those in the preceding paragraph reveal that it is highly implausible such biases account for much, if any, of the association of reported *S. dublin* and raw milk seen in this study. Because the association appears far stronger than values commonly taken as definitive evidence of a causation, we are not concerned about any downward biases that may exist in our estimate.

We think it important to note that persons with compromised host defenses appear particularly vulnerable to severe and even fatal outcomes of *S. dublin* exposure. Thus we would recommend that such persons, especially those with HIV infection, be warned to avoid raw milk consumption, and that raw milk carry a label warning of the possible hazard to such persons.

In this paper we have not considered the issue of transmission of other hazardous bacteria (such as *Campylobacter*), through raw milk, in part because the case fatality rate associated with such infections is much lower than for overt *S. dublin* infection. However, other diseases associated with milk products, such as listeriosis infection, may have equally high case fatality rates. As a result, regulators may also wish to consider these diseases when evaluating the hazards of raw milk.

References

1. Richwald, G. A., et al.: An assessment of risks associated with raw milk consumption in California. UCLA School of Public Health, Los Angeles, CA, 1986.
2. Askerkoff, B., Schroeder, S. A., and Brachman, P. S.: Salmonellosis in the United States—a five year review. Am J Epidemol 92: 13-24 (1970).
3. Rothman, K. J.: Modern epidemiology. Little Brown, Boston, 1986.
4. Kleinbaum, D. G., Kupper, L. L., and Morgenstern, H.: Epidemiologic research: principles and quantitative methods. Lifetime Learning, Belmont, CA, 1982.
5. California State Department of Health Services: *Salmonella dublin* in California: increasing incidence and increasing association with raw milk. California Morbidity, No. 12, Mar. 30, 1984.

NIDR—40 Years of Research Advances in Dental Health

PATRICIA G. SHERIDAN

Ms. Sheridan is a technical writer-editor in the Office of Planning, Evaluation, and Communications, National Institute of Dental Research, National Institutes of Health, Public Health Service.

Tearsheet requests to Ms. Patricia G. Sheridan, NIDR, Bldg. 31/2C-35, NIH, Bethesda, MD 20892.

Synopsis

The National Institute of Dental Research (NIDR) was created by President Harry S Truman on June 24, 1948, as the third of the National Institutes of Health. NIDR's legislation contained the mandate to conduct research and research training to improve oral health. An impetus for federally funded dental research was the finding in World War II that the major cause of rejection for military service was missing teeth. Because of the population's widespread tooth decay problems, early NIDR research focused on eliminating dental caries. NIDR scientists confirmed the safety and effectiveness of the use of fluoride in tooth decay prevention, leading to one of the nation's most successful public health efforts, community water fluoridation.

During the past 40 years, NIDR scientists have provided research advances and fostered technologies which changed the philosophy and practice of dentistry and brought dental sciences into the mainstream of biomedical research. Dental researchers contribute to studies of such diseases and problems as AIDS, cancer, arthritis, cystic fibrosis, diabetes, herpes, craniofacial anomalies, pain, and bone and joint disorders.

NIDR's 40th anniversary in 1988 recognizes its continuing commitment to oral disease prevention and health research, and to achieving the goal of people maintaining their natural dentition for a lifetime.

"THE PURPOSE OF THIS ACT is to improve the dental health of the people of the United States through the conduct of researches, experiments and studies relating to the cause, diagnosis and treatment of dental diseases and conditions . . ."(*1*).

President Harry S Truman, in approving the National Dental Research Act, began a research effort which over time has helped to revolutionize oral health care. In the following 40 years, the National Institute of Dental Research (NIDR) has been at the forefront of new advances and technologies that have changed both the philosophy and practice of dentistry and have brought dental sciences into the mainstream of biomedical research.

Early Days

NIDR today has a permanent staff of nearly 400 persons, a comprehensive multidisciplinary research program, and a $126 million annual budget. The early days of federally-supported dental research, however, largely consisted of the efforts of one man, Dr. H. Trendley Dean, investigating a condition known as mottled tooth enamel. Studies by Dr. Frederick S. McKay and Dr. G. V. Black in the early 1900s drew scientific attention to the problem of permanently stained teeth among residents of some western communities (*2*). Subsequent testing linked this defect with high concentrations of naturally occurring fluoride in drinking water. Dr. Dean, a member of the Commissioned Officer Corps of the Public Health Service, was the first dental officer at the newly established National Institute of Health, as it was known when he was assigned in 1931. He made up the one-person Dental Hygiene Unit in the Division of Pathology and Bacteriology and became the first Director of NIDR in 1948, serving until 1953.

Research not only showed that mottled enamel was a problem of national scope, but confirmed its cause. Whereas others had observed that persons with fluorosis seemed to have fewer cavities, Dr. Dean provided the first solid evidence correlating the amount of fluoride in drinking water with the incidence of dental decay. He established that 1 ppm fluoride would not cause fluorosis, yet would be sufficient to protect teeth against cavities. The findings led to the first controlled community drinking water fluoridation project, begun in 1945 in Grand Rapids, MI, whose water supply was nearly fluoride-free. Fluoridation was the beginning of disease prevention in dentistry.

Legislation

During World War II, the primary medical reason for rejection of those examined for military service was dental defects. Nearly 9 percent did not meet dental standards, which required six opposing teeth in each jaw. Manpower shortages led to much lower requirements and to a large scale program of dental rehabilitation among recruits.

In 1944, a Senate subcommittee investigated the health problems of servicemen, including dental disease. As a result, Senator Claude Pepper of Florida and Senator James Murray of Montana supported the establishment of a dental research institute as part of NIH. The first such bill (S. 190), was introduced in the Senate on January 20, 1945, with the support of the American Dental Association.

During the next 3 years, similar legislation followed in both the House and Senate. HR 6726, introduced by Dr. Walter Brehm, a dentist and Representative from Ohio, received approval of both houses of Congress, and President Truman signed the National Dental Research Act on June 24, 1948.

With Dr. Dean as its first director, NIDR opened with 25 employees and a budget of about $237,000. Key organizational decisions in the first days reflected the belief that solutions to clinical problems were to be found through fundamental research. The Institute was set up by basic disciplines for laboratory research and by disease and applied categories for clinical investigations. A section for epidemiology and biometry completed the organization.

During the 1950s and 1960s, NIDR expanded its research base as well as its physical plant. Congress allocated funds for a new dental research facility at the Institute, and President Dwight D. Eisenhower on August 1, 1958, signed the appropriation for construction. Building 30, a seven-level red brick structure to house 200 investigators, opened May 26, 1961.

NIDR Comes of Age

Discoveries in the 1960s led to the understanding that dental caries is an infectious, transmissible disease. Researchers identified the caries process as a combination of the effects of a cariogenic diet, susceptible tooth surface, and the bacterium *Streptococcus mutans*.

In 1969, NIDR proposed targeted research on caries with the establishment of a National Caries

Program, a concept that was adopted as a special health initiative by President Richard M. Nixon. Two years later, the program became an organizational component of the Institute.

Concurrent with its efforts on dental caries, NIDR broadened the scope of its basic investigations. Institute scientists pioneered research on the structure and properties of collagen, and by 1970, NIDR was an acknowledged leader in the field. These studies opened new avenues of research, including developmental biology, tissue formation, and bone metabolism. On another front, NIDR pursued enzyme research and made early and significant contributions to the identification of enzymatic processes in tissues. Like collagen research, enzyme studies were of benefit to other areas of science and attracted investigators from other disciplines.

NIDR's research was expanded into microbiology and immunology in response to the need to explore the origins of periodontal disease. Studies in the 1950s revealed the infectious nature of this group of diseases, but their etiology and mechanisms of progression remained obscure. Research in the 1960s confirmed a bacterial role in periodontal disease and demonstrated that immunological reactions to these bacteria in affected gum tissues played an important part in the disease process. Findings by NIDR investigators had broadened the knowledge base, not only in dental disorders, but in a range of biomedical disciplines.

The demands of the growing research effort prompted NIDR to offer intramural and extramural research training opportunities which successfully expanded the country's supply of trained manpower in scientific fields related to dental research. The dental sciences had come of age.

Dr. H. Trendley Dean, the first dental officer at the National Institutes of Health when he was assigned in 1931, was the first director of the National Institute of Dental Research, serving from 1931 to 1953

The Dental Research Section, shown in 1946. Front row, l. to r., Dr. Stanley Ruzika, William Poole, Bertha Blue, and Dr. David B. Scott. Back row, Dr. Edwin Short, Dr. H. Trendley Dean, Dr. Frank J. McClure, and Dr. Francis A. Arnold, Jr.

Dental Science and Biomedical Research

Studies carried out in the 1970s gained NIDR international recognition for its achievements in virology research, emphasizing the commonality of the causes of many dental and medical conditions. NIDR scientists showed that viruses could produce diabetes in experimental animals by destroying insulin-producing beta cells, that susceptibility to this endocrine disorder is genetically controlled, and that the disease could be prevented in laboratory mice by a vaccine. In a landmark study, investigators isolated a virus from the pancreas of a person with insulin-dependent diabetes mellitus, confirming a long-suspected viral role in this disease in man. Investigators today are continuing this

A worker adds fluoride to water in Grand Rapids, MI, in 1945 as part of the first community water supply experiment to demonstrate the efficacy of the caries prevention treatment

President Harry S Truman signs the National Dental Research Act in 1948, with (l. to r.) Dr. C. Willard Camalier, Sr., Director of the Washington office of the American Dental Association; Rep. Walter E. Brehm of Ohio, author of the act; Dr. H. B. Washburn, President of the ADA; Dr. Bruce D. Forsyth, Chief Dental Officer of the Public Health Service; Dr. Carl O. Flagstad, Chairman of the ADA Committee on Legislation; Dr. Daniel F. Lynch, past-president of the District of Columbia Dental Society; and Dr. H. Trendley Dean, Dental Director, National Institutes of Health

line of research to unravel the interplay among viral, environmental, and genetic factors, not only in this type of diabetes, but in other autoimmune diseases, such as rheumatoid arthritis and systemic lupus erythematosus.

Studies were carried out on the herpes simplex virus (HSV) type 1, the organism responsible for cold sores, and HSV type 2, the cause of genital herpes infection. NIDR investigators traced the path of herpesvirus from the point of viral penetration, through its travels up the nerve, to the site of subsequent establishment of latent infection. The heightened understanding of this viral process laid the groundwork for the development of a herpes vaccine a decade later.

Mineralized tissue research produced major gains during this decade in the understanding of the structure and development of bone and teeth. Advanced laboratory techniques enabled dental scientists to analyze in detail the factors and sequence of events involved in bone formation and resorption, and to isolate and purify substances found in bone matrix. This research has led to the discovery of new proteins and other agents that participate in bone growth, turnover, and repair, and has provided clues to what goes awry in the body as bone diseases develop.

The periodontal diseases, which exhibit many of the features of such chronic and debilitating disorders as diabetes and arthritis, began to yield to persistent investigation by intramural and extramural scientists. Three clinical research centers were targeted specifically to this oral health problem. Cellular immunologists brought new perspectives to the inflammatory process, accumulated data on the mechanism of bone destruction in periodontal diseases, and made inroads in understanding the roles and interactions of bacteria in the development of oral disease.

During the 1970s, NIDR expanded its role in the social and behavioral sciences to explore the relationships between these disciplines and dental health. Program goals were aimed at determining how behavioral, social, cultural, and economic factors influence oral health and at devising strategies to modify American's oral health behavior to encourage disease prevention.

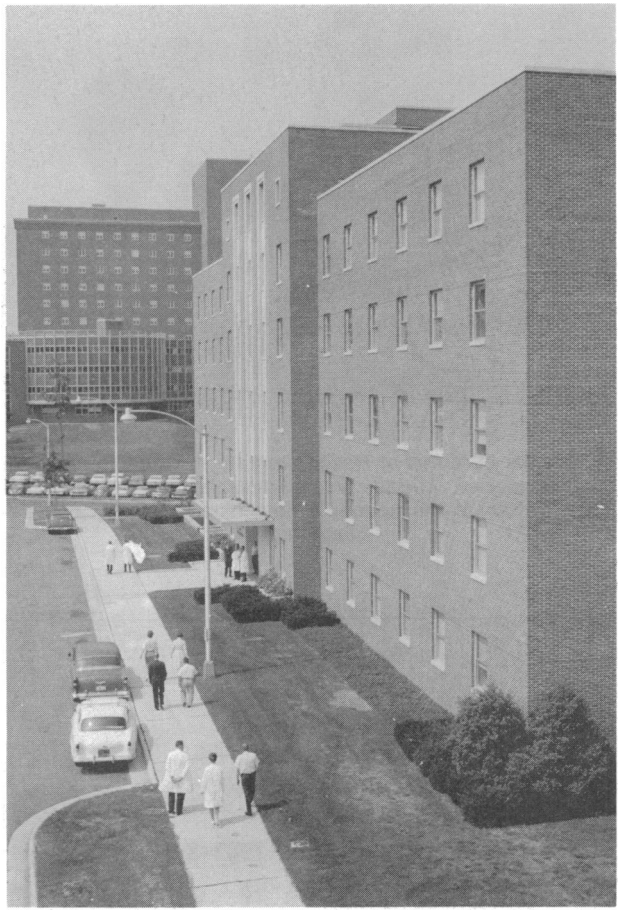
In the mid-1970s, the National Caries Program initiated school-based fluoride mouth-rinse demonstration projects. Public education efforts on the benefits of fluoride were underway and basic research on caries continued. Dental sealants, controlled-release devices for administering fluoride, and other preventive measures were developed

and tested. In other studies, nutritional scientists explored the cariogenicity of foods and the safety and palatability of artificial sweeteners.

In 1979, NIDR initiated its first nationwide survey of the dental health of school children aged 5 to 17 years. The survey, regarded as a report card for the Institute's caries prevention efforts, revealed a dramatic decrease in tooth decay. One-third of the children were caries free; for the remainder, the prevalence of tooth decay was half what it had been a generation before, a long step toward the goal of a nation of caries-free children.

Dental scientists have adopted techniques originally developed in cellular and molecular biology, such as recombinant DNA and monoclonal antibody methodologies. The new tools are helping to advance knowledge of cell function mechanisms common to many tissues and are contributing to understanding a range of disorders. Research advances are being translated into new diagnostic techniques, innovative treatment protocols, and realistic opportunities for disease prevention.

As research interests expanded, there was a growing need for trained investigators in the dental sciences. To encourage clinician-scientist training, in 1984 NIDR began a research career development program called the Dentist Scientist Award. The award helps candidates prepare for careers as research investigators.

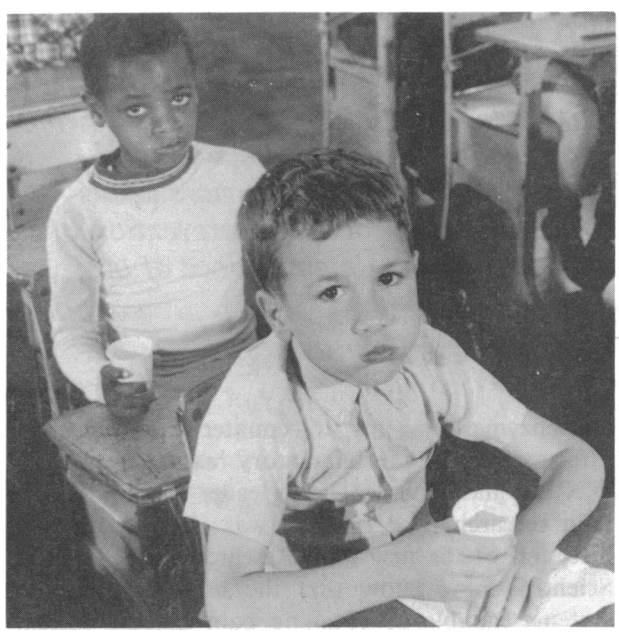


The National Institute of Dental Research, Building 30, opened in 1961

Dental Science and Health

Dental science has matured from a narrow concern with teeth and gums to encompass all the oral tissues; their normal metabolism, function, and pathology; and the behaviors associated with the cause and prevention of disease and the maintenance of oral health. The expanded domain of dental research is seen in current studies of oral viral infections; genetic anomalies; bone and joint diseases; oral cancers; acute and chronic pain conditions; salivary gland dysfunctions, which led to the establishment of the NIDR Dry Mouth Clinic; and behavioral and social aspects of oral health and disability.

These investigations have led to such recent achievements as the development of a model *in vitro* system to measure the invasiveness of tumor cells as well as the development of new antimetastatic drugs, the isolation of protein growth factors for bone, the identification of the region of immunoglobulin receptors responsible for hypersensitivity reactions, experimental vaccines against oral herpesvirus infections, and anti-inflammatory and



A school-based fluoride study, begun in 1972, involved the combined use of three fluoride agents, which were shown to reduce the prevalence of dental cavities by 65 percent among children in a study in rural Nelson County, VA

A National Institutes of Health program of research into pain and its causes, effects, and controls, is directed by NIDR investigators at the country's first multidisciplinary pain research clinic

NIDR Directors

H. Trendley Dean, 1948–53
Francis A. Arnold, Jr., 1953–66
Seymour J. Kreshover, 1966–75
David B. Scott, 1976–81
John F. Goggins (Acting, 1982–83)
Harold Löe, 1983–

'Dental science has matured from a narrow concern with teeth and gums to encompass all the oral tissues; their normal metabolism, function, and pathology; and the behaviors associated with the cause and prevention of disease and the maintenance of oral health.'

anti-enzymatic agents to counter the destructive effects of chronic inflammatory reactions.

NIDR has emerged as a leader in the field of pain research, and in 1983 was charged with the direction of the new Pain Research Clinic at NIH. Scientists now know that the brain has its own systems capable of blocking pain signals, systems which a person might be able to learn to regulate at will. NIDR studies have validated the pain-relieving effects of many pharmacologic agents. New ways to measure pain are standardizing the sensory and behavioral qualities of pain. Current studies are targeting pain associated with acquired immunodeficiency syndrome (AIDS); cancer; and other chronic, debilitating conditions.

In response to the need for research on the underlying mechanisms involved in AIDS, dental scientists are identifying early oral changes associated with the disease, such as hairy leukoplakia and candidiasis, and documenting the history of oral changes that occur as the disease progresses. NIDR immunologists have established that protective monocytes are not destroyed by human immunodeficiency virus (HIV), but, in fact, may be the vehicle by which the virus is spread throughout the body. Studies are in progress on salivary gland secretions, searching for evidence of pathological changes in HIV-infected patients; on microorganisms associated with opportunistic infections and malignancies in the oral cavity; and on potential measures to control them. Recently, NIDR researchers showed that human saliva contains a factor that blocks HIV from infecting cells. Other AIDS-related research is in progress.

Assessing the Nation's Oral Health

NIDR undertook a nationwide survey in 1985 to gauge the oral health and oral health behaviors of the employed and senior population, compiling data on 21,000 adults from 18 to 103 years of age in a sample representing 105 million persons (*3*). The most dramatic finding was the almost complete absence of toothlessness before age 40. Furthermore, only 4 percent of working adults aged 65 years and younger were missing all their teeth, and half the adult population younger than 65 had lost, at most, one tooth. The findings are measures of the progress of dental research and its impact on dental practice during the last four decades, the lifetime of NIDR.

Today's older generation, however, includes people who grew up before World War II and did not benefit from programs of prevention. NIDR is addressing oral health problems among the growing numbers of older people and finding a need for new knowledge of normal aging of the oral tissues, not only the teeth and gums, but the entire tissue complex involved in speaking, chewing, and swallowing, and the senses of taste, smell, touch, temperature, and pain. The research is exploring what happens to oral tissues in relation to changes in immunity, endocrine gland function, and other body systems, and how oral health affects, and

is affected, by systemic disease common in old age.

In 1986–87, NIDR conducted a follow-up survey of children's oral health to assess further the effectiveness of community and school-based caries prevention efforts. The survey of 40,000 children, representative of all school children aged 5–17 years, showed that the decline in the caries rate is continuing in the United States. Today, 50 percent of American school children are caries-free.

Not only are fewer children getting cavities today, but those who do are getting fewer. In 1980, children had an average of almost 5 decayed, missing, or filled surfaces on their permanent teeth, out of 128 possible surfaces in those with a full set of permanent teeth. In 1987, they had an average of three decayed, missing, or filled tooth surfaces. The average number of decayed or filled surfaces on the baby teeth of 5- to 9-year-olds dropped from more than 5 in 1980 to fewer than 4 in 1987. Although the survey did not address the question of what is causing the decline in dental caries, NIDR officials believe the widespread use of fluoride in water supplies, toothpaste, and other forms, is responsible. Combining this study with the adult survey, NIDR is able to assess the oral health of about 150 million Americans.

A Look to the Future

In the course of four decades, research has made historic strides in understanding oral diseases, and providing methods to prevent them. The next 40 years will bring new discoveries, new treatments, and, probably, new diseases.

New capabilities gained from research will contribute to progress in a major task that NIDR has proposed for the remainder of this decade and the 1990s, the development of a research and action program to unite biomedical and behavioral scientists, the dental profession, industry, and the general public in working toward the elimination of toothlessness, improvements in oral health, and prevention of diseases and disorders of the mouth.

In perhaps another 40 years, the major oral diseases that have plagued mankind since ancient times may be under control for much of the population. Scientific advances will allow dentists to expand their role to address the full range of diseases and disorders that affect the oral and facial tissues. Dentists will strengthen their partnership with other biomedical specialists, and by virtue of their broader diagnostic and therapeutic scope and skills, physicians of the mouth may be able to maintain the health of the teeth and associated tissues over a lifetime.

'In the course of four decades, research has made historic strides in understanding oral diseases, and methods to prevent them. The next 40 years will bring new discoveries, new treatments, and probably new diseases.'

References

1. U.S. Congress. National Dental Research Act, P. L. 80–755, June 24, 1948.
2. McKay, F. S., and Black, G. V.: Mottled teeth: an endemic developmental imperfection of the enamel of the teeth heretofore unknown in the literature of dentistry. Dental Cosmos, 1916.
3. National Institute of Dental Research. The National Survey of Oral Health in U.S. Employed Adults and Seniors: 1985–1986. NIH Publication 87–2868, National Institutes of Health, Bethesda, MD, 1987.