiene. Today, the prevalence of dental caries has been profoundly reduced, the management of periodontal diseases has progressed, and less than 10 percent of the adult population is edentulous. More people are dentate, free of pain and discomfort, and living longer than ever before in human history.

The mission of NIDR is to improve and promote craniofacial, oral, and dental health through research. The legislation that Congress enacted and President Harry S. Truman signed into law in 1948 to create NIDR entrusted it with national leadership in dental research, granted it authority to conduct and support research and training, and mandated that it promote science transfer and dissemination of information (**Table 1**). And NIDR has delivered.

Since its 1948 origins, NIDR training support has benefited this nation's universities and, in particular, schools of dentistry and medicine with a faculty educated and trained in the biological, physical, chemical, behavioral, and clinical sciences (**Table 2**).

Clinical dentistry directly benefited from the NIDR-sponsored science that has revolutionized diagnostics, therapeutics, and dental and medical devices, and provided remarkable health promotion and disease prevention approaches to improve craniofacial, oral and dental health (**Table 3**).

Imagine how science and technology have changed the face of dentistry. Science has fostered enhanced knowledge and expertise regarding all aspects of the human condition in health and disease. Today, we consider not only the prevention and control of dental caries and periodontal diseases, but we also address craniofacial-oral-dental malformations; other infectious diseases (viral, bacterial, yeast, and parasitic); oral and pharyngeal cancers; temporomandibular joint diseases and disorders; acute and chronic oral-facial pain; and oral manifestations of medically compromised patients with AIDS, osteoarthritis, osteoporosis and diabetes, to mention a few.[1,2] Today, we use scientific evidence to educate the general and professional public and to evaluate oral health determinants such as nutrition, lifestyle choices (tobacco cessation, alcohol reduction, and exercise), and environmental exposures.[3-6]

TABLE 1

Directors of NIDR (1948 to Present)

Name	From	To
Trendley Dean	Sept. 17, 1948	March 31, 1953
Francis A. Arnold Jr.	April 1, 1953	February 1966
Seymour J. Kreshover	February 1966	June 30, 1975
Clair L. Gardner (acting)	July 1, 1975	Dec. 31, 1975
David B. Scott	Jan. 1, 1976	Dec. 31, 1981
John F. Gogginss (acting)	Jan. 1, 1982	Dec. 31, 1982
Harold Loe	January 1983	June 1, 1994
Dushanka V. Kleinman (acting)	June 2, 1994	July 1995
Harold C. Slavkin	July 1995	—

Just look around a typical dental clinic in the 1990s. Bench science has moved into mainstream clinical dentistry, often at a very rapid pace. Consider the contributions from NIDR, ADA, the National Bureau of Standards, and private industry-sponsored research and development, which have resulted in:

- The high-speed dental handpiece;
- Panorex radiography;
- Digitized radiography;
- The inorganic and organic chemistry for dental materials;
- Dental sealants;
- Improved amalgam alloys;
- The science of infection management and control (from AIDS to xerostomia);
- The science of soft- and hard-tissue wound healing;
- The science of chemo- and neurosensory processes with attendant advances in analgesia;
- The biochemistry of tissue-specific mineralization; and
- The science of steroidal and nonsteroidal anti-inflammatory drugs.[7]

Just look at the community-based and community-wide prevention opportunities we have and can build upon. Oral health professionals are part of a comprehensive health promotion team, helping to advance health promotion and disease prevention, which is a profound strength of our dental profession. Imagine increased public/private partnerships and collaborations designed to improve student health, science and technology literacy. To begin to address these wonderful opportunities, NIDR is planning a network of regional Centers of Discovery, each thematically and programmatically dedicated to improving the health of the American people through research that extends from the bench to the community. In addition, NIDR has been designated by Health and Human Services Secretary Donna Shalala to be the lead federal agency in the first Surgeon General's Report on the Oral Health of the American People, scheduled to be completed by the Spring of 1999 (access to which can be obtained through the Internet at www.nidr.nih.gov)

NIDR celebrates its 50th anniversary

on June 24, 1998.

Investments in science have served as the fuel for the engine of technology that improves clinical dentistry and oral health. And as we approach the 21st century, what should we anticipate for the next 50 years? How should we prepare for the new millennium? Consider preparation in the context of major changes in demography, disease patterns, management of health care, international immigrations, and the global economy. By the year 2020,

Understanding gene testing for human dental, oral and craniofacial diseases and disorders.

the U.S. population will reach 300 million people, and one in every five Americans will be 65 or older. In this context, the goal of the NIDR will continue to be to reduce or eliminate inherited, infectious, neoplastic, and chronic craniofacial-oral-dental diseases and disorders.[8]

To help realize these goals, scientists will complete the sequencing of the entire human genome as well as a number of microbial and animal genomes by the year 2005.[9] Essentially every gene in the genetic lexicon of significant organisms will be identified and available in hard copy or through the Internet.

Bioinformatics will enable the rapid discovery of more sensitive and specific drugs for the treatment and management of human diseases and disorders. Bioinformatics will also enable dental and medical records to be readily accessible anywhere on the planet Earth. Biomimetics will enable the design and fabrication of novel biomaterials for body part replacements, including teeth, salivary glands, muscle, cartilage, bone and joints. Novel imaging techniques will enable detection of early caries lesions, and innovative remineralization strategies will be used to optimize and preserve the health of dental tissues. Increased knowledge and technology will enable improved oral diagnostics for inherited and acquired systemic diseases using saliva, buccal epithelial cells, and gingival crevicular fluids. During the first half of the 21st century, we envision oral health professionals addressing the challenges of chronic diseases and disorders coupled with medically compromised patients using gene-mediated diagnostics and therapeutics. All of these changes will require increased efforts in the dental and medical school curriculum and continuing education in the areas of epidemiology, genetics, biostatistics, bioinformatics, pharmacology, and physiology and a thorough understanding of the connection between oral and systemic health and diseases.

Our nation's decision to invest in the biomedical and behavioral scientific enterprise has reaped enormous health, social, and economic benefits for the American people as we celebrate this golden anniversary of NIDR. And as we anticipate the next millennium, it becomes very useful to consider the rates and magnitude of changes that have taken place in the demography and patterns of disease in our nation. Further, this is a time to evaluate our goals, where we have been, and where we plan to go as a profession. The future seems bright when we consider the enormous progress of biomedical and behavioral research, the advances in our understandings from the principles of oral infectious diseases, the promise of the microbial and human genomic era, and the emerging opportunities for oral health professionals to address health promotion and disease prevention. Virtually everything important to health care professionals, patients and society – diagnostic

TABLE 2

NIDR Appropriations

Fiscal Year	**Total** (in thousands)
1950	$1,780
1960	10,019
1970	28,754
1980	68,303
1990	135,749
1995	174,021
1996	183,478
1997	195,825
1998	209,415
1999 President's Budget	229,457

TABLE 3

The Top 16 Dental Schools*

University of Washington
University of California at San Francisco
University of Alabama at Birmingham
Forsyth Dental Center (a research organization that also provides training to dental hygienists)
University of Texas Health Science Center, San Antonio
University of Michigan
State University of New York at Buffalo
University of North Carolinaa
University of Iowa
University of Southern California
University of Rochester
University of Minnesota
University of Florida
University of Pennsylvania
Boston University
University of California at Los Angeles

* In fiscal year 1997, each of the above schools received $2 million or more from NIDR through competitive peer-review process.

techniques, understanding the etiology and pathogenesis of diseases, methods of treatment, approaches to prevention, health care management, dental and medical education, legal and ethical issues – will change through information technology, biotechnology, genetic dentistry and medicine, and our nation's expanding partnerships among federal, state, local governments, and the private sector as we enter the 21st century.

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To request a printed copy of this article, please contact/ Harold C. Slavkin, Office of the Director, National Institute of Dental Research, National Institutes of Health, 32 Center Drive, Bldg. 31C, Room 2C-39, Bethesda, MD 20892.

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Reducing the Burden of Oral and Pharyngeal Cancers

By Deborah M. Winn, PhD; Ann L. Sandberg, PhD; Alice M. Horowitz, PhD; Scott R. Diehl, PhD; Silvio Gutkind, PhD; Dushanka V. Kleinman, DDS, MScD

ABSTRACT In the United States, oral and pharyngeal cancers continue to result in significant morbidity and mortality. Dental professionals play a pivotal role in all facets of controlling the burden of oral and pharyngeal cancer – from efforts to prevent its occurrence, to ensuring that oral cancers are detected at the earliest possible stage, to treating these cancers, and to ensuring maximum quality of life and function for oral and pharyngeal cancer survivors. Individually and by making linkages within the community and beyond, dentists can help patients modify their risk of these cancers and can take steps to screen for them, thereby potentially improving survival and function of those who develop oral cancer. Creative partnerships between community dentists and academic and other research centers will help move knowledge of the biological processes involved in carcinogenesis and innovations in treatment into clinical practice. Partnerships between dental and medical professionals may also help efforts to reduce the morbidity related to oral and pharyngeal cancers. Local, state and national multidisciplinary initiatives are emerging that focus more broadly on risk factor control or oral and pharyngeal cancer issues. These many forms of cooperative approaches offer excellent opportunities to make a significant impact on reducing the incidence of and in treating these debilitating and disfiguring malignancies.

AUTHORS

Deborah M. Winn, PhD, is a senior investigator in the Division of Intramural Research, National Institute of Dental Research, National Institutes of Health.

Ann L. Sandberg, PhD, is director of the Neoplastic Diseases Program and the Comprehensive Oral Health Research Centers of Discovery Program in the Division of Extramural Research, National Institute of Dental Research, National Institutes of Health.

Alice M. Horowitz, PhD, is a senior scientist in the Office of Science Policy and Analysis, National Institute of Dental Research, National Institutes of Health.

Scott R. Diehl, PhD, is chief of the Molecular Genetic Epidemiology Section in the Division of Intramural Research at the National Institute of Dental Research, National Institutes of Health.

Silvio Gutkind, PhD, is chief of the Oral and Pharyngeal Cancer Branch, Division of Intramural Research, National Institute of Dental Research, National Institutes of Health.

Dushanka V. Kleinman, DDS, MScD, is deputy director, National Institute of Dental Research, National Institutes of Health.

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TABLE 1

Oral and Pharyngeal Cancer Electronic Information Resources
The home page for the National Institutes of Health: www.nih.gov
The home page for the National Institute of Dental Research, one of the National Institutes of Health: www.nidr.nih.gov
The home page for the National Cancer Institute, one of the National Institutes of Health: www.nci.nih.gov
The home page for the National Oral Cancer Awareness Program, an ongoing program to inform both the public and health care professionals about oral cancer and related topics: www.oralcancer.org
The home page for the Centers for Disease Control and Prevention: www.cdc.gov
The home page for the American Cancer Society: www.cancer.org

During the past 25 years, remarkable progress has been made in both the elucidation of the molecular bases of cancers and their treatment. Yet monumental challenges remain. Cancers of the oral cavity, lip and pharynx affect more than 30,000 people each year;[1] and, collectively, they remain the sixth most common cancer among U.S. white males and the fourth most common among U.S. black males.[2] These malignancies are among the most debilitating and disfiguring of all cancers, and annual costs of care are estimated to be about $2 billion.[3] Tobacco and alcohol are major risk factors for these cancers.[4]

It is encouraging that oral and pharyngeal cancer incidence (the number of new cases of oral and pharyngeal cancers per 100,000 people) has declined recently. This decline has been most notable among white males. Only in the past few years has a decline in incidence rates for black males occurred. This, fortunately, is a reversal of rates that increased by 1.6 percent per year during the period 1973-1992. Very recently, the incidence rates for black and white females have also declined.[5] However, the U.S. population is increasing, and the baby boomers are aging. Thus, the actual number of individuals with oral and pharyngeal cancers has increased by about 20 percent from 1973 to 1992. Similarly, the number of people with many other forms of cancer is also increasing.[5]

A decline in the overall mortality (deaths per 100,000 people) from oral and pharyngeal cancers has also occurred.[5] However, a striking exception to this finding is that, among people younger than 40, mortality from cancers of the tongue, the most common cancer site within the oral cavity, has been rising for decades.[5] The mortality from oral and pharyngeal cancers in California is similar to that in the United States.[6] However, California has a greater number of these malignancies than most states because of its large population. Of the newly diagnosed patients with oral and pharyngeal cancers in the United States in 1995, 3,000, or 11 percent, were in California.6 Nasopharyngeal cancers may be more common in California than elsewhere in the United States since a disproportionately large number of people of Chinese descent, who appear to be more susceptible to these specific cancers,[7] reside in California.

The overall survival rate for individuals with oral and pharyngeal cancers is 52 percent at five years after diagnosis. This is lower than that for colon cancer, cancer of the cervix, and breast cancer.[2] Although survival has improved for many cancers, the five-year survival of individuals with oral and pharyngeal cancers has not increased over the past four decades. The survival of blacks has actually decreased.[2] Most oral and pharyngeal cancers (64 percent) are not diagnosed at an early and more easily treatable stage; black people with oral cancer are even less likely to have an early stage diagnosis (**Figure 1**). Yet, it is clear that survival is better when the cancer is found at an early stage (**Figure 2**). Also, individuals who survive an initial primary oral cancer are at an elevated risk of developing new primary tumors. The rate of second primaries among oral and pharyngeal cancer patients exceeds that for any other type of cancer.[8,9]

Oral and pharyngeal cancers, like other cancers, result from a multistage accumulation of genetic aberrations. The genetic changes that have been associated with oral and pharyngeal cancers are not localized to any one chromosome but, rather, are found on many human chromosomes. Mutations in certain genes may promote uncontrolled cell growth by overproducing either growth stimulatory factors or their receptors that, following ligand binding, trigger numerous intracellular processes. Mutations in other genes result in a loss of tumor suppressors, proteins that prevent excessive cell growth. Additional genetic alterations favor vascularization of tumors or enable oral tumor cells to invade the surrounding tissues and migrate within lymph nodes to the lymph nodes in the neck. The intricacies of cancers are further increased by genetic aberrations in transcription factors that regulate the expression of other genes.[10]

Oral cancers are often preceded by premalignant lesions including leukoplakia (white mucosal changes) and erythroplakia (red mucosal changes) or mixed white and red lesions.[11] Biomarkers are cellular, biochemical, or molecular alterations measurable in human tissues and fluids.[12] Alterations in certain genes may occur in premalignant lesions and may, therefore, provide excellent biomarkers

for determination of those individuals who require close monitoring or who may benefit from chemoprevention, that is, the use of natural or synthetic chemicals such as vitamin A-related compounds to prevent oral cancer.[13] Major efforts are currently under way to identify genetic biomarkers both for the early detection of oral and pharyngeal cancers and as indicators for prognosis.[14] For example, the normal p53 suppressor gene inhibits cell growth. Mutations of the gene (resulting in failure of the normal inhibitions of growth) are common in oral cancers.[15] In addition, p53 alterations appear in premalignant oral lesions[16] and also predict recurrence and second head and neck primary cancers.[17] Behavioral and molecular factors are both important in oral cancer etiology. Of interest are recent studies suggesting that individuals with a genetic predisposition to rapidly metabolize alcohol and who also consume large quantities of alcohol are at the highest risk for development of oral and pharyngeal cancers.[18]

The primary objective of any therapeutic regimen for treatment of head and neck cancers is cure. However, current modalities also focus on preservation or restoration of function and appearance. Surgery or radiotherapy, either alone or in combination, is generally utilized for early stage tumors. Although surgery is commonly favored, radiotherapy may be essential because of the size or location of the tumor. In late-stage disease (tumor greater than 4 cm and/or lymph node involvement), more aggressive treatment, with resultant functional consequences, may be necessary. Chemotherapy is often added to the treatment regimen in advanced tumors or tumors of certain sites in the hope of increasing control;[19] by itself, chemotherapy is only palliative.[20] New techniques and approaches in treatment are emerging. For example, for instances when reconstruction of the mandible or soft tissue is required, techniques have now been developed for tumor resection and bone or skin grafting in a single surgical procedure. Investigators also are now exploring the possibilities of applying immunotherapy and gene therapy to the treatment of cancers of the head and neck.

Although we are moving ahead in understanding the etiology and pathogenesis of this disease, there are actions that can be taken now to prevent and control it. Reducing the burden of oral and pharyngeal cancers will require multiple approaches to prevent tobacco use and excessive alcohol consumption, identify precancerous lesions and tumors at the earliest possible stage, ensure prompt and coordinated treatment of people with oral cancer, and move promising scientific discoveries rapidly into practice. Dental professionals can contribute to these efforts to reduce the burden of the occurrence of oral cancer and its potentially devastating effects through practice-based efforts to reduce or eliminate patients' risk behaviors and by diagnosing these cancers earlier. Dental professionals can also make a difference through partnerships with the greater community, state and nation.

National and State Programs

Over the past several years, the Centers for Disease Control and Prevention, the National Institute of Dental Research, and the American Dental Association have developed a strategic plan for the prevention and reduction of oral cancer in the United States.21 It is hoped that this plan will stimulate an effective national campaign for the prevention and control of oral and pharyngeal cancers. Recommendations are made in five broad areas:

- Advocacy, collaboration, and coalition-building;
- Public health policy;
- Public education;
- Professional education and practice; and
- Data collection, evaluation, and research.

Implementation of the plan is under way and involves a wide range of dental, medical, and social service organizations that work with oral cancer patients and those at risk for oral cancer. The national health promotion and disease prevention objectives for the nation have highlighted oral cancer reductions and actions needed for tobacco control.[22]

There are several other initiatives at the national level that specifically focus on prevention and control of tobacco use and involve dental professionals. For the past several years, the National Dental Tobacco-Free Steering Committee under the sponsorship of the National Cancer Institute has mobilized a consortium to:

- Assess recent developments in tobacco use intervention strategies;
- Define opportunities of dental involvement in tobacco use intervention activities; and
- Promote cooperation among dental and other professional and public interest organizations.

A national program focused on chewing tobacco and snuff, the National Spit Tobacco Education Progam, has been under way since 1994. This program was initially funded by Oral Health America, the National Institute of Dental Research, and the National Cancer Institute and is now funded by the Robert Wood Johnson Foundation. Six regional coordinating centers across the country have been established. The National Cancer Institutes' COMMIT program, an acronym for Community Intervention Trial for Smoking Cessation, also included a focus on dental professionals.[23]

One example of a state-initiated program focuses on spit tobacco use. The

Spit Tobacco Education and Prevention Plan for the State of Texas is funded by the Texas Cancer Council and administered by the Dental Oncology Education Program in cooperation with the Texas Dental Association. The extremely high use of spit tobacco in Texas stimulated this special initiative. The goal is to diminish and eliminate use of spit tobacco through collaborative integrated research, education, and public policy activities.[24]

The development, implementation, and evaluation of state models has been suggested as one approach to oral cancer prevention and early detection.[21,25] A state model is defined as a comprehensive plan that includes implementation and evaluation criteria of appropriate interventions based on the needs of the particular state. The rationale for this approach is that each state has different oral cancer incidence, mortality, and survival rates; racial and ethnic groups; practice acts for health care providers; and laws concerning tobacco use and enforcement practices, as well as differences in both smoking and chewing patterns. Thus, no one model could fit the needs of all states. Today, no state has a comprehensive state model for oral cancer prevention and early detection, but several states have taken some initial steps to do so. For example, Maryland has begun a partnership for the prevention and early detection of oral cancers. The partnership, which is spearheaded by the state dental director, includes representatives from provider associations, advocacy and consumer agencies, organizations, and other interested groups. It is the intent of the partnership to assist Maryland dental and medical practitioners, policy-makers, and residents in receiving the benefits of appropriate and quality oral cancer prevention, education, and training and by advocating oral cancer-related policies that promote and protect health and support healthy behaviors and lifestyles.

Oral Cancer Prevention

Finding innovative means of preventing people from using tobacco and alcohol and developing effective methods to get users to quit will be essential in reducing the occurrence of new cases and the risks of second primary cancers. Based on a very large epidemiologic study in four areas of the United States, it is estimated that about three-fourths of oral and pharyngeal cancers are associated with the use of any form of tobacco and heavy alcohol intake.[26] Tobacco and alcohol independently increase the risk of oral and pharyngeal cancer, and people who use both are at much higher risk than would be expected from the risks among those who only smoke or only drink.[26] Quitting smoking reduces the risk of oral and pharyngeal cancer.[26] An advisory group to the surgeon general stated that smokeless tobacco (snuff and chewing tobacco) can cause cancer in humans.[27] Although cigarette smoking rates have been declining in adults and have probably contributed to the declines in incidence rates of these cancers, disturbing trends have emerged. Cigarette smoking is increasing among adolescents.[28] Smokeless tobacco use remains common, based on a survey in 1995 that found that 11.4 percent of high school youth had used smokeless tobacco in the previous month; for white adolescents the figure was 25.1 percent.[29] Also of serious concern is the recent popularity of cigar smoking. Compared to non-users of cigars, cigar smokers experience a four to tenfold higher risk of dying from oral, laryngeal, and esophageal cancer.[30]

Dentists seldom determine patients' use of tobacco and alcohol products.[31] Currently, one-third of dental schools do not assess patient risk behavior on their standard patient history forms;[32] also, routine risk behavior assessments are not universally used in medical and dental hygiene schools.[33,34] Provider knowledge of the patient's risk profile is an essential first step in changing patient behavior.

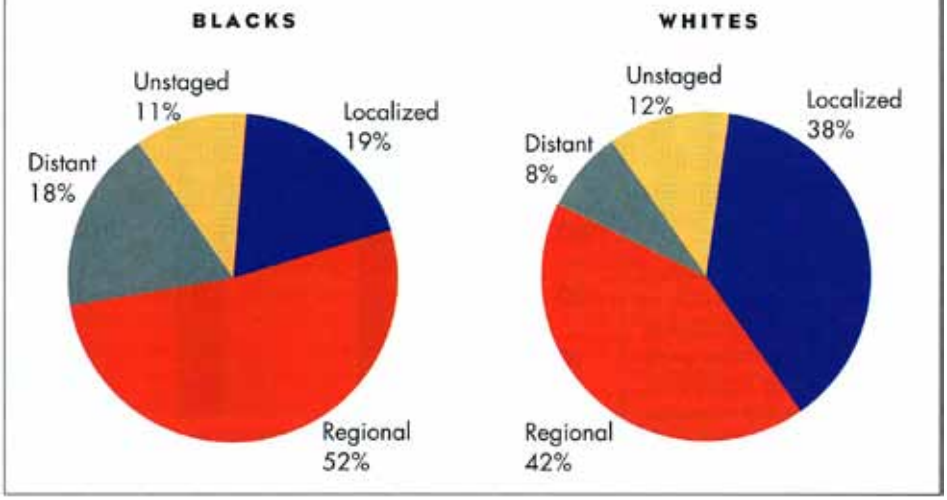
Emerging evidence is demonstrating that interventions in the dental practice setting may be effective in reducing use of tobacco. One recent study compared methods to stimulate smokeless tobacco users to quit. The intervention compared usual care with a routine oral examination, an explanation of the health risks of smoking, unequivocal advice to quit, and a nine-minute video, a self-help manual, and a brief counseling session with a dental hygienist. This intervention led to a 50 percent increase in the number of quitters at one year compared to usual care.[35] Brief interventions for smokers and other tobacco users suitable for the dental office have also been developed and made available.[36,37]

New approaches to help tobacco users quit are emerging. One promising strategy is suggested by the recent results of a clinical trial of the anti-depressant Bupropion. The results indicated that 19.6 percent of smokers receiving the lowest dosage of the anti-depressant were abstinent after one year of follow-up compared to 12.4 percent among the placebo group, and rates of abstinence for higher dosages of Bupropion were even greater.[38] However, because those at highest risk of oral and pharyngeal cancer are smokers who also abuse alcohol, interactions between drugs designed to curb tobacco and alcohol and the challenges of multiple drug dependencies must be considered.

Other mechanisms are also being used to influence tobacco use behaviors. California, for example, has had remarkable success in reducing tobacco consumption through Proposition 99, the tobacco tax initiative. The result

Figure 1.

Distribution of Oral and Pharyngeal Cancer by Stage at Diagnosis, 1986-91.[5]



of implementation of Proposition 99, which raised taxes on tobacco products and used the funds from the increase to fund tobacco control activities, has been a 27 percent decline in the prevalence of tobacco use in California from 1988 to 1993, a rate of decline three times that of the rest of the United States.[39]

Early Identification

Identifying cancers at the earliest possible stage is another critical component in mitigating the burden of oral and pharyngeal cancer. Both the patient and the dentist can play a role. White and/or reddish lesions in the oral cavity can progress to malignancies.[40] Nonhealing sores, pain and swelling are additional signals to a patient to seek a medical or dental examination. However, early detection of oral and pharyngeal cancers is impeded by the public's poor understanding of the risk factors for and the signs and symptoms of oral cancers.[41,42] For example, only 25 percent could identify one early sign of oral cancer, and 44 percent responded that they did not know any early signs.[42] Dental professionals can educate patients about their risk for oral and pharyngeal cancer and encourage compliance with visits and examinations to monitor oral and pharyngeal mucosal health. This function in part depends upon undergraduate training and practical experience, as well as continuing education updates.

Oral cancers may be diagnosed and treated earlier if dentists provide oral cancer examinations. Currently, only 14 percent of U.S. adults report that they have ever had an oral cancer examination and only 7 percent had the exam in the past year,[43] the frequency recommended by the American Cancer Society for adults 40 years of age and older.6 Based on a recent survey in two Maryland counties,[44] many dentists and other health care providers do not examine all adult patients for oral cancers. In addition, a recent national pilot study showed that dentists' level of knowledge regarding risk factors for and signs and symptoms of oral cancer is inconsistent and less than optimal.[45] Many dentists have not attended a continuing education course on oral cancer during the past five years.[45]

There are additional barriers to reducing the proportion of oral cancers that are diagnosed at late stage. A significant problem is the lack of reimbursement for oral cancer examinations under the Medicare and Medicaid systems.

Professional Education and Association Opportunities

Dental and dental hygiene schools are uniquely positioned to provide additional training in oral cancer prevention, detection, and care. Also, educational programs have been developed by non-academic groups including state American Cancer Society groups, the National Oral Cancer Awareness Program, and the National Oral Health Information Clearinghouse, the latter in conjunction with an advisory group that has representatives from patient groups, the Centers for Disease Control and Prevention, the American Dental Association, and the Federation of Special Care.

Associations of dental professionals, working with their medical and other health care personnel colleagues, can also contribute to efforts to reduce oral cancer and encourage activities that improve early detection. State dental and medical boards could require that dental and medical personnel take a special course on oral cancer prevention and early detection prior to licensure and relicensure.[41] Such a requirement has several precedents in California, for example, the newly enacted requirement for all dental personnel to complete continuing education in infection control. Many state and local dental/dental hygiene organizations sponsor cancer education programs at their annual or periodic meetings.

Dental, Medical, and Research Partnerships

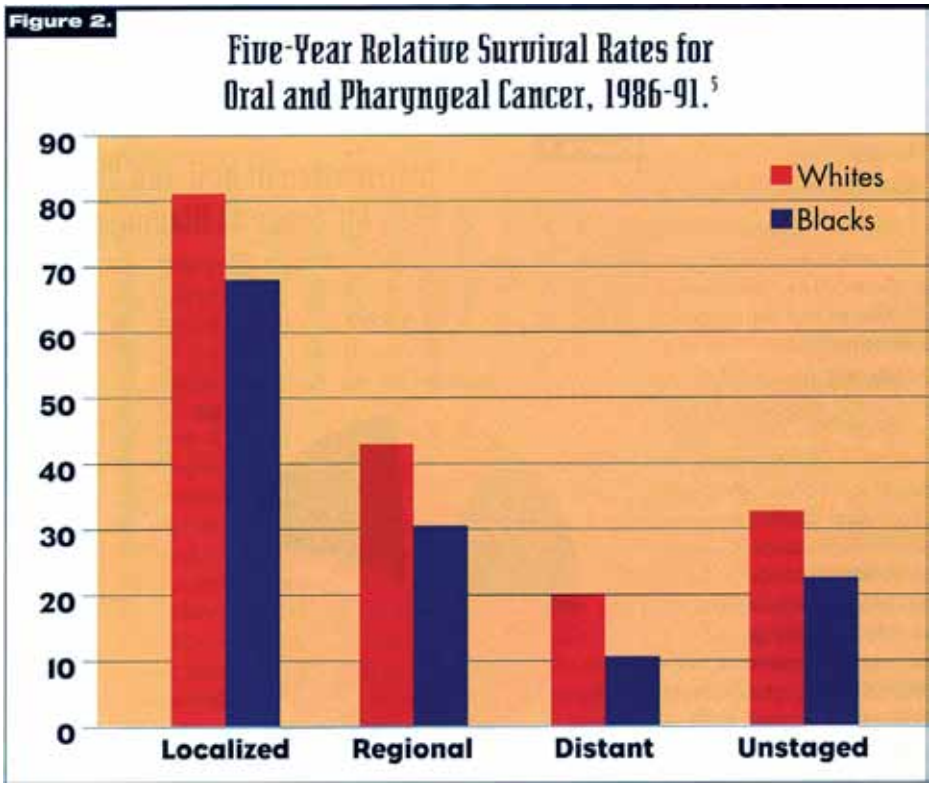
Partnerships can focus attention on particular public health problems,

potential solutions, and mechanisms for implementing those solutions. Two special types of partnerships will be important: those with the medical community and those with the research community. Other, broader partnerships will be important as well.

Concerted and coordinated effort on the part of dental and medical professionals is essential to make an impact in risk factor management. Responsibility for diagnosis is shared between the dental and medical professions because of the nature of the presenting symptoms, which may lead patients to seek out dentists, otolaryngologists, or internal medicine specialists, among others. The patterns of health care utilization by older people suggest that both medical and dental professionals may have opportunities to screen for previously undetected lesions. For example, in one study of head and neck cancer patients residing in Boston, subjects had a median of 10.5 health care visits in the 24-month period just prior to diagnosis, and these visits included a wide range of health care professions and care settings.[46] Thus, monitoring through both the medical and dental care systems can potentially optimize early detection. Efforts are under way to increase the diagnostic capacity of all health professionals and to introduce preliminary examinations in settings such as the health service centers for homeless shelter residents.[47]

The medical, psychological, and social problems associated with both tobacco use and alcohol abuse are well-known. Thus, it is clear that the individuals at highest risk for oral cancer may have enormous difficulty quitting either of these habits. They may also have medical or emotional problems that can compromise compliance with health care appointments intended to monitor risk factors or oral lesions. Smoking and alcohol abuse and their consequences may complicate oral cancer treatment. Finally, once diagnosed and treated for oral cancer, many patients face functional and other problems that impact oral and systemic health and must be closely monitored for recurrences and new primaries. Ongoing dental-medical communication and coordination should help maximize function, quality of life, and early detection of new problems in these patients.

Figure 2.



The research community and dental practitioners can form new relationships in the future to take advantage of scientific innovations. The Internet provides the practicing dentist with excellent opportunities to follow these advances: The National Institute of Dental Research and the National Cancer Institute Web pages are constantly updated with new research findings. The research community needs to establish links with dentists in communities as a source of patients for studies and as a possible setting for studies of the effectiveness of procedures for risk factor control, early detection, and follow-up after diagnosis and initial therapy.

Conclusion

Dental professionals play a pivotal role in all facets of oral and pharyngeal cancers. They must be involved in attempts to prevent occurrence of these malignancies through promotion of tobacco and alcohol control and be well-versed in examination procedures to detect lesions at the earliest possible stages. They must also be instrumental in reducing the morbidity and mortality of oral pharyngeal cancers by promptly referring patients for appropriate treatment and, subsequently, monitoring them for recurrence or the development of second primary tumors. Close teamwork among dentists, hygienists, physicians, maxillofacial or head and neck surgeons,

radiation and medical oncologists, prosthodontists, psychologists or psychiatrists, and rehabilitation specialists would optimize diagnosis, therapy, and maintenance or restoration of function and quality of life. Consortia that focus on the control of oral and pharyngeal cancers in the United States have been established. Their multidisciplinary cooperative approaches, in addition to escalated progress in research and more rapid translation of research findings to a clinical setting, would make a significant impact on reducing the incidence of and treating these debilitating and disfiguring malignancies.

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To request a printed copy of this article, please contact/ Deborah Winn, PhD, Division of Intramural Research, National Institute of Dental Research, Natcher Building, Room 4AS-19F, 45 Center Drive, Bethesda, MD 20892-6401.

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The Mouth is a Gateway to the Body: Gene Therapy in 21st Century Dental Practice

By Bruce J. Baum, DMD, PhD; Jane C. Atkinson, DDS; Lorena Baccaglini, DDS, MS; Mark E. Berkman; Jaime S. Brahim, DDS, MS; Clifford Davis, BS; Henry E. Lancaster, DMD; Yitzhak Marmary, DMD; Anne C. O'Connell, BDS, MS; Brian C. O'Connell, BDS, PhD; Songlin Wang, DDS, PhD; Yanying Xu, DDS, PhD; Hisako Yamagishi, DDS, PhD; Philip C. Fox, DDS

ABSTRACT Gene therapy may become an integral tool in dental practice early in the 21st century. It, and other biological therapies, are expected to be applied to oral diseases and disorders during the midpractice lifetime of today's dental students. If the applications of oral gene transfer are expanded to systemic diseases, oral health care providers in the future could routinely be "gene therapists" with therapeutic targets well outside the oral cavity.

AUTHORS

Bruce J. Baum, DMD, PhD, is the chief of NIDR's Gene Therapy and Therapeutics Branch (GTTB).

Jane C. Atkinson, DDS, is a senior staff dentist (oral medicine) in the GTTB. Lorena Baccaglini, DDS, MS, is an oral medicine fellow at NIDR.

Mark E. Berkman is a dental student at Ohio State University and for 1997-98 is a Howard Hughes Medical Institute-NIH research scholar working in the GTTB.

Jaime S. Brahim, DDS, MS, is a senior staff dentist (oral and maxillofacial surgery) at NIDR.

Clifford Davis, BS, is a dental student at UCLA and for 1997-98 is a NIH-Clinical Research Training Program fellow working in the GTTB.

Henry E. Lancaster, DMD, is an oral medicine fellow at NIDR.

Yitzhak Marmary, DMD, was a visiting scientist in the GTTB during 1996-97 and is head of oral and maxillofacial radiology at the Hebrew University-Hadassah School of Dental Medicine, Jerusalem, Israel.

Anne C. O'Connell, BDS, MS, is director of the NIDR Clinical Research Core Facility.

Brian C. O'Connell, BDS, PhD, is the head of the Gene Regulation and Expression Unit, GTTB.

Songlin Wang, DDS, PhD, was a visiting scientist at the GTTB during 1995-97 and is head of the Salivary Gland Disease Center at Capital University, Beijing.

Yanying Xu, DDS, PhD, was a visiting scientist at the GTTB during 1996-97 and is an associate professor in the Department of Oral Medicine, School of Stomatology, Beijing Medical University, Beijing.

Hisako Yamagishi, DDS, PhD, is a visiting fellow from Tokyo Dental College, Tokyo, working in the GTTB.

Philip C. Fox, DDS, is clinical director, NIDR, and chief, Clinical Investigations Section, GTTB.

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Currently, the practice of dentistry reflects an educational system whose essential elements were structured following the publication of the Gies Report in 1926.[1] Dental students today are taught basic biomedical sciences and excellent technical skills in the course of a four-year predoctoral curriculum in preparation for careers as the primary oral health providers in our system of health care delivery. Gies' report brought dental education fully into the university community, where it remains today. However, while many relevant components of this community have experienced significant pedagogical changes as a result of new knowledge and scholarship (e.g., in biology, medicine, materials science, and bioengineering), the impact has been limited within dental education.[2,3] The basic formula for producing a dentist – and, thus, by extension the definition of oral health care in America – has changed little in the past 50 years with a few notable exceptions.[4] Elsewhere in health care, the exponential growth in biology has dramatically altered approaches to clinical care.[5] Arguably, the most dramatic example of such change is in the transfer of nucleic acids into cells for the purpose of altering a disease or disorder, so-called gene therapy.[6] It is the authors' expectation that gene therapy will also become an integral tool in oral health care, i.e., dental practice, early in the 21st century.

Gene Transfer

Three years ago, two of the authors wrote an essay in the Journal of the American Dental Association[7] titled, "The impact of gene therapy on dentistry." In it, they described the fundamental biological principles that underlie gene transfer, as well as methods in place at that time for its clinical application. They also reported several initial attempts, by their own and other laboratories, to apply gene transfer technology for orally relevant problems. Since that time, progress has been considerable, markedly exceeding the authors' most optimistic expectations. Although not yet ready for human use, many potential applications derived from test tube/cell culture experiments have entered the preclinical, animal model stage. The technology is still far from perfect and certainly has substantive problems, but clinical gene therapy is maturing and showing even more, and broader, potential then originally believed.[6]

One area of application is of particular importance for the oral health community to recognize: the use of genes as pharmaceutical agents. This is a use of clinical gene transfer barely appreciated initially by medicine.[6,8] There are certainly many oral-specific, corrective applications of gene transfer possible, e.g., repair of irradiated salivary glands or treatments of oral cancer. However, it is conceivable that somewhat analogous to the conventional medications taken by mouth, a number of systemic gene therapeutics may also follow a route of oral delivery because it is convenient.

How might such future gene therapeutics work? Could dentists routinely perform gene transfer? Many natural gene products (proteins) intended for use in one body locale have their site of synthesis elsewhere. Because of the ease of access, it seems reasonable to consider oral tissues as a target for use in systemic gene therapeutics. And who is better trained to manipulate oral tissues than dentists? In the mouth, there are many sites to which a foreign gene might be delivered advantageously (and presumably be expressed) and from which the gene product might enter the upper gastrointestinal tract or the circulation. These sites include the salivary glands, mucosa, gingival crevice, and tongue. While other health care practitioners can be trained to perform oral procedures,[9] this area is within the purview of dentistry. The following describes examples of such applications using salivary glands.

TABLE 1

Vectors Used to Transfer Genes in Vivo.

Viruses
Retrovirus* **
Adenovirus*
Adeno-associated virus* **
Lentivirus**
Nonviral Methods
Cationic liposomess*
Macromolecular conjugates

* In clinical use at present (for retroviruses, ex civo only). Al l virus ventors used are replication deficient.

** Can lead to integrated (within the host chromosome), stable gene transfer.

Methods of Gene Transfer

The delivery of genes or other nucleic acids into salivary glands is straightforward, employing the approach clinically used for sialography.[10] While sialography is not a procedure commonly performed by most dentists, the manual skills required are within a dentist's repertoire. The procedure involves cannulating the main excretory ducts (Stensen's and Wharton's) of the major salivary glands (parotid and submandibular/sublingual, respectively). A suspension of the gene transfer vector is subsequently retrograde-infused slowly into the gland. Since almost all epithelial cells in a gland abut the duct lumen,11 the gene transfer vector potentially has most cells in the gland as targets.

How are genes transferred (**Table 1**)? A vector is the carrier of the gene to be transferred. There are essentially two ways to transfer genes at present,

TABLE 2

Genes Transferred to Mammlian Salivary Glands*

Gene	Function	Reference
B-Galactosidase	marker bacterial enzyme	10
Chloramphenicol-Acetyltransferase	marker bacterial enzyme	26
1-Antitrypsin	protease inhibitor	10, 22
Growth hormone	systemically active hormone	24, 25
Insulin	systemically active hormone	25
Histatin 3	anti-candidal protein	18
Aquaporin 1	membrane water channel	27
Aquaporin 5	membrane water channel	28
E2F-1	transcription factor	29

*All studies used either rat parotid or submandibular glands with foreign genes delivered via cannulation of the main excretory duct.

i.e., two types of vectors: viral and nonviral. Viruses have evolved highly efficient mechanisms to transfer genes. However, they may pose a safety risk, even though all forms currently used are replication-deficient (cannot multiply). For example, viruses can lead to a potent immune reaction that limits their activity and precludes their readministration. Nonviral gene transfer usually involves a formulation of condensed DNA within a lipid capsule. Nonviral methods have a low safety risk but thus far have proven to be markedly less efficient than viruses at gene transfer in vivo. Whatever the vector used, it is recognized in some way (a specific protein receptor or electrostatic charge) by the target cell, internalized, and transported to the nucleus with varying degrees of efficiency. Once in the nucleus, the gene is either integrated into the chromosome (e.g., retrovirus, adeno-associated virus, or lentivirus) or it exists in an epichromosomal (free) location (adenovirus and nonviral methods). There is no single idealized gene transfer vector for all clinical purposes at present, nor is there likely to be one in the near future. There have been major improvements in vector technology recently,[6] but the methods used now leave considerable room for improvement.

Salivary glands seem to provide an excellent target site for gene transfer (Table 2), including gene transfer for the production of a secreted protein product. As noted above, these glands are easily accessed, and almost all of the parenchymal cells contact the lumen into which the gene transfer vector is infused. Further, most of the cells in the gland are acinar and thus designed to manufacture considerable protein for export, albeit typically into the mouth. The latter, normal secretory process could be augmented, for example, by transferring a gene into the gland, which would prevent or correct disorders of the upper gastrointestinal tract. Alternatively, since it is known that at least some exocrine proteins can reach the bloodstream,[12] glands could be engineered to secrete a gene product for general systemic use. Recent in vivo animal studies have shown that both of these possibilities appear feasible in the near future.

Upper GI Tract Gene Therapeutics

One of saliva's physiological roles is to protect and nurture the tissues of the upper GI tract.[13] Despite the fact that saliva contains many beneficial factors, including various antimicrobial, lubricatory, remineralizing and cell growth-promoting proteins, the tissues of the upper GI tract do suffer significant morbidities. Dentists know well the continuing problems of caries, periodontal diseases, aphthous ulcers, and mucosal candidiasis. Despite advances in conventional tools to manage several of these conditions, these oral disorders remain significant. The authors chose to address mucosal candidiasis as a prototypical problem. While it is less common for dentists to treat candidiasis than caries or periodontal diseases, this infection is potentially life-threatening in a medically compromised individual. At the time the authors began their efforts in gene transfer (late 1991), it was widely accepted that gene transfer technology primarily should be applied to clinical conditions with mortal risk, a view no longer widely held.[14] The initial strategy was quite simple. Saliva contains naturally potent anticandidal proteins called histatins.[15,16] These are believed to help control oral flora and are reported to be reduced in AIDS-immunosuppressed patients,17 thus rendering the individuals susceptible to mucosal candidiasis. This is particularly dangerous if Candida species develop that are resistant to common azole-type, oral antifungal drugs (e.g., fluconazole). The authors reasoned that if they could increase the production of histatins in such patients by gene transfer to the salivary glands, they could prevent or eliminate such infections. Although the specific mechanism of action by which histatins kill Candida is not yet clearly known, it appears to be different from that of azole drugs. Therefore, histatins may be effective against azole-resistant Candida species. Furthermore, the authors reasoned, it would not be necessary for the gene transfer to be

permanent. Rather, it seemed likely that a "therapeutic" course of gene expression (10 to 14 days) would be adequate for this purpose. This meant that the authors could probably employ the current generation of adenoviruses as a gene transfer vector.[10]

They constructed a recombinant adenovirus encoding histatin 3[18] one of the histatin protein family members with demonstrated anticandidal action.[16,17] They showed that this virus was able to direct the expression of authentic histatin 3 in a cell culture model and, more importantly, lead to the secretion of histatin 3 in rat saliva after infection of rat salivary glands with the vector. This is particularly noteworthy since rats do not normally make histatin 3. Further, the levels of histatin 3 found in rat saliva were as high as ~1.5 mg/ml, more than tenfold that seen normally in humans.[18] Of greatest significance, recombinant histatin 3 was able to kill azole-resistant Candida in vitro.[18] The authors are now engaged in a preclinical series of experiments, using immunosuppressed rabbits, to determine if this virus, and the researchers' approach, will be useful under more therapeutic conditions. If these studies are successful, the authors expect to be able to apply this gene transfer treatment to patients within a reasonable time.

The authors have also begun to test various strategies to augment saliva with proteins that could disrupt or limit dental plaque formation.[19] Although this has not yet provided the positive results seen with the anti-Candidal strategy described above, they believe it shows considerable promise conceptually. The value of limiting dental plaque to prevent dental disease has been long recognized and is widely applied with conventional pharmacotherapeutics.[20] Thus far, these conventional approaches have been only partially successful. A gene transfer approach likely would be entirely complementary to conventional methods and may substantially increase the extent to which dental plaque can be diminished. The authors expect that this approach, or another not yet conceived, will be able one day to reduce dental plaque formation substantially and eliminate caries and periodontal disease.

Systemic Gene Therapeutics

For many years, scientists have suggested that salivary glands are able to secrete in an endocrine (directly to the bloodstream) manner as well as use their common exocrine (external secretion) pathway.[12,21] While the data supporting such a view are intriguing, they have not been fully convincing, and the notion of salivary glands as secondary endocrine organs never widely took hold. Gene transfer offered a way to test this possibility in a clear manner. The authors transferred the gene for human 1-antitrypsin (hAT), using an adenoviral vector, into the salivary glands of adult rats.[22] HAT is a protein normally made in the liver and secreted into the bloodstream to function as an inhibitor of proteolytic enzymes. It is not normally made by salivary glands. Furthermore, the authors were able to measure hAT without any interference from the rat homologue. Hence, any hAT in the rat bloodstream would have had to come from the salivary glands subsequent to gene transfer. They were able to show this clearly, and their studies demonstrated unequivocally that a mammalian salivary gland was capable of endocrine secretion.

The human disease spectrum includes many conditions that result from a deficiency of a single protein. There are inborn errors of metabolism present from birth, including an endocrinopathy such as growth hormone deficiency or a hematologic (bleeding) disorder such as Factor VIII deficiency (hemophilia A), or conditions that develop later in life, such as diabetes. Although it is currently possible to treat such protein deficiencies via the injection of purified recombinant (genetically engineered) proteins, it is widely recognized that such injections do not represent an ideal therapeutic approach.[23] Consequently, there is considerable effort in the biomedical science community to develop novel, more practical, convenient, and cost-effective ways to treat single, circulating-protein deficiency disorders. Gene transfer offers a viable approach to these issues.

The authors hypothesized that it might be possible to use salivary glands as a natural, endogenous slow-release device to secrete therapeutic proteins into the bloodstream after a single gene transfer. For a test case, they studied the expression of human growth hormone (hGH) by salivary glands. As above with hAT, they had excellent measurement tools available to assay protein production. Further, and most importantly, physiological responses to this increase in hGH could be followed preclinically in a rat model because, conveniently, rats are able to respond to the human hormone. They constructed an adenovirus encoding hGH and showed that it directed the production of hGH in, and secretion into the bloodstream by, rat salivary glands.[24] The levels of hormone achieved were on average well-above that needed for therapy in humans. In adult rats, these hGH levels were also able to induce several serologic responses clearly indicative of the hormone's systemic activity (increased triglycerides and increased BUN/creatinine ratio).[24] Thus, at least in rats for a short-term experiment, the authors' hypothesis was proved.

Another research group, at the University of California at San Francisco, has addressed this hypothesis in a slightly different manner.[25] They transferred genes into adult rat salivary glands, however they used nonviral means rather than viruses. The genes transferred include hGH and insulin. Although the serum hormone levels achieved were substantially lower than those seen when viral-mediated gene transfer is employed, they were adequate to induce certain physiological responses. Thus, two separate studies support the use of salivary glands for the secretion of therapeutic proteins into the bloodstream. These results prove a principle. While the approach is not ready for application to patients, it lacks only refinement. The gene transfer field is experiencing explosive growth, and it can reasonably be anticipated that such refinement will come in the near future.

Dentists as Gene Therapists

The title of this section may at first sound strange, however it represents a real possibility in the next 20 or more years. To most people, and most dentists, clinical dentistry is primarily directed at the technical repair of the dentition and supporting structures. In its simplest form, gene transfer can also be viewed as a "technique," albeit one with a seemingly more obvious biological basis than treating caries or periodontitis. If it can be used to prevent or treat oral conditions more successfully than conventional techniques, why not use it?

A major advantage for all such studies is the ready accessibility of oral tissues. The mouth has long been said to serve as a convenient window to the body. The authors are confident that gene transfer, and other biological therapies, will be applied to oral diseases and disorders during the midpractice lifetime of today's dental students. If the applications of oral gene transfer are expanded to systemic diseases, such as those mentioned above, oral health care providers in the future could routinely be "gene therapists" with therapeutic targets well outside the oral cavity. However, for dentists to be able to use such techniques, and maintain their place as key oral health care providers, they must understand modern biology at a practical level. This means that today's schools of dentistry need to give students a biological foundation for their future.[3] It also means that active practitioners, especially those who are relatively recent graduates and who have limited facility in biology and biomedicine, would be well-served by acquiring this same foundation.

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To request printed copies of this article, please contact/Bruce J. Baum, TKTK, GTTB/NIDR/NIH, 10 Center Drive, MSC 1190, Bldg. 10, Room 1N113, Bethesda, MD 20892.

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A Caries Nation

Robert E. Horseman, DDS

Most of us are only dimly aware of the existence and function of the National Institute for Dental Research. Indeed, the machinations of the International Monetary Fund are like a shining beacon of clarity compared to our knowledge of the NIDR. Being dimly aware, as opposed to being totally cognizant, has been found to be a comfort in so many avenues of our daily lives, but in failing to recognize the contributions of this federally funded organization, we do the NIDR a great disservice.

Pure research, to the particular breed of cats that pursues it, does not necessarily have to have a goal. It can take many paths, detour, veer off on seemingly unrelated tangents, and frequently end up back at the proverbial Square One. At the moment, there is a waiting period of more than six months to even register for admittance to Square One, but that's inconsequential. As long as the funding holds out, a serendipitous result could occur at any moment.

A case in point: After six years of exhaustive research by dedicated scientists studying every conceivable facet of pink vulcanite denture material, irrefutable evidence pointed to the fact that it bore no more resemblance to actual human tissue than AstroTurf does to dichondra or Pamela Lee to real women. This conclusion was later confirmed by the Psychic Friends Network under the direction of Dionne Warwick.

Without the people who unselfishly devote their professional lives to pushing the envelope of R & D – research and development to we laypeople – we'd still be using one-fluted burs made from pot metal, trying to cope with nondesigner toothbrush handles, and denying the public the benefits of carbamide peroxide.

Not all of the dental research is being performed at the spacious NIDR headquarters in Washington, D.C. Grants are farmed out to projects deemed to be worthy, regardless of their venue. We dropped in to check up on the progress of Dr. Alfredo Schmutz, a reclusive party on the order of Howard Hughes, who conducts his esoteric experiments in an unwindowed, unventilated demolition-bound annex to his garage.

If Dr. Schmutz were to grow a full head of finger-in-the-light-socket hair and lop a full meter off his stature, he would bear a stunning resemblance to Albert Einstein, famous for his trivia answer E=MC2. It has long been the controversial contention of Dr. Schmutz, who comes from a long line of eccentrics, that the Germ Theory, as applied to dental decay,

is criminally wrong. Recall that it was his grandfather, Dr. Percival Schmutz, who first discovered the basic unit of tooth decay, the carey, which he named after the musical lament "Carry Me Back to Old Virginny," a popular ditty of his time. After lengthy experimentation on little woodland creatures, he learned that the carey could not function as a viable entity except when bonded molecularly with one or more other caries and that's why one almost never hears the singular term "carey" any more. It was the elder Dr. Schmutz's belief, now largely discounted, that dental decay was the result of "parlous and vitreous humours" incurred by the excessive consumption of rhubarb.

Eyes bright as new pennies, cheeks glowing like twin Pippins, I enjoin Schmutz at his door.

"How goes the research, Doctor?"

"Who wants to know?" he replies, eyeing me narrowly through the peephole. "You come poking around here from Hanes or Fruit of the Loom?"

"No, why?" After reluctantly granting me admittance, he quickly obscures some papers lying on his desk and slams a drawer on a partially consumed pastrami on rye while flicking a dollop of French's Spicy Mustard off his tie.

"Because," he says, lowering his voice and hastily securing the door behind him with multiple locks and a length of chain, "word has leaked that I'm on the verge of a scientific breakthrough, and I fear I may be targeted for termination by mercenary gunsels of the dry goods trade, obliged to expunge me from this mortal coil."

"Good Lord, Schmutz, what have you discovered?"

"Sure you're not from Jockey, Manhattan or Cambridge Classics?" he casts about fearfully, peering myopically under his desk.

"Why would these people want to do you a mischief for God's sake?"

"Because – are you ready for this? – I have found that dental decay, caries if you count yourself among the cognoscenti, is directly related to too-tight underwear! You might as well know; it'll be in all the journals within a fortnight."

"I thought that was an infertility problem," I offer tentatively.

Schmutz scoffs, "That's what they all thought. I have researched the dental records of Willie Shoemaker and other top riders. I've looked into lawyers' briefs, studied Italian falsettos and dropouts from the Vienna Boys Choir. Rampant caries, every one of 'em!"

"I don't understand the correlation," I puzzled.

"Well, you wouldn't, would you?" he snaps, waspishly, "You're not a trained researcher whose grant is about to expire in six weeks. The underwear manufacturers are not going to take this lying down, Buster. I've just a short time to record the DMF statistics of 5,000 boxer-shorts-wearing people to prove my hypothesis ere I'm taken out by the underwear consortium. Good day, Sir!"

Unconventional, yes; controversial, of course; nuttier than a fruitcake, perhaps, but Alfredo Schmutz and other researchers of similar determination and single-mindedness of purpose cannot help but take our breath away and point to the dawn of a new tomorrow.