Dental Caries

A Medical Dictionary, Bibliography,
and Annotated Research Guide to
Internet References

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and Philip M. Parker, Ph.D., Editors

ICON Health Publications
ICON Group International, Inc.
4370 La Jolla Village Drive, 4th Floor
San Diego, CA 92122 USA

Printed in the United States of America.

Last digit indicates print number: 10 9 8 7 6 4 5 3 2 1

Publisher, Health Care: Philip Parker, Ph.D.
Editor(s): James Parker, M.D., Philip Parker, Ph.D.

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Cataloging-in-Publication Data

Parker, James N., 1961-
Parker, Philip M., 1960-

Dental Caries: A Medical Dictionary, Bibliography, and Annotated Research Guide to Internet References / James N. Parker and Philip M. Parker, editors
p. cm.
Includes bibliographical references, glossary, and index.
ISBN: 0-497-00346-5
1. Dental Caries-Popular works. I. Title.

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Acknowledgements

The collective knowledge generated from academic and applied research summarized in various references has been critical in the creation of this book which is best viewed as a comprehensive compilation and collection of information prepared by various official agencies which produce publications on dental caries. Books in this series draw from various agencies and institutions associated with the United States Department of Health and Human Services, and in particular, the Office of the Secretary of Health and Human Services (OS), the Administration for Children and Families (ACF), the Administration on Aging (AOA), the Agency for Healthcare Research and Quality (AHRQ), the Agency for Toxic Substances and Disease Registry (ATSDR), the Centers for Disease Control and Prevention (CDC), the Food and Drug Administration (FDA), the Healthcare Financing Administration (HCFA), the Health Resources and Services Administration (HRSA), the Indian Health Service (IHS), the institutions of the National Institutes of Health (NIH), the Program Support Center (PSC), and the Substance Abuse and Mental Health Services Administration (SAMHSA). In addition to these sources, information gathered from the National Library of Medicine, the United States Patent Office, the European Union, and their related organizations has been invaluable in the creation of this book. Some of the work represented was financially supported by the Research and Development Committee at INSEAD. This support is gratefully acknowledged. Finally, special thanks are owed to Tiffany Freeman for her excellent editorial support.

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Table of Contents

FORWARD

In March 2001, the National Institutes of Health issued the following warning: "The number of Web sites offering health-related resources grows every day. Many sites provide valuable information, while others may have information that is unreliable or misleading."[1] Furthermore, because of the rapid increase in Internet-based information, many hours can be wasted searching, selecting, and printing. Since only the smallest fraction of information dealing with dental caries is indexed in search engines, such as **www.google.com** or others, a non-systematic approach to Internet research can be not only time consuming, but also incomplete. This book was created for medical professionals, students, and members of the general public who want to know as much as possible about dental caries, using the most advanced research tools available and spending the least amount of time doing so.

In addition to offering a structured and comprehensive bibliography, the pages that follow will tell you where and how to find reliable information covering virtually all topics related to dental caries, from the essentials to the most advanced areas of research. Public, academic, government, and peer-reviewed research studies are emphasized. Various abstracts are reproduced to give you some of the latest official information available to date on dental caries. Abundant guidance is given on how to obtain free-of-charge primary research results via the Internet. **While this book focuses on the field of medicine, when some sources provide access to non-medical information relating to dental caries, these are noted in the text.**

E-book and electronic versions of this book are fully interactive with each of the Internet sites mentioned (clicking on a hyperlink automatically opens your browser to the site indicated). If you are using the hard copy version of this book, you can access a cited Web site by typing the provided Web address directly into your Internet browser. You may find it useful to refer to synonyms or related terms when accessing these Internet databases. **NOTE:** At the time of publication, the Web addresses were functional. However, some links may fail due to URL address changes, which is a common occurrence on the Internet.

For readers unfamiliar with the Internet, detailed instructions are offered on how to access electronic resources. For readers unfamiliar with medical terminology, a comprehensive glossary is provided. For readers without access to Internet resources, a directory of medical libraries, that have or can locate references cited here, is given. We hope these resources will prove useful to the widest possible audience seeking information on dental caries.

The Editors

[1] From the NIH, National Cancer Institute (NCI): **http://www.cancer.gov/cancerinfo/ten-things-to-know**.

CHAPTER 1. STUDIES ON DENTAL CARIES

Overview

In this chapter, we will show you how to locate peer-reviewed references and studies on dental caries.

The Combined Health Information Database

The Combined Health Information Database summarizes studies across numerous federal agencies. To limit your investigation to research studies and dental caries, you will need to use the advanced search options. First, go to **http://chid.nih.gov/index.html**. From there, select the "Detailed Search" option (or go directly to that page with the following hyperlink: **http://chid.nih.gov/detail/detail.html**). The trick in extracting studies is found in the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Journal Article." At the top of the search form, select the number of records you would like to see (we recommend 100) and check the box to display "whole records." We recommend that you type "dental caries" (or synonyms) into the "For these words:" box. Consider using the option "anywhere in record" to make your search as broad as possible. If you want to limit the search to only a particular field, such as the title of the journal, then select this option in the "Search in these fields" drop box. The following is what you can expect from this type of search:

- **Diagnosis and Treatment of Dental Caries: A Microdentistry Approach**

  Source: Dentistry Today. 20(7): 66, 68, 70-71. July 2001.

  Contact: Available from Dentistry Today Inc. 26 Park Street, Montclair, NJ 07042. (973) 783-3935.

  Summary: Accurate early caries (cavities) detection of the pit and fissure areas of the teeth has been elusive, despite many efforts. The complex occlusal (how the jaws come together) anatomy has greatly contributed to the difficulties of early caries diagnosis. Pit and fissure decay can reach a significant size before becoming clinically detectable. This article discusses two clinical cases where a new diagnostic technology was used to detect caries. The author first explains the rationale for the need for this type of early detection, then describes the technology itself. The technology used was the

DIAGNOdent (KaVo), a small, battery powered diode laser designed to diagnose caries presence under pits and fissures. The author outlines the recommended techniques to use, then reports two case studies, one representing early detection and one representing hidden advanced caries. In the two cases described, the DIAGNOdent proved successful in detecting caries. 19 figures. 15 references.

- **Evidence-based Prevention, Management, and Monitoring of Dental Caries**

  Source: Journal of Dental Hygiene. 76(4): 270-275. Fall 2002.

  Contact: Available from American Dental Hygienists' Association. 444 North Michigan Avenue, Chicago, IL 60611. (312) 440-8900. Website: www.adha.org.

  Summary: Dental caries (cavities), not unlike periodontal diseases, is now recognized as an infectious, transmissible, multifactorial disease of bacterial origin. Current evidence-based emphasis is on the need to recognize a carious lesion in its earliest stage before demineralization has produced a cavitated lesion that requires restoration by a dentist. This article describes the dental hygienist's role as a prevention specialist in determining the **dental caries** risk factors for patients of all ages and in introducing remineralization strategies into the patient's dental hygiene care plan. Conservative strategies of a concentrated program include initial infection control with a chlorhexidine rinse; extra daily fluoride exposures; placement of pit and fissure sealants where indicated; control of sucrose exposures; use of sugar substitutes, particularly xylitol-containing sugar-free chewing gum; and an emphasis on a daily bacterial plaque removal routine. Evidence supports the management and monitoring of **dental caries.** Caries risk level must be reevaluated at each maintenance appointment. Appropriate in-office strategies to preserve tooth structure should be carried out and followed by applicable home regimens that are based on need, not age. 3 tables. 24 references.

- **Immunization Against Dental Caries**

  Source: Vaccine. 20(16):2027-2044. May 15, 2002.

  Contact: Available from Elsevier Science, Regional Sales Office, Customer Support Department. P.O. Box 945, New York, NY 10159-094. (888) 4ES-INFO (437-4636). Fax: +1 212 633 3680. Email: usinfo-f@elsevier.com. Website: www.elsevier.com/locate/vaccine.

  Summary: Dental caries is one of the most common infectious diseases. Of the oral bacteria, mutans streptococci, such as Streptococcus mutans and Streptococcus sobrinus, are considered to be causative agents of **dental caries** (cavities) in humans. This article reviews current work on immunization against **dental caries.** To control **dental caries,** vaccines have been produced using various cell surface antigens of these organisms. Progress in recombinant DNA technology and peptide synthesis has been applied to the development of recombinant and synthetic peptide vaccines to control **dental caries.** Significant protective effects against **dental caries** have been shown in experimental animals, such as mice, rats and monkeys, which have been subcutaneously, orally, or intranasally immunized with these antigens. Only a few studies, however, have examined the effectiveness of **dental caries** vaccines in humans. Recently, local passive immunization using mouse monoclonal antibodies, transgenic plant antibodies, egg-yolk antibodies, and bovine milk antibodies to antigens of mutans streptococci have been used to control the colonization of the organisms and the induction of **dental caries** in humans. The authors conclude that such immunization procedures may be a safer approach for controlling human **dental caries** than active immunization. 3 tables. 190 references.

- **Is Asthma a Risk Factor for Dental Caries?: Findings from a Cohort Study**

  Source: Caries Research. 35(4): 235-239. July-August 2001.

  Contact: Available from S. Karger Publishers, Inc. 26 West Avon Road, P.O. Box 529, Farmington, CT 06085. (800) 828-5479 or (860) 675-7834. Fax (860) 675-7302. Website: www.karger.com.

  Summary: It has been suggested that children with asthma may have a higher risk for **dental caries** (cavities), both as a result of their medical condition and the physical and physiological effects of their medication regimen (pharmacotherapy). By examining the association over time between asthma and caries increment, this study tested the hypothesis that childhood asthma is associated with an increased caries increment. In a long standing New Zealand cohort study, participants' long term asthma histories and the 3 year net caries increment between the ages of 15 and 18 years were examined. Of the 781 children who were examined at 15 and 18 years, 39 participants were consistently taking anti asthma medication at the ages of 9, 11, 13, and 15 years (and were labeled in this study as 'medication determined asthmatics'), 56 were identified as consistent wheezers at the ages of 9, 11, 13 and 15 years ('wheeze determined asthmatics') and 36 were members of both groups. A smaller group (n = 9) was identified as being very long term asthmatics (asthma at 5 years of age and at the ages of 9, 11, 13 and 15 years). Some 206 study members were identified as having no history of asthma, asthma medication or significant wheeze at any time up to and including 18 years The overall mean net caries increment between the ages of 15 and 18 was 2.06 surfaces. There were no significant differences in caries increment between the 206 asthma free participants and any of the asthma groups. The authors conclude that their results provide little evidence for an asthma-caries causative relationship.

- **Pulp-Dentin Biology in Restorative Dentistry. Part 4: Dental Caries: Cahracteristics of Lesions and Pulpal Reactions**

  Source: Quintessence International. 32(9): 717-736. October 2001.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com.

  Summary: The infectious disease **dental caries** (cavities) results in lesions that may affect enamel, dentin, pulp, and cementum. This article, the fourth in a series on pulp-dentin biology in restorative dentistry, discusses the characteristics of these lesions and pulpal reactions that accompany **dental caries.** The authors stress that if a caries lesion has progressed to the stage at which it requires restorative intervention, it is important that the clinician understand the tissue changes in the dentin that are likely to have taken place during lesion development. Until the present, no major distinction between the restorative treatment of active (rapidly progressing) and arrested (slowly progressing) lesions has been made, despite the fact that the two conditions exhibit major differences in tissue changes in the pulp-dentin complex. Intratubular changes and tertiary dentin formation will affect the outcome of the restorative treatment. In unaffected dentin and in rapidly progressing lesions, permeable tubules persist, and when the preparation of carious teeth results in the opening of unaffected dentin, greater care must be taken in all phases of the restorative procedures than if the dentin is impermeable. An active, deep lesion can be changed to an arrested lesion by a two-step excavation approach. The authors conclude that optimal assessment of the prevailing clinical conditions can only be made on the basis of thorough knowledge of the biology of the pulp-dentin organ. 42 figures. 104 references.

- **Recommendations for using fluoride to prevent and control dental caries in the United States**

  Source: Morbidity and Mortality Weekly Report: Recommendations and Reports. 50(RR-14): 1-42. August 17, 2001. 2001. 42 pp.

  Contact: Available from Centers for Disease Control and Prevention, Epidemiology Program Office, Atlanta, GA 30333. Telephone: (404) 639- 3661. Available from the Web site at no charge.

  Summary: The recommendations in this report guide dental and other health professionals, public health officials, policymakers, and the public in the use of fluoride to achieve maximum protection against **dental caries** while reducing the likelihood of enamel fluorosis. The recommendations address public health and professional practice, self-care, consumer product industries, and health agencies. Extensive references conclude the report.

- **Dental Caries in Older Adults with Diabetes Mellitus**

  Source: SCD. Special Care in Dentistry. 19(1): 8-14. January-February 1999.

  Contact: Available from Federation of Special Care Organizations in Dentistry. 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2660.

  Summary: This article describes a study that determined the prevalence of coronal and root surface caries in older adults with diabetes and assessed the effect of glycemic control on **dental caries.** The study population consisted of 24 people who had diabetes and 18 nondiabetic controls who were 54 to 86 years old. Coronal and root surface caries and restorations were evaluated. People who had diabetes had fewer teeth than people who did not have diabetes, especially those with poorer glycemic control. The mean decayed or filled surface (DFS) and filled surface (FS) values were higher, and the mean decayed surface (DS) and missing surface (MS) values were lower in people who did not have diabetes compared with those who did have diabetes and in people with well-controlled compared to those with poorly controlled diabetes. After adjusting for missing teeth, the data were expressed as a percentage of the available surfaces, and the significant differences in DFS and FS disappeared. However, the p values for mean number of DS and MS remained very similar to those for percent DS and percent MS. The number of root surface caries was higher for people who had diabetes compared with people who did not have diabetes, but no corresponding difference was observed between people with well-controlled and poorly controlled diabetes. Results suggest that diabetes and poor glycemic control may not be associated with an increased prevalence of past coronal and root surface caries in older adults. However, findings suggest that older adults with diabetes may have more active **dental caries** and tooth loss than people without diabetes. 4 tables. 63 references. (AA-M).

- **Dental Caries in HIV-Infected Children Versus Household Peers: Two-Year Findings**

  Source: Pediatric Dentistry. 22(3): 207-214. May-June 2000.

  Contact: Available from American Academy of Pediatric Dentistry. Publications Department, 211 East Chicago Avenue, Suite 700, Chicago, IL 60611-2616.

  Summary: This article reports a two year comparison of the incidence and baseline prevalence of **dental caries** found in both the primary and permanent dentition among a cohort of HIV-infected children as compared to household peer control subjects who were not HIV-infected. The subjects in the report were from an initial cohort of 171

children (104 HIV-positive and 67 HIV-negative), who were participants in the Children's Hospital AIDS Program in Newark, NJ, from 1993 to 1995. This analysis reports the findings on the children who completed baseline through Year 02 examinations (n = 121), aged 2 to 15 years old (68 HIV-positive, 53 HIV-negative). While the DMFS (decayed, missing, filled surfaces-noted in capital letters for permanent teeth and in lower case letter for primary teeth) incidence at Year 02 among the 6 to 11 year old control subjects was 17 percent higher than that of the HIV-infected cases (2.1 versus 1.8, respectively) this same incidence was eight fold higher for the control subjects among the 12 to 15 year olds (e.g., 8.1 versus 1.0, respectively). The mean cumulative dmfs score to date for HIV-infected cases was higher than for the control subjects for both the 2 to 5 year olds and the 6 to 11 year olds. In all three age groups, HIV-infected cases had a greater number of primary teeth and fewer number of permanent teeth than the control subjects. The authors conclude given that HIV-infected cases had lower DMFS scores and higher dmfs scores than their household peer controls, the fewer mean number of permanent teeth among the HIV-infected cases suggests that this delayed tooth eruption pattern in permanent teeth contributed to the lower DMFS scores seen in the HIV-infected cases. 4 figures. 6 tables. 26 references.

- **Sickle Cell Anemia and Dental Caries: A Literature Review and Pilot Study**

  Source: SCD. Special Care in Dentistry. 22(2): 70-74. March-April 2002.

  Contact: Available from Special Care Dentistry. 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2660.

  Summary: This article reports on a cohort study undertaken to determine whether individuals with sickle cell anemia (SCA) were more susceptible to **dental caries** (cavities) than non SCA control subjects. Thirty-five cases of SCA (aged 6 years and older) were identified from a screening of 15,900 current patient files at the Howard University College of Dentistry Dental Clinic. A total of 140 non SCA control subjects was selected. While there was virtually no difference in DMFS (decayed, missing, filled surfaces) between SCA cases and controls for 6 to 19 years olds, for subjects aged 20 and older, the DMFS was 30.4 percent higher in the SCD cases. For all ages, the M component for SCA cases was 40.7 percent higher, and the D component was 20.0 percent higher, while the F component was only 3.5 percent higher than for controls. Untreated decay was 24.4 percent higher in the SCA cases. The findings from this pilot study suggest that SCA cases have a higher susceptibility to **dental caries** or that SCA patients may have different treatment pathways once caries is detected. The authors conclude that while none of the observed differences were statistically significant, these findings were of clinical interest and should be pursued in future large scale studies. 3 figures. 2 tables. 24 references.

- **Risk Factors for Dental Caries in Children with Cerebral Palsy**

  Source: SCD. Special Care in Dentistry. 22(3): 103-107. 2002.

  Contact: Available from Special Care Dentistry. 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2660.

  Summary: This article reports on a study conducted to examine the oral condition and the salivary and microbiological parameters associated with **dental caries** (cavities) in 62 children with cerebral palsy, who came from households of low socioeconomic status (study group). This group had mixed 96 to 11 years old) and permanent (11 to 16 years old) dentition. Dental examinations were performed to measure **dental caries,** plaque index, salivary levels of mutans streptococci and lactobacilli, salivary flow rate, pH of

stimulated saliva, and buffer capacity of saliva. A group of 67 non-handicapped children from similar socioeconomic backgrounds also were examined using these parameters (control group). The results showed that children with cerebral palsy who had permanent dentitions had a higher mean decayed, missing and filled surfaces (DMFT) index, as well as a higher plaque index for both sexes. Microbiological examination revealed higher levels of mutans streptococci among study group subjects with mixed dentition than in the control group. Also, lactobacillus counts were higher in the study group, regardless of sex of dentition. With respect to salivary flow rate, pH and buffering capacity, lower mean values were obtained for the study group. 2 tables. 31 references.

- **Dental Caries Prevalence and Treatment Need Among Racial/Ethnic Minority Schoolchildren**

  Source: New York State Dental Journal (NYSDJ). 68(8): 20-23. October 2002.

  Contact: Available from Dental Society of the State of New York. 7 Elk Street, Albany, NY 12207. (518) 465-0044.

  Summary: This article reports on a study that was undertaken to estimate **dental caries** (cavities) prevalence and treatment need among racial and ethnic minority schoolchildren in the Bronx. Oral examinations were conducted on 148 second graders, 194 fourth graders, and 299 sixth graders in three different schools. A single examiner trained to use the DMFS index according to National Institute of Dental and Craniofacial Research (NIDCR) diagnostic criteria and procedures examined all the children between November 1999 and July 2000. The study revealed that 39 percent of the children exhibited **dental caries** experience in their permanent dentition (mean decayed, missing or filled surfaces-DMFS = 1.45), treatment need (28 percent); and 26.4 percent of children in their primary dentition (dmfs = 1.01) and treatment need (18 percent). Hispanic children (DMFS = 1.71) had higher **dental caries** experience compared to African-Americans (DMFS = 1.14). This was found to be statistically significant. Treatment need in Hispanics was 30 percent in permanent dentition and 17 percent in primary dentition; in African-Americans it was 30 percent in permanent dentition and 18 percent in primary dentition. Treatment need was highest among sixth grade African Americans in their permanent dentition and in second grade Hispanics in the primary dentition. 2 tables. 21 references.

- **Relationship of Socioeconomic Background to Oral Hygiene, Gingival Status, and Dental Caries in Children**

  Source: Quintessence International. 33(3): 195-198. March 2002.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com.

  Summary: This article reports on a study undertaken to assess the relationship between socioeconomic status and oral hygiene, gingival (gum) condition, and **dental caries** (cavities) among 12 to 15 year old children. Children of low to moderate socioeconomic status (n = 674) attending 10 public schools were chosen randomly from each of the five geographic areas in Irbid, Jordan. Children of high socioeconomic status (n = 347) attending 10 private schools were also included. Significantly higher proportions of children attending public schools had bleeding on brushing and calculus. Mean plaque and gingival scores were higher in public school children than in private school children, but the difference was not statistically significant. The public school children

had higher overall scores for decayed, missing, or filled teeth (DMFT) and surfaces as well as higher scores for decayed teeth and surfaces, but there was no statistically significant difference between groups. However, children attending private schools had significantly more missing and filled teeth and surfaces. The author concludes that the findings for oral hygiene, gingival status, and **dental caries** were worse, but not significantly worse, among poor children than they were among rich children. Therefore, dental health education is recommended for both socioeconomic groups. 3 tables. 20 references.

- **National Institutes of Health Consensus Development Conference Statement: Diagnosis and Management of Dental Caries Throughout Life, March 26-28, 2001**

  Source: JADA. Journal of the American Dental Association. 132(8): 1153-1161. August 2001.

  Contact: Available from American Dental Association. ADA Publishing Co, Inc., 211 East Chicago Avenue, Chicago, IL 60611. (312) 440-2867. Website: www.ada.org.

  Summary: This article reports on the National Institutes of Health Consensus Development Conference on the Diagnosis and Management of **Dental Caries** Throughout Life, convened in March 2001. The conference was undertaken to provide health care providers, patients, and the general public with a responsible assessment of the currently available data regarding the diagnosis and management of **dental caries** (cavities) throughout life. A nonfederal, nonadvocate 13 member panel representing the fields of dentistry, epidemiology, genetics, medicine, oral biology, oral radiology, pathology, periodontics, public health, statistics, and surgery, as well as a public representative, was convened. In addition, 31 experts in these same fields presented data to the panel and to a conference audience of approximately 700. The evidence included presentations by experts; a systematic review of the dental research literature; and an extensive bibliography of **dental caries** research articles. Scientific evidence was given precedence over clinical anecdotal experience. The article reports the findings in six areas: the best methods for detecting early and advanced **dental caries** (the validity and feasibility of traditional and emerging methods); the best indicators for an increased risk of **dental caries;** the best methods available for the primary prevention of **dental caries** initiation throughout life; the best treatments available for reversing or arresting the progression of early **dental caries;** clinical decisionmaking regarding prevention or treatment, based on detection methods and risk assessment; and new research directions for the prevention, diagnosis, and treatment of **dental caries.** The full Consensus Development Conference statement is available on the Web (www.consensus.nih.gov). The article concludes with a list of the panel members and conference presenters and their affiliations.

- **Dental Caries: Diagnosis and Treatment**

  Source: New York State Dental Journal. 68(2): 38-40. February 2002.

  Contact: Available from Dental Society of the State of New York. 7 Elk Street, Albany, NY 12207. (518) 465-0044.

  Summary: This article reviews the current thinking about the diagnosis and treatment of **dental caries** (cavities). Topics include a definition of tooth decay, etiology, epidemiology, risk assessment, examination and diagnosis of the initial lesion, and specific considerations including white spot lesions, active lesions, hidden lesions, variations among dentists, and instruments. The authors stress that the diagnosis of tooth decay must go beyond the clinical detection of a carious lesion. The practitioner

should assess the individual's risk factors as well as the activity of the lesion. The traditional instrumentation has limitations. Therefore, researchers are urged to find new diagnostic tools to allow earlier detection, to predict disease activity, and to assess the susceptibility of an individual. In addition, patients' cooperation is the main factor for the success of a preventive dentistry program; the authors consider how the dentist's role can have a positive impact on patient compliance. 21 references.

- **Soft Drinks and Dental Caries: A Current Controversy**

  Source: Oral Care Report. 11(3): 5-6. 2001.

  Contact: Available from Oral Care Report. Dr. Chester W. Douglas, Department of Oral Health Policy, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115. E-mail: colgateoralcarereport@hms.harvard.edu. Website: www.colgate.com.

  Summary: This newsletter article, from a summary journal of advances in dentistry and oral health care, considers the relationship between soft drinks and **dental caries** (cavities). According to the United States Department of Agriculture, per capita soft drink consumption has increased by almost 500 percent in the last 50 years. Half of all Americans, and most adolescents, consume sugar-sweetened soft drinks every day. The authors report on evidence both for and against an association between this soft drink consumption and **dental caries.** The authors note that in addition to their cariogenic (cavity causing) properties, both carbonated soft drinks and fruit juices are acidic and can cause erosion and demineralization. A final section considers the role of sugar-free soft drinks. The authors conclude that the best advice for individuals would be to reduce their overall consumption of soft drinks, as opposed to switching to sugar free drinks. One table summarizes the findings of five research studies. 1 figure. 1 table. 8 references.

Federally Funded Research on Dental Caries

The U.S. Government supports a variety of research studies relating to dental caries. These studies are tracked by the Office of Extramural Research at the National Institutes of Health.[2] CRISP (Computerized Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other institutions.

Search the CRISP Web site at **http://crisp.cit.nih.gov/crisp/crisp_query.generate_screen**. You will have the option to perform targeted searches by various criteria, including geography, date, and topics related to dental caries.

For most of the studies, the agencies reporting into CRISP provide summaries or abstracts. As opposed to clinical trial research using patients, many federally funded studies use animals or simulated models to explore dental caries. The following is typical of the type of information found when searching the CRISP database for dental caries:

[2] Healthcare projects are funded by the National Institutes of Health (NIH), Substance Abuse and Mental Health Services (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDCP), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH).

- **Project Title: A LONGITUDINAL STUDY OF LEAD EXPOSURE AND DENTAL CARIES**

  Principal Investigator & Institution: Watson, Gene E.; Associate Professor; Community and Prev Medicine; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 30-JUN-2004

  Summary: The long-term goal of our research is to elucidate underlying mechanisms by which the physical and social environments result in health disparities. Our previous work has shown that the hypothesis that lead exposure is a risk factor for **dental caries** is plausible and could have significant public health impact, especially for individuals in impoverished circumstances (Watson et al., 1997; Moss et al., 1999). We will study **dental caries** risk due to environmental lead exposure in a birth cohort of 245 Cincinnati children that have been participants in the Cincinnati Lead Cohort Study since late 1979. The on-going study of 15-16 year-olds is currently in its third year of funding (R01 ES08158, Early Exposure to Lead and Adolescent Development, P.I.: K. Dietrich). This group of African-American and white Appalachian children is arguably the most well-described longitudinal cohort ever studied for prenatal and postnatal lead exposure (prenatal maternal blood lead concentration, neonatal blood lead concentration, quarterly assessments of the concentration of lead in blood from birth to 5 years and semi-annually thereafter). This cohort is unique among the major longitudinal studies of lead and child health in that a substantial number of subjects were exposed to clinically significant levels of lead during early development. Peak lead exposure in this cohort ranges from 5 to over 80 micrograms/dL. We will collect additional data specifically related to **dental caries** risk and perform laboratory microanalytic assessments of lead in plaque and enamel. This will allow us to test a series of hypotheses that relate environmental lead exposure to risk for **dental caries** development in adolescents. The work of this project will focus on four specific aims related to 1) Demonstrating the strength of the association between environmental lead exposure and risk for **dental caries** and ruling out alternative explanations; 2) Assessing the utility of permanent tooth enamel, deciduous tooth enamel, deciduous tooth dentin and supragingival plaque as biomarkers for lead exposure using microanalytic techniques; 3) Testing mechanistic hypotheses that show lead exposure a) reduces salivary gland function; b) acts as an effect modifer to reduce the protective effect of salivary fluoride; c) is most strongly linked to caries when measured during enamel formation; 4) Exploring more broadly the basis for oral disease disparities in disadvantaged groups by examining the interplay of lead, nutrition, and social factors.

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- **Project Title: A STUDY OF ORAL HEALTH DISPARITIES IN ADULT ASIAN & PAC***

  Principal Investigator & Institution: Easa, David; Associate Dean for Clinical Research; Pediatrics; University of Hawaii at Manoa Honolulu, Hi 96822

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): The primary objective of this application is to develop collaborative affiliations in preparation for conducting an R01 study on molecular and epidemiological correlates of oral health disparities in Asian & Pacific Islanders (APIs). Specifically, these collaborative affiliations will be fostered through training and network development. The training component will involve the University of North Carolina Dental Research Center (UNC) providing mentorship and consultation for the University of Hawaii (UH) through seminars, development of

educational materials, and travel between the universities by faculty, post-doctoral fellows and principal investigators. The network development component will focus on establishing a collaborative oral health research network comprised of UNC, UH's Medical and Nursing and Dental Hygiene Schools and Clinical Research Center, the Dental Division of the State of Hawaii Department of Health, the Hawaii Primary Care Association, Community Health Centers, and the Area Health Education Center in Hawaii. An Advisory Committee comprising representatives from these entities will meet to identify priorities for future research in oral health, and focus groups will meet to identify barriers and facilitators to conducting oral health research, identify community research questions, and provide education for the community relating to oral health disparities in APIs. The final component, preliminary studies will assist in the development of the knowledge base needed to test the science proposed in the R01. The second objective is to evaluate the planning stage by refining and implementing a project evaluation plan and systematically using findings to monitor the process of the above collaborative affiliations, training, network, development, and pilot study development. Achievement of these objectives will enhance the research capacity of UH and the broader community to conduct research that will lead to innovative strategies designed to reduce oral health disparities in the ethnically diverse population of the State of Hawaii.

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- **Project Title: AMYLASE BINDING STREPTOCOCCI DENTAL PLAQUE AND CARIES**

  Principal Investigator & Institution: Scannapieco, Frank A.; Professor and Associate Chair; Oral Biology; State University of New York at Buffalo Suite 211 Ub Commons Buffalo, Ny 14228

  Timing: Fiscal Year 2004; Project Start 30-SEP-1992; Project End 31-DEC-2008

  Summary: Dental plaque is the oral biofilm responsible for the etiology of **Dental caries** and periodontal disease. A number of salivary proteins have been shown to interact with bacteria in plaque, and such interactions likely play critical roles in plaque formation. One such interaction is that between amylase, the most abundant enzyme in saliva, and the amylase-binding streptococci (ABS), which are numerous in plaque. Based on our recent findings generated during the previous funding period, this once-amended competitive renewal application seeks to continue our studies of the biochemical, physiological, cariological and ecological consequences of amylase-binding to ABS. We found that while amylase binding-deficient mutants adhere less well to amylase-coated surfaces and demonstrate defective biofilm formation in vitro, they colonize rat teeth better than wild type strains, out-compete their parental strains in rats fed sucrose/starch diet. These surprising findings led to the realization that AbpA inhibits sucrose-dependent colonization determinants such as, but perhaps not limited to, GtfG of S. gordonii. Thus, our Aims for the next funding period are to: 1) investigate potential interactions of genes and proteins involved in amylase binding (abpA and abpB) and genes involved in glucan synthesis (rgg and gtfG). We will evaluate the transcription of abpA, abpB and gtfG in mutant strains to determine if Abp modulates gtfG expression (or vice versa) at the transcriptional level. 2) compare wildtype and mutant strains in standard in vitro adhesion and biofilm models. 3) assess the physical interaction between Gtf and amylase-binding proteins using proteomic approaches such as Western blot-ligand binding assays, Maldi-Tof (Matrix-assisted, Laser-Desorption-Ionization/Time of Flight) mass spectrometry, or phage display. 4) determine if amylase-binding mutations in Gtf-deficient or -proficient S. gordonii modulate S.

gordonii oral colonization and cariogenicity in rats. 5) determine if S. gordonii-amylase interactions modulate S. mutans colonization competition and cariogenicity and if strains of S. mutans made to express AbpA show altered colonization and/or cariogenic abilities. Integration of in vitro with in vivo studies is crucial for mechanistic understanding of Dental plaque formation.

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- **Project Title: ANALYSIS OF BIOFILMS ON NATURAL AND SYNTHETIC DENTAL SURFACES**

  Principal Investigator & Institution: Khajotia, Sharukh S.; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, Ok 73126

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 30-JUN-2008

  Summary: Microbial colonization of exposed tooth surfaces (enamel and cementum) in the oral cavity has been demonstrated to be associated with biofilm formation and subsequent periodontal disease or **dental caries.** Studies have demonstrated that tooth surfaces and the surfaces of certain dental biomaterials that have higher surface roughness values have increased microbial attachment and adhesion in comparison with similar substrates that have been polished or glazed. However, initial investigations into the reduction of surface roughness or incorporation of antibacterial monomers in polymer-based restorative biomaterials have had limited success in reducing biofilm formation. The overall goal of this project is to determine the utility of selected topographical and physical properties as predictors of in vitro biofilm formation by Streptococcus mutans and by Streptococcus gordonii. The specific aims of this investigation are: 1) to characterize selected topographical and physical properties of tooth and restorative biomaterial surfaces and to measure biofilm accumulations of S. mutans and S. gordonfi on those surfaces, and 2) to quantify the effect of laser, chemical and mechanical treatments of tooth and restorative biomaterial surfaces on selected topographical and physical properties and S. mutans and S. gordonfi biofilm accumulation. The studies comprising this project will utilize atomic force microscopy to obtain non-destructive 3-dimensional topographical and nanohardness characteristics of the surfaces tested. A contact angle goniometer will be used to measure the surface energy and wettability/hydrophobicity of the substrates, and a confocal laser scanning microscope will be used to quantify the biofilms formed in an in vitro batch culture apparatus. It is hypothesized that accurate characterization of the topography of natural and synthetic dental substrates will provide significant fundamental information on the role of those surfaces in biofilm development, particularly in the proximity of restorations. The knowledge gained from this project will also be useful in the modification of the topography of existing dental restorative materials and periodontal treatments, or in the formulation of guidelines for new restorative materials and treatments. In the long-term, this knowledge could help to reduce the incidence of disease connected with biofilm formation, thereby realizing substantial cost savings and improved oral care for dental patients.

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- **Project Title: ANTIGENS OF STREPTOCOCCUS MUTANS IN CARIES IMMUNITY**

  Principal Investigator & Institution: Russell, Michael W.; Professor of Microbiology & Immunology; Microbiology and Immunology; State University of New York at Buffalo Suite 211 Ub Commons Buffalo, Ny 14228

  Timing: Fiscal Year 2002; Project Start 01-JAN-1984; Project End 31-DEC-2003

Summary: This project is focused on three aspects in the development of novel genetically engineered mucosal immunogens constructed primarily from a saliva-binding region (SBR) of surface protein AgI/II of Streptococcus mutans and a nontoxic component of cholera toxin (CT), the A2/B subunits, as potential candidates for inclusion in a vaccine against **dental caries.** Specific Aim 1 will address the mechanisms underlying immunological memory that maintains long-term and recallable salivary IgA antibody responses when SBR-CTA2/B is administered to mice by the intranasal route, which has previously been shown to be particularly effective for inducing these responses. The following will be investigated: the generation and characteristics of antigen-specific memory B and T cells, and the cytokines they produce, in the nasal lymphoid tissue and the cervical lymph nodes that drain it; the ability of these cells to serve as precursors of IgA antibody-secreting cells in salivary glands; and the uptake and retention of antigen by these tissues. Specific Aim 2 will develop and refine further mucosal immunogens based on the same technology, to improve the production and immunological properties of SBR-CTA2/B, to construct and evaluate immunogens from other segments of AgI/II that may be important for protection against **dental caries,** and to evaluate the use of similar immunogens constructed from S. mutans glucosyltransferase. The immunogens will be evaluated for their immunogenicity in terms of the salivary IgA and serum antibodies induced in mice when administered by the intragastric and intranasal routes. Specific Aim 3 will determine the ability of SBR-CTA2/B to induce salivary IgA and serum antibody responses to S. mutans AgI/II in adult human volunteers immunized orally or intranasally with this immunogen. This is planned as a small-scale, preclinical experiment, that takes advantage of the known safety and immunogenicity of CTB itself when administered to humans by these routes, and the previously demonstrated ability of CTB to serve as a carrier for other protein antigens coupled to it either chemically or genetically when these are administered to experimental animals by oral or intranasal routes. The information obtained will permit clinical trials to be proposed for the evaluation of these and similar immunogens are vaccines against **dental caries,** and demonstrate the utility of this technology for inducing mucosal immune responses that may be applicable against other human infections.

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- **Project Title: BACTERIAL GENE EXPRESSION IN MODEL ORAL BIOFILMS**

  Principal Investigator & Institution: Jacques, Nicholas A.; Principal Research Scientist; Institute of Dental Research 2 Chalmers St Sydney,

  Timing: Fiscal Year 2001; Project Start 20-SEP-1999; Project End 31-JUL-2004

  Summary: It is now recognised that the transition of microbial species from a free-living, suspended or planktonic state to a component of an adherent community involves fundamental behavioural change. Both **dental caries** and periodontal diseases are essentially dependent on the polymicrobial plaque that develops with increasing complexity after the initial colonization of salivary components that coat the tooth surface. While there has been extensive analysis of the growth of dental plaque organisms as mixed communities in the planktonic state, to date there is little knowledge of interactions between adherent bacteria. The proposed studies will employ two powerful and complementary new technologies to monitor changes in gene expression occurring during initial colonisation and maturation of a model biofilm. Recognition of the factorial expansion of complexity in polymicrobial systems limits detailed analysis to two key microorganisms, Streptococcus gordonii as a major early coloniser of the acquired salivary pellicle and Streptococcus mutans which is strongly

implicated as a major pathogen initiating **dental caries.** Both organisms can be genetically manipulated. The technique of In Biofilm Expression Technology (IBET) will enable comprehensive analysis of new gene expression patterns during biofilm formation on saliva-coated hydroxyapatite while Proteome analysis will facilitate recognition of altered protein profiles, particularly at the cell surface. Structural and time course analysis of altered gene expression patterns in situ will be enhanced by Confocal Laser Scanning Microscopy. Regulatory mechanisms relating to surface adhesins, the influence of extracellular sugar polymers, the response to unfavourable environments including acidic conditions and to the activity of key enzyme activities will be a focus. These parameters are highly pertinent and are the subject of study at the Institute. This program of research will provide essential data necessary for a therapeutic strategy aimed at the establishment and maintenance of a non-pathogenic dental plaque.

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- **Project Title: BINDING PROTEINS AND ORAL STREPTOCOCCAL ENDOCARDITIS**

  Principal Investigator & Institution: Holt, Robert G.; Associate Professor; Meharry Medical College 1005-D B Todd Blvd Nashville, Tn 37208

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-JUL-2007

  Summary: Infective endocarditis is the most common serious and life-threatening cardiac infection in the United States. The number of cases is expected to increase because of the increasing numbers of intravenous drug users and elderly individuals with underlying valvular degenerative changes. Both groups are at risk for the development of the disease. Over 50% of all cases of infective endocarditis are caused by oral streptococci of the mitis group and the mutans group of streptococci, where historically many members were called viridans streptococci. The generally nonnivasive Streptococcus mutans is a member of the dental caries-causing mutans group streptococci and is the most frequent species of the mutans streptococci isolated from the oral cavity of humans. The long term goal of this study is to broaden the understanding of the pathogenesis of infective endocarditis caused by oral streptococci. We hypothesize that mutans streptococcal cells have specific receptors that bind extracellular matrix molecules and fibrinogen and this interaction functions to facilitate colonization of heart tissue in the pathogenesis of endocarditis caused by mutans streptococci. The goal of this project is to identify and characterize the bacterial cell surface molecules that are involved in the adherence of heart tissue by mutans streptococci. Binding studies in our laboratory have indicated that S. mutans cells have the ability to bind to the human extracellular matrix molecules, fibronectin, laminin, and collagen type I, and the plasma protein, fibrinogen. Also, we have determined that an isogenic antigen I/II (spaF)-deficient mutant strain of S. mutans has a reduced ability to bind fibronectin, collagen and fibrinogen which suggests that antigen I/II contributes to the interaction of S. mutans cells with these molecules. The specific aims of this study are: 1) to clone and characterize genes encoding proteins that mediate the interaction of S. mutans cells with extracellular matrix molecules (fibronectin, taminin and collagen) and fibrinogen; 2) to construct mutant S. mutans strains having defects in their ability to bind extmcellular matrix molecules and fibrinogen; 3) to evaluate using a rat model of experimental endocarditis the role of binding of S. mutans cells to extracellular matrix molecules and fibrinogen in the pathogenesis of infective endocarditis; and 4) to examine the virulence of an antigen I/II(P 1) mutant strain using the rat model of endocarditis. The results of these studies should identify candidate antigens for the

production of protective immunity against infective endocarditis caused by oral streptococci as well as provide information on virulence mechanisms that function during infective endocarditis.

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- **Project Title: BIODURABILITY OF DENTIN-ADHESIVE RESIN BOND JOINT**

  Principal Investigator & Institution: Armstrong, Steven R.; Dental Research; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2004

  Summary: (provided by applicant): A more reliable, technique-insensitive and durable adhesive resin bond to dentin is required if the full benefit of bonded restorations is to be realized. This is especially important due to the fact that caries remains a major health problem, dentin sensitivity affects greater than 40 million Americans, and root caries is increasing with our aging population. Adhesive bonding to enamel has proven to be highly successful; however, bonding to dentin remains poorly understood and unreliable. Resin adhesion to dentin is thought to be primarily micromechanical by the interdiffusion of adhesive monomers into the acid demineralized organic matrix; through steps not dissimilar to any other adhesive procedure, i.e. surface preparation, wetting and solidification. The long-range goal of our program of research is the conservative restoration of teeth, prevention of demineralization, and desensitization of exposed dentin surfaces through dentin bonding. The specific objective of this application is to identify resin-dentin bond degradation involved with the wetting process. The central hypothesis of this work is that the mineral depleted dentin surface must be completely and homogeneously infiltrated by the adhesive system for a successful dentin bond. Preliminary mechanical, fractographic and analytical work provide evidence that current dentin adhesive systems incompletely infiltrate the dentin surface, phase separate, polymerize sub-optimally, and hydrolytically degrade, leading to clinical restorative failure. The rationale for the proposed research is that, once mechanisms of dentin bond formation and failures are understood, evidence-based novel approaches for successful dentin adhesion can be developed. Aim 1 will determine probability failure rates and debond pathways of the dentin-resin composite bond exposed to simulated bacterial and tissue inflammatory responses utilizing a novel accelerated aging model. Aim 2 will identify the resin monomer degradation products from the storage media from Aim 1. Aim 3 will identify resin infiltration and stability throughout the hybrid layer using micro-Raman spectroscopy. We expect to demonstrate a decrease in bond strength, a changing debond pathway and a decreasing amount of adhesive monomer in the hybrid layer. This study is significant, because the knowledge gained will improve the understanding of dentin adhesion and biodurability; leading to hypothesis-driven clinical trials examining the wetting conditions required for a clinically successful dentin bond.

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- **Project Title: BIOFILM FORMATION AND METABOLISM ON DENTAL SURFACES**

  Principal Investigator & Institution: Ferretti, Joseph J.; Senior Vice President & Provost; Microbiology and Immunology; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, Ok 73126

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 30-JUN-2008

Summary: (provided by applicant): The present Center of Biomedical Research Excellence (COBRE) proposal is designed to grow oral health related research, and increase the competitiveness of investigators associated with the University of Oklahoma College of Dentistry and affiliated institutions with common interests in dental research. At the center of this proposal are the junior investigators who will take a multidisciplinary approach to study microbial biofilm formation and metabolism on natural and artificial dental surfaces. The establishment and evolution of microbial biofilms on smooth surfaces in the oral cavity leads to **dental caries,** gingivitis, and periodontitis, accounting for the majority of all dental disease. To approach this problem from a number of vantage points, project investigators in the present proposal were drawn from complementary fields, including microbiology and genetics, pathology and cell biology, periodontics, and dental materials. An administrative core will oversee and work with the junior investigators, providing mentoring from senior investigators, enhanced core facilities, and an external advisory committee of internationally recognized scientists in the thematic topic of microbial biofilms on dental surfaces. In addition, a training program for students at all levels will be initiated as well as an outreach program to identify faculty and students at other institutions in the state interested in dental biofilm research. The university administration has committed to expand this effort with the addition of two permanent faculty positions from institutional resources. This COBRE proposal provides the necessary resources, infrastructure, and mentoring required for Oklahoma dental researchers to be successful in competing for future NIH funding as independent investigators. The ultimate benefit of this program will be the translation of research knowledge to treatment and prevention of oral diseases.

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- **Project Title: BIOFILM GROWTH AND DETACHMENT OF AN ORAL PATHOGEN**

  Principal Investigator & Institution: Kaplan, Jeffrey B.; Oral Biology; Univ of Med/Dent Nj Newark Newark, Nj 07107

  Timing: Fiscal Year 2004; Project Start 01-JUL-2004; Project End 31-MAR-2008

  Summary: Biofilms are communities of bacteria growing attached to a surface. Biofilms are responsible for more than 80% of bacterial infections in humans. Examples of diseases caused by biofilms include **Dental caries,** periodontitis, cystic fibrosis pneumonia, and infective endocarditis, and infections of various medical devices such as intravenous catheters, artificial joints and contact lenses. Little is known about the detachment of bacteria from biofilms, a process necessary for the spread of infections to new sites. Biofilm detachment represents an important area of future research that is expected to lead to novel strategies for treating biofilm infections The Gram-negative oral bacterium Actinobacillus actinomycetemcomitans has been implicated as the causative agent of localized juvenile periodontitis, a severe and rapid form of periodontal disease that affects 70,000 primarily African-Americans in the U.S. annually. A. actinomycetemcomitans also causes several non-oral infections including bacteremias, brain abscesses and infective endocarditis. A striking feature of fresh clinical isolates of A. actinomycetemcomitans is their ability form extremely tenacious biofilms on surfaces such as glass, plastic and saliva-coated hydroxyapatite, a property that has been shown to be essential for virulence in a rat model. Tight adherence to surfaces also makes A. actinomycetemcomitans an excellent model for studying biofilm growth and detachment in vitro. Genetic and microscopic studies in this laboratory have shown that A. actinomycetemcomitans cells grown attached to surfaces in broth form highly-differentiated biofilm colonies that are capable of releasing cells into the medium.

Biochemical and genetic studies indicate that A. actinomycetemcomitans biofilm colonies are held together by a sticky, extracellular polysaccharide. The proposed experiments are a continuation of our preliminary studies which have identified an enzyme produced by A. actinomycetemcomitans which causes the degradation of the sticky polysaccharide coating and detachment of A. actinomycetemcomitans cells from the biofilm aggregate. We plan to use genetic techniques to understand how production of this enzyme is regulated in the bacterial cell, and biochemical techniques to determine the structure of the polysaccharide substance on the surface of the cell. Preliminary data indicate that this enzyme is capable of degrading biofilms produced by other species of Gram-negative and Gram-positive bacteria, indicating that it may represent a novel anti-biofilm therapeutic with broad spectrum potential.

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- **Project Title: BIOMARKERS FOR TOTAL BODY BURDEN OF FLUORIDE**

  Principal Investigator & Institution: Lampi, Kirsten J.; Oral Molecular Biology; Oregon Health & Science University Portland, or 972393098

  Timing: Fiscal Year 2004; Project Start 01-SEP-2003; Project End 31-AUG-2005

  Summary: (provided by applicant): While the benefit of fluoridation in the prevention of **dental caries** has been overwhelmingly substantiated, the effect of fluoridation on other chronic health problems is less clear. For example, fluoridation has been linked with osteoporosis, bone cancer, uterine cancer, fertility rates, testosterone levels, gastro-duodenal manifestations, and otosclerosis. The majority of studies evaluating the impact of fluoridation on chronic health conditions, however, have been ecological. In ecological studies, the unit of analysis is an aggregate on individuals rather than the individual itself and, in most cases both exposure status and disease status are based on the aggregate. Aggregating exposure and disease status data can lead to inappropriate conclusions regarding relationships at the individual level (ecological fallacy). The purpose of this research is to identify a biomarker for long-term fluoride exposure that can be used in future epidemiologic research on the impact of fluoride exposure on human health. Developing a fluoride biomarker will improve the precision of fluoride exposure measures and provide better estimates of individual level fluoride exposure. This will reduce misclassification of fluoride exposure, thereby enhancing our ability to detect dose-response relationships between fluoride exposure and health outcome measures. The fluoride content of bone appears to reflect total body burden of fluoride and is an appropriate "gold standard" for a fluoride biomarker. For this reason, we will recruit 210 patients scheduled for primary total hip or total knee replacement surgery in Portland and Salem, OR. Excised bone tissue along with fasting blood, fasting ductal saliva, and demographic information will be obtained from each study participant and analyzed for fluoride content at the Medical College of Georgia. While controlling for confounding variables, we will correlate bone fluoride to tissue fluoride in order to determine which tissue, if any, is the "best" biomarker for long-term fluoride exposure. In addition, we will obtain additional tissue samples from a subset (n=30) to evaluate the precision of the biomarker. This research is a collaborative effort between Oregon Health Sciences University and the Medical College of Georgia.

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- **Project Title: BIOTECH & MATERIALS RESEARCH TO REDUCE CARIES DISPARITY**

  Principal Investigator & Institution: Milgrom, Peter M.; Professor of Dental Public Health Scienc; Dental Public Health Sciences; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2004; Project Start 01-JUN-2004; Project End 31-MAY-2005

  Summary: (provided by applicant): This is a revision of Grant application No. R13DE015798-01 for a scientific workshop with the aim to: (1) Produce a state-of-the-art assessment of the public health approaches and their limitations in preventing early childhood **dental caries** in disparity populations. Important in this assessment will be differentiating applied problems of engineering and technology versus fundamental science. (2) Assess recent emerging research in the prevention of **dental caries** including: specific species bacterial adhesion prevention, biofilm ecology manipulation, circumvention of sucrose driven acid production, genetically engineered antibiotic production in situ, and fluoride- and other antimicrobial-release coatings. (3) Promote a dialogue between end-users, oral microbiologists, and materials and bioengineering experts in order to develop novel prevention technologies and implement the transfer of such technologies to industry and practice. (4) Address the question of what can be done to more effectively use the large body of basic and applied caries science already available to speed solutions to the public health community. (5) Develop a research agenda that will help state, federal, and private funding agencies identify critical research needs; not only for novel technological solutions but also on outreach mechanisms to transfer such novel technologies to industry and public health practice. The rationale for the workshop is that science and technology have not produced sufficient practical tools for public health practitioners and the private delivery system to address the plaque of **dental caries** that exists for children and adults from families with low incomes and for numerous ethnic minority and racial groups. The 2 1/2 day conference is to be held Winter 2005 in Seattle and involve participants from basic and applied academic dental research, bioengineering and biotechnology, government, and industry. The conference will be co-sponsored by the Northwest/Alaska Center to Reduce Oral Health Disparities, the University of Washington UWeb Bioengineering Center, and the Salivary Diagnostics Project.

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- **Project Title: CARIES PREVENTION IN ALASKAN NATIVE INFANTS**

  Principal Investigator & Institution: Grossman, David; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2003

  Summary: Alaska Native children are disproportionately affected by early childhood caries, compared to all U.S. children. Dental care needs for adults and children in rural Alaska far exceed the acute care and prevention resources available. As a result, there is a high level of dental morbidity present among adults that likely contributes to early transmission of mutants streptococci (MS) from adult caregivers to infants in the household. Furthermore, the cultural practice of per- mastication of solid food for infant feeding amplifies the transmission of oral secretions from adult to child. The prevention of early MS acquisition and subsequent caries in infants and toddlers required efforts starting at birth. Since Alaska Natives are a rural population at high risk for caries, interruption of vertical transmission of MS using a combination of improved oral hygiene practice, and topical antimicrobials and bacteriostatic agents may be an ideal

prevention strategy for childhood caries. Chlorhexidine and xylitol are two agents that have been shown to reduce dental decay and MS counts. The specific aim of this proposal is to conduct a community based, randomized blinded trial to determine if the serial use of chlorhexidine and xylitol in 250 mothers will reduce the vertical transmission of caries between Alaska Native mothers and infants. The Yukon-Kuskokwim (YK) Delta of southwestern Alaska is the site of the study. We hypothesize that a two week period of twice-daily chlorhexidine mouthwash use prior to deliver followed by a subsequent two year period of maternal xylitol gum use, will lead to a significant reduction in the age-specific prevalence of early childhood caries at 12 and 24 months of age among the offspring of mothers in the intervention group, compared to control group mothers. We also hypothesize that, compared to controls, mothers and children in the intervention group will have significant reductions in oral MS counts at each follow-up interval. If proven successful, this intervention could have a significant impact on the prevalence of caries among young Alaska Native children and other population groups at high risk for childhood caries.

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- **Project Title: CHILDHOOD VACCINES AND DENTAL CARIES IMMUNITY**

  Principal Investigator & Institution: Smith, Daniel J.; Senior Member of Staff; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-AUG-1982; Project End 30-APR-2003

  Summary: (Adapted from investigator's Abstract): A continuing long-term goal of the research conducted under this grant is to develop a **dental caries** vaccine that mediates protection via the mucosal immune system. The patterns of infection and initial human responses to mutans streptococcal antigens have revealed parameters of time and specificity for potential pediatric application of **dental caries** vaccines, and have suggested novel pathways for vaccine therapy. A direct result of this study has been the identification of Streptococcus mutans glucan binding protein (GBP59) as a new mutans streptococcal target for vaccine therapy. This discovery permits a broader based approach to immunologically mediated control of **dental caries** than previously possible. Preliminary studies with novel mucosal adjuvants and bioadhesive microparticles have suggested new, or more refined, methods of enhancing the induction of immunity to mucosally applied antigens such as GBP59. To build on these important discoveries, the investigators will explore the molecular characteristics of S. mutans GBP59 by cloning and sequencing the gene responsible for its synthesis. Epitopes associated with caries protection will then be identified using deduced sequence homologies with functionally important regions of other proteins, and by using immunologic probes. The potential use of these epitopes in subunit vaccines will then be tested in a rodent caries model. Also, the presence of human T and B lymphocyte responsiveness to these epitopes will be explored. The success of mucosal-based vaccines is dependent, not only on inclusion of appropriate epitopes, but also on the ability to induce an adequate immune response. Thus, the investigators propose to explore the potential for Clostridium difficile toxin A (TxA) to serve as a novel mucosal adjuvant for important caries vaccine antigens, such as GBP59, as well as its potential to contribute epitopes to which caries-protective antibody may be induced. Targeted delivery of antigen to appropriate lymphatic sites can also contribute to the success of mucosal vaccines. Hence, the proposed studies will investigate the ability of a novel bioadhesive microparticle system to deliver immunogenic doses of these antigenic constructs to inductive sites in the GALT and BALT, and to induce protective immune responses, alone, and in combination with TxA.

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- **Project Title: CHRONIC DENTAL DISEASE AND CARDIOVASCULAR DISEASE**

  Principal Investigator & Institution: Joshipura, Kaumudi J.; Assistant Professor; Oral Health Policy & Epidem; Harvard University (Medical School) Medical School Campus Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 30-SEP-1998; Project End 31-JUL-2004

  Summary: Several recent reports have found significant associations between periodontal disease, tooth loss and increased coronary heart disease (CHD). Possible associations between **dental caries** and CHD and between dental disease and stroke have also been reported. Recent literature also supports the possible role of other chronic bacterial and viral infection, fibrinogen and other inflammatory mediators in increasing CHD risk. We propose to study the relation between periodontal disease, caries and tooth loss, and risk of incidence of coronary heart disease and stroke and to assess if these associations are independent of common risk factors including behavioral factors. Additionally, we propose to evaluate two possible explanations for these associations: (1) tooth loss leads to reduced masticatory efficiency, which could lead to reduced intake of dietary antioxidant and fiber, which in turn has been associated with increased risk for cardiovascular disease; and (2) chronic dental disease could lead to hyperfibrinogenemia which is strongly and probably causally associated with increased risk of CHD. We will also evaluate C-reactive protein, von Willebrand factor, tissue plasminogen activator, and Factor VII as additional mediators. Participants include 51,529 men enrolled in the Health Professionals Follow-Up Study since 1986 and 90,000 females enrolled in the Nurses Health Study since 1976 who reported their dental status in 1992. The follow-up in these cohorts is excellent and has been consistently over 90 percent. The outcome measures will include incident cases of CHD and stroke in 15 years of follow-up among men and 9 years of follow-up among women free of cardiovascular disease and cancer at baseline. Over 4500 incident cases of CHD and stroke are anticipated. Biomarker assays will be performed for a sub-population consisting of new CHD cases incident after the time of initial blood collection, and one matched control per case. Blood samples were provided by 32,000 nurses in 1989-90 and by 18,100 male health professionals in 1993-94, allowing for sufficient follow-up to include an estimated 600 incident cases among males and 600 cases among females for the biomarker analyses. The high prevalence of dental infection makes its potential association with inflammatory and dietary mediators, and ultimately increased risk of CHD and stroke very important with implications for millions of Americans.

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- **Project Title: CLONING ANALYSIS OF S. MUTANS PUTATIVE COLLAGENASE**

  Principal Investigator & Institution: Dao, My Lien L.; Associate Professor; Biology; University of South Florida 4202 E Fowler Ave Tampa, Fl 33620

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-MAY-2005

  Summary: Dental root decay is prevalent among older individuals as their gum recesses exposing Dental root surface to attack by cariogenic bacteria. In a study involving 449 subjects of an age range of 79-101 years, 96% had coronal decay experiences, and 64% had root caries experience with 23% of the group having untreated root caries (ADA News Releases, 2000). Streptococcus mutans, an etiologic agent in the development of coronal caries, has also been implicated in Dental root decay; data in support of this implication include the finding of S. mutans in Dental root section, its ability to bind

collagen, and to degrade FALGPA, a known synthetic peptide substrate for collagenase. Bacterial collagenases are considered as virulence factors as they facilitate the invasion and destruction of host tissues by the pathogens. It is not yet known whether S. mutans produces a true collagenase enzyme. Considering the increase in incidence of Dental root caries as the population lives longer, the long-term goal of the current study is to develop effective and safe methods to control this disease, and improve the nutrition and quality of life of the population at risk. In order to determine whether the collagenolytic enzyme in S. mutans is a good candidate antigen for vaccine development, the Specific Aim of the current research is to learn more about the S. mutans enzyme in order to explore this avenue. A putative S. mutans collagenase gene has been obtained previously, and sequence analysis showed a high homology with the 35-kDa collagenase of various clinical isolates of Porphyromonas gingivalis, a bacterium causing periodontitis. The plan is to clone the 1.2 kbp putative collagenase coding sequence into an expression plasmid under the control of a strong promoter in order to obtain the corresponding protein, which in turn will be isolated and characterized by biochemical methods. Antibody will be prepared against the S. mutans enzyme and tested for the ability to block collagen binding and/or collagen degrading properties. The data obtained will be compared with other known bacterial collagenases. This information is essential in determining future directions for research on the role of S. mutans in Dental root caries, and other diseases that may involve collagen binding and collagen degrading activity such as periodontitis and endocarditis.

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- **Project Title: CONTROLLED-RELEASE SEALANT TO PREVENT SECONDARY CARIES**

  Principal Investigator & Institution: Anusavice, Kenneth J.; Professor; Dental Biomaterials; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 15-SEP-2001; Project End 31-AUG-2005

  Summary: (Applicant's abstract verbatim) The cost of dental care in the United States was $45.8 billion in 1995. Replacement of dental restorations accounts for 75 percent of all operative work, and secondary caries at the margins of restorations is the most frequently identified reason for replacement (Kidd, 1996). Thus, dental patients can realize considerable cost savings and improved oral health care if the lifetime of defective restorations can be extended through the use of tooth preservation therapies. The overall objective of this study is to test the hypothesis that application to marginal crevices of a sealing resin that releases chlorhexidine and/or fluoride (when the pH decreases to below 6.0) can extend the service life of defective amalgam and composite restorations and enhance remineralization of demineralized adjacent enamel. We propose to test the following hypotheses- (1) polymer microspheres loaded with chlorhexidine diacetate alone, a dispersed mixture of either CaF2 or ZnF2 and chlorhexidine diacetate, or one of these fluoride agents alone will exhibit an onset of ion release when the solution pH decreases below 6.0 and will terminate ion release when the pH increases above 6.0; (2) the controlled-release microspheres when loaded in a resin matrix (bis GMA/TEGDMA/HEMA), will exhibit an initial release rate when the solution pH decreases below 6.0 and will reduce its release rate when the solution pH increases above 6.0; (3) Test the hypothesis that microbial accumulation (plaque) and site specific levels of S. mutans on tooth enamel adjacent to defective amalgam or composite restorations are significantly better predictors of secondary caries than the width of the marginal crevice and; whole mouth levels of S. mutans; and (4) a crevice-sealing resin containing a dispersed mixture of chlorhexidine and fluoride microspheres

will more effectively inhibit demineralization and enhance remineralization of enamel adjacent to composite restorations than resins containing only one of these two therapeutic agents. Clinically relevant aspects of this project include: (1) use of a monoclonal antibody test for site specific analyses of S. mutans on selected approximal tooth surfaces with amalgam or composite restorations; (2) use of a dispersed mixture of polymer microspheres that will release an antibacterial agent (chlorhexidine) simultaneous with a remineralizing agent (fluoride) to prevent secondary caries in situ; and (3) analysis of extracted restored teeth to determine the best of four predictors for secondary caries (plaque levels-at the margins of restorations, whole mouth concentrations of S. mutans, site specific levels of S. mutans at the margins of amalgam and composite restorations, and the width of marginal crevices adjacent to amalgam and composite restorations).

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- **Project Title: DETROIT CENTER FOR RESEARCH ON ORAL HEALTH DISPARITIES**

  Principal Investigator & Institution: Ismail, Amid I.; Professor; Cariology/Restor Sci/Endod; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2002; Project Start 30-SEP-2001; Project End 31-JUL-2008

  Summary: (Provided by the applicant) - The Detroit Center for Research on Oral Health Disparities aims to promote oral health and reduce disparities within the community of low-income African American children (0-5 years) and their main caregivers (14 + years) living in the City of Detroit. The driving theme of the center's research program is to identify determinants and design interventions to answer the following question: why do some low-income African American children and their main caregivers have better oral health than others who live in the same community? The proposed center will focus on studying intra-group disparities in oral health. The community based partners, the City of Detroit Department of Health (DDH) and the Voices of Detroit Initiative (VODI) have strongly supported this theme. The Center will include 3 support cores, 5 research core projects and 1 pilot study. The Center's Methodology Core will select a multistage random sample of African American families living in the poorest 39 Census Tracts in the City of Detroit. A total of 1,529 families will be sampled and interviewed in their homes. It is estimated that 994 families will be examined at community centers in year 2 (2002) funding. Based on extensive data collected by the investigative team (R01 MH58299) in Detroit, the investigators predict that 760 families will be retained by the third examination phase in year 6 (2006). The research teams will investigate the social characteristics of parents, families, and neighborhoods, that are associated with disparities in oral health (dental caries and periodontal diseases) of children and their caregivers; lead levels in saliva of children and saliva and blood (finger prick) of the main caregivers; dietary intake; and genetic, behavioral, social and bacteriologic risk factors of periodontal disease in adults. Using information from 3 core research projects, the investigators propose to develop a tailored multi-media educational intervention (Project #3), based on the transtheoretical model of behavioral change, which will be administered using a randomized controlled design in year 4 of funding, just prior to the second examination phase. Additionally, the center will evaluate the impact on access to dental care of the state-funded experiment on utilization where Medicaid children are managed like privately insured patients (Project #4). The center will support health professionals from the DDH and VODI and the University of Detroit Mercy to receive research training. Doctoral students in three programs targeting

minorities in the Schools of Public health and Social Work will be offered stipends to conduct research on health disparities. All families will have access to dental care in a DDH dental clinic (funded by DDH, HRSA, Delta Dental of Michigan and VODI).

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- **Project Title: DEVELOPMENT OF A VACCINE FOR HUMAN PERIODONTITIS**

  Principal Investigator & Institution: Page, Roy C.; Professor; Periodontics; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2001; Project Start 20-SEP-1999; Project End 31-JUL-2004

  Summary: (adapted from the Investigator's abstract): Periodontitis is a major cause of tooth loss in adults in the US and worldwide. There is a compelling need for new approaches to prevention and control. Use of a vaccine may be possible since the disease is caused by a small group of gram-negative bacteria among which Porphyromonas gingivalis predominates. Vaccine development is hampered by a gap in our fundamental knowledge about the role of immune responses in modulating periodontal tissue destruction. Studies in animal models are necessary to obtain the needed information. The Principal Investigator has shown that immunization of the nonhuman primate Macaca fascicularis, using a killed P. gingivalis vaccine, suppresses or blocks periodontal destruction as assessed by alveolar bone loss. The mechanisms may involve antibody-mediated reduction in levels of PGE2 and other inflammatory mediators, and immune neutralization of P. gingivalis virulence factors as well as opsonization. Immunization studies are likely to continue to close the gaps in our understanding of the pathogenesis. The Principal Investigator and others have demonstrated that a vaccine containing cysteine protease from P. gingivalis has high potential for inducing protection. The Principal Investigator in a pilot study has demonstrated that immunization of M. fascicularis with a vaccine containing porphypain-2 was more effective that the whole cell vaccine in reducing bone loss. PGE2 levels in crevicular fluid were significantly reduced. The Principal Investigator proposes to confirm and extend these observations by studying 10 animals immunized with gingipains and 10 control animals using their well-established protocol. The primary outcome measure will be radiographic assessment of alveolar bone status. Titers and functional biologic properties of serum, salivary, and GCF antibodies will be measured, and P. gingivalis and five other bacteria in the flora monitored by DNA probes. Effects of immunization on levels of PGE2, IL-1beta, and TNF-alpha in GCF will be determined and antibody mediated modulation of P. gingivalis virulence factors assessed. Gingival biopsies will be taken to evaluate the effect of immunization on the cellular infiltrate by immunocytochemistry and inflammatory mediator expression by in situ hybridization. Additional safety data will be obtained by necropsy of some of the animals at the end of the study. These observations will contribute in a major way to closing the gaps in our knowledge of the role of the host immune response in the pathogenesis of periodontitis.

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- **Project Title: DIABETES ASSOCIATIONS WITH CARIES AND TOOTH LOSS**

  Principal Investigator & Institution: Taylor, George W.; Professor; Cariology/Restor Sci/Endod; University of Michigan at Ann Arbor 3003 South State, Room 1040 Ann Arbor, Mi 481091274

  Timing: Fiscal Year 2004; Project Start 01-JUL-2004; Project End 30-APR-2006

  Summary: Diabetes mellitus is a common chronic disease. The prevalence of diabetes in the U.S, particularly type 2 diabetes, is increasing. Its complications impose a large

burden on a high proportion of people with diabetes. This burden of diabetes is even higher in certain minority populations. While both **Dental caries** and tooth loss are also common conditions in the U.S. population, their prevalence is generally decreasing. Nevertheless, for important subgroups of the population, particularly certain minority and economically disadvantaged groups, there is a disproportionately higher burden of **Dental caries,** tooth loss, and periodontal diseases. Substantial evidence exists to support the role of diabetes and poorer glycemic control as important risk factors for periodontal disease. Nevertheless, the impact of diabetes on caries and tooth loss remains unclear. There is limited U.S. population-based evidence to support or refute an adverse effect for diabetes on these two common oral conditions. Recent epidemiological evidence is further defining the role of tooth loss in adverse systemic health outcomes through effects on dietary intake and nutritional status. Given the special role of diet in the health of people with diabetes and the status of cardiovascular diseases as a major complication of diabetes, tooth loss, and specifically tooth loss due to caries, can therefore have particular importance. The 2 Specific Aims of this proposed study are to: (1) determine whether diabetes mellitus is associated with an increased prevalence of **Dental caries** and **Dental caries** experience, and (2) determine whether diabetes mellitus is associated with an increased prevalence of tooth loss. These Aims will be accomplished by testing a series of detailed hypotheses using rigorous and thorough multivariable statistical analyses appropriate for the complex sample design NHANES ill data. The results of this study wilt provide important, population-based evidence to substantiate (or refute) associations of diabetes with caries and tooth loss. If a significant adverse effect is estimated for diabetes, then the results of this project will provide important data to aid in the design of intervention studies to prevent or reduce the occurrence of **Dental caries** and tooth loss in people with diabetes. Results may also impact on existing clinical practice protocols, and promote new public policy in matters related to diabetes.

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- **Project Title: EARLY CARIES DETECTION AND INTERVENTION**

  Principal Investigator & Institution: Wefel, James S.; Professor and Director; Dows Inst for Dental Research; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 01-MAR-2001; Project End 31-DEC-2005

  Summary: The title for this multi-site program grant application (PO1) is "Early Caries Detection and Intervention." One of the goals of this P01 is to determine the ability of various diagnostic techniques to measure early changes in enamel demineralization. Currently available techniques include quantitative light fluorescence (QLF), infrared laser fluorescence (IR), and electrical conductivity (EC). There is a tremendous need to validate the application of all new developing clinical detection methods, both for primary and secondary caries. It has been stated that "The Diagnosis of early care lesions can be regarded as the cornerstone of cost- effective health care delivery and quality of dental care." (ORCA Symposium on Caries Diagnosis). Three projects will be used to validate the use of these newer diagnostic techniques and then apply those techniques in clinical trials of both primary (Indiana, Proj. 3) and secondary caries (Texas/Indiana, Proj. 2). The interventions will first be tested in Project 1 for effectiveness and if acceptable used as an intervention for primary and/or secondary clinical caries trials. Teeth that are exfoliated during the trials will be analyzed at Iowa for the presence and/or extent of lesion formation using polarized light microscopy as the "gold standard" The interrelationships between the projects and complimentary nature of the research objectives will produce a synergism that offers far more than merely individual

projects at individual sites. These series of studies are expected to: 1) Validate new imaging technologies for the detection of both primary and secondary **dental caries** at a much earlier stage of development than is currently possible; 2) Determine the most effective intervention methods using the appropriate in vitro and in situ models; 3) Use these early caries detection methods to monitor clinically effective interventions for primary and secondary caries. An Administrative Core and a Biostatistics Core will support the projects. The project director will receive advice and review from both an internal Steering Committee and External Advisory Committee. The collaborative efforts of the three research-intensive Universities, the long- standing expertise and diverse populations offer a unique combination of resources for this P01.

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- **Project Title: EARLY CARIES DETECTION WITH NEAR-IR LIGHT**

  Principal Investigator & Institution: Fried, Daniel; Associate Professor in Residence; Preventative and Restorative Dental Sciences; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-MAY-2005

  Summary: The overall objective of the proposed research is to develop non-invasive optical devices for the detection and diagnosis of early **dental caries** (dental decay). New, more sophisticated diagnostic tools are needed for the detection and characterization of caries lesions in the early stages of development. If carious lesions are detected early enough, they can be arrested/reversed by non-surgical means through fluoride therapy, anti-bacterial therapy, dietary changes, or by low intensity laser irradiation. The principal factor limiting optical imaging through the enamel of the tooth in the visible range of 400-700-nm is light scattering. Light scattering in sound enamel and dentin is sufficiently strong in the visible range to obscure light transmission through the tooth. The magnitude of light scattering in dental enamel decreases markedly with increasing wavelength. Therefore, we hypothesize that the near-IR region from 830-1550-nm offers the greatest potential for new optical imaging modalities due to the weak scattering and absorption in sound dental hard tissue. At longer wavelengths, absorption of water in the tissue increases markedly reducing the penetration of IR light. The overall objectives of this proposal will be achieved through the following specific aims: (1) Measure the optical constants and light scattering anisotropy and phase function of sound dental hard tissue at wavelengths in the near-IR between 660 and 1550-nm for polarized and unpolarized light and determine the changes in those optical parameters that occur upon demineralization during the caries process; (2) Develop near-IR polarization sensitive optical coherence tomography (PS-OCT) for the detection, diagnosis, and imaging of early caries lesions and for the monitoring of lesion progression in simulated caries models; (3) Develop near-IR transillumination for the detection and imaging of early interproximal caries lesions. It is likely that if these studies and future clinical trials are a success, that this novel technology for imaging dental hard tissue will be employed for the detection and monitoring of early carious lesions without the use of ionizing radiation, thereby enabling conservative non-surgical intervention and the preservation of healthy tissue structure. Moreover, it is probable that this proposed imaging technology would enable the clinician to detect and quantify the severity of occlusal lesions that are not resolvable with conventional radiography due to the surrounding sound tissue structure.

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- **Project Title: EARLY CHILDHOOD CARIES--PREVENTION AND TREATMENT OUTCOMES**

  Principal Investigator & Institution: Weintraub, Jane A.; Lee Hysan Professor & Chair; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2003

  Summary: Early Childhood Caries (ECC), previously called Baby Bottle Tooth Decay and Nursing Caries, is a form of **dental caries** that affects infants and young children. The often severe disease is difficult and expensive to treatment. Strategies to identify very young children at risk for ECC and rigorous testing of interventions are not well developed. This project has two major components with different research designs; both will determine in certain factors are associated with increased ECC incidence, but will involve very different study populations: A) a population-based retrospective cohort study among 6,058 children born between 1986-1993 to members of the Kaiser Permanente Health Plan in the Pacific Northwest (KPNW) and B) a prospective, randomized clinical trial (RCT) among initially caries-free children under age three at two public health facilities in San Francisco, one serving a primarily Latino and one a primarily Asian population. A) Factors to be assessed from KPNW patient records include information about the child, the parents, the mother (i.e., medications prescribed during pregnancy), the siblings, and the dental providers. Behavioral information (i.e., bottle use, oral hygiene) will be ascertained from questionnaires. Among children born between 1986-90, we will determine if ECC in the primary dentition increases the risk of caries treatment on first permanent molars. B) The RCT will 1) Compare the efficacy of once or twice/year fluoride varnish (FV) application plus counseling to counseling alone in preventing ECC; 2) Assess pre-intervention salivary markers (biologic an chemical), behavioral and demographic factors as predictors of ECC; 3) Compare the efficacy of these interventions between sites serving different ethnic populations with a high prevalence of ECC; and 4) Determine the salivary fluoride release profile from fluoride varnish applied to a sub-set of subjects. If successful, this study will provide methods for targeting children at risk for ECC and evidence that an intervention is efficacious in preventing ECC in this young age group. Collaboration among UCSF, KPNW, the San Francisco public health community and industry will facilitate translation of findings into the dental public health and private sectors.

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- **Project Title: ENVIRONMENTAL AGENTS AS MODULATORS OF DISEASE PROCESSES**

  Principal Investigator & Institution: Cory-Slechta, Deborah A.; Professor; Environmental Medicine; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 01-AUG-1980; Project End 31-MAR-2005

  Summary: OVERALL (Taken from the Applicant's Description) Despite a marked increase in the human life span, questions about the role of environmental and occupational agents as modulators of disease and dysfunction continue to arise. These questions are provoked by such observations as the increased incidence of asthma in children, reports that Parkinson's disease (PD) has an environmental rather than a genetic basis, of correlations between ultra fine particles and cardiovascular respiratory morbidity and even mortality, and of endocrine-like chemical and reproductive dysfunction, among others. The goal of the University of Rochester NIEHS Environmental Health Sciences Center (EHSC) is to define the scope of the contribution of toxic agents to disease processes and dysfunctions and to understand the mechanisms

by which they occur. The Center strives to provide a sound scientific basis for evaluating the health risks posed by chemical exposures to human populations and ultimately to prevent their occurrence. This is achieved through the efforts of four Research Cores. Studies within the Neurotoxicology Research Core seek to identify mechanisms by which toxicants affect nervous system function and thereby contribute to behavioral, neurological and psychiatric disturbances of the nervous system, such as Parkinson's disease, autism, and cognitive impairments. The Osteotoxicology Research Core focuses primarily on the extent to which lead exposure serves as a risk factor for disturbances of skeletal function, particularly its involvement in **dental caries** in osteoporosis. The Pulmonary Toxicology Research Core examines inflammatory and oxidative stress-induced mechanisms of lung injury and how disease states such as asthma, chronic obstructive pulmonary disease and others modulate these mechanisms. The Protein Modulators of Toxicity Research Core seeks to identify the ways in which toxicants modulate biologically active proteins critical to normal homeostatic function, thereby inducing changes contributing to disease processes. The scientific efforts of the Research Cores are promoted and assisted through five Facility/Service Cores: Transgenic Services, Pathology/Morphology/Imaging, Biostatistics, University Facilities and Shared Instrumentation. In addition, collaborations and new directions are significantly enhanced through the Enrichment Program of the EHSC, which includes a Pilot Project Program, a Visiting Scientist Program, the EHSC Seminar Series and the Rochester Conference Series. The Community Outreach and Education Program with its new Director, has instituted a Community Advisory Board that provides communication between the EHSC and the Community and has established educational programs for various segments of the community, including students and teachers, medical professionals and even senior scientists

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- **Project Title: ENVIRONMENTAL INFLUENCES AND DENTAL CARIES**

  Principal Investigator & Institution: Bowen, William H.; Welcher Professor of Dentistry; Eastman Dentistry; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 01-SEP-1995; Project End 31-DEC-2005

  Summary: Despite significant reduction in the prevalence of **dental caries** in some segments of the population it remains a major public health problem, particularly for those least able to bear the burden. The decline in prevalence has generally been attributed to increased exposure to fluoride through a variety of routes. Prior to and during the increased use of fluorides ingestion with food preservatives was also increasing by over 25 fold. Food preservatives have properties in common with fluoride in that they behave as weak acids they are protonated at low pH values, can diffuse into cells, reduce acid tolerance and acid adaptation by mutants streptococci. Recognizing the importance of saliva on the plaque environment, we will examine the relationship of mammalian and non- mammalian components of whole saliva samples collected over a three- year period, to the incidence of **dental caries** in the same group of subjects. We believe this proposal is highly novel and offers the possibility of developing approaches to enhance the diagnosis of caries and methods for its prevention.

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- **Project Title: FAMILY AND CULTURAL INFLUENCES ON INFANT FEEDING**

  Principal Investigator & Institution: Barton, Sharon J.; None; University of Kentucky 109 Kinkead Hall Lexington, Ky 40506

Timing: Fiscal Year 2003; Project Start 01-FEB-2003; Project End 31-JAN-2005

Summary: (provided by applicant): The goal of this program of research is to improve infant feeding practices and long-term health outcomes of infants and children. Infant health, growth, and development depend on what and how the infant is fed during the first year of life. The purpose of this longitudinal ethnographic study is to investigate cultural influences or family beliefs about infant feeding and the manner in which these beliefs are translated into feeding practices. The proposed research will help meet Healthy People 2010 objectives by identifying key points and reasons during infant feeding through the first year when breast or formula feeding alone ceases and where feeding practices are begun that lead to poor nutrition, over-feeding, and increased potential for **dental caries.** Previous research by the PI suggests that mothers' feeding decisions are influenced by fathers, grandmothers, and cultural practices, despite availability of published feeding guidelines. The specific aims are to (1) describe cultural influences on family beliefs and practices related to the introduction of solid foods and beverages during the first year of life; (2) examine personal and contextual factors that determine family beliefs and practices related to infant feeding and the introduction of solid foods and beverages; (3) develop a culturally sensitive theory about infant feeding during the first year of life. Longitudinal data will be collected during the infant's first year of life, using ethnographic methods. A purposive sample of families will be recruited from health clinics in two rural Kentucky counties. Fieldwork will consist of home observations and in-depth interviews with family members and with participants from community agencies that deal with infant feeding (e.g. WIC). Data also will be gathered from published infant feeding resources and observation of daily life in the community. Constant-comparative methods will be used to describe, analyze, and interpret data. Credibility of the findings will be strengthened through detailed field notes and an audit trail. This research will provide an understanding of and theory pertaining to the complex cultural issues surrounding infant feeding. The findings will provide the basis for developing and testing culturally sensitive nursing interventions to improve infant feeding practices and long-term health outcomes of infants and children.

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- **Project Title: FLUORIDE REQUIREMENTS FOR THERAPEUTIC EFFICACY**

  Principal Investigator & Institution: Carey, Clifton M.; Grants Administrator; American Dental Association Foundation Chicago, Il 60611

  Timing: Fiscal Year 2004; Project Start 15-MAR-2004; Project End 31-JAN-2009

  Summary: The goal of this proposal is to establish the minimum concentration of fluoride needed to prevent enamel and root caries. The lack of knowledge about "the target concentration of fluoride required in the oral environment to optimize its potential for caries prevention" has inspired the NIDCR to issue a program announcement (PA-01-121) indicating a high priority status for this subject. After 60 years of community water fluoridation we still do not know how much F is required to prevent caries. This may be because no one has systematically performed in vitro studies that separate the significant factors under conditions that closely mimic those of the oral environment and then validated those findings in intraoral studies. This proposal details such a systematic study to identify the significant factors and their interactions as related to the efficacy of fluoride to prevent caries. A predictive model that takes into account the conditions of each person is to be developed from in vitro studies and then validated through intraoral studies. In the mouth, fluoride originates either from the saliva at a relatively low and fairly constant concentration (0.1 ppm; Carey et al., 1986) or from fluoride rinses, gels, and dentifrices, which is transient and

can range in concentration up to 15,000 ppm. In Aim 1 the continuous flow model is used to optimize the amount of fluoride that is needed to prevent enamel caries when there is a steady, low concentration of fluoride at all times. Aim 2 is focused on determining the amount of fluoride on a time-weighted basis that is required to prevent enamel caries when the fluoride is provided as a bolus treatment twice daily. Recognizing that root dentin is a very different substrate than enamel, Aims 3 and 4 are focused on determining the therapeutic amounts of fluoride required to prevent root caries under conditions of constant exposure (Aim 3) and periodic high concentration fluoride exposures (Aim 4). Aim 5 will establish the amount of fluoride required to prevent caries when proteins or other permselective macromolecules are adsorbed on the surfaces of the enamel or root dentin. In Aim 6, the relationships between saliva composition, salivary flow and the amount of fluoride required to prevent caries established with the continuous flow model will be tested by use of an intraoral model. In this Aim 6 the effect of fluoride exposure on the prevention of caries will be determined. Together these studies should, for the first time, be able to demonstrate the minimum therapeutic levels of fluoride necessary to have a prophylactic effect. Additionally, the potential of this project to develop predictive models that can be used to indicate the required amount of F as a function of a specific environment is particularly significant because the profession will be able to tailor F regimes as appropriate. This is particularly important in the treatment of populations that are at higher risk.

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- **Project Title: GENERAL CLINICAL RESEARCH CENTER-FORSYTH DENTAL INSTIT**

  Principal Investigator & Institution: Flier, Jeffrey S.; Professor; Beth Israel Deaconess Medical Center St 1005 Boston, Ma 02215

  Timing: Fiscal Year 2003; Project Start 01-DEC-1977; Project End 30-NOV-2004

  Summary: (provided by applicant): The BIDMC's GCRC proposes to form a satellite with the Forsyth Dental Institute (FDI), a world class center for clinical investigation of oral disease. This proposal describes a spectrum of investigations involving treatment of periodontal diseases, development of a vaccine for **dental caries,** testing of mercury amalgam toxicity and investigation of oral cancer. Sixteen projects are described that will be conducted at the Satellite Center that include microbiology, microbial genomics, microbial taxonomy, immunology and toxicology as these studies relate to conditions of oral health and disease and microbial biofilms. The proposed Satellite Center will include a Dental Clinic Core, a Laboratory Core and Biostatistics/Informatics support. Specific areas of investigation in this application include: 1) comparison of conventional and antibacterial_supplemented treatments of periodontal disease; 2) investigation of means to prevent periodontal disease; 3) studies on familial distribution of oral bacteria; 4) studies of oral bacteria as examples of naturally occurring biofilms; 5) studies of oral bacteria that penetrate cells; 6) studies of the ways in which early lesions of periodontal disease are initiated; 7) investigation of the microbiology associated with oral cancer; 8) studies that contribute to the development of a **dental caries** vaccine; 9) investigation of the potential toxicity of mercury amalgams; and 10) studies of the uncultivable bacteria of the oral cavity with planned development of a microbial microarray for oral bacteria identification. In addition to the planned studies as outlined above, a strategy to create bi_directional linkage between parent and satellite GCRC's is described in which a dental facility will be established at the BIDMC GCRC to be staffed by Forsyth personnel. Through this facility, it is envisioned that future studies on the oral health

effects of systemic disease, and the converse, effects of systemic disease on oral health will be investigated. It is also stressed that this facility will encourage closer affiliation between the Joslin Diabetes Center (JDC) Satellite and the Forsyth Satellite. It is envisioned that this proposal will expand the research horizon of the FDI and contribute new technology to the research of the parent.

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- **Project Title: GENETIC DETERMINANTS OF DENTAL FLUOROSIS**

  Principal Investigator & Institution: Everett, Eric T.; Assistant Professor; Oral Facial Development; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-APR-2007

  Summary: (provided by applicant): During amelogenesis a strong correlation has been repeatedly demonstrated between the amount of fluoride consumed and the incidence of dental fluorosis. Greater than optimal amounts of fluoride (taken systemically) have been shown to contribute to a greater risk in developing fluorosis in a dose dependent manner. Concurrent with the decline in **dental caries** has been an increase in the prevalence of dental fluorosis, a side effect of fluoride exposure. The prevalence of dental fluorosis in recent years ranges between 7.7% and 80.9% of the population in communities with fluoridated water and from 2.9% to 42% in communities with nonfluoridated water. We hypothesize that genetic determinants also influence to an individual's susceptibility or resistance to develop dental fluorosis. In other words, the environment interacts with the genotype to produce the final phenotype. Our initial test of this hypothesis consisted of using a mouse model system where continuous eruption of the mouse incisors permit investigation of active amelogenesis over a relatively short period of time and where we could rigorously control genotype, age, gender, food, housing, and drinking water fluoride level. That study involved 12 genealogically disparate inbred strains of mice, and showed differences in dental fluorosis susceptibility/resistance between the strains. Furthermore, we found clustering of strains into distinct phenotypic groups. The A/J mouse strain is highly susceptible, with a rapid onset and severe development of dental fluorosis compared to the other strains tested. The 129P3/J mouse strain is least affected with negligible dental fluorosis. Those observations directly support the contribution of a genetic component in the pathogenesis of dental fluorosis and have allowed us to develop a central hypothesis; that in addition to the environmental component (increased amounts of fluoride that can be ingested) genetic determinants/factors that encode proteins and pathways underlie fluorosis susceptibility or resistance. The goal of the proposed studies, to identify genes involved in dental fluorosis susceptibility/resistance, will be pursued in the following two specific aims. Specific Aim: To identify candidate loci that convey susceptibility / resistance to dental fluorosis. Two approaches will be used. First, through the modeling of gene action in the susceptible A/J strain and second, to perform quantitative trait loci (QTL) mapping using the A/J and 129P3/J inbred mouse strains in the generation of F2 progeny, and developing linkage maps at a resolution of 20-cM for the chromosomal regions containing putative susceptibility to fluorosis loci. These studies will allow us to identify genetic determinants that directly or indirectly contribute to an individual's susceptibility or resistance to dental fluorosis. Future studies will investigate the cellular roles and functions of these genes and pathways during the pathogenesis of fluorosis. This knowledge will allow optimal use of fluorides for an individual in the prevention of **dental caries** while minimizing the risks of excessive fluoride.

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- **Project Title: GENETIC FACTORS TO ORAL HEALTH DISPARITIES IN APPALACHIA**

  Principal Investigator & Institution: Marazita, Mary L.; Professor; Cleft Palate Research Center; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-SEP-2002; Project End 31-MAY-2009

  Summary: There is no doubt that there are genetic, environmental and behavioral components to the expression of oral health status in all populations. Furthermore, it is clear that there will be interactions between these components and that each of these components may be transmissible (in a broad sense) within families. Therefore, in this project we will apply state-of-the-art statistical and molecular genetic approaches to two study samples: a representative W.V. cohort of 500 families, and a subset of approximately 80 "high-risk" families (i.e., ascertained through index through index cases in the top 10% of the distribution of the DMFS index) The ultimate goal of the studies described in this project is to develop an array of functional genetic polymorphisms that are related to oral health, in order to characterize individuals (and populations) as to their genetic risk factors. This array could ultimately be implemented via a DNA chip, or other high throughput platform, for rapid and cost- effective genotyping. To begin to develop such an array, we will focus on approximately 25-30 genes that are known to be important in oral health in the broad categories of growth factors and receptors, homeodomain genes, signaling and transcription factors, xenobiotic detoxification and metabolism, inflammation, and behavior. The Appalachian population has never been characterized with respect to these categories of genes and such characterization will be the first aim of this study. Then, the genotypes at these genetic loci will be analyzed simultaneously with oral health phenotypes, microbiological status, and health behaviors in order to discover the transmission pattern of the phenotypes (adjusted for the effects of the microbiology and behavior covariates) and the potential co- segregation of phenotypes and genotypes, in order to identify the genes that are important in oral health in this population. The major orofacial disease outcome of interest to COHRA is caries, and caries will therefore provide a major focus for the genetic studies outlined in this proposal. However, similar strategies will pertain for the other orofacial phenotypes, such as periodontal status, assessed on the study subjects.

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- **Project Title: GLUCAN BINDING PROTEINS OF ORAL STREPTOCOCCI**

  Principal Investigator & Institution: Banas, Jeffrey A.; Associate Professor; Ctr/Immunol/Microbial Disease; Albany Medical College of Union Univ Albany, Ny 12208

  Timing: Fiscal Year 2003; Project Start 01-AUG-1992; Project End 30-APR-2008

  Summary: Streptococcus mutans possesses three distinct glucosyltransferases (GTFs) and at least three different nonenzymatic glucan binding proteins (GBPs). The precise contributions of each GTF and GBP to plaque development are unknown. Recently we showed that the loss of a glucan-binding protein (GbpA), accomplished through allelic replacement, dramatically altered the architecture of the biofilm formed by cultures of S. mutans. Based on these data we engineered strains with inactivation in genes encoding other extracellular proteins. The loss of GbpC, FruA, or P1 also resulted in changes in the biofilm architecture. To explain these observations we posit that the loss of an

extracellular protein may result in specific physical and/or biochemical changes to the organism, or to its immediate environment that affect the structure of the mature biofilm formed by that organism. The Specific Aims of this application are designed to test these possibilities. Since work with the GbpA has progressed the furthest, investigations of specific GbpA properties are also included in the Aims. Aim 1) Examine the physical properties of the knockout strains including hydrophobicity, surface charge, and their interactions with cations such as calcium which are important in the development of a biofilm. Aim 2) Use a flow chamber to examine the events associated with the initial attachment of the knockout strains to the substratum and correlate the results with the structure of the mature biofilms. Aim 3) Examine how the ratio of GbpA to glucan synthesis correlates with the structure of the biofilm. Aim 4) Delete or replace the amino terminal domain (non glucan-binding domain) of GbpA and examine how this change affects the phenotypic properties of Streptococcus mutans compared to the wild-type and GbpA knockout strains. Aim 5) Express phenotypic properties of formation. Aim 6) Utilize architecture influence gene GbpA in the heterologous host Streptococcus gordonii and examine the organism in the context of sucrose-dependent adhesion and biofilm microarrays to determine how the loss of extracellular proteins and biofilm expression.

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- **Project Title: GOLD STANDARD METHODS FOR FLUORIDE ANALYSIS**

  Principal Investigator & Institution: Martinez-Mier, Esperanza A.; Preventive Community Dentistry; Indiana Univ-Purdue Univ at Indianapolis 620 Union Drive, Room 618 Indianapolis, in 462025167

  Timing: Fiscal Year 2002; Project Start 01-AUG-2002; Project End 31-JUL-2004

  Summary: (provided by applicant): Fluoride is widely recognized for reducing the prevalence of **Dental caries.** Therefore, either studies aimed to enhance its beneficial effects or to reduce its detrimental effects continues to be relevant. Such studies can benefit from improvements in the techniques employed for the analysis of fluoride. In addition, meaningful international studies in this field can only be conducted if standardized methods for measuring the levels, ingestion and concentrations of fluoride, are available. Currently available fluoride measurement techniques are not standardized and a universal standard for fluoride determination has not been established. Although a variety of techniques are available, none have been accepted for universal use. The current project Aims to collaborate with established analytical laboratories to develop standard, global methods for analyzing fluoride in different types of samples. In order to develop these standard, global methods for fluoride analysis, the Fluoride Laboratory at the Oral Health Research Institute proposes to collaborate with six, additional, well-established laboratories that are currently conducting fluoride analyses. The proposed collaboration will include the analysis of the fluoride content of a series of 180 biological and environmental samples using the methods in current use in each laboratory. Results of these analyses and descriptions of the analytical procedures used will be collected and distributed from each laboratory to all collaborators. A plan will be then developed to resolve any differences in results and to identify preferred analytical procedures in a meeting of all collaborators at the Oral Health Research Institute. Analyses of another series of biological samples by all laboratories using the preferred analytical methods will be then conducted and, finally a scientific paper reviewing the data collected and the preferable analytical procedures will be developed for publication. The proposed investigation will provide an opportunity for seven recognized laboratories to collaborate in order to reach consensus

about detailed protocols that will identify and describe gold standard techniques for fluoride analysis of specific types of samples. The proposed study will provide an opportunity to resolve discrepancies that currently make it difficult to compare the results of the many studies dealing with fluoride analyses.

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- **Project Title: GOLDENSEAL(HYDRASTIS CANADENSIS)REMEDY FOR ORAL DISEASES**

  Principal Investigator & Institution: Wu, Christine D.; Associate Professor; Periodontics; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 15-APR-2001; Project End 31-MAR-2004

  Summary: (APPLICANT'S ABSTRACT): Complementary and alternative medicine (CAM) has recently gained popularity with the American public. Research validating CAM has focused mainly on the treatment and prevention of systemic medical diseases while less attention has been paid to oral diseases. Oral diseases including **dental caries** and periodontal disease, are a major cause of loss of work and school days. Chemical and mechanical means have been used to control dental plaque bacteria, the etiologic agent of caries and periodontal disease. However, none of the available agents is ideal and frequently cause adverse effects. This justifies further search and development of alternative agents from natural sources that are safe and effective. The North American plant, Hydrastis canadensis L. (Ranunculaceae), known commercially as "Goldenseal," has been used for centuries as an antiseptic to treat skin disorders and as an antidiarrheal, antiseptic, astringent, hemostatic, and vasoconstrictor agent. Goldenseal is one of the major phytomedicines ("herbal remedies") sold in health food stores and pharmacies in the U.S. Several mouthrinses and toothpastes containing Goldenseal are available on the market. Although claims have been made by the manufactures regarding its ability to fight gum diseases and prevent caries, no scientific data is available to substantiate these claims. The goal of the proposed research is to evaluate the potential of Goldenseal as a remedy in prevention and treatment of oral diseases and to maintain oral health. It is hypothesized that antimicrobial compounds that are safe for humans can be identified from H. canadensis. These compounds may have potential as dental prophylactic/therapeutic agents and may also serve as lead compounds for the subsequent design and synthesis of new agents that are even more effective than the existing ones. The Specific Aims of this study are: SA1: To isolate and identify active antimicrobial compounds from H. canadensis by activity-guided fractionation and characterization; SA2: To determine antimicrobial activity of the purified compounds against cariogenic and periodontal pathogens; SA3: To investigate mixtures of purified antimicrobial compounds from H. canadensis for synergistic antimicrobial activities; SA4: To correlate bioactivity of various commercially available Goldenseal-containing oral hygiene products with levels of active alkaloids identified in SA2. The proposed research is innovative in that it represents collaboration between an oral microbiologist and a natural product chemist that will assure the speedy discovery of novel or known active compounds from Goldenseal and will provide scientific explanation as to the remedy's efficacy. It will also serve as a model system for the evaluation of existing herbal remedies for their oral health related claims. This application of CAM research will help to achieve better oral health and oral disease prevention, one of the to priority areas of focus specified b the U.S. Public Health Service in "Health People 2000."

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- **Project Title: HEALTH EFFECTS OF DENTAL AMALGAMS IN CHILDREN**

  Principal Investigator & Institution: Mckinlay, Sonja M.; New England Research Institutes, Inc. 9 Galen St Watertown, Ma 02472

  Timing: Fiscal Year 2002; Project Start 30-SEP-1996; Project End 31-JUL-2006

  Summary: The safety of silver amalgam as a dental restorative material has been controversial since its introduction 150 years ago, but-until recently it has been generally assumed that the exposure to mercury from dental amalgam is limited to the acute placement phase. Some recent studies (mostly observational and primarily of adults) have demonstrated chronic release of mercury vapor from amalgam fillings during chewing and brushing, raising new safety concerns. The randomized trial, Children's Amalgam Trial (CAT) is designed as a comprehensive assessment of the relative safety of silver amalgam, compared to the alternate, mercury-free materials, demonstrating equivalence of cognitive and renal outcomes. Children aged 6-10 at last birthday with no prior dental restoration (to minimize prior mercury exposure) and mixed (primary and permanent) dentition were recruited from two New England communities (rural Main and inner city Boston/Cambridge, Massachusetts) to represent, to the extent feasible, the likely effects in children in the US. Children were chosen for this trial as they are most likely to be amalgam-free at randomization and, given their smaller body mass and developmental stage, more likely to demonstrate adverse effects (if any) of increased body mercury burden. This 5-year competing continuation will enable completion of 6 years of observation of the trial subjects/randomized from August 1997 to September 1999). Current funding, through July 2001, will include two years of observation only. Given the obvious public health significance of the potential long range impact of mercury on cognitive function, the primary endpoint measure is the full scale IQ score of the Wechsler Intelligence Scale for Children: Third Edition (WISC III) and the primary outcome is the estimated change in the score between Baseline and 6 years post randomization, adjusted for the baseline IQ score. Secondary outcomes include more immediately measured safety endpoints that will be monitored annually, including: urine mercury levels; a dip-stick screening test for urinary protein (confirmed by albumin level); and gamma-glutamyl transpeptidase (gamma-GTP). Other endpoints include other aspects of cognitive function from an extensive neuropsychological test battery, while key covariates include a measure of dietary mercury (hair levels) and the dose of amalgam summarized in "surface-years" of exposure. To date, 534 subjects have been randomized (107%) and follow-up through the 12 month visit, although not yet complete, indicates that the initial (12 month) response rate should be at least 92%. Subsequent losses are expected to be negligible (about 2% per year). A non- orthogonal analysis of covariance will test for equivalence on IQ scores between treatments arms similar modeling will be used to address secondary aims.

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- **Project Title: IMAGE ANALYSIS ALGORITHM FOR EARLY CARIES DETECTION**

  Principal Investigator & Institution: Dunipace, Kenneth R.; Therametric Technologies, Inc. 5080 E 161St St Noblesville, in 46060

  Timing: Fiscal Year 2004; Project Start 01-MAY-2004; Project End 30-APR-2005

  Summary: In spite of the remarkable decline in the prevalence of **Dental caries** observed in the U.S. during the past 25 years, **Dental caries** continues to be the most common Dental disease and additional measures for the prevention and control of this disease are needed. The ability to detect **Dental caries** at an earlier stage of development would markedly facilitate the development of more effective measures for the prevention and

control of this disease and their use in Dental practice. Conventional visual-tactile-radiographic procedures for caries detection are unable to detect the caries process until it has progressed through 300-500 microns of enamel and such lesions are difficult to reverse/remineralize with restorative procedures frequently required. Research during the past decade has demonstrated that a new technology, Quantitative Light Fluorescence (QLF) is not only capable of detecting the caries process much earlier but is able to quantify changes in the mineral content, i.e., demineralization and remineralization, as they occur in situ. This capability will allow Dental practitioners to: (a) identify early lesions reflecting caries risk prior to cavitation; (b) implement appropriate interventions to reverse the disease process at an earlier stage with more efficient outcomes; and, (3) monitor the success (or failure) of the applied intervention measures. Nevertheless, we believe that the presently available QLF instrumentation could be significantly improved to permit the detection of the caries process shortly after initiation through the development of a mathematical algorithm that utilizes all characteristics of the images. The effectiveness of these analyses would be greatly enhanced if there were more distinctive change between the appearance of sound and carious tissue. The purpose of this application is to develop and demonstrate a unique method for displaying these changes.

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- **Project Title: IMMUNOLOGIC DISEASES AND BASIC IMMUNOLOGY**

  Principal Investigator & Institution: Cooper, Max D.; Investigator; Medicine; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2002; Project Start 01-JUL-1976; Project End 31-DEC-2006

  Summary: (provided by applicant): The Institutional Training Program described in this application reflects the commitment of this university to the training of highly motivated pre-doctoral students and Ph.D. and M.D. graduates who seek research and teaching careers in immunology. The major strength of the program is the broad base of expertise and research interests of its faculty, covering a broad spectrum of modem immunology. Basic research opportunities are available in lymphocyte differentiation; cellular immunology; molecular immunology; gene organization, structure and function of immunoglobulins, T cell receptors, complement, and lymphokines; secretory immunity; transgenic models of immune function; immunogenetics; host responses to infectious diseases, transplantation immunology, and neuroimmunology. Because a large number of the preceptors are involved in the care of patients with immunologic diseases in addition to their research programs, the program provides an interface between basic and applied immunology and its primary focus remains the elucidation of pathogenetic mechanisms operative in diseases of immune etiology. Opportunities directly related to human diseases are available in autoimmune diseases, vaccine development, immunodeficiencies, neoplastic diseases, immune-complex diseases, host-defense defects, **dental caries,** microbial and parasitic pathogenesis, and transplantation immunology. We believe that the diversity of interests and high quality of the faculty participating in this program assure students that the training they receive will enable them to make significant contributions in the field of immunology. Predoctoral trainees are selected from among the graduate students already enrolled in the interdisciplinary Cellular and Molecular Biology Program who have successfully completed their first year of study. Postdoctoral trainees are selected among individuals with a M.D., Ph.D. or equivalent terminal degree on the basis of prior academic and research performance, letters of recommendation, and personal interviews. Major criteria for selection include a high motivation for research and commitment to a research and teaching career in

academic immunology. Research training will be carried out in modem, well-equipped laboratory and office space occupied by UAB investigators. Classrooms, conference rooms, and small group libraries are available for complementary activities. Special research facilities include modem immunocytometry equipment, an electron microscope laboratory , a transgenic mouse facility, and core facilities for oligonucleotide synthesis, nucleic acid sequencing, protein sequencing, and hybridomas. Preceptors of the program have access to the Hospitals and Clinics of the Medical Center.

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- **Project Title: INFLUENCE OF CRANBERRY ON PLAQUE-RELATED DISEASES**

  Principal Investigator & Institution: Koo, Hyun; Eastman Dentistry; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2004; Project Start 01-JAN-2004; Project End 30-NOV-2006

  Summary: (provided by applicant): **Dental caries** is the most common oral infectious disease that afflicts humans. More than 95% of all adults have experienced this disease. It is more common than asthma, hay fever or chronic bronchitis in 5-17 year old children. The American public spends close to $40 billion per year to treat this disease or its consequences. **Dental caries** results from the interaction of specific bacteria with constituents of the diet on a susceptible tooth surface. Dental plaque accumulation is the first clinical evidence of this interaction; dental plaque is a biofilm which is comprised of a population of bacteria growing on the tooth surface enmeshed in a polysaccharide matrix. Acid can be formed rapidly by acidogenic bacteria, such as Streptococcus mutans, within the matrix and its persistence results in dissolution of the tooth. Furthermore, plaque is also the major aetiological factor in gingivitis. Cranberries, like other natural products, harbor a plethora of biological compounds such as flavonoids (e.g. quercetin and myricetin), phenolic acids (benzoic acid), anthocyanins, condensed tannins, and others. We have shown that many of these substances can: (i) inhibit enzymes associated with the formation of the plaque polysaccharide matrix, (ii) block adherence of bacteria to surfaces, (iii) prevent acid formation, and (iv) reduce acid tolerance of cariogenic organisms. For example, quercetin and myricetin are effective inhibitors of glucosyltransferases (GTFs), enzymes responsible for the synthesis of glucans; glucans synthesized by GTFs mediate the adherence and accumulation of cariogenic streptococci on the tooth surface. Weak acids, such as benzoate (benzoic acid), affect the acid production by S. mutans and have been shown to reduce **dental caries** in rats. We propose a comprehensive plan to explore the influence of cranberry on many of the biological aspects involved in the pathogenesis of dental plaque formation and caries. We also propose to examine the ability of cranberry to prevent or reduce caries in our well-proven rodent model and to investigate the effects of cranberry on plaque formation and gingivitis in vivo.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: LASER EFFECTS ON DENTAL HARD TISSUES**

  Principal Investigator & Institution: Featherstone, John D.; Chairman; Preventative and Restorative Dental Sciences; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2001; Project Start 01-AUG-1992; Project End 31-JUL-2004

  Summary: (adapted from the Investigator's abstract): The overall objective of the research is to develop an understanding of the interactions of laser light with dental hard tissues and to establish a scientific basis for the safe and effective use of lasers for

treatment of dental hard tissues including caries prevention and caries removal. There are seven specific aims. The first specific aim is to determine the absorption coefficients for enamel and dentin, with emphasis on the 9.3 and 9.6 um wavelengths which were not able to be fully studied with the lasers available previously. The investigators now have access to a CO2 laser with a shorter pulse duration which will enable measurement of the high absorption at these wavelengths (in vitro). The second specific aim is study the thermal behavior of enamel and dentin follower laser irradiation at selected wavelengths and to model with computer simulations using 1-, 2-, and 3-D finite difference heat conduction numerical codes. This aim improves on their previous 1-D modeling efforts (in vitro). The third specific aim is to study the thermal decomposition kinetics of enamel and dentin during laser irradiation. This aim will utilize six techniques: (1) thermal response analysis based on infrared radiometry measurements of surface temperature, (2) glancing x-ray diffraction, (3) FTIR reflectance spectroscopy, (4) evolved gas analysis, (5) acid dissolution rate measurements, and (6) scanning electron microscopy (in vitro). The fourth specific aim is to carry out safety studies in humans in vivo to establish degree and effects of heat transfer to the pulp during laser irradiation. The study involves 25 volunteers scheduled for removal of 3rd molar teeth in which thermocouple placed at the pulp-dentin junction any temperature rise during laser irradiation (in vivo). Specific Aim 5 is to determine the laser irradiation parameters, with and without fluoride treatments, that optimally inhibit the progression of caries-like lesions in enamel and tooth roots. An acid dissolution assay is used to generate a measure to tooth material hardening by the laser (in vitro). The sixth specific aim is to conduct intra-oral studies in humans involving the placement of dental materials, pretreated in vitro by the laser, into the oral cavity of human volunteers for prolonged periods to study the ability of laser irradiation to harden dental materials. This assay will be conducted through a subcontract with the University of Indiana (in vivo). The seventh specific aim is to study the inhibition of secondary caries around restorations by laser irradiation (in vitro).

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- **Project Title: LONGITUDINAL STUDY OF CARIES IN A RURAL WIC POPULATION**

  Principal Investigator & Institution: Warren, John J.; Prev and Community Dentistry; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-AUG-2005

  Summary: (provided by applicant): While the prevalence of **dental caries** has declined for the majority of U.S. children in recent decades, there are profound disparities in **dental caries** experience where young children from low-income or minority families suffer a disproportionate share of the disease burden. To effectively address the problem of caries in the primary dentition of high-risk children, preventive efforts should be directed at these children beginning at a very early age. The WIC supplemental nutritional program is one of the very few programs that serves children at very young ages, and it also serves children from low-income families. However, there are limited data available about the oral health of WIC-enrolled populations, and studies have not longitudinally followed subjects in such a population. Thus, the goals for the proposed study are to longitudinally track caries experience in WIC-enrolled children; to assess methods to enhance subject recruitment and retention in these populations and to gather longitudinal caries risk data on WIC populations. We will also explore how S. mutans clonal types change over time, as well as how they interact with host genetic markers and predict caries development in these high-risk young children. Specifically,

the study will follow a cohort of WIC-enrolled 1-year-old children for 18 months in Muscatine and Louisa counties in Iowa - two rural counties with large Hispanic populations. Collection of pilot data in this population will allow our research team and others to continue research aimed at reducing oral health disparities, including longitudinal trials of preventive interventions. Moreover, interventions centered at WIC programs have the potential to become sustainable caries-prevention programs for high-risk children throughout the country. We will collect data on caries occurrence, beverage consumption, fluoride exposures, S. mutans levels and clonal type, and host genetic markers, and we will assess different methods of recruiting and retaining subjects in this high-risk population. Data from this pilot study will be of great value and will position the study team to effectively conduct future intervention studies to reduce oral health disparities.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: LUXS-MEDIATED QUORUM SENSING IN STREPTOCOCCUS MUTANS**

  Principal Investigator & Institution: Wen, Zezhang; Oral Biology; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2003; Project Start 15-JUN-2003; Project End 31-MAY-2005

  Summary: (provided by applicant): Streptococcus mutans is recognized as the principal etiological agent of **dental caries,** the most prevalent infectious disease of humans. The ability to metabolize carbohydrates and generate acids, to survive acidic pH and other adverse conditions, and to adhere to and form tenacious biofilms on the tooth surface are believed to be critically associated with the cariogenicity of this human pathogen. Known for its high degree of acid tolerance (aciduricity) and its high capacity to produce acid (acidogenicity), S. mutans lives primarily on the tooth surface at high cell-density in a high diversity ecosystem better known as dental plaque, the structure and composition of which is known to be largely influenced by such factors as the source and availability of nutrients, the pH in the oral cavity and by the ability of the biofilm organisms to adapt to the fluctuations in environmental conditions. Quorum sensing is a cell density--dependent regulatory mechanism that is known to be involved in regulation of a variety of physiologic processes and virulence in both Gram (+) and Gram (-) bacteria. We have recently generated evidence that the S. mutans possesses a gene encoding a functional homologue of the new family of autoinducer synthases (LuxS) that are responsible for production of autoinducers of the quorum sensing system 2, AI-2. This study is designed to yield novel information concerning LuxS-mediated quorum sensing and virulence regulation in S. mutans, which will contribute to our understanding of the pathogenesis of this microorganism and the ecology of the oral flora. The Specific Aims of this proposed study are: 1) to investigate the role of luxS in acid tolerance by S. mutans. By using functional assays, reporter gene fusions, Northern hybridization, and proteomics, we will investigate acid tolerance and its regulation by luxS, and identify novel factors (proteins) that are involved in luxS-regulated acid tolerance responses. 2). To use confocal laser scanning microscopy (CLSM) and mixed, known-species consortia to determine the impact of luxS of S. mutans on bacterial adherence by S. mutans and the inter- and intra-generic interactions between S. mutans and other oral bacteria in terms of biofilm initiation development and structure.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: LYSIS OF CARIOGENIC BACTERIA BY PHAGE-ENCODED ENZYMES**

  Principal Investigator & Institution: Delisle, Allan L.; Associate Professor; Oral & Craniofacial Biol Scis; University of Maryland Balt Prof School Baltimore, Md 21201

  Timing: Fiscal Year 2002; Project Start 15-SEP-2000; Project End 31-AUG-2004

  Summary: The long-range, health-related goal of this proposal is to develop species-specific, cell wall-hydrolyzing enzymes encoded in the genomes of phages specific for Streptococcus mutans and Actinomyces naeslundii as new therapeutic treatments for **dental caries.** S. mutans is the primary etiological agent of human enamel caries, whereas A. naeslundii (A. viscosus), an early colonizer of dental plaque, has long been believed to be involved in gingivitis and root surface (cementum) caries. The major objective of the research proposed herein is to isolate, purify and characterize the enzymes which enable phages specific for these species to lyse their host cells. The lysis genes of two previously studied phages which are specific for S. mutans and A. naeslundii will be isolated, cloned and sequenced. To accomplish this, the complete genomes of these two phages will be sequenced, which will allow direct PCR subcloning of their holin and endolysin genes and characterization of their respective products. The DNA sequences of these holin/lysin gene pairs will provide information on their regulatory mechanisms and further our knowledge of the evolutionary relatedness of these viral proteins. Comparative analyses of their deduced primary amino acid sequences may also reveal conserved protein domains that are important in determining their structural and functional properties. Additional cloning experiments will be employed to isolate holin genes, and nearby endolysin genes, from these two phages and three additional oral phages, in order to develop a generally applicable method for directly isolating oral phage lysis genes. Phage DNA libraries will be constructed in a phage vector having a defective holin gene, which will allow recombinants expressing oral phage holins to be selected by complementation (plaque formation) of the defect in the phage vector. Inserts will then be sequenced to identify the phage holin genes and primers complementary to the ends of these genes will then be used to sequence, directly from the phage genomes, the adjacent, downstream endolysin genes. Selected endolysin genes will be subcloned, by PCR, from phage genomic DNAs, or from recombinant phage vectors, into expression vectors and introduced into E. coli in order to isolate and purify their gene products. The enzymatic activities of these proteins will then be extensively characterized, including determining the specific bonds which they cleave in the cell walls of their respective hosts. Purified preparations of these lytic enzymes might ultimately be used to kill, in a species-specific manner, S. mutans and A. naeslundii in dental plaque.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MEMBRANES OF THE DENTAL PATHOGEN STREPTOCOCCUS MUTANS**

  Principal Investigator & Institution: Brady, L Jeannine.; Oral Biology; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 01-MAR-1986; Project End 29-FEB-2004

  Summary: (Adapted from investigator's Abstract): Streptococcus mutans is recognized as the major etiologic agent of **dental caries** in humans. Its pathogenicity is enhanced by a number of virulence factors including an adhesin (P1), which promotes colonization in the absence of dietary sucrose and the ability of this species to withstand the effects of low pH caused by the homofermentation of sugars. The present application focuses on

each of these virulence traits. The gene encoding the P1 adhesin, spaP, has been cloned and sequenced and the gene product is well characterized. Nothing is known, however, of environmental or genetic regulatory mechanisms controlling its expression. Environmental regulation will be studied by growing a heterodiploid strain containing a chromosomal spaP::lacZ reporter gene fusion construct in a chemostat under varying growth conditions. Both adherent and non-adherent cells will be assayed for gene expression by measuring beta-galactosidase activity. Genetic regulatory loci will be interrupted by using transposon Tn 917 or random chromosomal fragments and screened for loss of adhesin expression. Regulatory genes will be characterized after marker rescue or cloning into E. coli. Also, putative enzymes and transport proteins that aid in the folding and localization of P1 will be isolated by affinity chromatography methods and responsible genes characterized as above. The second thrust of this proposal involves the Ffh-dependent protein translocation system, only recently discovered in S. mutans. An acid-sensitive mutant, known to be interrupted in the ylxM-ffh (sat) operon and unable to assemble optimal amounts of membrane-bound H+/ATPase, will be studied by two-dimensional gel electrophoresis. Major proteins differentially expressed between mutant and wild-type membranes will be recovered, subjected to N-terminal amino acid sequence analysis and appropriate degenerate oligonucleotides synthesized for use in screening the investigator's genomic libraries for responsible genes. By this approach, the investigator hopes to determine the key proteins transported into membranes by the Ffh-pathway. The yeast two-protein hybrid technique will be employed to analyze the binding of S. mutans Ffh-containing fusion proteins to those containing S. mutans ATP-ase subunits or other relevant gene products in vivo in Saccharomyces cerevisiae. Such reactions will be confirmed by affinity chromatography on Ffh- GST columns. Finally, environmental regulation will be studied by growing a heterodiploid strain containing a chromosomal ylxM promoter::lacZ reporter gene fusion construct in a chemostat under varying growth conditions including pH, osmolarity, and nutrient sources.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MICROBIAL DIVERSITY AND GENETIC CHARACTERIZATION**

  Principal Investigator & Institution: Caufield, Page W.; Professor and Director; Diagnostic Science and Urgent Care; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2002; Project Start 15-JUN-2002; Project End 31-MAY-2005

  Summary: The proposed studies are anticipated to yield important new information as to the composition of the bacterial biota that comprises the caries-associated plaque biofilm. The long-term benefit of such information should lead researchers to devising both diagnostic and preventative strategies for **dental caries** based on addressing its etiological agents. This proposal will focus on children with a severe forms of **dental caries** called Early Childhood Caries (ECC). Using a powerful technique of gradient electrophoresis will be used to separate 16S rDNA markers from an array of bacteria in plaque biofilms. These gels should show differences between the microfloras of ECC and caries-free children. This profiling, in turn, will allow us to identify or approximate those bacteria, some likely to be uncultivable, associated with caries. Another hypothesis to be tested is whether strains of mutans streptococci, or the entire caries-biofilm differ in their ability to cause disease. Subtraction DNA hybridization will be used to discover unique genetic loci present in mutans streptococci or dental plaques of caries-prone children. Further development of subtraction DNA hybridization will lead to our overall objective, i.e., to characterize from whole plaque a constellation of genetic loci

within the caries-active biofilm, irrespective of the limitation of first cultivating specific bacteria. This will set the groundwork for subsequent studies in which a set of DNA probes can be compiled and tested, which will be useful for predicting whether a particular child is at risk for caries. Knowing the function of these genetic loci and the bacterial host from which they arise will give important information as to the causation of caries. Moreover, having genetic markers for disease may eliminate the costly and imprecise practice of cultivating bacteria from dental plaque. The research proposed will likely impact on these more serious forms of caries, leading to its eventual prevention.

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- **Project Title: MMP-20 AND MMP-20 DOMAIN FUNCTION IN FORMING ENAMEL**

  Principal Investigator & Institution: Bartlett, John D.; Assistant Member; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-JAN-2002; Project End 31-DEC-2006

  Summary: (provided by applicant): The goal of this application is to characterize the role that the matrix metalloproteinase enamelysin (MMP-20) plays during dental enamel and tooth development. The enamel proteins (amelogenin, ameloblastin, enamelin) are cleaved soon after they are secreted into the enamel matrix. Enamelysin is expressed simultaneously with the enamel proteins and recombinant enamelysin will cleave recombinant amelogenin at virtually all of the precise sites previously observed in vivo. Thus, enamelysin is an important amelogenin processing enzyme. As for all MMPs, enamelysin contains a propeptide that must be cleaved if the enzyme is to become active. Enamelysin also has a hemopexin domain that is not functionally well defined. An enamelysin knockout (-/-) mouse was engineered to characterize the contribution of enamelysin to tooth and enamel development (Aim 1). The enamelysin -/-mouse is the only MMP -/- mouse with a profound phenotype that survives to breed. Thus, we can define the limits of the enamelysin promoter (Aim 2) so that it may be used to express an enamelysin transgene in the -/- background and revert the -/- phenotype back to normal. Furthermore, because the -/- mouse has a profound phenotype and can breed, we are in possession of the only MMP -/- mouse that can be utilized to characterize the mechanistic function of the MMP propeptide and/or hemopexin domain. So, we propose to introduce two enamelysin promoter transgenes into the -/-background. The first transgene will allow enamelysin to be secreted as an active enzyme (propeptide removed intracellularly) so that we may characterize the role of the enamelysin propeptide in tooth development (Aim 3). The second transgene will encode enamelysin without its' hemopexin domain so that the contribution of the hemopexin domain in tooth development may be characterized (Aim 4). The long-term goals of this project are to contribute to the understanding of enamel formation so that eventually synthetic enamel can be engineered for the repair of damaged (**dental caries**) or diseased (amelogenesis imperfecta) dental enamel. This application builds on results from a highly productive R29 grant (DE12098).

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: MOLECULAR ANALYSIS OF THE BIOFILM IN CARIES AND HEALTH**

  Principal Investigator & Institution: Griffen, Ann L.; Professor; Pediatrics; Ohio State University 1960 Kenny Road Columbus, Oh 43210

  Timing: Fiscal Year 2004; Project Start 01-AUG-2004; Project End 30-APR-2009

Summary: Dental caries is the most common chronic disease of childhood, and is the biggest unmet health care need among America's children. Socioeconomic disparities in both rates of disease and treatment are a major public health issue. To date, effective biological interventions to prevent caries have not been developed. Dental plaque contains several hundred different organisms, many of which are poorly studied. A number of species have been shown to produce sufficient acid to drive pH below critical levels and to tolerate low pH. Research has primarily focused on Streptococcus mutans as the etiologic agent in caries, but based the work of previous investigators using cultivation and on our preliminary findings using molecular methods, S. mutans is not always present in caries, is often found at low levels, and additional and unexpected bacterial species may be important. In addition, comparatively little attention has been paid to identifying health-associated and potentially beneficial bacterial species that may reside in the oral cavity. For the proposed project, bacterial species present in childhood caries and health will be identified by cloning and sequencing bacterial 16S ribosomal genes amplified from DNA isolated from plaque samples. This open ended approach will allow the detection and identification of all bacterial species present, including novel, uncultivated or unexpected species. The presence and quantities of the species identified by this approach as potentially associated with caries or health will then be determined using quantitative, real-time PCR. This dual-technique approach will allow the examination of a much larger sample size than is possible by cloning and sequencing alone. Accomplishment of the proposed studies will identify the pathogens associated with the onset and progression of severe caries of the primary and young permanent dentition, and identify those bacterial species associated with a healthy dentition. This study will also provide a comprehensive catalog of the supragingival flora in children based on molecular technology. The significance of the proposed work is that identification of additional caries pathogens would provide alternative targets for biological interventions, and identification of beneficial health-associated species could provide the basis for therapeutic interventions to establish caries-resistant microbial communities.

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- **Project Title: MOLECULAR BIOLOGY OF ORAL ALKALI PRODUCTION**

  Principal Investigator & Institution: Burne, Robert A.; Professor & Chair; Oral Biology; University of Florida Gainesville, Fl 32611

  Timing: Fiscal Year 2002; Project Start 01-AUG-1992; Project End 30-JUN-2006

  Summary: (provided by applicant): Alkali generation, in the form of ammonia, is a major impediment to the initiation and progression of **dental caries.** There is also indirect evidence to support that ammonia production impacts calculus deposition by promoting mineral precipitation, and it may also exacerbate periodontal diseases by impairing the function of normal host immune and repair processes. There are two major sources of ammonia in the mouth: urea and arginine, which are hydrolyzed by ureases and the arginine deiminase system (ADS) of oral bacteria, respectively. During the previous funding periods, substantial insight was gained about the molecular architecture, genetic regulation, the role of ureases of oral bacteria in physiologic homeostasis and the importance of alkali generation in caries inhibition. This proposal builds on our previous studies with the ureases of oral bacteria, focusing on two fundamental areas directly related to the molecular biology, physiology and role in oral diseases of ammonia production. The first continues the studies we have developed during the previous funding periods on the molecular biology of urea catabolism by oral microorganisms and the second goal is to thoroughly characterize the arginine

deiminase systems (ADS) of two oral streptococci. To accomplish our goals, we have organized the project under two specific aims: Aim 1. Continued analysis of the genetics, physiology and role in oral ecology and disease of bacterial ureases focusing primarily i) on the pH- and carbohydrate-dependent expression of the urease of Streptococcus salivarius, but also ii) on the utility of recombinant, urease-producing bacteria in inhibition of **dental caries** and iii) on factors that may affect the ability of oral microorganisms to carry out ureolysis in the human oral cavity. Aim 2. Molecular analysis of the arginine deiminase system of Streptococcus gordinii and Streptococcus rattus focusing i) on the cis- and trans-acting factors governing induction by arginine, and repression by glucose or oxygen, ii) analysis of the role of the ADS in inhibition of the initiation and progression of **dental caries** using of ADS-deficient mutants of S. gordonii and S. rattus, or recombinant, arginolytic S. mutans, and iii) physiological analysis of arginine transport and analysis of the effects of fluoride on alkali-generation via the ADS. This research will provide insights into new ways to control caries and other oral infectious diseases by manipulating the capacity or oral microorganisms to produce ammonia and to modulate the pH of oral biofilms.

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- **Project Title: MOLECULAR DYNAMICS IN CLASS II COMPOSITE RESTORATIONS**

  Principal Investigator & Institution: Bohaty, Brenda S.; Pediatric Dentistry; University of Missouri Kansas City Kansas City, Mo 64110

  Timing: Fiscal Year 2002; Project Start 15-MAR-2002; Project End 28-FEB-2007

  Summary: (provided by applicant) The goal of the Mentored Patient-Oriented Research Career Development Award (K23) is to facilitate training clinical practitioners in the area of patient-oriented clinical research. The application is separated into didactic and research components. The didactic component will provide education experiences that include introductory, specialty, and integrative courses. The combination of these courses will allow the candidate to develop independence and confidence in her ability to apply the scientific method. The research component will provide the candidate an opportunity to work closely with experienced clinical and basic science investigators. The research project combines 1) in vivo evaluations of Class II composite restorations placed in pediatric patients with 2) in vitro chemical, mechanical, and morphologic analyses of these restorations following exfoliation of the treated teeth. The candidate will develop a unique database that includes for each composite restoration clinical features e.g. surface staining, marginal integrity, recurrent caries, etc. The candidate working with her mentors will complete chemical, mechanical and morphologic characterization on the exfoliated samples, paying particular attention to breakdown at the composite/tooth interface. The juxtaposition of these analyses will provide critical, new data on changes within the composite material and/or at the material/tooth interface during function in the pediatric dental patient. The overall hypotheses of this project are that the clinical performance of Class II composite restorations placed in primary molars depends on the development of an impervious seal at the gingival margin and that a pre-treatment regimen that provides complete adhesive resin encapsulation of the treated dentin will result in a superior bond at these sites of the preparation. The specific aims will test the following hypotheses: in comparison to dentin pre-treatment regimen that acid-etches the dentin separately, self-etching adhesive will provide 1) improved bonding at the gingival margin of Class II composite restorations placed in primary molars, in vivo; 2) superior clinical performance at the gingival margin of Class II composite restorations placed in primary molars for up to 36

months in vivo; 3)enhanced infiltration of the dentin at the gingival margin of Class II composite restorations (in recovered specimens) as measured by Raman chemical imaging of the dentin/hybrid/adhesive/composite (d/h/a/c)interface; 4) greater modulus of elasticity with the dentin at the gingival margin as measured by scanning acoustic microscopy; 5) enhanced structural integrity at the d/h/a/c interface at the gingival margin.

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- **Project Title: MOLECULAR EPIDEMIOLOGICAL APPROACH TO DETERMINE S.MUTANS**

  Principal Investigator & Institution: Li, Yihong; Assistant Professor; Basic Science and Craniofacial Biology; New York University 15 Washington Place New York, Ny 10003

  Timing: Fiscal Year 2004; Project Start 01-JUL-2004; Project End 30-APR-2006

  Summary: (provided by applicant): **Dental caries** is the single most common chronic childhood disease. Each year, more than 51 million school hours are lost due to dental-related illness and over $40 billion is spent on the treatment of this disease. Epidemiological and clinical studies have suggested that mutans streptococci, particularly Streptococcus mutans, are the major microbial pathogens associated with **dental caries.** The most commonly used technique to identify S. mutans is cultivation on selective media. The major limitations of the method include inadequate detection of S. mutans in saliva particularly when S. mutans is present at low levels; morphology varies depending upon the medium used; and it is costly and labor-intensive. To date, the most reliable technique to rapidly and specifically identify bacterial species is PCR. But for S. mutans, the lack of species-specific probes and primers continues to limit high-throughput research on prevalence and colonization of S. mutans. Therefore, the objective of this project is to develop highly sensitive and species-specific probes and primers that can be used in PCR-based assays to rapidly, accurately, and effectively identify S. mutans in clinical oral specimens. Our goal will be accomplished by pursuing the following specific aims. (1) To identify potentially unique sequences in S. mutans genome that will enable us to develop species-specific probes and primers for the detection of S. mutans in the clinical specimens. (2) To validate the probes and to demonstrate the high sensitivity and specificity of the species-specific probes and primers. (3) To compare the species-specific probes and primers with the conventional culture method. From these experiments, we should be able to obtain well-defined S. mutans-specific probes and primers and to prove the superiority of the newly developed probes to the findings obtained from the culture method. The new molecular markers will enable us to conduct molecular epidemiological studies of S. mutans infection and high-throughput research so that we can improve our understanding of the polymicrobial etiology of **dental caries,** ascertain a child's risk potential prior to disease development, and evaluate the effectiveness of caries interventions. Application of the new molecular tools will have a substantial impact on improving the oral health of children.

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- **Project Title: MOLECULAR EPIDEMIOLOGY OF DENTAL CARIES SUSCEPTIBILITY**

  Principal Investigator & Institution: Slayton, Rebecca L.; Pediatric Dentistry; Oregon Health & Science University Portland, or 972393098

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 31-AUG-2004

Summary: (provided by applicant): **Dental caries** is one of the most common diseases of childhood. It occurs in children of all socioeconomic classes and in every country around the world. In the United States, there is disparity in caries prevalence such that 80% of the caries occur in 20% of the children, primarily minority children or those from low income families. Although there is clear evidence that **dental caries** is a multifactorial infectious disease with many environmental contributory factors, there is also strong evidence for a host genetic component in the etiology of this disease. Currently, the most reliable predictor of a child's future risk for caries is the presence of one or more carious teeth. Other environmental factors contribute to this risk but do not provide the level of specificity needed for the targeting of effective preventive measures. The objective of this application is to screen candidate genes to identify sequence polymorphisms that occur more frequently in subjects with **dental caries** than in those without caries. A secondary objective is to initiate the collection of families with multiple affected children to be used for a genome scan in a future application. The central hypothesis of the application is that sequence variations in one or more candidate genes, combined with environmental factors, can be used to predict caries risk prior to the occurrence of disease. Two hundred affected children aged 3 to 4 years and age and race matched controls will be ascertained from Iowa for linkage disequilibrium studies. Families with multiple affected siblings will be ascertained whenever possible. Candidate genes will include genes involved in enamel mineralization and in salivary buffering. Collection of families will be done to facilitate future genome wide scans for caries susceptibility loci. Identification of genetic markers for **dental caries** will provide us with a better understanding of the caries process on an individual basis, a more reliable method to assess caries risk and will facilitate the development of targeted preventive strategies.

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- **Project Title: MOLECULAR GENETIC ANALYSIS OF S. MUTANS CARIOGENICITY**

  Principal Investigator & Institution: Kuramitsu, Howard K.; Professor; Oral Biology; State University of New York at Buffalo Suite 211 Ub Commons Buffalo, Ny 14228

  Timing: Fiscal Year 2002; Project Start 01-SEP-1978; Project End 30-JUN-2005

  Summary: This application will focus on characterizing essential genes in Streptococcus mutans involved in plaque formation and growth. Utilizing model in vitro systems, genes essential for biofilm formation will be identified and characterized following insertion duplication mutagenisis of S. mutans GS5. In addition, two genes recently identified in our laboratory as important for this process, comB and sgp, will be further analyzed as to their respective roles in biofilm formation. Potential signal transduction mechanisms involving both genes will be investigated using gene expression techniques in addition, the role of the com system in inraspecies quorum sensing relative to gene transfer and biofilm formation will be assessed. A novel approach developed in this laboratory to identify essential genes in any transformable microorganism will be utilized to identify such genes in S. mutans this approach, based upon antisense RNA induction, has the potential of identifying target sites for the development of specificanticaries agents. In addition, this approach can be readily used to identify essential genes in ubiquitous bacteria for development of broad- spectrum antibacterial agents. The specific aims of this proposal are designed to provide new information regarding essential virulence factors of S. mutans which could be exploited to design novel anticaries strategies.

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- **Project Title: MOLECULAR/MECHANICAL IMAGING OF DENTIN BONDING SUBSTRATE**

  Principal Investigator & Institution: Wang, Yong; Oral Biology; University of Missouri Kansas City Kansas City, Mo 64110

  Timing: Fiscal Year 2003; Project Start 01-AUG-2003; Project End 31-MAY-2008

  Summary: (provided by applicant): The candidate for the proposed "Mentored Quantitative Research Career Award" has multidisciplinary training and research experience in polymer chemistry and materials science. His expertise in the field of polymer chemistry, material science and vibrational spectroscopy has placed him in a unique position to apply this strong knowledge base to the area of biomaterials and biomedical/tissue engineering. The program outlined in this career development application adds a biological/clinical foundation to the candidate's background. The candidate will build his research knowledge, experience and understanding of the biological aspects of oral tissue development, disease processes involving oral and craniofacial tissues, and molecular biologic techniques through a multidisciplinary program that combines education, mentoring and completion of an innovative research study. The candidate's long-term goal is to establish himself as a productive, independent research scientist in biomaterials/tissue engineering with a specific focus on the development of replacement materials for oral and craniofacial tissues. Research activities will be completed in the newly created Center for Research in Interfacial Structure and Properties at the UMKC School of Dentistry. A fundamental goal of the Center, which is under the direction of the candidate's mentors: Drs. Paulette Spencer and J. Lawrence Katz, is to provide a research environment that serves as a catalyst for collaborative investigations focused on applying the principles of biological systems to the hierarchal design, synthesis and application of biomaterials. The candidate proposes to use novel high-resolution analytical techniques for direct in situ detection of the molecular structure and micro-mechanics of the bond formed at the adhesive interface with caries-affected dentin and sclerotic dentin. The work will identify the structure/property characteristics that inhibit the formation of a durable bond at the adhesive interface with these clinically relevant dentin substrates. Results from this work will provide critical, new insight into failure mechanisms at the dentin/adhesive interface; failure that can ultimately lead to premature breakdown of the composite restoration.

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- **Project Title: MULTIVARIATE EXAMINATION OF CARIES RISK ASSESSMENT**

  Principal Investigator & Institution: Perrin, Nancy A.; Kaiser Foundation Research Institute 1800 Harrison St, 16Th Fl Oakland, Ca 946123433

  Timing: Fiscal Year 2002; Project Start 30-SEP-2002; Project End 29-SEP-2004

  Summary: (provided by applicant): This project uses structural equation modeling to examine the predictive validity of dentists' caries risk assessments and tests the congruence between patients' caries risk classifications and the caries preventive treatment they receive. The provision of caries preventive treatment linked to a patient's individually determined level of risk for the development of new lesions is increasingly being advocated as the standard of care for caries management. However, the predictive validity of dentists' assessment of caries risk, the degree to which patients with elevated risk classifications receive appropriate preventive treatment, and the effectiveness of preventive methods in patients with elevated risk have not been fully evaluated. These interrelated questions require a longitudinal multivariate approach. The proposed

evaluation uses existing data from two staff model dental HMOs that have applied the risk-based management approach for several years to investigate the validity of caries risk assessment and the impact of subsequent treatment.

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- **Project Title: NOVEL ANTIMICROBIALS: SALIVARY MUC7 PEPTIDES**

  Principal Investigator & Institution: Bobek, Libuse A.; Professor of Oral Biology; Oral Biology; State University of New York at Buffalo Suite 211 Ub Commons Buffalo, Ny 14228

  Timing: Fiscal Year 2004; Project Start 15-MAR-1992; Project End 31-AUG-2008

  Summary: With the emergence of pathogens resistant to conventional antimicrobials, and toxicity of some antimycotics, there is an urgent need for development of new agents with novel mechanisms of action. One promising source is cationic antimicrobial peptides. We have discovered that human salivary mucin MUC7 peptides (derived from the N-terminus) possess significant and broad-spectrum antimicrobial activity m vitro. These cationic peptides are effective against a variety of fungi (e.g., C. albicans and C. neoformans, organisms responsible for the common opportunistic infections in immunocompromised patients, particularly those with HIV/AIDS), and both Gram-positive and negative bacteria (e.g. S. mutans, implicated in **Dental caries** and P. gingivalis, implicated in periodontal diseases). MUC7 20-mer and 12-mer retain considerable candidacidal activity in physiological-like conditions found in the oral cavity. The 12-mer in combination with histatin-5-12-mer or amphotericin-B acts in a synergistic or additive manner against C. albicans and C. neoformans. A newest addition, 12-mer-D isomer exhibits more potent candidacidal activity in high-ionic strength buffers and in saliva, and is less hemolytic than the 12-mer-L (natural form). These finding support and strengthen our hypothesis that these novel peptides are indeed suitable candidates for therapeutic and preventive antimicrobials. Further, that they will show little or no toxicity toward mammalian cells and will have low tendency to elicit resistance. The work proposed in this application will further evaluate the MUC7 peptide potential as therapeutic agents in vitro and m vivo, and continue to examine their mechanism of action. In Specific Aim 1, MUC7 12-mer peptide antimicrobial activity will be examined in detail, including in combination with other antimicrobial agents. In Specific Aim 2, we will address the mechanism of MUC7 peptide action, including intracellular target(s), potential binding to nucleic acid, inhibition of protein and nucleic acid synthesis, and the effect of MUC7 peptide on C. albicans and S. cerevisiae by gene expression profiling. Specific Aim 3 will address the formulation and in vitro testing of biodegradable polymeric and/or hydrogel polymeric delivery systems for these peptides. In Specific Aim 4, we will test the efficacy of the specifically design delivery systems against fungal infections in vivo models. Altogether, these efforts attempt to move the MUC7 peptides toward the long-range goal of clinical application.

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- **Project Title: NOVEL BIOACTIVE GLASS DENTIFRICE FORMULATIONS**

  Principal Investigator & Institution: Greenspan, David C.; Usbiomaterials Corporation 1 Progress Blvd, #23 Alachua, Fl 32615

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 15-MAY-2003

  Summary: (provided by applicant): The Long-term goal of this research is to develop novel dentifrice formulations containing bioactive glasses that will replace or be an

adjuvant to fluoride as an anti-cares agent. The initial focus of the research will be to develop reduced fluoride formulations which have equivalent or superior anti-caries efficacy to commercially available formulation. These formulations will be beneficial to the general population and to segments of the population where the potential benefits of using a standard fluoride dentifrice formulation is reduced. Bioactive glasses have been successfully used clinically as a bone grafting material for over fifteen years. Recently it has been documented that fine particulate bioactive glasses incorporated into an aqueous dentifrice have demonstrated an ability to clinically reduce tooth hypersensitivity through the occlusion of dentinal tubules. In vitro studies have demonstrated significant occlusions and remineralization of prepared bovine dentin and remineralization of precarious surface lesions. Other in vitro studies have demonstrated significant anti-microbial effect towards caries pathogens. The Specific Aims of this Phase I application are to: 1) test single phase anhydrous and dual phase aqueous dentifrice formulations to characterize their efficacy, 2) conduct accelerated stability testing of the most promising formulations, 3) test selected formulations from Aim 2 for anti-microbial activity and, 4) evaluate them using established in vitro subsurface caries models to predict in vivo efficacy.

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- **Project Title: NOVEL NANO CALCIUM PHOSPHATE FOR PULP GENE DELIVERY**

  Principal Investigator & Institution: Sfeir, Charles S.; Assistant Professor; Oral Medicine and Pathology; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2004; Project Start 01-FEB-2004; Project End 31-JAN-2006

  Summary: (provided by applicant): Gene therapy holds promise for treatment of a variety of diseases. However, transfer techniques using biological vectors is not without serious problems. Therefore, gene delivery using non-viral approach is highly preferable due to convenience of delivery, ease of manufacturing, cost effectiveness, and biocompatibility. However, these techniques are limited by low transfection efficiency. To address this problem, we have developed nano-sized calcium phosphate particles, NanoCaPs, as a novel delivery system for plasmid DNA transfection. We hypothesize that NanoCaPs will serve as a superior transfection system because the reduced crystalline dimensions will result in increased surface-active DNA binding and greater cellular uptake and enhanced transfection efficiency. This elegant non-viral gene delivery system could be used alone or incorporated into synthetic or natural polymers to deliver genes in a sustained manner. To prove our hypothesis we propose to synthesize NanoCaPs incorporated in a biodegradable fibrin matrix to enhance both the in vitro and in vivo transfection efficiency of plasmid DNA (pDNA). This technology will increase the uptake and expression of marker genes (luciferase and/or beta-galactosidase) as well as therapeutic transfectents. A dentin regenerative therapy model will be used to locally administer plasmid DNA vectors encoding rat bone morphogenetic protein-7 (BMP-7) in a composite nano-sized calcium phosphate carrier matrix to enhance dentin regeneration. Our preliminary in vitro and in vivo data is in excellent agreement with our objective to design and develop this efficient plasmid gene therapy system. These results suggest the potential successful application of our approach for dentin regeneration. The present study will provide a concrete foundation for conducting further applied and basic science research related to dentin plasmid gene therapy and will also provide a model to study the biology for dentin repair and regeneration. The specific aims have been formulated to provide solutions to fundamental questions related to in vitro and in vivo pDNA transfection efficiency and

the specific application of the pDNA bound NanoCaPs embedded in a fibrin matrix for dentin therapy thus providing key information currently missing.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ORAL HEALTH DISPARITIES IN THE FIRST 4 DECADES OF LIFE**

  Principal Investigator & Institution: Thomson, William M.; Associate Professor & Division Head; University of Otago Leith St Dunedin,

  Timing: Fiscal Year 2004; Project Start 01-JAN-2004; Project End 30-NOV-2007

  Summary: (provided by applicant): Objective: The proposed research aims to use a life-course approach to develop a better understanding of the interplay of biological, environmental and behavioral determinants and antecedents of oral conditions from childhood to oral health by elucidating the nature, scale, persistence and potential mutability of oral health disparities in a population-based cohort of adults. Methods: The Dunedin Study has traced the development of a representative 1972 birth cohort of 1,000 New Zealand men and women at birth and ages 3, 5, 7, 9, 11, 13, 15, 18, 21 and 26. New data will be gathered at age 31, enabling analysis of oral health disparities data from childhood to age 31. The research will: (1) document the natural history of oral conditions through to the 4th decade of life; (2) examine the influence of earlier SES (and SES transitions) on adult oral health; (3) using periodontal disease as a model, test hypotheses about gene-environment interactions in the origins of poor adult oral health; and (4) determine the extent to which poor oral health is an important contributor to (a) poor physical health and (b) experience of adverse life outcomes by the 4th decade of life. The planned research will provide unique information on the scale, persistence and potential mutability of disparities in oral health through the first four decades of life, and will assist in identifying those clinical, public health and policy interventions, which are likely to be most appropriate and efficacious in reducing oral health disparities. The Dunedin Study offers a unique opportunity to conduct such an investigation because of the comprehensive data archive, which has already been assembled. Implications: The persistence of oral health disparities has not been investigated through the entire life course to date, and close examination of the degree to which the Dunedin cohort's early-life disparities in oral health persist into adulthood would be invaluable in determining whether (and to what extent) such inequalities can be reduced by clinical, public health or policy interventions. The outcome of this important work will inform and determine the nature of measures which are taken to reduce oral health disparities.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: ORAL HEALTH OF OLDER TYPE 1 DIABETIC PATIENTS**

  Principal Investigator & Institution: Moore, Paul A.; Professor and Institute Director; Dental Public Health; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 01-SEP-2001; Project End 30-JUN-2004

  Summary: (provided by applicant): This revised grant submission describes a collaborative follow-up study of the oral health complications of Type 1 diabetes and the potential interrelationships between diabetes complications and oral diseases. This revision includes progress since the March 2000 submission and responses to study section's concerns and recommendations (INTRODUCTION: Response to Study Section). Since 1985, the NIH supported Epidemiology of Diabetes Complication Study (EDC) at the University of Pittsburgh Graduate School of Public Health (R0l-DK34818; TJ Orchard, PI) has been evaluating the medical complications of type 1 juvenile onset

diabetes mellitus. In 1991, the Oral Health Science Institute (OHSI) of the School of Dental Medicine initiated a collaboration with the EDC to perform a comprehensive oral health examination of these patients (NIH-NIDR-l-91-R4; PA Moore, PI). The demographics, oral physiology and health behaviors of this unique population were characterized and the point prevalence rates for tooth loss, edentulism, periodontal disease, **dental caries,** soft tissue pathologies, salivary functions and Candida infections have been published. Analyses of associations between oral diseases and diabetic complications (nephropathy, neuropathy, retinopathy, vascular disease) within this insulin dependent population have also been completed. Advanced age, disease duration, glycemic control and smoking appear to be significant factors in many of the analyses performed to date and our initial results suggest that the oral health complications associated with Type 1 diabetes are likely to become even more clinically significant as the age of these patients increases. The ability to continue our collaboration with the EDC and collect longitudinal oral health data is an extraordinary opportunity. Our plan for this NIDCR resubmission is to continue our collaboration with the EDC by providing a second oral health examination of this unique population. The goals of this follow-up oral health evaluation are: 1) to determine the prevalence, incidence and disease progression rates for tooth loss, periodontal disease, coronal and root caries, soft tissue pathologies, salivary dysfunctions and oral health behaviors of this type 1 diabetic cohort, and 2) to assess the interrelationships between oral health complications and systemic diabetic complications to evaluate possible mechanisms for these interrelationships and to develop strategies for control and prevention. This overall plan will permit us to understand the etiology of these complications and to define specific subpopulations and risk factors appropriate for future prospective oral health prevention and intervention trials.

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- **Project Title: ORAL IMMUNOLOGY/MICROBIOLOGY ANNUAL MEETING**

  Principal Investigator & Institution: Fine, Daniel H.; Professor and Chair; Oral Biology; Univ of Med/Dent Nj Newark Newark, Nj 07107

  Timing: Fiscal Year 2003; Project Start 01-DEC-2002; Project End 30-NOV-2003

  Summary: (provided by applicant): The Oral Immunology/Microbiology Research Group was founded in 1991 as a means of promoting collegial interaction and collaboration among individuals interested in the immunology and microbiology of the oral cavity, particularly as related to oral disease (dental caries and periodontal disease). Formed in response to a general perception that large meetings such as the IADR/AADR General Sessions do not provide a forum suitable for intimate discourse and collaboration, the OIMRG is comprised of more than seventy investigators representing thirty-nine universities, research centers, and commercial organizations in the U.S. and abroad. Once each year the group convenes for an annual meeting, which consists of three scientific sessions, each focusing upon a distinct area of oral immunology and microbiology. It is primarily, but not exclusively, through the annual meeting that the objectives of the Oral Immunology/Microbiology Research Group are achieved. These objectives include the following: 1. To foster interaction and collaboration among scientists interested in oral immunology and microbiology. 2. To promote information exchange and collaboration between academicians and their colleagues in the private sector who are engaged in basic and clinical studies pertaining to oral health and disease. 3. To provide a forum through which new investigators entering the fields of oral immunology/microbiology can begin to "network" with more established investigators and to establish contact with representatives of federal and

non-federal agencies which may be a potential source of funding for future studies. The 13th annual meeting of the Oral ImmunologylMicrobiology Research Group has been scheduled for January 9-12, 2003, at the Longboat Key Hilton in Longboat Key, FL Session topics will include: a) host responses to oral bacteria, b) mechanisms of microbial pathogenesis employed by oral bacteria, and c) mechanisms of host mediated injury to oral tissues. Two guest lecturers will be invited, one discussing a topic related to the broad area of host immunity, the other pertaining to bacterial virulence factors. Perpetuation of the OIMRG and its annual meetings greatly enhances the spirit of collegial interaction/collaboration among investigators with expertise in immunology and microbial pathogenesis as related to oral health and disease.

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- **Project Title: PREVENT TRANSMIS OF MUTANS STREPTOC FR MOTHER TO CHILD**

  Principal Investigator & Institution: Bretz, Walter A.; Assistant Professor; Dental Public Health; University of Pittsburgh at Pittsburgh 350 Thackeray Hall Pittsburgh, Pa 15260

  Timing: Fiscal Year 2002; Project Start 15-SEP-2000; Project End 30-JUN-2005

  Summary: Dental decay is the most prevalent affliction in children worldwide. In recent years the occurrence of dental decay has declined dramatically in many industrialized countries subsequent to the wide spread availability of fluoride in the water supply and dentifrices. However, in newly industrialized countries such as Brazil, the occurrence of decay is still high, especially among lower income groups. The mutans streptococci (MS) have been convincingly associated with human dental decay, and clinical protocols which seek to reduce the levels of the MS invariably result in a significant reduction in decay. One of the most important observations from these studies is the possibility that decay and the establishment of MS can be reduced and/or prevented in young children by treating those mothers who are highly infected with MS prior to the eruption of the primary teeth. Other studies indicate that if the primary teeth are not colonized by the MS in the first year after their eruption, they are likely to remain caries free, during the following years. These findings indicate that dental decay may be prevented by delaying the colonization of the MS in primary dentition. The ideal population for such a study could be found in communities without water fluoridation, with a high level of unmet dental care, and who would have frequent access to sugar. Populations in many newly industrialized countries would meet these qualifications. However, it is difficult to perform an interceptive study, such as preventing the transmission of the MS from mother to infant in such countries, as the local dental community has neither the financial and physical resources nor the trained dental personnel. We have found an exception to this in the city of Bauru, Sao Paulo, Brazil. This community of 250,000 residents is situated in the sugar cane growing region of Brazil and boasts the leading dental school in South and Central America. In the investigation to be described, we will collaborate with the Bauru investigators in a longitudinal randomized clinical trial with the following specific aims: 1) to determine whether the salivary levels of the MS can be reduced in mothers of young infants by an intervention program which may include restorative procedures, topical fluorides, the use of xylitol chewing gum, and chlorhexidine varnishes; 2) to determine whether this intervention reduces or delays the acquisition of MS in the infants and whether this in turn reduces the subsequent caries incidence in children.

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- **Project Title: PREVENTION OF DENTAL CARIES**

  Principal Investigator & Institution: Takagi, Shozo; American Dental Association Foundation Chicago, Il 60611

  Timing: Fiscal Year 2003; Project Start 01-JUL-1978; Project End 31-MAY-2006

  Summary: New treatments are proposed to induce the deposition of "cariostatic" concentrations of fluoride (F), calcium (Ca), and phosphate (P) in oral substrates. Their "anti-caries" potential will be evaluated using well established in situ Demineralization-Remineralization (Demin/Remin) models to prepare them for future clinical trials: 1) A Fluoridating Gel for Pits and Fissures. A new gel system for increasing "tooth-bound" F in pits and fissures will be compared to an APF gel in an in situ Demin/Remin model. 2) Calcium and Phosphate Releasing Chewing Gum. Gums containing separate Ca and P sources will be evaluated for their ability to deposit a substantive bioavailable Ca-P reservoir in plaque. These gums will then be evaluated in the in situ Demin/Remin model. 3) Controlled Calcium Release Fluoride Rinses and Dentifrices. The previously developed controlled F-release type rinses were more effective in an in situ Demin/Remin model than a NaF rinses due to their enhanced deposition of bioavailable F as CaF2. Nevertheless, interferences from "nonactive" mouthrinse/dentifrice ingredients, and problems in formulating low-F rinses were encountered. A solid/liquid rinse is proposed that maximizes oral CaF2 deposition by controlling Ca release into in a NaF solution. These Ca-release type rinses are less subject to interferences and more suitable for formulating potent Iow-F rinses and dentifrices. Part 1 of this study, seeks basic information on kinetics of CaF2 formation and deposition needed to formulate prototype Ca-release mouthrinses/dentifrices. Part 2 formulates prototype 12, 6 and 3 mM F Ca-release mouthrinses and dentifrices. These mouthrinses and dentifrices will be evaluated in vivo and in situ using the Demin/Remin model. These treatments are inexpensive, compatible with existing procedures and, potentially, very effective. They provide an increased "anti-caries" effect at a low total F exposure. Thus, these treatments should have a strong impact on public health. Moreover, the information on the "cariostatic" effects of "tooth-bound" F or Ca and P supplements and the knowledge of bioavailable F deposition in the oral environment, should be valuable for the future development of "anti-caries" treatments and strategies.

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- **Project Title: PREVENTION OF EARLY CHILDHOOD CARIES IN MEDICAL PRACTICE**

  Principal Investigator & Institution: Rozier, Richard G.; Professor; Health Policy and Administration; University of North Carolina Chapel Hill Aob 104 Airport Drive Cb#1350 Chapel Hill, Nc 27599

  Timing: Fiscal Year 2002; Project Start 15-AUG-2001; Project End 30-JUN-2006

  Summary: The purpose of this research is to evaluate an already funded and ongoing intervention to prevent early childhood caries (ECC) in children of low-income families. The intervention began in 10 North Carolina counties in Jan 2000. Pediatricians and nurses are providing preventive dental services, including screening and fluoride varnish applications for infants and toddlers up to 36 months of age, and health education for their primary caregivers. Community coordinators help ensure the fist visit at 9 months of age and at six-month intervals thereafter. The quasi-experimental design will use information from 10 matched counties for comparison. The evaluation consists of three separate studies designed to determine the impact of the intervention on ECC outcomes. In the first study, short-term effectiveness of the intervention will be

determined by comparing the prevalence and severity of noncavitated and cavitated carious lesions in 900 3-year-olds, who began the intervention at 9 months of age, with children from the control group. Historical controls from the intervention and comparison counties will account for secular trends in ECC. An interview of caregivers will provide control variables and secondary outcomes, including knowledge, behaviors and quality of life. The second study will determine carryover effects of the intervention on ECC in children 5 years of age, two years after their participation in the intervention ends. Its justification is the need to know if results from early, medical-based interventions continue after children are no longer eligible and before they enroll in school-based preventive dentistry programs. Caries increments derived from public health surveillance of kindergarten students, which includes 95 percent of the 8,000 students in the 20 study counties, will be compared for intervention and control children who were observed in the first study, as well as concurrent controls and historical controls from 4 years before. Interactions between the medical-based interventions and preventive services provided by dentists will be tested using Medicaid and CHIP dental claims. The third study will determine the effects of the ECC interventions for 1- and 2-year-olds on cumulative caries-related (CR) treatment and costs of dental services provided by the Medicaid and CHIP programs through 3 and 4 years of age. The likelihood of hospital use will be analyzed separately from total CR treatment and costs because of its expense. Most analyses will focus on whether net intervention costs (community outreach and provider reimbursements) are offset by reductions in CR treatment costs. We will do a limited assessment of the cost pe oral health- related quality of life.

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- **Project Title: PRIMARY CARE PROVIDER AND PREVENTIVE ORAL HEALTH**

  Principal Investigator & Institution: Lewis, Charlotte; Route 1, Box 216; Pediatrics; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 31-JUL-2006

  Summary: This K23 proposal is from a pediatric physician who has a history of a strong interest in oral health in children, and the development of the pediatrician as a positive force in assuring that appropriate attention is paid to oral health in young children. Poor and minority children are disproportionately affected by **dental caries** and are more likely to have difficulty accessing dental care. Low-income children may have more secure access to regular visits with Primary Care Health Providers (PCHPs). Using the PRECEDE-PROCEED model as a planning framework, this proposal aims to assess the feasibility of a health care model in which PCHPs are substantially involved in oral health. Five interrelated projects seek to determine how PCHPs can successfully expand their scope of practice to include preventive oral health from the provider, practice, and patient-parent perspective. Analysis of Washington State Medicaid claims data will be performed to measure the degree to which PCHPs have unique opportunities to provide preventive oral health counseling and care to their low-income patients who otherwise are not accessing dental care. The final project will be a randomized trial using a pretest-posttest design. The PCHP practices will be randomly selected to participate in an expanded oral health preventive package. Control practices will receive limited intervention. The number of claims submitted to Medicaid for fluoride varnish application, as an indicator of expanded PCHP involvement in preventive oral health, will be compared between treatment and control practices. At the completion of these projects, it is expected to have developed a rich model whereby PCHPs may expand their involvement in preventive oral health as a means to improve access to preventive

dental care for underserved and other vulnerable groups of children. In addition, this career development award is expected to provide to Dr. Lewis the didactic and experiential training necessary to become an independent clinical investigator focusing on pediatric and dental health services research.

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- **Project Title: QUANTITATION OF ENAMEL DEMINERALIZATION MECHANISMS**

  Principal Investigator & Institution: Higuchi, William I.; Professor; Pharmaceutics and Pharmaceutl Chem; University of Utah Salt Lake City, Ut 84102

  Timing: Fiscal Year 2002; Project Start 01-NOV-1982; Project End 31-JAN-2006

  Summary: (Adapted from the Investigator's Abstract): The long term objectives of the proposed research are to gain a better understanding of the mechanisms of **dental caries** and to provide rational bases for improved preventive or therapeutic regimens. The Principal Investigator proposes to do basic studies of the anomalous solubility behavior of carbonated apatites (CAPs) and human dental enamel (HE) with the general objective of establishing how the solubility depends on the composition of the mineral phase, the crystallinity of the mineral phase, an the composition of the external dissolution medium. The studies will rely heavily on the metastable equilibrium solubility (MES) distribution paradigm and the surface complex hypothesis developed just prior to the beginning of the past project period. The MES and the surface complex concepts have dictated entirely new approaches to both experimental design and data interpretation and have provided the framework for understanding the interrelationship between mineral composition, mineral crystallinity, solution composition and the observed solubility of biominerals and synthetic apatites. There are four specific aims. Aim 1 proposes studies to establish for the CAPs the quantitative relationships between the magnitude of the MES, the CAP crystallinity (especially crystallite microstrain), and carbonate content, and the stoichiometry of the MES governing surface complex. In Aim 2, studies are proposed to quantitatively establish the influence of solution foreign ions (strontium and fluoride) on the magnitude of the MES and the stoichiometry of the MES governing surface complex. In Aim 3, studies are proposed to quantitatively establish the possible crystal lattice effects of these foreign ions on the magnitude of the MES. Aim 4 proposes to establish the relevance of the findings in the CAP studies (above) to the solubility behavior of HE. Two major experimental breakthroughs of the past project period make it possible for accomplishing these aims. The first of these is a procedure of relatively high accuracy for deducing the dissolution driving force function (and therefore the stoichiometry of the MES governing surface complete) from analysis of the MES distribution data obtained as a function of several independent variables (e.g., buffer pH, solution common ions, and solution foreign ions). The other is a procedure for separating and quantifying the contributions of crystallite size and microstrain to CAP crystallinity using X-ray diffraction data and the Rietveld method of whole-pattern-fitting structure-refinement. Taken together, these two methods permit addressing the questions associated with each of the Specific Aims.

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- **Project Title: REGULATION AND CONTROL OF MINERALIZATION IN TEETH**

  Principal Investigator & Institution: Margolis, Henry C.; Head, Department of Biomineralization; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2003; Project Start 01-APR-2003; Project End 31-MAR-2008

Summary: (provided by applicant): The proposed studies are designed to improve our understanding of how biomimetic approaches can be used to remineralize carious enamel and properly restore normal tooth enamel structure and properties. Our working hypothesis is that the restoration or regeneration of proper tooth structure and function can be achieved through the regulation of mineral ion diffusion, crystal growth kinetics and crystal orientation. Studies will be guided by a working mathematical model that will be developed to describe the dynamics and interrelationships of these key events, based on experimental data generated using a novel chemical approach to remineralize in vivo-like incipient carious lesions. Using this model as a basis, novel biomimetic approaches to remineralize and regenerate tooth structures will be studied. The proposed biomimetic strategies are based on our current state of knowledge of how mineral deposition and organization are regulated in developing mineralized tissues. Given the high prevalence of **dental caries,** there is a tremendous need for restorative procedures that are superior to those presently available. The long-term goal of these studies is to develop new procedures to regenerate normal tooth structure and function. In general, these studies consider the importance of ion diffusion and driving forces for dissolution and precipitation in human enamel, along with the role of synthetic and biologically relevant molecules that regulate the rate and shape of growing enamel mineral crystals. Specifically, we propose: 1. To determine the mechanism and potential effectiveness of novel acidic remineralizing solutions in vitro; 2. To determine the mechanism and remineralization effectiveness of supersaturated calcium phosphate solutions that are stabilized by selected salivary proteins and peptides; 3.To determine the remineralization effectiveness of novel supersaturated calcium phosphate solutions that are stabilized by pyrophosphate, where remineralization kinetics are regulated by added phosphatases; 4.To develop an in vitro system to study the remineralization of enamel fissure lesions using microradiography, polarized light microscopy and X-ray microtomography; and 5. To determine the possible role of stabilized amorphous calcium phosphate (ACP) as a precursor for the epitaxial growth of mature enamel crystals, with particular attention on the remineralization and regeneration of carious enamel fissure tissue.

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- **Project Title: REGULATION OF GTF GENE EXPRESSION IN S MUTANS**

  Principal Investigator & Institution: Goodman, Steven D.; Basic Sciences; University of Southern California 2250 Alcazar Street, Csc-219 Los Angeles, Ca 90033

  Timing: Fiscal Year 2002; Project Start 01-AUG-2001; Project End 30-JUN-2006

  Summary: Streptococcus mutans is a causative agent of **dental caries.** It's ability to inflict damage is strongly linked to the production of long chain glucose polymers (glucans) derived from dietary sucrose which allow the bacteria possesses a family of genes that express enzymes called glucosyltransferases (GTF). There are three GTFs in S. mutans. They share 50 percent sequence identity and are encoded by the homologous gtfB, gtfC and gtfD genes. The gtfB and gtfC gene are found in direct repeat with a mere 198 base paries separation between coding sequences. Although mutations in either gtfB or gtfC produce a colonizing deficient phenotype, little is known about their regulation. Until recently, the only effector known to regulate these genes was sucrose, the substrate of the GTFs. Supplemented sucrose transiently induces a 3-fold increase in a gtfB transcriptional fusion. Now we have demonstrated that both gtfB and gtfC show coordinated growth phase- dependent expression. For both genes, expression peaks prior to exponential growth and falls over 100-fold by early stationary phase. In this proposal, we intend to further study this phenomenon including identifying critical cis

and trans acting elements and through mutagenesis determine how these elements affect gtf gene expression. Since these gtf genes are involved in the colonization process, the genetic elements that are found here will need to be examined in terms of the bacteria's pathogenic mechanisms.

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- **Project Title: REGULATION OF IMMUNE RESPONSE IN THE ORAL CAVITY**

  Principal Investigator & Institution: Michalek, Suzanne M.; Professor; Microbiology; University of Alabama at Birmingham Uab Station Birmingham, Al 35294

  Timing: Fiscal Year 2002; Project Start 01-JUN-1988; Project End 31-MAY-2004

  Summary: Public awareness of emerging infectious diseases and that infectious diseases continue to be the leading cause of morbidity and mortality worldwide has fostered a need to develop better means for prevention and treatment. The evidence that most infectious agents cause disease by colonization of or penetration through mucosal surfaces has prompted novel vaccination strategies that would lead to increased protection of the mucosae as well as surfaces bathe by mucosal secretion, e.g., teeth. Secretory IgA antibodies in saliva are important in protection against oral diseases, including Streptococcus mutans-induced **dental caries,** and are induced following stimulation of the common mucosal immune system (CMIS). However, little information in known about the human CMIS, especially with respect to salivary IgA responses. The overall goals of this grant is to evaluate compartmentalization within the human CMIS, especially with respect to the salivary IgA response, and to develop a human caries vaccine. The purpose of the present studies is to establish the effectiveness of the intranasal (IN) route of immunization for inducing human salivary IgA responses protective against infection with S. mutans. Specifically, we will: 1) Determine the immunization regimen for the effective induction of human salivary IgA responses after IN immunization of S. mutans antigens and mucosal adjuvants. The recombinant (r) S. mutans antigens to be used are the saliva-binding region (SBR) of the adhesin AgI/II and the catalytic domain (CAT) and glucan-binding domain (GLU) of glucosyltransferase. The adjuvants to be used are the B subunit of cholera toxin (rCTB) and monophosphoryl lipid A (MPL). Adult volunteers will be used in this aspect of the study. The quality and quantity of antibody in saliva, nasal wash, and serum and of circulating antibody-secreting cells will be measured at various times up to 6 months after IN immunization with each antigen alone, antigen and an adjuvant, or a combination of antigens and an adjuvant. The oral microflora will be assessed for the number of S. mutans/total streptococci. These results should determine the effectiveness of IN immunization with S. mutans antigens in inducing salivary IgA responses, the usefulness of adjuvants in promoting the response, and whether the response was protective. 2) Determine the longevity of the human salivary IgA response after IN immunization and evaluate memory in the CMIS in terms of salivary IgA responses after subsequent IN immunization. The immune responses in serum and secretion from adult subjects used in aim 1) will be followed to evaluate the duration of the response. When the response wanes, these subjects will be boosted with the original vaccine and immunologic and microbiologic parameters will be measured to establish the effectiveness of the immunization regimen for inducing prolonged salivary responses and to learn more about memory in the human CMIS. 3) Determine the effect of age on human salivary IgA responses after IN immunization with S. mutans antigens and mucosal adjuvants. Since **dental caries** is a childhood disease, it is important to learn if the information we are obtaining in adults regarding the human CMIS also applies to children. In this portion of the study, children will be immunized by the IN

route with antigen alone or antigen with an adjuvant. By analysis over time of antibody activity in saliva, nasal wash, and serum, we will be able to define similarities/differences in the CMIS of children and adults. By monitoring the oral microflora, we will be able to tell if the induced response was effective in reducing the level of S. mutans and in preventing the colonization by S. mutans of erupting molars. The results of this study should establish the effectiveness of the IN route of immunization, the suitability of the rSBR, rCAT and rGLU proteins of S. mutans for a combination vaccine, and the benefit of a mucosal adjuvant (CTB or MPL) for inducing a human salivary response which affords immune protection against S. mutans infection. This study will provide valuable information on the human CMIS which will help in the development of mucosal vaccines and bring us closer to establishing a human caries vaccine.

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- **Project Title: REGULATION OF STREPTOCOCCUS MUTANS VIRULENCE BY COVR/S**

  Principal Investigator & Institution: Spatafora, Grace A.; Associate Professor; Biology; Middlebury College Old Chapel Bldg Middlebury, Vt 05753

  Timing: Fiscal Year 2003; Project Start 01-JAN-2003; Project End 31-DEC-2004

  Summary: (provided by applicant): Two component signal transduction systems are widely used by pathogenic bacteria to regulate the expression of their virulence factors in response to changing environmental cues during the infectious process. Streptococcus mutans is exposed to the transient environments of the human oral cavity where it is the primary etiologic agent of **Dental caries.** Specifically, changes in pH, oxygen content, and nutrient availability are likely to necessitate a rapid bacterial response to promote S. mutans-induced cariogenesis. We identified a gene pair in S. mutans that is homologous to the covR/S two-component signal transduction system in the group A streptococci (GAS). CovR/S is known to regulate the expression of multiple genes associated with GAS virulence, including basal which is necessary for capsule production and ska, which encodes a plasminogen activator. Work conducted in5laboratory implicates the S. mutans covR/S homologs in the regulation of fructosyltransferases (ftf) that mediate the sucrose-dependent production of fructans necessary for bacterial adherence to the tooth pellicle. Since S. mutans produces a multitude of factors that promote its survival and persistence in the human host, we posit that CovR/Smay function as a global regulator of S. mutans genes whose products promote disease in the oral cavity. The major goal of this research application is to define a putative role for CovR/S in S. mutans virulence control. The Specific Aims include: 1. Characterization of a S. mutans covR- mutant recently constructed in5laboratory, and analysis of its cariogenic potential in germfree rats; 2. Identification of the S. mutans gene(s) that are subject to CovR/S control in environments that approximate the oral cavity using differential display polymerase chain reaction (ddPCR) and 2D proteomic approaches; 3. construction of S. mutans knockout mutants and reporter gene fusions to functionally characterize CovR/S-regulated genes and analyze their expression. Taken collectively, these studies will elucidate S. mutans mechanism(s) of virulence gene control, and so enable prevention and/or intervention in the pathogenic process that leads to the development of **Dental caries.**

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- **Project Title: REMINERALIZING PULP-CAPPING CEMENTS & BONDING AGENTS**

  Principal Investigator & Institution: Dickens, Sabine H.; American Dental Association Foundation Chicago, Il 60611

  Timing: Fiscal Year 2002; Project Start 15-SEP-2001; Project End 14-SEP-2004

  Summary: The long-term goals of the proposed research are to demonstrate the cariostatic properties and biocompatibility of a previously developed Ca-PO4 Resin Cement (CP-RC) and to investigate the in vitro and in vivo properties of a novel Ca-PO4-enriched Bonding Agent (CP-BA). Both CP-RC and CP-BA are based on acidic- and other dimethacrylate resins, Ca-PO4 fillers and fluoride additives. The cement will provide the handling characteristics necessary for its clinical use as a direct or indirect pulp-capping agent. It has high pH during and after setting, moderate fluoride release, and has been shown in vitro to remineralize artificial tooth lesions. However, while the cement has shown moderate adhesive properties, its bond strength to dentin is low compared to those of current bonding agents. Moreover, preliminary tests showed that bonding agents placed between CP-RC and dentin with artificial caries-like lesions significantly reduced their remineralization. Thus, there is a need to explore novel dentin bonding agents with remineralizing/cariostatic properties and strong adhesion to normal and mineral-deficient dentin. Such adhesives could serve as conventional restorative bonding agents and for pulp-capping purposes. The specific aims are to 1. evaluate CP-RC effectiveness for preventing secondary caries formation in adjacent dentin and enamel; 2. (i) analyze qualitatively and quantitatively leachable components from the cement; and (ii) determine the in vitro cytotoxicity and effects on odontoblast cell culture and compare the in vitro biocompatibility and cytodifferentiation of CP-RC with the results from an (ongoing) in vivo animal study on the pulp-capping efficacy of the cement; 3. investigate bonding systems containing the same adhesive resin and Ca-PO4 fillers as the CP-RC and characterize their bioactivity effects and reinforcing mechanisms 4. evaluate the biocompatibility and cytodifferentiation of an optimized CP-BA and 5. address the controversial question of whether adhesive bonding agents can be successfully applied to pulp-capping procedures by evaluating the in vivo pulp-capping efficacy of this novel biocompatible, bioactive bonding agent. Completion of this research will lead to a remineralizing pulp-capping/lining cement and a bioactive Ca-PO4 dentin adhesive The CaPO4 resin cement will provide a method to reliably treat mechanical and small carious pulp exposures by stimulating the natural formation of dentin bridging with a base that has moderate adhesion to prevent leakage and the strength to allow the immediate placement of a permanent restoration. A remineralizing adhesive will provide methods of adhering to mineral-deficient dentin and for covering exposed pulps. The proposed studies will also provide a valuable comparison of in vivo test results to pulp cell response in vitro.

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- **Project Title: RISK FOR ENAMEL FLUOROSIS AMONG NORWEGIAN CHILDREN**

  Principal Investigator & Institution: Pendrys, David G.; Associate Professor; Behav Scis & Community Health; University of Connecticut Sch of Med/Dnt Bb20, Mc 2806 Farmington, Ct 060302806

  Timing: Fiscal Year 2002; Project Start 01-JUN-2001; Project End 31-MAY-2004

  Summary: The increase in the prevalence of enamel fluorosis in the US, Norway, and elsewhere in the Western world has been a cause of concern within the dental research

and public health community. Enamel fluorosis has important public health importance since fluoride is an important caries preventive agent. Thus there is need to very specifically identify early fluoride exposures responsible for this increase in enamel fluorosis prevalence. Findings in Norway have important relevancy to the US. Evidence suggests fluoride supplement use under pre-1994 US protocols was an important risk factor for enamel fluorosis. In 1994, a lower dosage protocol was accepted in the US, which is remarkably similar to a protocol under which current middle school age children in Norway were supplemented from infancy. This creates an opportunity to investigate whether there is continued fluorosis risk associated with this protocol, years in advance of our ability to conduct such an investigation in the US. In contrast to the US, Norway has never artificially fluoridated any of its drinking water supplies, and the presence of naturally occurring fluoride is relatively rare, so there is no fluoride "halo effect." Thus estimates of fluorosis risk associated with fluoride supplement and early fluoride dentifrice use derived from an investigation of a Norwegian population will represent conservative minimum estimates of the fluorosis risk potential of these fluoride sources in the US. This case-control study will investigate fluorosis risk factors among Norwegian children, age 11-13 years, living in Bergen, Norway. The methodology, including use of the Fluorosis Risk Index (FRI) and a mailed questionnaire, has been consistently used successfully in 5 previous risk factor studies. The FRI has consistently demonstrated good reliability. The questionnaire has consistently demonstrated a high response rate, high test/re-test reliability, and the ability in conjunction with FRI subject fluorosis categorization to identify strong associations between age-specific exposures and surface area-specific enamel fluorosis. Logistic regression analyses will be used to derive adjusted odds ratio estimates of the relative risk of enamel fluorosis associated with early fluoride exposures as well as adjusted estimates of attributable risk. Caries examination will allow comparison with fluorosis and early fluoride exposures.

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- **Project Title: ROCHESTER COLLABORATIVE TO REDUCE ORAL HEALTH DISPARITI***

  Principal Investigator & Institution: Billings, Ronald J.; Professor; Eastman Dentistry; University of Rochester Orpa - Rc Box 270140 Rochester, Ny 14627

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): The partnership of Eastman Dental Center with the City of Rochester and Rochester City Schools to prevent or reduce disparities in oral health began in 1915 with a gift from George Eastman enabling the creation of the Rochester Dental Dispensary. Today, that partnership extends to the University of Rochester Medical Center, including the School of Medicine and Dentistry. However, despite this rich history of collaboration and an extensive network of community-based oral health facilities, fewer than 30% of children from the most impoverished neighborhoods in the city receive regular oral health care. Further, little is known about disparities in oral diseases or dentofacial disorders among Rochester-dwelling Hispanic families from Puerto Rico and Central America. On the basis of regularly scheduled oral health surveys of Rochester school children, a comprehensive database on the distribution of **dental caries** has been compiled. However, little data on caries prevalence or incidence by race or ethnic group are available. Similarly, while we know that fewer than 30% of Medicaid eligible Rochester children utilize oral health care services, there are no data on barriers to utilization of the abundant and conveniently located neighborhood and school-based oral health care facilities, nor have effective

interventions been developed to improve utilization. Little attention has been given to cultural and behavioral characteristics of minorities that may profoundly influence utilization. Given the rich infrastructure and abundant resources available to us, we have formed a community partnership and a multidisciplinary research collaborative to undertake research on preventing or reducing oral health disparities. In this proposal, we describe three specific aims to: 1) organize research teams; 2) link research and community partners; and 3) refine research questions and design studies that will address the following four lines of research: 1) Assess the distribution of oral disease/disorders, with emphasis on **dental caries;** investigate factors associated with any excess morbidity observed in Rochester-dwelling Hispanic children and contrast findings with matched cohorts of African-American and Caucasian children; 2) Determine the impact of existing oral health care programs on disparities in oral disease morbidity; 3) Identify barriers to effective utilization of the oral health care system; and, 4) Develop intervention strategies that will prevent or reduce disparities in both the levels of oral diseases as well as in access to, and effective utilization of, the oral health care system.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: S. MUTANS: ITS MUTACIN ANTIBIOTIC**

  Principal Investigator & Institution: Qi, Fengxia; Oral Biology/Medicine/Orofacial Pain; University of California Los Angeles 10920 Wilshire Blvd., Suite 1200 Los Angeles, Ca 90024

  Timing: Fiscal Year 2003; Project Start 03-MAR-2003; Project End 30-NOV-2007

  Summary: Streptococcus mutans is the major etiologic agent responsible for **Dental caries,** the most prevalent disease in the developed and developing countries. Most clinical isolates of S. mutans produce antimicrobial peptides called mutacins. Mutacins are active against a wide spectrum of Gram-positive bacteria including pathogens and oral commensals. Thus, mutacin production by S. mutans may play a double role: it provides the producing strain with a competitive edge in gaining dominance in the Dental plaque, leading to **Dental caries.** On the other hand, it may protect the human host from Gram-positive bacterial infections. The proposed research Aims to study the genetic, biochemical and biological aspects of mutacin biogenesis and regulation with the following approaches: Aim 1, to characterize the trans-acting factors for mutacin gene regulation. Aim 2, to characterize the cis-acting factors that regulate mutacin gene expression. Aim 3, to determine the structure/function of the mutacin molecule and improve the properties of mutacins by genetic engineering. Aim 4, to enhance mutacin biosynthesis and improve fermentation conditions. The proposed research will have a significant impact on two fronts. The first is the alarming surge in resistance to the existing battery of antibiotics by emerging and existing pathogens, and the increasing threat of bioterrorist attack using genetically engineered pathogens resistant to all existing antibiotics. These threats underpin the importance and urgency of finding unconventional antibiotics, to which resistance has not been developed. The second front is understanding the mechanism of gene regulation for mutacin production in S. mutans. This knowledge will help design effective control measures to curb the growth and virulence of S. mutans in the Dental plaque.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SALIVA TEST FOR CARIES RISK**

  Principal Investigator & Institution: Denny, Paul C.; Professor; Proactive Oral Solutions, Inc. 2921 St. Albans Dr Los Alamitos, Ca 907204456

Timing: Fiscal Year 2004; Project Start 15-JUL-2002; Project End 31-MAR-2006

Summary: Ultimately, the goal of this project is to produce a simple, non-invasive saliva test, which is able to assess caries risk. Within the Dental community, there is a trend to include prevention in the treatment plan. The test facilitates this move by offering the Dental professional, and ultimately the patient, the tool to determine the risk for caries development. Those patients who are identified as high or medium risk, can then be targeted for a personalized prevention program. Past caries experience, DFS (number of decayed and filled tooth surfaces) has been the best predictor for risk level of future caries development; however, it is an unreliable measure. There is need for a test that provides standard identification criteria and leads to an accurate diagnosis of caries risk through childhood and young adulthood. Preliminary studies showed a strong correlation between MUC7 mucin in saliva and DFS. The completed Phase I study included more than 100 children and young adults, extending correlations to individual caries experience in children 7-9 years old. A new set of predictors was identified that are more universal than mucins alone. Lectin assays revealed carbohydrate moieties, some of which are blood group antigen-like, that resulted in correlations with DFS in whole, unfractionated saliva that are even more precise than with mucin alone. The methods for assessing the levels of the newest predictors for caries risk are easier and less cumbersome than for mucin quantitation, thus opening opportunities to develop very simple, reliable tests that will be easy to commercialize. The goal of the Phase II Study is to produce working models of these tests, which use the relevant technology for each application. Also during Phase II, the data base will be increased by collecting samples from additional young adults and children expanding to different ages, and races or ethnicities, with the goal of further "universalizing" the test. In addition to a chair-side test that can be used by the Dental professional, the strip test could have world-wide impact on oral health by targeting those in most need where resources are limited.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SALIVARY AMYLASE--ROLE IN DENTAL CARIES PATHOGENESIS**

  Principal Investigator & Institution: Ramasubbu, Narayanan; Associate Professor; Dental Research Center; Univ of Med/Dent Nj Newark Newark, Nj 07107

  Timing: Fiscal Year 2002; Project Start 01-APR-1999; Project End 31-MAR-2003

  Summary: Salivary amylase provides an excellent example of the multifunctionality exhibited by salivary proteins. The multifunctional nature of amylase includes: 1) starch hydrolysis; 2) binding to hydroxyapatite (enamel); and 3) binding to bacteria (e.g. viridans streptococci) in solution and when bound to hydroxyapatite. For salivary amylase, its binding to bacteria in solution may result in bacterial clearance (protective) while its presence in the enamel pellicle may facilitate dental plaque formation (harmful). Its binding to viridans streptococci both in solution as well as when bound to the hydroxyapatite surface is dependent upon the maintenance of its native conformation. The goals of this proposal are to elucidate the structure-function relationships of amylase in the context of its role(s) in oral physiology. Characterization of these relationships at the molecular level will improve the understanding of basic mechanisms responsible for the early colonization of streptococci in the oral cavity. The underlying hypothesis of this proposal is that the multifunctionality of this enzyme can play a significant role in **dental caries** development. In particular, we feel that the structural domains of salivary amylase are critical in the caries process. In this grant period, we propose to generate distinct mutants with biochemical and physiological defects targeted against each of the three functions of salivary amylase. The mutants will

be generated using a facile baculovirus expression system and the biological activities of the mutants will be screened with specific assays for bacterial binding, starch hydrolysis or hydroxyapatite binding. The structure of these mutants will be determined using protein crystallography for understanding the effect of mutation on the function. These first generation mutants will provide clues regarding how augmenting or weakening of one function affects the other two. We will obtain these clues from the in vitro biological assays and structure analysis of mutants which exhibit significantly altered activity. Based upon these results, additional mutants representing second and third generations will be constructed. Such mutants will permit the design of strategies to manipulate human salivary amylase-bacterial interactions that favor the host and thus reduce the potential for caries.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STATIONARY PHASE BEHAVIOR IN ORAL STREPTOCOCCI**

  Principal Investigator & Institution: Piggot, Patrick; Microbiology and Immunology; Temple University 406 Usb, 083-45 Philadelphia, Pa 19122

  Timing: Fiscal Year 2003; Project Start 01-JUL-2003; Project End 30-APR-2007

  Summary: Streptococcus mutans is the primary agent of **Dental caries.** We think that stationary-phase bacteria are critical to the behavior and survival of S. mutans in the Dental plaque biofilm, and hence to its role in **Dental caries.** They are surely a critical part of the feast-or-famine lifestyle of S. mutans, as famine causes entry into the stationary phase. Yet, most studies of S. mutans have been of exponentially growing bacteria. We propose to test the general hypothesis that stationary-phase bacteria in biofilms behave differently from vegetative bacteria and have an important role in determining the properties of mature biofilms, and in particular in their persistence. We propose using single-species biofilms formed in flow cells to test this hypothesis. We propose to test how well stationary-phase bacteria survive prolonged carbon-source starvation in biofilms and how they respond to nutrient restoration and acid shock. We will test the effect of different treatments on the shedding of bacteria from stationary-phase biofilms, and test how effectively the shed bacteria can initiate secondary biofilm formation in a second flow cell. We propose to use the fluorescing protein GFPmut3b* as a probe to locate bacteria expressing known stationary-phase-specific genes and those expressing vegetative-phase specific genes. This will help clarify the difference in properties between the two bacterial types. We will screen for new stationary-phase expressed genes. These genes will enable testing if there are different types of stationary-phase bacteria with different resistances and different responses to nutrient. They will give an indication of the sorts of function that are expressed during stationary phase. We propose to test the roles of these genes. We propose to identify and characterize the regulators of stationary phase gene expression. These studies should lead to a better understanding of how S. mutans in mature Dental plaque biofilm persists and responds to fluctuations in its environment.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STREPTOCOCCUS MUTANS SUGAR TRANSPORT & BIOFILM FORMATION**

  Principal Investigator & Institution: Ajdic, Dragana; University of Oklahoma Hlth Sciences Ctr Health Sciences Center Oklahoma City, Ok 73126

  Timing: Fiscal Year 2003; Project Start 30-SEP-2003; Project End 30-JUN-2008

Summary: Sugar transport and metabolism by Streptococcus mutans is directly related to the onset and formation of human **dental caries** (tooth decay). In S. mutans, sugar substrates are taken up by ABC transporters (e.g., the maltose transport and multiple sugar metabolism transport (MSM) systems), by specific permeases, and most commonly by phosphoenolpyruvate (PEP)-sugar phosphotransferase systems (PTS). To better understand this important dental pathogen, we have sequenced the entire DNA sequence of the genome of strain UA159 at the University of Oklahoma. Detailed computational analyses of the S. mutans genome showed the presence of five ABC transporters and fourteen PTS systems for the probable transport of sugars or sugar alcohols including glucose, sucrose, maltose, lactose and fructose. Since the uptake and metabolism of carbohydrates is the key step in the formation and release of cariogenic acid, and since completion of the genomic DNA sequence of S. mutans strain UA159 now permits us to locate all of the predicted coding regions, this proposed work will examine the global gene response in S. mutans. Additionally, because S. mutans grows in a plaque that is a natural biofilm, it is crucial to determine the alterations in gene expression in biofilm cultures. Therefore, the specific aims of this proposal are to 1) analyze the differences in global gene expression observed when S. mutans UA159 is grown in the presence of the most common dietary sugars (sucrose, maltose, lactose, glucose, and fructose) in planktonic culture and in biofilm, and 2) identify multiple transporters for the same sugar (as well as genes influenced by transport systems) in S. mutans planktonic and biofilm cultures by individually inactivating those systems. We hypothesize that many genes will have differential patterns of expression in response to the availability of carbohydrate source and culture state. The information obtained from the proposed study should dramatically advance our understanding of this important human pathogen and facilitate new approaches for treatment and intervention aimed at reducing the incidence of **dental caries.**

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STUDY PLANS OF COMMUNICATION AND ORAL HEALTH DISPARITIES**

  Principal Investigator & Institution: Koerber, Anne; Pediatric Dentistry; University of Illinois at Chicago 1737 West Polk Street Chicago, Il 60612

  Timing: Fiscal Year 2002; Project Start 15-SEP-2002; Project End 31-AUG-2004

  Summary: (provided by applicant): This is a proposal for a planning grant to develop research approaches to discover whether dentist-patient communication leads to disparities in the prevalence of caries and periodontal disease in African American and Hispanic patients, and to identify testable methods to improve communication to avoid or alleviate those disparities. The specific aims are: Aim One: To create a research team and form an Advisory Board for the development of research plans, and to obtain training for the team. Aim Two: To look for methods of studying the effect of dental team communication on caries and periodontal disease of Hispanic and African American dental school patients. Aim Three: To determine what methods promote compliance and good communication between practitioners and Hispanic and African American patients, to identify training methods for the dental team, and to develop evaluation protocols to test the methods that can be used to apply for pilot funding or R01 funding, as appropriate. If dental teams are more likely to alienate or fail to make an effective working relationship with African American or Hispanic patients than with White patients, then they are less likely to obtain important information from that patient, they are less likely to have a positive influence on the patient's dental attendance or home care behavior, and they are less likely to convince the patient of the

appropriate treatment plan. This is especially true if the treatment plan consists of regimens that require specific patient behaviors, such as plaque control programs. The methods to be used are 1) literature searches to identify variables and methods, 2) interviews and focus groups with patients, dental students, dental hygiene students, faculty and dental school staff to uncover potential difficulties and assure that important areas are identified, 3) an advisory board to review and advise about potential difficulties with the measures and methods, identify areas that should be explored, and to review the value of proposed research plans, 4) consultation and training with experts in measuring communication and in teaching cultural competence, and 5) statistical advice on measurement and analyses. A two year plan is proposed with the expectation of producing several research proposals aimed at both measuring the effect of doctor-patient communication on disparities and evaluating training methods to help dental providers communicate better with minorities.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: STURCTURE/PROPERTIES OF ALTERED FORMS OF DENTIN AND CEMENTUM**

  Principal Investigator & Institution: Marshall, Grayson W.; Professor & Chair; University of California San Francisco 500 Parnassus Ave San Francisco, Ca 941222747

  Timing: Fiscal Year 2002; Project Start 01-AUG-1991; Project End 31-JAN-2007

  Summary: (provided by the applicant) The main objective of Project 8, Structure/Properties of Altered Forms of Dentin and Cementum, is to determine specific material "signatures" for key variations and alterations of dentin and cementum in both primary (deciduous) and permanent teeth. The material "signature" will be defined by characteristic microstructures, composition and selected properties (mechanical and demineralization) for each form or variation of dental hard tissue. We hypothesize that the "signatures" will provide a unique identifier for each alteration. These "signatures" should prove instrumental for developing improved clinical approaches to preventive and conservative, restorative dentistry. We will carry out this work in an ordered, repeated measures design involving a variety of advanced methods including x-ray tomographic microscopy (XTM), atomic force microscopy (AFM) for imaging, demineralization and nanoindentation measurements, small angle x-ray scattering (SAXS) and other standard tools, allowing determination of characteristics of mineral, and collagen fibril structure, repeat distances and cross-links. Aim 1 will define the "signature" for transparent dentin associated with coronal caries and attrition in primary and permanent dentin; sclerotic cervical lesions, endodontically treated teeth, and aging of the root. It will also evaluate the mineral level, structure and nanomechanical properties variations of the zones in active and arrested root caries, and identify unique characteristics of dentin associated with Dentinogenesis Imperfecta (DI-II). Aim 2 will focus on changes associated with collagen cross-link patterns and fibril structure for each variation. Aim 3 evaluates the "signature" of secondary and tertiary dentin in primary and permanent teeth, and evaluates the dependence of tertiary dentin "signature" on the nature of the stimulus. Aim 4 will determine the age-dependent key components of the "signature" i.e., structure and properties of cellular and acellular cementum, the cementun-dentin junction (CDJ), and the cementun-enamel junction (CEJ) using the same approach and generally the same teeth as those used for dentin. The "signatures" from this project will provide fundamental information that will be used to develop a model in Project II, understand the substrate for bonding in Project III and will serve as a baseline for comparison with the "signatures" of mouse teeth in Project IV.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: SYNTHETIC PEPTIDE VACCINES FOR DENTAL CARIES**

  Principal Investigator & Institution: Taubman, Martin A.; Senior Member and Head; Forsyth Institute Boston, Ma 02115

  Timing: Fiscal Year 2002; Project Start 01-MAY-1996; Project End 30-JUN-2006

  Summary: Our overall aim is to develop immunization constructs, vectors, and strategies which have the best chance of inducing protective immune responses to mutans streptococcal infections in susceptible pediatric populations. We have previously identified several glucosyltransferases (GTF) enzyme sequences which can induce immune response in rodents which will alter GTF activity and reduce subsequent **dental caries.** To enhance the induction of protective immune responses we will first identify sequences from glucosyltransferase (GTF) enzymes from S. mutans and S. sobrinus associated with potent Class II MHC binding in humans. Peptides based on these and on novel GTF epitopes, recently shown to influence catalytic activity and transitional state stability of the enzyme (activity associated) will be synthesized and evaluated for immunogenicity and protective effect. These epitopes, together with other functionally significant peptides derived from the catalytic and glucans binding domains of GTF previously shown to induce protective responses, well be incorporated into conjugate vaccines with tetanus toxoid (TT). Intranasal routes for mucosal immunization with TT- GTF peptide conjugate vaccine will be investigated for the ability to induce protective levels of immunity in the oral cavity in the well established rodent model of experimental **dental caries.** Since the intranasal route may be contraindicated in children with upper respiratory conditions such as asthma, the colo-rectal route of administration will also be explored using constructs combined with or without mucosal adjuvants such detoxified mutant E. coli enterotoxin (LT) or unmethylated CpG oligodinucleotides. The protective effect of systemic immunization with TT-GTF peptide conjugate vaccine studies will also be investigated as an approach to minimizing the frequency of visits required for childhood immunizations, since evidence suggests that this route of immunization can induce salivary IgA antibody in young children. Various of the mist effective peptide(s) as determined by TT-GTF peptide conjugate vaccine studies will be expressed recombinantly in attenuated Salmonella typhi vectors which can target these epitopes to appropriate mucosal inductive sites. Caries protection will be evaluated after intranasal immunization with these attenuated Salmonella vectors. Our goal is to design a vaccine that contains a combination of immunologically potent and functionally relevant epitopes, in formats, by routes, and with adjuvants that result in sustained levels of protection from **dental caries** and that will be acceptable for human use.

  Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: TRIALS TO ENHANCE ELDERS' TEETH/ORAL HEALTH (TEETH)**

  Principal Investigator & Institution: Kiyak, H A.; Professor; Institute on Aging; University of Washington Grant & Contract Services Seattle, Wa 98105

  Timing: Fiscal Year 2002; Project Start 30-SEP-1997; Project End 31-JUL-2005

  Summary: (provided by applicant): The proposed project is a competing renewal of the TEETH ("Trials to Enhance Elders' Teeth and Oral Health") study funded by NIDCR (R01 DE012215, 9/30/97 - 7/31/02). This double blind, randomized clinical trial, supervised by a Data and Safety Monitoring Board (DSMB), was designed to provide unequivocal evidence regarding the impact of regular rinsing with a 0.12%

chlorhexidine solution on tooth loss in low income, community dwelling older adults. A sample of 1101 people aged 60-75 was recruited between 05/98 and 08/99, with 701 in Seattle, 400 in Vancouver, B.C. (under a subcontract to the University of British Columbia). Random assignment resulted in 550 elders in the active rinse, 551 in the placebo. As of the last DSMB meeting in 07/01, the tooth loss rates in groups A and B were 13 and 16 lost teeth per 1000 tooth-years, respectively (p=0.44). The attrition rate and non-compliance rate were lower than projected and were not dependent on treatment assignment. No treatment-related adverse effects have been identified to date. Mortality rates in both groups are similar, and the most common oral lesion - lichen planus - has a similar prevalence in both groups. Surrogate measures of periodontitis and caries are reported annually to the TEETH DSMB. The purpose of this competing renewal is to complete the data follow-up until 12/04, including following up with dentists who have extracted teeth in these subjects during their enrollment in TEETH. Group comparisons will assess the impact of the low-cost chlorhexidine rinse regimen on 5-year incidence of root and coronal caries, attachment loss, and the true endpoint, tooth loss. Clinical data, radiographs, and health histories will aid in determining reasons for tooth loss, in addition to the impact of rinsing with the active vs. placebo solution. The same research team will continue to monitor, analyze, and conduct the TEETH study at both sites, using the protocol stipulated in the initial application, including the modifications provided by the DSMB. Every indication to date suggests a successful completion of this trial as projected.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

- **Project Title: XYLITOL ENHANCEMENT OF BACTERIAL KILLING BY AIRWAY**

  Principal Investigator & Institution: Zabner, Joseph; Associate Professor; University of Iowa Iowa City, Ia 52242

  Timing: Fiscal Year 2003; Project Start 01-SEP-2003; Project End 31-AUG-2008

  Summary: Chronic infection in the airways is the most common cause of morbidity and mortality in cystic fibrosis. The link between CFTR mutations and infection remains uncertain. While many diverse hypotheses have been advanced, one point is clear: CF patients manifest some defect in host defense, and this defect is localized to the airway surface. Airway surface liquid (ASL) has antimicrobial properties that help keep the lungs sterile. The antimicrobial properties of ASL are enhanced when the salt conentration is low. This suggests that, regardless of the baseline salt concentrations in the ASL in vivo, further lowering it would improve antimicrobial activity. A strategy that could lower the salt concentration in the airways would be to apply a non-absorbable osmolyte to the ASL. This could reduce ASL NaCI concentration by substituting the osmotic effect of NaCI with a non-ionic osmolyte. Xylitol is a simple 5-carbon sugar, commonly used as a non-metabolizable sweetener. Xylitol has been shown to prevent or decrease the progression of **dental caries** and decrease the incidence of acute otitis media when used prophylactically. Our preliminary data are very encouraging: xylitol has low permeability across epithelia, it can reduce ASL salt concentrations, it does not inhibit ASL antimicrobial factors, and most importantly, xylitol can enhance ASL-mediated bacterial killing in vitro and in vivo. Our long-term hypothesis is that xylitol administration will prevent or delay the onset of CF airway infections. Towards that goal we propose to test the efficacy of xylitol in augmenting ASL killing in mice, sheep and adults with CF. We have 3 hypotheses. Administering xylitol to the airways will increase bacterial killing in mice. We will study the effect of xylitol on several CF bacterial pathogens administered to mouse lung. Aerosolized xylitol will prevent airway colonization/infection in large animals. We will ask if xylitol

administration increases airway killing of a sheep airway pathogen M. haemolytica. Airway administration of xylitol is safe and reduces the bacterial burden in patients with CF. Xylitol has been given to humans intravenously and orally as a food additive. We will first ask if aerosolized xylitol is safe in normal volunteers and determine how long it stays in the ASL compartment. We will then ask if xylitol administration is safe in CF patients and whether it can decrease the bacterial burden in their lungs.

Website: http://crisp.cit.nih.gov/crisp/Crisp_Query.Generate_Screen

E-Journals: PubMed Central[3]

PubMed Central (PMC) is a digital archive of life sciences journal literature developed and managed by the National Center for Biotechnology Information (NCBI) at the U.S. National Library of Medicine (NLM).[4] Access to this growing archive of e-journals is free and unrestricted.[5] To search, go to **http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=Pmc**, and type "dental caries" (or synonyms) into the search box. This search gives you access to full-text articles. The following is a sample of items found for dental caries in the PubMed Central database:

- **Adherence Inhibition of Streptococcus mutans: an Assay Reflecting a Possible Role of Antibody in Dental Caries Prophylaxis.** by Olson GA, Bleiweis AS, Small PA Jr.; 1972 Apr; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=422387
- **Amount and avidity of salivary and serum antibodies against Streptococcus mutans in two groups of human subjects with different dental caries susceptibility.** by Lehtonen OP, Grahn EM, Stahlberg TH, Laitinen LA.; 1984 Jan; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=263427
- **Comparison of an Adherence Domain and a Structural Region of Streptococcus mutans Antigen I/II in Protective Immunity against Dental Caries in Rats after Intranasal Immunization.** by Hajishengallis G, Russell MW, Michalek SM.; 1998 Apr; http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=108112
- **Effect of neonatal thymectomy on dental caries in rats.** by Ebersole JL, Taubman MA, Smith DJ.; 1982 Dec; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=347867
- **Effects of Local Immunization with Glucosyltransferase Fractions from Streptococcus mutans on Dental Caries in Hamsters Caused by Homologous and Heterologous Serotypes of Streptococcus mutans.** by Smith DJ, Taubman MA, Ebersole JL.; 1978 Sep; http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=422074

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[3] Adapted from the National Library of Medicine: **http://www.pubmedcentral.nih.gov/about/intro.html**.

[4] With PubMed Central, NCBI is taking the lead in preservation and maintenance of open access to electronic literature, just as NLM has done for decades with printed biomedical literature. PubMed Central aims to become a world-class library of the digital age.

[5] The value of PubMed Central, in addition to its role as an archive, lies in the availability of data from diverse sources stored in a common format in a single repository. Many journals already have online publishing operations, and there is a growing tendency to publish material online only, to the exclusion of print.

- **Effects of Local Immunization with Streptococcus mutans on Induction of Salivary Immunoglobulin A Antibody and Experimental Dental Caries in Rats.** by Taubman MA, Smith DJ.; 1974 Jun;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=414936
- **Immune response and dental caries incidence in Streptococcus faecalis-monoassociated Harvard caries-resistant and caries-susceptible rats.** by Peri BA, Wagner M.; 1977 Jun;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=421033
- **Immunization with purified protein antigens from Streptococcus mutans against dental caries in rhesus monkeys.** by Lehner T, Russell MW, Caldwell J, Smith R.; 1981 Nov;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=350881
- **Inhibition of Experimental Dental Caries by Antibiotics.** by Fitzgerald RJ.; 1972 Apr;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=444211
- **Interdental Localization of Streptococcus mutans as Related to Dental Caries Experience.** by Gibbons RJ, Depaola PF, Spinell DM, Skobe Z.; 1974 Mar;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=414831
- **Intranasal Immunization against Dental Caries with a Streptococcus mutans-Enriched Fimbrial Preparation.** by Fontana M, Dunipace AJ, Stookey GK, Gregory RL.; 1999 May;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=103731
- **Non-cariogenicity of the disaccharide palatinose in experimental dental caries of rats.** by Ooshima T, Izumitani A, Sobue S, Okahashi N, Hamada S.; 1983 Jan;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=347905
- **Oral passive immunization against dental caries in rats by use of hen egg yolk antibodies specific for cell-associated glucosyltransferase of Streptococcus mutans.** by Hamada S, Horikoshi T, Minami T, Kawabata S, Hiraoka J, Fujiwara T, Ooshima T.; 1991 Nov;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=259011
- **Prevalence of dental caries in 4- to 5-year-old children partly explained by presence of salivary mutans streptococci.** by Granath L, Cleaton-Jones P, Fatti LP, Grossman ES.; 1993 Jan;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=262623
- **Protection of gnotobiotic rats against dental caries by passive immunization with bovine milk antibodies to Streptococcus mutans.** by Michalek SM, Gregory RL, Harmon CC, Katz J, Richardson GJ, Hilton T, Filler SJ, McGhee JR.; 1987 Oct;
  http://www.pubmedcentral.gov/picrender.fcgi?tool=pmcentrez&action=stream&blobtype=pdf&artid=260710

- **Tonsillar Application of Formalin-Killed Cells of Streptococcus sobrinus Reduces Experimental Dental Caries in Rabbits.** by Fukuizumi T, Inoue H, Tsujisawa T, Uchiyama C.; 1999 Jan;
  http://www.pubmedcentral.gov/articlerender.fcgi?tool=pmcentrez&artid=96329

The National Library of Medicine: PubMed

One of the quickest and most comprehensive ways to find academic studies in both English and other languages is to use PubMed, maintained by the National Library of Medicine.[6] The advantage of PubMed over previously mentioned sources is that it covers a greater number of domestic and foreign references. It is also free to use. If the publisher has a Web site that offers full text of its journals, PubMed will provide links to that site, as well as to sites offering other related data. User registration, a subscription fee, or some other type of fee may be required to access the full text of articles in some journals.

To generate your own bibliography of studies dealing with dental caries, simply go to the PubMed Web site at **http://www.ncbi.nlm.nih.gov/pubmed**. Type "dental caries" (or synonyms) into the search box, and click "Go." The following is the type of output you can expect from PubMed for dental caries (hyperlinks lead to article summaries):

- **A Caries Vaccine? The state of the science of immunization against dental caries.**
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  Author(s): Condon M.
  Source: Afr Dent J. 1988 March; 2(1): 22-5. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3272732

- **Virulence factors of Streptococcus mutans and dental caries prevention.**
  Author(s): Hamada S, Koga T, Ooshima T.
  Source: Journal of Dental Research. 1984 March; 63(3): 407-11.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6230378

- **Wearing of removable partial dentures in relation to dental caries.**
  Author(s): Tuominen R, Ranta K, Paunio I.
  Source: Journal of Oral Rehabilitation. 1988 November; 15(6): 515-20.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3236123

- **What do the public and profession know about dental caries prevention in Korea?**
  Author(s): Johng-bai K.
  Source: Int Dent J. 1998 August; 48(4): 399-404.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9779124

- **Widening the war on dental caries.**
  Author(s): Polakoff PL.
  Source: Occup Health Saf. 1983 September; 52(9): 48-50. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6634009

- **Will complacency allow return of dental caries?**
  Author(s): Woodall I.
  Source: Rdh. 1990 October; 10(10): 8, 32. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2089458

- **With HAART success, managing dental caries is again important.**
  Author(s): Mosca N.
  Source: Hiv Clin. 2002 Winter; 14(1): 6-7. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11833447

- **Would you believe, decreases in dental caries and increases in the demand for dental care?**
  Author(s): Waldman HB.
  Source: Asdc J Dent Child. 1989 July-August; 56(4): 257-61. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2668364

- **Xylitol and dental caries.**
  Author(s): Makinen KK, Scheinin A.
  Source: Annual Review of Nutrition. 1982; 2: 133-50. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6764729

- **Xylitol and dental caries: an overview for clinicians.**
  Author(s): Lynch H, Milgrom P.
  Source: J Calif Dent Assoc. 2003 March; 31(3): 205-9. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12693818

- **Xylitol chewing gum and dental caries.**
  Author(s): Tanzer JM.
  Source: Int Dent J. 1995 February; 45(1 Suppl 1): 65-76. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7607747

- **Xylitol for prevention of dental caries.**
  Author(s): Lee B, Sue D.
  Source: Dicp. 1989 September; 23(9): 691-2. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2800584

CHAPTER 2. NUTRITION AND DENTAL CARIES

Overview

In this chapter, we will show you how to find studies dedicated specifically to nutrition and dental caries.

Finding Nutrition Studies on Dental Caries

The National Institutes of Health's Office of Dietary Supplements (ODS) offers a searchable bibliographic database called the IBIDS (International Bibliographic Information on Dietary Supplements; National Institutes of Health, Building 31, Room 1B29, 31 Center Drive, MSC 2086, Bethesda, Maryland 20892-2086, Tel: 301-435-2920, Fax: 301-480-1845, E-mail: ods@nih.gov). The IBIDS contains over 460,000 scientific citations and summaries about dietary supplements and nutrition as well as references to published international, scientific literature on dietary supplements such as vitamins, minerals, and botanicals.[7] The IBIDS includes references and citations to both human and animal research studies.

As a service of the ODS, access to the IBIDS database is available free of charge at the following Web address: **http://ods.od.nih.gov/databases/ibids.html**. After entering the search area, you have three choices: (1) IBIDS Consumer Database, (2) Full IBIDS Database, or (3) Peer Reviewed Citations Only.

Now that you have selected a database, click on the "Advanced" tab. An advanced search allows you to retrieve up to 100 fully explained references in a comprehensive format. Type "dental caries" (or synonyms) into the search box, and click "Go." To narrow the search, you can also select the "Title" field.

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[7] Adapted from **http://ods.od.nih.gov**. IBIDS is produced by the Office of Dietary Supplements (ODS) at the National Institutes of Health to assist the public, healthcare providers, educators, and researchers in locating credible, scientific information on dietary supplements. IBIDS was developed and will be maintained through an interagency partnership with the Food and Nutrition Information Center of the National Agricultural Library, U.S. Department of Agriculture.

The following information is typical of that found when using the "Full IBIDS Database" to search for "dental caries" (or a synonym):

- **Diagnosis and management of dental caries throughout life.**
  Source: NIH-Consens-Statement. 2001 March 26-28; 18(1): 1-23 1080-1707
- **Recommendations for using fluoride to prevent and control dental caries in the United States. Centers for Disease Control and Prevention.**
  Source: Anonymous MMWR-Morb-Mortal-Wkly-Repage 2001 August 17; 50(RR-14): 1-42 0149-2195
- **Reduction in dental caries with four concentrations of sodium fluoride in a dentifrice: a meta-analysis evaluation.**
  Author(s): The Procter & Gamble Company, Health Care Research Center, Mason, Ohio, USA. bartizekrd@pg.com
  Source: Bartizek, R D Gerlach, R W Faller, R V Jacobs, S A Bollmer, B W Biesbrock, A R J-Clin-Dent. 2001; 12(3): 57-62 0895-8831

Federal Resources on Nutrition

In addition to the IBIDS, the United States Department of Health and Human Services (HHS) and the United States Department of Agriculture (USDA) provide many sources of information on general nutrition and health. Recommended resources include:

- healthfinder®, HHS's gateway to health information, including diet and nutrition: **http://www.healthfinder.gov/scripts/SearchContext.asp?topic=238&page=0**
- The United States Department of Agriculture's Web site dedicated to nutrition information: **www.nutrition.gov**
- The Food and Drug Administration's Web site for federal food safety information: **www.foodsafety.gov**
- The National Action Plan on Overweight and Obesity sponsored by the United States Surgeon General: **http://www.surgeongeneral.gov/topics/obesity/**
- The Center for Food Safety and Applied Nutrition has an Internet site sponsored by the Food and Drug Administration and the Department of Health and Human Services: **http://vm.cfsan.fda.gov/**
- Center for Nutrition Policy and Promotion sponsored by the United States Department of Agriculture: **http://www.usda.gov/cnpp/**
- Food and Nutrition Information Center, National Agricultural Library sponsored by the United States Department of Agriculture: **http://www.nal.usda.gov/fnic/**
- Food and Nutrition Service sponsored by the United States Department of Agriculture: **http://www.fns.usda.gov/fns/**

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering food and nutrition. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=174&layer=&from=subcats**

- Family Village: **http://www.familyvillage.wisc.edu/med_nutrition.html**
- Google: **http://directory.google.com/Top/Health/Nutrition/**
- Healthnotes: **http://www.healthnotes.com/**
- Open Directory Project: **http://dmoz.org/Health/Nutrition/**
- Yahoo.com: **http://dir.yahoo.com/Health/Nutrition/**
- WebMD®Health: **http://my.webmd.com/nutrition**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**

The following is a specific Web list relating to dental caries; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **Food and Diet**

  Sugar Alcohols
  Source: Healthnotes, Inc.; www.healthnotes.com

  Water
  Source: Healthnotes, Inc.; www.healthnotes.com

CHAPTER 3. ALTERNATIVE MEDICINE AND DENTAL CARIES

Overview

In this chapter, we will begin by introducing you to official information sources on complementary and alternative medicine (CAM) relating to dental caries. At the conclusion of this chapter, we will provide additional sources.

National Center for Complementary and Alternative Medicine

The National Center for Complementary and Alternative Medicine (NCCAM) of the National Institutes of Health (**http://nccam.nih.gov/**) has created a link to the National Library of Medicine's databases to facilitate research for articles that specifically relate to dental caries and complementary medicine. To search the database, go to the following Web site: **http://www.nlm.nih.gov/nccam/camonpubmed.html**. Select "CAM on PubMed." Enter "dental caries" (or synonyms) into the search box. Click "Go." The following references provide information on particular aspects of complementary and alternative medicine that are related to dental caries:

- **"Don't just treat a tooth. treat the whole patient!".**
  Author(s): Nagel DW.
  Source: J Mich Dent Assoc. 2003 October; 85(10): 34-6, 38. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=14618770

- **"Tooth worms", poverty tattoos and dental care conflicts in Northeast Brazil.**
  Author(s): Nations MK, Nuto Sde A.
  Source: Social Science & Medicine (1982). 2002 January; 54(2): 229-44.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11824928

- **An In vitro microbial-caries model used to study the efficacy of antibodies to Streptococcus mutans surface proteins in preventing dental caries.**
  Author(s): Fontana M, Buller TL, Dunipace AJ, Stookey GK, Gregory RL.

Source: Clinical and Diagnostic Laboratory Immunology. 2000 January; 7(1): 49-54.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=10618276

- **Another update for Canadian dentists regarding chlorhexidine varnish therapy for the prevention of dental caries.**
Author(s): Lewis DW.
Source: Journal (Canadian Dental Association). 1994 August; 60(8): 717-20; Discussion 721-2, 725.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8087680

- **Antibacterial activity of Camellia sinensis extracts against dental caries.**
Author(s): Rasheed A, Haider M.
Source: Arch Pharm Res. 1998 June; 21(3): 348-52.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9875456

- **Assessing risk indicators for dental caries in the primary dentition.**
Author(s): Vanobbergen J, Martens L, Lesaffre E, Bogaerts K, Declerck D.
Source: Community Dentistry and Oral Epidemiology. 2001 December; 29(6): 424-34.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11784285

- **Black tea extract and dental caries formation in hamsters.**
Author(s): Linke HA, LeGeros RZ.
Source: International Journal of Food Sciences and Nutrition. 2003 January; 54(1): 89-95.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12701240

- **Canadian Consensus Conference on the appropriate use of fluoride supplements for the prevention of dental caries in children.**
Author(s): Limeback H, Ismail A, Banting D, DenBesten P, Featherstone J, Riordan PJ.
Source: Journal (Canadian Dental Association). 1998 October; 64(9): 636-9. Review.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9812431

- **Changing patterns of dental caries in Ethiopian adolescents who immigrated to Israel.**
Author(s): Sarnat H, Cohen S, Gat H.
Source: Community Dentistry and Oral Epidemiology. 1987 October; 15(5): 286-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3477362

- **Control of dental caries.**
Author(s): Newbrun E.
Source: Southern Medical Journal. 1977 October; 70(10): 1161-4.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=910166

- **Dental caries and dental fluorosis among schoolchildren who were lifelong residents of communities having either low or optimal levels of fluoride in drinking water.**
  Author(s): Selwitz RH, Nowjack-Raymer RE, Kingman A, Driscoll WS.
  Source: J Public Health Dent. 1998 Winter; 58(1): 28-35.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9608443

- **Dental caries experience in Indians of the Upper Xingu, Brazil.**
  Author(s): Rigonatto DD, Antunes JL, Frazao P.
  Source: Revista Do Instituto De Medicina Tropical De Sao Paulo. 2001 March-April; 43(2): 93-8.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11340483

- **Dental caries in nineteenth century upper Canada.**
  Author(s): Saunders SR, De Vito C, Katzenberg MA.
  Source: American Journal of Physical Anthropology. 1997 September; 104(1): 71-87. Erratum In: Am J Phys Anthropol 1998 March; 105(3): 405.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9331454

- **Dental caries in South African rural black women who had large families and long lactations.**
  Author(s): Walker AR, Dison E, Walker BF.
  Source: J Trop Med Hyg. 1983 December; 86(6): 201-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6672228

- **Dental caries prevalence and the use of fluorides in different European countries.**
  Author(s): Kalsbeek H, Verrips GH.
  Source: Journal of Dental Research. 1990 February; 69 Spec No: 728-32; Discussion 820-3.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2312894

- **Dental caries prevention by traditional Chinese medicines. Part II. Potent antibacterial action of Magnoliae cortex extracts against Streptococcus mutans.**
  Author(s): Namba T, Tsunezuka M, Hattori M.
  Source: Planta Medica. 1982 February; 44(2): 100-6.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7071194

- **Dental caries, fluoride levels and oral hygiene practices of school children in Matebeleland South, Zimbabwe.**
  Author(s): Sathananthan K, Vos T, Bango G.
  Source: Community Dentistry and Oral Epidemiology. 1996 February; 24(1): 21-4.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8833509

- **Dental caries, fluorosis, and fluoride exposure in Michigan schoolchildren.**
  Author(s): Szpunar SM, Burt BA.

Source: Journal of Dental Research. 1988 May; 67(5): 802-6. Review.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3284939

- **Dietary phosphate supplementation and its effects on dental caries and salivary and serum concentrations of calcium and inorganic phosphate in the rat.**
  Author(s): Dawes C, Shaw JH.
  Source: Archives of Oral Biology. 1965 July-August; 10(4): 567-77.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=5226824

- **Does raw sugar cane juice protect against dental caries.**
  Author(s): Fox FW, Noriskin JN.
  Source: South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde. 1976 December 25; 50(55): 2146.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1013866

- **Effect of amino acid supplements on dental caries in the syrian hamster.**
  Author(s): Englander HR, Keyes PH, Fitzgerald RJ.
  Source: Archives of Oral Biology. 1965 July-August; 10(4): 599-604.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=5226825

- **Effect of dietary supplements of fluoride on development of dental caries in the rat.**
  Author(s): Joost Larsen M, Poulsen S, Thylstrup A.
  Source: Caries Research. 1978; 12(3): 180-2.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=272955

- **Effect of long-term consumption of a probiotic bacterium, Lactobacillus rhamnosus GG, in milk on dental caries and caries risk in children.**
  Author(s): Nase L, Hatakka K, Savilahti E, Saxelin M, Ponka A, Poussa T, Korpela R, Meurman JH.
  Source: Caries Research. 2001 November-December; 35(6): 412-20.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11799281

- **Effects of propolis on dental caries in rats.**
  Author(s): Ikeno K, Ikeno T, Miyazawa C.
  Source: Caries Research. 1991; 25(5): 347-51.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=1836157

- **Effects on dental caries incidence of frequent ingestion of small amounts of sugars and stannous EDTA in chewing gum.**
  Author(s): Glass RL.

Source: Caries Research. 1981; 15(3): 256-62.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6783308

- **Incidence of dental caries in Lucknow school-going children.**
  Author(s): Chandra S, Chawla TN.
  Source: J Indian Dent Assoc. 1979 April; 51(4): 109-10. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=296202

- **Letter: Does raw sugar cane juice protect against dental caries?**
  Author(s): Fox FW, Noriskin JN.
  Source: South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde. 1976 May 8; 50(20): 760.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=935949

- **Oolong tea polyphenols inhibit experimental dental caries in SPF rats infected with mutans streptococci.**
  Author(s): Ooshima T, Minami T, Aono W, Izumitani A, Sobue S, Fujiwara T, Kawabata S, Hamada S.
  Source: Caries Research. 1993; 27(2): 124-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8319255

- **Oral lesions and dental caries status in perinatally HIV-infected children in Northern Thailand.**
  Author(s): Pongsiriwet S, Iamaroon A, Kanjanavanit S, Pattanaporn K, Krisanaprakornkit S.
  Source: International Journal of Paediatric Dentistry / the British Paedodontic Society [and] the International Association of Dentistry for Children. 2003 May; 13(3): 180-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12752917

- **Patterns of breast and bottle feeding and their association with dental caries in 1- to 4-year-old South African children. 1. Dental caries prevalence and experience.**
  Author(s): Roberts GJ, Cleaton-Jones PE, Fatti LP, Richardson BD, Sinwel RE, Hargreaves JA, Williams S.
  Source: Community Dent Health. 1993 December; 10(4): 405-13.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=8124629

- **Prevention of dental caries by acupuncture.**
  Author(s): Shimura N, Nakamura C, Hirayama Y, Turumoto A, Okada S.
  Source: Bull Tokyo Med Dent Univ. 1980 September; 27(3): 137-9.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6936090

- **Prevention of dental caries by Oriental folk medicines--active principles of Zizyphi Fructus for inhibition of insoluble glucan formation by cariogenic bacterium**

Streptococcus mutans.
Author(s): Kohda H, Kozai K, Nagasaka N, Miyake Y, Suginaka H, Hidaka K, Yamasaki K.
Source: Planta Medica. 1986 April; (2): 119-20.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3725931

- **Proposed approach to dental caries and oral hygiene via a mouthwash.**
Author(s): Oliver VM.
Source: Meharri Dent. 1968 June; 27(3): 16. No Abstract Available.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=4970874

- **Question from the clinician: fluoride supplementation and dental caries.**
Author(s): Gleiner S.
Source: Pediatrics in Review / American Academy of Pediatrics. 2002 May; 23(5): 186-7.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=11986495

- **Relationship between dental caries and vegetarian and non-vegetarian diets.**
Author(s): Rahmatulla M, Guile EE.
Source: Community Dentistry and Oral Epidemiology. 1990 October; 18(5): 277-8.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2249415

- **Relationship of betel chewing and dental caries.**
Author(s): Chandra S, Desai VM.
Source: J Indian Dent Assoc. 1970 November; 42(11): 269-76. No Abstract Available.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=4395934

- **Risk factors in dental caries.**
Author(s): Hunter PB.
Source: Int Dent J. 1988 December; 38(4): 211-7. Review.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3063664

- **Short-term consumption of probiotic-containing cheese and its effect on dental caries risk factors.**
Author(s): Ahola AJ, Yli-Knuuttila H, Suomalainen T, Poussa T, Ahlstrom A, Meurman JH, Korpela R.
Source: Archives of Oral Biology. 2002 November; 47(11): 799-804.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=12446187

- **Stress, relaxation and saliva: relationship to dental caries and its prevention, with a literature review.**
Author(s): Morse DR, Schacterle GR, Furst ML, Esposito JV, Zaydenburg M.

Source: Ann Dent. 1983 Winter; 42(2): 47-54. Review. No Abstract Available.
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6399971

- **Studies on dental caries prevention by traditional medicines. VIII. Inhibitory effect of various tannins on glucan synthesis by glucosyltransferase from Streptococcus mutans.**
  Author(s): Kakiuchi N, Hattori M, Nishizawa M, Yamagishi T, Okuda T, Namba T.
  Source: Chemical & Pharmaceutical Bulletin. 1986 February; 34(2): 720-5.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=2939967

- **Studies on dental caries prevention by traditional medicines. X. Antibacterial action of phenolic components from mace against Streptococcus mutans.**
  Author(s): Hattori M, Hada S, Watahiki A, Ihara H, Shu YZ, Kakiuchi N, Mizuno T, Namba T.
  Source: Chemical & Pharmaceutical Bulletin. 1986 September; 34(9): 3885-93.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=3815609

- **Studies on the mechanism of early dental caries.**
  Author(s): Yardeni J.
  Source: Journal of Dental Research. 1965 September-October; 44(5): 873-84.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=4953279

- **Sugar consumption and dental caries.**
  Author(s): Nadanovsky P.
  Source: British Dental Journal. 1994 October 22; 177(8): 280-1.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=7946663

- **The relation between betel chewing and dental caries.**
  Author(s): Moller IJ, Pindborg JJ, Effendi I.
  Source: Scand J Dent Res. 1977 January; 85(1): 64-70.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=265084

- **The relative effects of three dietary supplements on dental caries.**
  Author(s): Finn SB, Jamison HC.
  Source: Asdc J Dent Child. 1980 March-April; 47(2): 109-13. No Abstract Available.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=6928859

- **The role of early dietary habits in dental caries development.**
  Author(s): Ismail AI.
  Source: Spec Care Dentist. 1998 January-February; 18(1): 40-5. Review.
  http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9791306

Additional Web Resources

A number of additional Web sites offer encyclopedic information covering CAM and related topics. The following is a representative sample:

- Alternative Medicine Foundation, Inc.: **http://www.herbmed.org/**
- AOL: **http://search.aol.com/cat.adp?id=169&layer=&from=subcats**
- Chinese Medicine: **http://www.newcenturynutrition.com/**
- drkoop.com®: **http://www.drkoop.com/InteractiveMedicine/IndexC.html**
- Family Village: **http://www.familyvillage.wisc.edu/med_altn.htm**
- Google: **http://directory.google.com/Top/Health/Alternative/**
- Healthnotes: **http://www.healthnotes.com/**
- MedWebPlus: **http://medwebplus.com/subject/Alternative_and_Complementary_Medicine**
- Open Directory Project: **http://dmoz.org/Health/Alternative/**
- HealthGate: **http://www.tnp.com/**
- WebMD®Health: **http://my.webmd.com/drugs_and_herbs**
- WholeHealthMD.com: **http://www.wholehealthmd.com/reflib/0,1529,00.html**
- Yahoo.com: **http://dir.yahoo.com/Health/Alternative_Medicine/**

The following is a specific Web list relating to dental caries; please note that any particular subject below may indicate either a therapeutic use, or a contraindication (potential danger), and does not reflect an official recommendation:

- **General Overview**

  Immune Function
  Source: Healthnotes, Inc.; www.healthnotes.com

  Multiple Sclerosis
  Source: Healthnotes, Inc.; www.healthnotes.com

- **Chinese Medicine**

  Bibo
  Alternative names: Long Pepper; Fructus Piperis Longi
  Source: Chinese Materia Medica

- **Herbs and Supplements**

  Chaparral
  Source: The Canadian Internet Directory for Holistic Help, WellNet, Health and Wellness Network; www.wellnet.ca

Green Tea
Alternative names: Camellia sinensis
Source: Healthnotes, Inc.; www.healthnotes.com

Gymnema
Alternative names: Gurmar; Gymnema sylvestre
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

Strontium
Source: Healthnotes, Inc.; www.healthnotes.com

Zizyphus
Alternative names: Jujube; Ziziphus sp.
Source: Alternative Medicine Foundation, Inc.; www.amfoundation.org

General References

A good place to find general background information on CAM is the National Library of Medicine. It has prepared within the MEDLINEplus system an information topic page dedicated to complementary and alternative medicine. To access this page, go to the MEDLINEplus site at **http://www.nlm.nih.gov/medlineplus/alternativemedicine.html**. This Web site provides a general overview of various topics and can lead to a number of general sources.

CHAPTER 4. DISSERTATIONS ON DENTAL CARIES

Overview

In this chapter, we will give you a bibliography on recent dissertations relating to dental caries. We will also provide you with information on how to use the Internet to stay current on dissertations. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical dissertations that use the generic term "dental caries" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on dental caries, we have not necessarily excluded non-medical dissertations in this bibliography.

Dissertations on Dental Caries

ProQuest Digital Dissertations, the largest archive of academic dissertations available, is located at the following Web address: **http://wwwlib.umi.com/dissertations**. From this archive, we have compiled the following list covering dissertations devoted to dental caries. You will see that the information provided includes the dissertation's title, its author, and the institution with which the author is associated. The following covers recent dissertations found when using this search procedure:

- **CHANGES IN DISPARITIES IN DENTAL CARIES EXPERIENCES IN UNITED STATES ADULTS** by LUBWAMA, ROBERT N., PHD from UNIVERSITY OF MICHIGAN, 2003, 140 pages
  http://wwwlib.umi.com/dissertations/fullcit/3079494
- **THE EFFECTS OF VISUAL AND AUDITORY ACUITY LOSSES AND DENTAL CARIES ON ACADEMIC ACHIEVEMENT AMONG DISADVANTAGED THIRD-GRADE CHILDREN.** by GASTON, ALONZO DUBOIS, EDD from UNIVERSITY OF CINCINNATI, 1974, 149 pages
  http://wwwlib.umi.com/dissertations/fullcit/7502329
- **WATER-BORNE MOLYBDENUM: A STUDY OF ITS RELATIONSHIP TO DENTAL CARIES IN COLORADO.** by LUDINGTON, THEODORA TSONGAS, PHD from UNIVERSITY OF COLORADO AT BOULDER, 1976, 167 pages
  http://wwwlib.umi.com/dissertations/fullcit/7623648

Keeping Current

Ask the medical librarian at your library if it has full and unlimited access to the *ProQuest Digital Dissertations* database. From the library, you should be able to do more complete searches via **http://wwwlib.umi.com/dissertations**.

CHAPTER 5. PATENTS ON DENTAL CARIES

Overview

Patents can be physical innovations (e.g. chemicals, pharmaceuticals, medical equipment) or processes (e.g. treatments or diagnostic procedures). The United States Patent and Trademark Office defines a patent as a grant of a property right to the inventor, issued by the Patent and Trademark Office.[8] Patents, therefore, are intellectual property. For the United States, the term of a new patent is 20 years from the date when the patent application was filed. If the inventor wishes to receive economic benefits, it is likely that the invention will become commercially available within 20 years of the initial filing. It is important to understand, therefore, that an inventor's patent does not indicate that a product or service is or will be commercially available. The patent implies only that the inventor has "the right to exclude others from making, using, offering for sale, or selling" the invention in the United States. While this relates to U.S. patents, similar rules govern foreign patents.

In this chapter, we show you how to locate information on patents and their inventors. If you find a patent that is particularly interesting to you, contact the inventor or the assignee for further information. **IMPORTANT NOTE:** When following the search strategy described below, you may discover non-medical patents that use the generic term "dental caries" (or a synonym) in their titles. To accurately reflect the results that you might find while conducting research on dental caries, we have not necessarily excluded non-medical patents in this bibliography.

Patents on Dental Caries

By performing a patent search focusing on dental caries, you can obtain information such as the title of the invention, the names of the inventor(s), the assignee(s) or the company that owns or controls the patent, a short abstract that summarizes the patent, and a few excerpts from the description of the patent. The abstract of a patent tends to be more technical in nature, while the description is often written for the public. Full patent descriptions contain much more information than is presented here (e.g. claims, references, figures, diagrams, etc.). We will tell you how to obtain this information later in the chapter. The following is an

[8]Adapted from the United States Patent and Trademark Office: **http://www.uspto.gov/web/offices/pac/doc/general/whatis.htm**.

example of the type of information that you can expect to obtain from a patent search on dental caries:

- **Antibodies against Streptococcus**

  Inventor(s): Lehner; Thomas (London, GB2), Smith; Roberta (London, GB2)

  Assignee(s): Council of Governors of the United Medical and Dental Schools of Guy's (London, GB2)

  Patent Number: 5,518,721

  Date filed: September 7, 1994

  Abstract: Monoclonal antibodies which bind the surface antigen I/II of Streptococcus sobrinus serotype d and cross react with the surface antigen I/II of Streptococcus mutans serotypes c, e, f and g and method for producing the antibody. Compositions comprising the antibody used in a method to combat **dental caries** in a mammal.

  Excerpt(s): Streptococcus mutans has been recognised for many years as the major organism responsible for the development of **dental caries** in mammals. Various vaccines have been proposed in the past based on various antigenic fragments of S. mutans. One such vaccine is described in British Patent No. 2,060,647 based upon the antigen known as I or I/II. Antigen I has a molecular weight, as determined by sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) of 146-155 Kd. Antigen I/II is believed to be a conjugate of antigen I and antigen II, this I/II antigen having a molecular weight determined by SDS-PAGE of 175-195 Kd. Published European Patent Application No. EP-A-0 116 472 describes antigen X which is a much smaller molecule having a molecular weight, determined by SDS-PAGE of about 3.5-4.5 Kd but which appears to include the same antigenic determinants included within antigens I and I/II. Antibodies against antigens I, I/II and X are known. The above-mentioned British Patent describes the raising of antibodies against antigens I and I/II by conventional procedures in experimental animals, for example rhesus monkeys, rabbits and mice. These antibodies are proposed primarily for the purification of the antigen by affinity chromatography but the Patent Specification mentions the possibility of using such antibodies for passive immunisation by conventional means. Conventional passive immunisation involves parenteral administration of the antibodies but while such techniques are theoretically available, as a practical matter, passive immunisation has never been regarded as clinically attractive and indeed, the British Patent refers to the preferred use of the antigenic materials for direct immunisation. All antibodies that have been raised against S. mutans serotype c or against the streptococcal antigen serotype c (SA.sub.c) exhibit a certain degree of cross-reactivity. It is well known that such antibodies are also cross-reactive with antigenic material originating from serotypes e and f of S. mutans. In clinical practice, it is found that serotypes c, e and f amount to about 90% of the bacterial S. mutans population so that the prophylactic or therapeutic use of antibodies raised against serotype c are of considerable practical value but fail to be effective in relation to the residual approximately 10% of the bacterial population. In some series serotype d is found in addition to serotype c in up to 50% of children examined.

  Web site: http://www.delphion.com/details?pn=US05518721__

- **Antibodies against streptococcus**

  Inventor(s): Lehner; Thomas (London, GB2), Smith; Roberta (London, GB2)

  Assignee(s): Council of Governors of the United Medical School and Dental Schools of (London, GB2)

  Patent Number: 5,612,031

  Date filed: June 7, 1995

  Abstract: Antibodies which bind the surface antigen I/II of Streptococcus sobrinus serotype d and cross react with the surface antigen I/II of Streptococcus mutans serotypes c, e, f and g and method to combat **dental caries** by applying the antibodies which bind the surface antigen I/II of Streptococcus sobrinus serotype d and cross react with the surface antigen I/II of Streptococcus mutans serotypes c, e, f and g.

  Excerpt(s): This invention relates to antibodies useful to combat **dental caries.** Streptococcus mutans has been recognised for many years as the major organism responsible for the development of **dental caries** in mammals. Various vaccines have been proposed in the past based on various antigenic fragments of S. mutans. One such vaccine is described in British Patent No. 2,060,647 based upon the antigen known as I or I/II. Antigen I has a molecular weight, as determined by sodium dodecyl sulphate polyacrylamide gel electrophoresis (SDS-PAGE) of 146-155 Kd. Antigen I/II is believed to be a conjugate of antigen I and antigen II, this I/II antigen having a molecular weight determined by SDS-PAGE of 175-195 Kd. Published European Patent Application No. EP-A-0 116 472 describes antigen X which is a much smaller molecule having a molecular weight, determined by SDS-PAGE of about 3.5-4.5 Kd but which appears to include the same antigenic determinants included within antigens I and I/II. Antibodies against antigens I, I/II and X are known. The above-mentioned British Patent describes the raising of antibodies against antigens I and I/II by conventional procedures in experimental animals, for example rhesus monkeys, rabbits and mice. These antibodies are proposed primarily for the purification of the antigen by affinity chromatography but the Patent Specification mentions the possibility of using such antibodies for passive immunisation by conventional means. Conventional passive immunisation involves parenteral administration of the antibodies but while such techniques are theoretically available, as a practical matter, passive immunisation has never been regarded as clinically attractive and indeed, the British Patent refers to the preferred use of the antigenic materials for direct immunisation.

  Web site: http://www.delphion.com/details?pn=US05612031__

- **Antibodies to S. mutans and uses thereof**

  Inventor(s): Hume; Wyatt R. (Los Angeles, CA), Shi; Wenyuan (Los Angeles, CA)

  Assignee(s): The Regents of the University of California (Oakland, CA)

  Patent Number: 6,231,857

  Date filed: August 20, 1999

  Abstract: The invention describes three monoclonal IgG antibodies, referred to as SWLA1, SWLA2, and SWLA3, which appear to recognize a species-specific lipooligosaccharide or lipopolysaccharide on the cell surface of S. mutans. The invention also describes a rapid method of detection of S. mutans without the need for prior growth of the bacteria in culture. The invention further describes a methods of utilizing

these antibodies for rapidly quantitatively detecting S. mutans. These methods are sensitive enough to detect the presence of a single S. mutans bacterial cell. These methods can be widely used in the clinical diagnosis and treatment of **dental caries** in humans.

Excerpt(s): The present invention relates to novel antibodies to the Streptococcus mutans bacteria that are naturally found in the mouth, and play a role in the development of **dental caries.** The invention relates to methods of detection of S. mutans using the antibodies of the invention or fragments or derivatives thereof. The invention also relates to diagnosing, monitoring, treating and protecting the teeth from **dental caries** using the antibodies of the invention or fragments or derivatives thereof. Throughout this application, various publications are referenced within parentheses and cited at the end of the application. The disclosures of these publications are hereby incorporated by reference herein in their entireties. Currently human **dental caries,** or cavities, are detected by changes in translucency, color, hardness or X-ray density of teeth. These technologies have limitations both in specificity and reproducibility. Further, they do not show, at a single time point, whether or not the disease is active.

Web site: http://www.delphion.com/details?pn=US06231857__

- **Anti-caries oral compositions**

Inventor(s): Acevedo; Ana Maria (Caracas, VE), Chatterjee; Robi (South Setanket, NY), Kleinberg; Israel (Smithtown, NY)

Assignee(s): The Research Foundation of State University of New York (Stony Brook, NY)

Patent Number: 5,762,911

Date filed: March 5, 1996

Abstract: The present invention relates to oral compositions containing anti-caries agents distributed in an oral vehicle. In particular, the present invention provides oral compositions containing calcium, arginine and a cariostatic anion distributed in an oral vehicle. A method for preparing oral compositions containing anti-caries agents is also provided by the present invention. A method of reducing **dental caries** is described which comprises delivering a therapeutically effective amount of an oral composition containing calcium, arginine and a cariostatic anion into the oral cavity.

Excerpt(s): Dental caries is a multi-factorial disease which occurs when cariogenic oral bacteria metabolize simple and complex sugars to produce acids which cause the dissolution of tooth enamel, thereby creating a caries lesion or cavity. The present invention provides oral compositions containing anti-caries agents distributed in an oral vehicle. In particular, the present invention describes oral compositions containing calcium, arginine, and a cariostatic anion distributed in an oral vehicle. A method for preparing oral compositions containing anti-caries agents is also described by the present invention. A method of reducing **dental caries** is described which comprises delivering a therapeutically effective amount of an oral composition containing calcium, arginine and a cariostatic anion into the oral cavity. Ever since Miller in 1890 first provided evidence that acid produced by the oral bacteria during the fermentation of carbohydrates is mainly responsible for the demineralization of teeth and the initiation of the **dental caries** process, the ability to retard or prevent the demineralization of teeth has been extensively studied. Miller W. D. (1890) "Micro-organisms of the human mouth," Reprinted 1973. Karger, Basel. Miller described the formation of **dental caries** as

a two step process. In the first step, oral bacteria, primarily Gram-positive bacteria, metabolize fermentable carbohydrates present in the oral cavity to produce acid. In the second step, the acids generated by the oral bacteria demineralize tooth enamel, dentine and/or cementum, thereby creating a caries lesion or cavity in the tooth crown or root. The primary source of fermentable carbohydrates metabolized by the oral bacteria in the first step of the Miller process is the diet. Glucose is the main sugar available from dietary carbohydrates. It is a constituent monosaccharide of sucrose, maltose, lactose and starch. Studies on pure cultures of oral bacteria have shown that glucose is readily fermented by the Gram-positive bacteria which contribute far more to the fermentation process than oral Gram-negatives. Such fermentation can be arbitrarily classified as either homofermentative, where lactic acid is the main product, or heterofermentative, where substantial amounts of products other than lactic, including formic, acetic, propionic and succinic acids, as well as ethanol and carbon dioxide can be produced. Platt and Foster (1958) J. Bacteriol., 75:453-459.

Web site: http://www.delphion.com/details?pn=US05762911__

- **Antimicrobial chewing gum**

  Inventor(s): Barry; John E. (Derry, NH), Trogolo; Jeffrey A. (Boston, MA)

  Assignee(s): AgION Technologies L.L.C. (Wakefield, MA)

  Patent Number: 6,365,130

  Date filed: November 23, 1998

  Abstract: The present invention provides a novel chewing gum product generally for the lysis and killing of oral microbes. In a preferred embodiment, the chewing gum product comprises an antimicrobial metal ion component and an inorganic ceramic carrier, and provides a concentration of such substances from about 0.05 to 50 weight percent of the chewing gum. In particular, these compositions may comprise zeolites ion-exchanged with antimicrobial metals, in addition to other oral care compounds. The present invention also relates to methods of using such compositions for treating and inhibiting **dental caries,** dental plaque and gingivitis, oral malodor and periodontal conditions. The compositions of the present invention may be incorporated into chewing gum according to conventional methods used in the art.

  Excerpt(s): The present invention relates to chewing gum products containing an antimicrobial agent for killing microbes, particularly oral bacteria, for reducing or preventing dental plaque and caries and gingivitis, and to methods for treating the same, and the like. There is a need in the dental arts for an improved means of promoting dental health and hygiene, including a means for reducing plaque and **dental caries,** gingivitis, and especially for killing microbes which cause these dental problems, as a result of improper and inadequate tooth brushing. Plaque may be removed to some extent by effective brushing of the teeth. However, some areas of the teeth, which are less accessible and cannot be easily reached by a toothbrush, are particularly susceptible to plaque formation and consequently to calculus. Left unhindered, the plaque increases in size and more tenaciously adheres to the teeth. Although brushing with a toothbrush and dentifrice is a widely recognized technique for maintaining dental health, the average person brushes only once a day for approximately one minute. Therefore, a great need exists for finding additional methods for improving daily oral hygiene. Dental caries, which cause the progressive decay of teeth, are manifested by localized demineralization, caused by acids produced from bacteria that ferment carbohydrate foods. The process may begin when bacteria in the

mouth adhere to a tooth surface, thereby forming a dental plaque. The plaque is a product of microbial growth, primarily derived from food residues in the mouth. Mucoproteins and minerals present in saliva and dead cells in the mouth also contribute to plaque formation. There is substantial evidence that dental plaque is the predominant etiological factor responsible for both **dental caries** and periodontal disease, due to the generation of acids within the plaque structure. Thus, dental compositions having antimicrobial properties are beneficial for killing oral bacteria that contribute to the formation of dental plaque.

Web site: http://www.delphion.com/details?pn=US06365130__

- **Apparatus for the treatment of dental caries**

  Inventor(s): Baysan; Aylin (London, GB), Holland; Gregory R. (Irvine, CA), Lynch; Edward (Belfast, GB), Mc Pherson; Roger (Cerritos, CA), Schemmer; Jurgen H. (King City, CA), Weisel; Tom (Mesa, CA)

  Assignee(s): Curozone Ireland Limited (IE)

  Patent Number: 6,454,566

  Date filed: November 13, 2000

  Abstract: Apparatus for the treatment of **dental caries** includes a source of oxidizing gas and a handpiece for delivering the gas to a tooth. A cup attached to the handpiece is provided for receiving the gas and exposing a selected area of the tooth to the gas. The cup includes a resilient edge for sealably the edge for engaging the tooth around the selected area to prevent escape of a gas therepast.

  Excerpt(s): The present invention generally relates to the treatment of **dental caries,** and more particularly is directed to apparatus for the treatment of **dental caries** utilizing an oxidizing gas. The role of specific micro-organism such as, for example, streptococcus mutants in **dental caries** is well documented. Enzymes produced by such micro-organisms synthesize dextran from the sucrose passing through the month with food or drink resulting in the formation of dental plaque and **dental caries.** Dental caries is the decay of teeth caused by demineralization of the enamel surface with organic acids produced by bacteria which adhere to teeth surfaces.

  Web site: http://www.delphion.com/details?pn=US06454566__

- **Bacteriophage-encoded enzymes for the treatment and prevention of dental caries and periodontal diseases**

  Inventor(s): Delisle; Allan L. (Sykesville, MD)

  Assignee(s): University of MD (College Park, MD)

  Patent Number: 6,635,238

  Date filed: September 14, 2001

  Abstract: A method for the treatment and prevention of **dental caries** and periodontal diseases using bacteriophages and phage-encoded anti-bacterial enzymes to inhibit establishment of bacteria in the oral cavity is provided. Also provided are methods for studying the cell wall of an oral bacterium, a method for preventing spoilage of perishable items and a method for removing dextrans from surfaces utilized in sugar

manufacture. Purified enzymes and the isolated DNA fragments encoding them are also provided.

Excerpt(s): This invention relates to bacteriophage-encoded enzymes useful in preventing **dental caries** and periodontal diseases. More specifically, this invention relates to lysozyme-like enzymes isolated from bacteriophages which are capable of killing cariogenic bacteria and other periodontal disease-causing organisms. The invention also relates to dextranase-like enzymes suitable for dental treatments (i.e., loosening plaque) and other applications where it is desired to remove dextran and other bacterial polysaccharides (i.e., mutan) synthesized from sucrose. With regard to their function in dental plaque, phages are likely to influence the plaque flora in several potentially significant ways. Prophages, for example, provide immunity to super-infection by homoimmune phages and would presumably assist lysogens which carry them in competing with other bacteria in plaque by killing phage-sensitive competitors in a manner analogous to bacteriocinogenic cells. The semi-solid nature of dental plaque provides an especially favorable environment for this type of competition. Alternatively, lytic phage would be expected to select for phage-resistant mutants of sensitive strains and for mucoid mutants (phenotypically phage-resistant), which could well have altered colonizing and pathogenic properties. Actinophage-resistant mutants have in fact already been used to study cell surface structures that appear to be involved in specific, intergeneric oral bacterial coagreggation reactions (Delisle, A. L. et al (1988) Infect. Immun. 56:54-59; Tylenda, C. A. et al (1985) Infect. Immun. 48:228-233), which are believed to play an important role in colonization of dental plaque (Kolenbrander, P. E. et al (1985) In, S. E. Murgenhagen and B. Rosan (eds) pp. 164-171, American Society for Microbiology, Washington, D.C.). The literature on S. mutans phages dates back to 1970, when Greer first claimed to be able to induce phages, by treatment with mitomycin C, from oral streptococcal strains AHT, BHT and HHT (Greer, S. W., et al (1970) IADR Abstr. 160; J. Dent. Res, 48A:88) and subsequently claimed that the same virus was present in all of eight cariogenic streptococci he examined, but not in non-cariogenic strains (Greer, S. W., et al (1971) J. Dent. Res. 50:1594-1604). He then reported that lysogens could be cured of their prophages by treatment with acridine orange (Greer, S. W., et al (1971) IADR Abstr. 57: J. Dent. Res. 49:67) and nitrosoguanidine (Greer, S. W., et al (1972) IADR Abstr. 68: J. Dent. Res. 50:65). The latter was used to isolate temperature-sensitive mutants, one of which was heat-inducible and could be used to obtain cured cells by brief heating. Greer also proposed a curing procedure based on radiosensitization of DNA by incorporating 5-bromodeoxyuridine lysogens (Ramberg, E. et al (1973) IADR Abstr. 113: J. Dent. Res. 52a), but its application to S. mutans was never subsequently reported. Greer never reported the successful isolation of an infectious phage which could be grown in S. mutans. Difficulties in repeating Greer's induction experiments led many microbiologists to assume that he was really working with enterococci, which were common contaminants in the oral streptococcal cultures being exchanged among various laboratories during this time.

Web site: http://www.delphion.com/details?pn=US06635238__

- **Bacteriostatic and antibacterial agent containing mango kernel component**

  Inventor(s): Arai; Megumi (Saitama, JP), Dosako; Shunichi (Saitama, JP), Furuya; Hirokazu (Saitama, JP), Hashiba; Honoo (Saitama, JP), Ito; Fumio (Saitama, JP), Kabuki; Toshihide (Saitama, JP), Nakajima; Hadjime (Saitama, JP), Tadokoro; Seiichiro (Saitama, JP)

  Assignee(s): Snow Brand Milk Products Co., Ltd. (Hokkaido, JP)

  Patent Number: 6,063,382

  Date filed: March 26, 1998

  Abstract: A mango kernel triturate or mango kernel extract has a bacteriostatic and antibacterial activity, and thus can be used in food products or cosmetics as a bacteriostatic and antibacterial agent. Furthermore, agents for preventing and treating acne or agents for preventing **dental caries** can be provided by adding said extract as an effective component.

  Excerpt(s): The present invention relates to a mango kernel triturate or a mango kernel extract, which has a bacteriostatic and antibacterial activity, and bacteriostatic and antibacterial agents containing them as an effective component. Furthermore, the present invention relates to beverages and foods to which said bacteriostatic and antibacterial agent is added. Furthermore, the present invention relates to cosmetics to which said bacteriostatic and antibacterial agent is added. Furthermore, the present invention relates to oral hygienic products to which said bacteriostatic and antibacterial agent is added. have been used as means to prolong shelf-life. The addition of antibacterial agents to foods has been a particularly effective means to control microbial contamination. Thus, recently, antibacterial agents derived from natural substances as well as chemically synthesized antibacterial agents have been developed. These antibacterial agents derived from natural substances are referred to as preservatives or shelf-life extenders for which various antibacterial agents derived from the extracts of natural substances, such as the thick-stemmed bamboo (Phyllostachy heterocycla MITF), yucca, Japanese horseradish, garlic and tea, have been used (Shokuhin to Kaihatsu, Vol. 30, pp. 27-33, 1996; Monthly Food Chemicals, August 1996). On the other hand, a plant mango (Mangifera indica), which belongs to family Anacardiaceae, order Rutales, is grown naturally or cultivated mainly in tropical and subtropical regions. The fruit of the mango tree is used for food. For example, about 9,000 metric tons of the fruit were imported to Japan from January to September in 1996. Further, the oil extracted from mango kernels has been used as a cocoa butter substitute in countries such as India, and the oil cakes obtained after extraction and pressing processes have been used, for example, as a food filler (JAOCS, Vol. 60, p. 88, 1983).

  Web site: http://www.delphion.com/details?pn=US06063382__

- **Caries treatment method with fluoride**

  Inventor(s): Connelly; John Jude (Ottawa, CA)

  Assignee(s): Knowell Therapeutic Technologies, Inc. (Ontario, CA)

  Patent Number: 5,738,113

  Date filed: March 12, 1996

  Abstract: A method for the control and reduction of **dental caries** is provided for individuals who are at risk of **dental caries.** The method comprising a first step of

applying an antimicrobial treatment followed shortly thereafter by a second step of applying a fluoride treatment.A method for the diagnosis, control and reduction of **dental caries,** the method comprising testing for Streptococcus mutans in an oral cavity of a patient and determining the patient's risk level for developing **dental caries,** to establish what treatment, if any, the patient requires in accordance with a set of treatment guidelines.

Excerpt(s): The present invention relates to a method for the diagnosis and reduction of **dental caries.** More specifically, the method of the present invention relates to uses of a Streptococcus mutans monitoring test in association with fluoride and chlorhexidine. More particularly the present invention relates to an improvement in the control and reduction of **dental caries** by the use of fluoride in association with an antimicrobial agent such as chlorhexidine and a Streptococcus mutans monitoring test. Affordability, predictability and true prevention as the bases for dental treatments are increasingly the concerns of more and more dental patients. Increasingly, dentists are required to provide more cost-effective services for both the insured patient and the uninsured patient. Effective medical management of **dental caries** is required particularly for those populations of patients that exhibit increased risk factors for caries. It is known that the presence of **dental caries** in certain patient subpopulations accounts for a substantial proportion of the **dental caries** seen in the population at large. In his article entitled, "The Medical Management of Dental Caries" (JADA, Vol. 125, January 1994, pp 31S to 39S), Edelstein quotes the U.S. Oral Health Coordinating Committee claim that 25% of U.S. children accounted for 75% of **dental caries** in 1986-1987. He also notes that caries among children world-wide is evident in many developing countries and much of Central Europe.

Web site: http://www.delphion.com/details?pn=US05738113__

- **Composite toothpaste products**

  Inventor(s): Aoki; Hideki (Inashiki-gun, JP), Aoki; Hidenao (Tokyo, JP), Aoki; Marehito (Tokyo, JP)

  Assignee(s): Tokyo Bioceramics Institute Co., Ltd. (Tokyo, JP)

  Patent Number: 6,358,494

  Date filed: December 1, 1999

  Abstract: A composite toothpaste product comprising a toothpaste containing a hydroxyapatite as a main active ingredient and another toothpaste containing a fluorine compound as a main active ingredient, which are enclosed with a container made of, for instance, a flexible tube but separated from each other by a partition united to the container. In the composite toothpaste product, the toothpastes are separated from each other with no contact when it is out of use, and are squeezed out of the container, when in use, in such a manner that the latter toothpaste is enclosed with the former. It is far more effective in removing bacterial plaque, improving tooth whiteness, and preventing **dental caries** than the conventional toothpaste products containing only either a hydroxyapatite or a fluorine compound.

  Excerpt(s): The present invention relates to a composite toothpaste product containing a fluorine compound and a hydroxyapatite in combination. In particular, the invention relates to an improved composite toothpaste product which imparts favorable effects to teeth by way of the activity of the fluorine compound as well as the activity of the hydroxyapatite, when the teeth are brushed. The toothpaste generally comprises water,

a wetting agent, and an abrasive. Until now, proposals to incorporate a variety of additives into the toothpaste for improving functions of the toothpaste have been made. Some of these proposals have been employed in the production of commercially available toothpastes. A representative additive is a fluorine compound. It has been confirmed that a fluorine compound is dissociated in an aqueous toothpaste to give a fluorine ion which reacts with a surface layer of the tooth to enhance the surface hardness of the tooth. A toothpaste containing a fluorine compound is described in Japanese Patent Provisional Publication No. 46-4150.

Web site: http://www.delphion.com/details?pn=US06358494__

- **Composition for treating dental caries caused by streptococcus mutans**

  Inventor(s): Fischetti; Vincent (West Hempstead, NY), Loomis; Lawrence (Columbia, MD)

  Assignee(s): New Horizons Diagnostics Corp (Columbia, MD)

  Patent Number: 6,399,098

  Date filed: September 28, 2000

  Abstract: The present invention discloses a method for treating baterial **dental caries** caused by Streptococcus mutans, comprising administering a composition comprising an effective amount of at least one lytic enzyme produced by a bacteriophage specific for Streptococcus mutans, with the lytic enzyme having the ability to exclusively digest a cell wall of the Streptococcus mutans infecting all or part of a mouth or teeth, and a toothpaste for delivering the enzyme to the mouth and teeth.

  Excerpt(s): The present invention discloses a method and composition for the treatment of bacterial infections by the use of a lysing enzyme blended with an appropriate carrier suitable for the treatment of the infection. In the past, antibiotics have been used to treat various infections. The work of Selman Waksman in the introduction and production of Streptomycetes, Dr. Fleming's discovery of penicillin, are well known as well as the work of numerous others in the field of antibiotics. Over the years, there have been additions and chemical modifications to the "basic" antibiotics in attempts to make them more powerful, or to treat people allergic to these antibiotics. Others have found new uses for these antibiotics. U.S. Pat. No. 5,260,292 (Robinson et al.) discloses the topical treatment of acne with aminopenicillins. The method and composition for topically treating acne and acneiform dermal disorders includes applying an amount of an antibiotic selected from the group consisting of ampicillin, amoxicillin, other aminopenicillins, and cephalosporins, and derivatives and analogs thereof, effective to treat the acne and acneiform dermal disorders. U.S. Pat. No. 5,409,917 (Robinson et al.) discloses the topical treatment of acne with cephalosporins.

  Web site: http://www.delphion.com/details?pn=US06399098__

- **Compositions for inhibiting dental caries and/or middle ear infections and uses thereof**

  Inventor(s): Aaltonen; Antti Sakari (Marttilantie 2as.6, FIN-03850 Pusula, FI), Suhonen; Jouko (663 Garth Ct., Yorktown Heights, NY 10598)

  Assignee(s): none reported

  Patent Number: 6,143,330

  Date filed: August 24, 1998

  Abstract: Compositions for treating or preventing **dental caries** and/or middle ear infections. These compositions comprise antibodies to **dental caries** and/or antibodies to bacteria causing middles ear infections and/or an agent preventing the adhesion, accumulation or reporduction of the pathogens of tooth or middle ear. The preferred agent is xylitol. Methods for using these compositions are also included.

  Excerpt(s): This invention relates to an immune milk preparation for the prevention of middle ear infections (otitis media) in children. The preparation contains antibodies produced against bacteria which cause middle ear infections and, if desired, also **dental caries** inhibiting agents. So called immune milk can be produced by vaccinating a pregnant cow against certain pathogens whereby the cow organism forms antibodies to these diseases, which antibodies are transferred to the colostrum. The remedying effects of immune milk have been known for a long time. Already since the beginning of the century immunized goat or cow milk has been tested in the treatment of various bacterial and viral diseases. The most important of the more recent studies are concentrated on the diseases dependent on the microbes of the gastrointestinal tract, i.a. rheumatoid arthritis, **dental caries,** gingivitis, diarrheas, dysentery, gastritis and cryptosporidiosis. A **dental caries** inhibiting product of immunized cow's milk, which contains specific antibodies to killed Streptococcus mutans cells, is known (U.S. Pat. No. 4,324,782). In the United States usual immune milk is produced by maintaining the antibody level with boosters. The amount of antibodies is rather small, and the effect is based on daily administration. In Taiwan immune milk is sold as a health drink. In Australia powder containing antibodies to rotavirus has been mixed into i.a. infant formulas (Murtomaa-Niskala, 1994). Whole milk products also contain non-specific antibacterial factors which may have effect of microbial flora (Takahashi et al., 1992). In Finland immune milk has been prepared against i.a. Helicobacter pylori infection (Oona et al., 1994), and antibodies to Streptococcus mutans and Streptococcus sobrinus, obtained from the colostrum of an immunized bovine (Loimaranta et al., 1996), have been studied at the Dental Department of the University of Turku (Prof. Jorma Tenovuo, personal communication). This immune milk has been produced at the Centre of Agricultural Research in Jokioinen.

  Web site: http://www.delphion.com/details?pn=US06143330__

- **Fluoridated micellar casein**

  Inventor(s): Berrocal; Rafael (St-Legier, CH), Neeser; Jean-Richard (Savigny, CH), Tachon; Pierre (Cugy, CH)

  Assignee(s): Nestec S.A. (Vevey, CH)

  Patent Number: 5,833,953

  Date filed: June 14, 1996

Abstract: Process for the preparation of fluoridated casein micelles, in which at least 100 ppm of a soluble fluoride salt are added of a solution comprising micellar casein and the fluoridated micellar casein is isolated. Food or pharmaceutical composition for treating **dental caries** or plaque comprising an effective quantity of fluoridated micellar casein or its micellar subunits.

Excerpt(s): The subject of the present invention is the fluoridation of the casein of a milk and the use of the fluoridated caseins as agents for treating dental pathologies. Cow's milks comprising fluorine salts, such as sodium fluoride, has already been proposed for reducing the incidence of **dental caries** in human health (Beddows G. et al., Analyst, 106, 1341-1344, 1981). Other studies have, moreover, shown that most of the fluoride exists in equilibrium in a cow's milk in a free ionic form, while a small part may be complexed by the milk calcium. The fluoride is not therefore necessarily complexed with the milk proteins, especially with the micellar casein (Beddows G. et al., J. Fd Technology, 17, 55-62, 1982).

Web site: http://www.delphion.com/details?pn=US05833953__

- **Fluoride ion sustained release preformed glass ionomer filler and dental compositions containing the same**

Inventor(s): Fuchigami; Kiyomi (Kyoto, JP), Ikemura; Kunio (Joyo, JP), Kitamura; Toshio (Uji, JP), Miyai; Kozo (Nara, JP), Roberts; Thomas Arwel (Congleton, GB)

Assignee(s): Shofu Inc. (Kyoto, JP)

Patent Number: 5,883,153

Date filed: July 15, 1997

Abstract: There is provided a fluoride-ion sustained release pre-formed glass ionomer filler comprising a powdery reaction product of polyalkenoic acid with a fluorine-containing glass, and a method of producing the same. There is also provided a dental composition containing the filler. The fluoride-ion sustained release pre-formed glass ionomer filler is long capable of releasing fluoride ions in the presence of water without involving disintegration. The dental composition of the invention is useful particularly for prevention of **dental caries** and like trouble.

Excerpt(s): The present invention relates to fluoride-ion releasable pre-formed glass ionomer fillers. More particularly, the invention relates to a pre-formed glass ionomer filler capable of stable and sustained fluoride ion release without involving elution and disintegration, and dental compositions containing the same. The pre-formed glass ionomer filler in accordance with the present invention is useful mainly for the preparation of dental compositions. Additionally, because of its sustained fluorine releasability feature, the pre-formed glass ionomer filler is also useful for hard tissues of a living body which take in fluorine, including teeth and bones in particular and, therefore, it is applicable for use in various fields, such as surgery, orthopaedic surgery, and plastic surgery, as well as in dentistry. Fluoride ion fluorinates the hydroxyapatite of dentin and thus strengthen the dentin. Therefore, fluoride ion has much to be expected of for use in inhibiting or preventing **dental caries.** Further, it is conceivable to use fluoride ions in combination with calcium ion and phosphoric ion for capping dental tuble, calcification thereof, and/or recalcification of softened dentin, through which much can be expected for protection of dental pulp and otherwise.

Web site: http://www.delphion.com/details?pn=US05883153__

- **Fluoride-releasing compositions**

  Inventor(s): Burgess; John O. (New Orleans, LA), Ding; Xingzhe (Aurora, CO), Ling; Long (Metairie, LA), Xu; Xiaoming (Metairie, LA)

  Assignee(s): Board of Supervisors of Louisiana State University and Agricultural and (Baton Rouge, LA)

  Patent Number: 6,703,518

  Date filed: March 5, 2003

  Abstract: Chelating monomers and fluoride-releasing compositions are disclosed that may be incorporated into dental composite restorative materials or other dental materials, to produce materials with high fluoride release rates, and high fluoride recharge capability. Such resins may be used in dental restorative materials to help reduce the level of **dental caries** in patients, particularly the level of caries occurring on the margins of the restorative materials.

  Excerpt(s): This invention pertains to compositions useful in dental composites or in other composite materials, particularly to compositions that release fluoride ion and that may be recharged with additional fluoride ion. Fluoride is the most widely used agent to prevent **dental caries** (tooth decay). Tooth decay can occur on the margins of dental restorations. Such recurring caries is a frequent cause for failure of dental restorations. Fluoride-releasing restorative materials have been used to try to reduce recurrent caries at restoration margins. The effectiveness of such fluoride-releasing materials varies widely. Fluoride-releasing materials generally fall into one of four categories: glass ionomers, resin-modified glass ionomers, compomers, and fluoride-releasing composite resins. In general, materials with higher levels of fluoride release tend to have poorer mechanical properties (e.g., a lower compressive strength) High fluoride-releasing materials have therefore been used clinically primarily to restore decayed, but non-biting areas. Glass ionomers and resin-modified glass ionomers release fluoride as a by-product during acid-base reactions between the ion-leachable fluoride glass and an acidic liquid. Glass ionomers and resin-modified glass ionomers generally have high fluoride release and recharge capabilities, but they have low strength and poor esthetic qualities. Composite resins have been widely used in restorative dentistry because they have high strength, good wear resistance, and excellent esthetics, but they release relatively small amounts of fluoride, and have low fluoride-recharge capabilities. There is an unfilled need for dental composite resins with high strength, good wear resistance, high fluoride release rates, and high fluoride recharge capability.

  Web site: http://www.delphion.com/details?pn=US06703518__

- **Image measuring apparatus**

  Inventor(s): Devaraj; Balasigamani (Yamagata, JP), Horiuchi; Hiroshi (Sendai, JP), Inaba; Humio (Sendai, JP), Ishihata; Hiroshi (Sendai, JP), Kobayashi; Masaki (Yamagata, JP), Takeda; Motohiro (Yamagata, JP), Usa; Masashi (Sendai, JP)

  Assignee(s): Biophotonics Information Laboratories Ltd. (Yamagata, JP)

  Patent Number: 5,818,587

  Date filed: May 10, 1996

  Abstract: An image measuring apparatus for measuring an image of a tooth or gum applies the radiation of a laser beam to permit extremely quick, reliable, safe detection of

dental caries and other dental pathological conditions. The low incident power of the laser radiation would not cause damage or pain to the tissue, such as the tooth or gum. The image measuring apparatus is equipped with a light source which emits light having at least a wavelength in a range of 500 nm or more to less than 600 nm; it uses the light emitted from the light source to obtain 2-dimensional images or computed tomographic images of a tooth or gum from the light, which has been transmitted through the tooth or gum, by using an optical heterodyne detection method.

Excerpt(s): The present invention relates to an imaging apparatus to obtain images of the internal structure of human teeth or gums and use the obtained images for diagnosis in dentistry. The detection or diagnosis of a decayed tooth is most important and essential in odontotherapy. Hitherto, radiographic diagnoses have generally been carried out. There is a danger, however, that X-rays adversely affect biomedical tissues and the requirements in carrying out radiographic diagnoses are becoming more strict to ensure safety. Besides, it is difficult to detect primary caries even by radiographic inspection.

Web site: http://www.delphion.com/details?pn=US05818587__

- **Material and apparatus for removing dental caries**

  Inventor(s): Horiguchi; Shoji (Hachioji, JP), Ochiai; Tetsuo (Nukata-gun, JP), Watanabe; Masatomo (Hashima, JP)

  Assignee(s): Sintobrator, Ltd. (Tokyo-To, JP)

  Patent Number: 6,132,212

  Date filed: October 27, 1998

  Abstract: There is disclosed a dental caries-removing material consisting of grinding granules ejected against **dental caries,** or pathological issues, to remove them. The granules are obtained by pulverizing untoxic stones of seeds and have Vickers hardness values (JIS Z 1051)(Hv) of 10 to 60 and granular diameters of 40 to 160.mu.m. This material is prepared by pulverizing and grading stones of seeds (such as peach, plum, apricot, or Japanese apricot).

  Excerpt(s): The present invention relates to a material and apparatus for selectively removing **dental caries** without damaging sound dentine. Dental caries occur and progress by the following mechanism. Dentine consisting of inorganic and organic components is bated by acids produced by bacteria and thus softens. Subsequently, the remaining organic components are decomposed by bacteria, creating voids. Dental caries would recur unless portions softened and invaded with bacteria are removed. Thus, caries must be fully removed.

  Web site: http://www.delphion.com/details?pn=US06132212__

- **Method and apparatus for electronically imaging a tooth through transillumination by light**

  Inventor(s): Elbaum; Marek (Dobbs Ferry, NY), Greenebaum; Michael (Brooklyn, NY), Jacobs; Adam (Glen Ridge, NJ), Keem; Sunguk (Cliffside Park, NJ), Schneiderman; Allen H. (Ridgewood, NJ), Shultz; Theodore S. (Larchmont, NY)

  Assignee(s): Electro-Optical Sciences (Irvington, NY)

  Patent Number: 6,201,880

  Date filed: December 31, 1996

  Abstract: A method and apparatus for imaging teeth includes illuminating a surface of a tooth and electronically imaging the tooth from a non-illuminated surface of the tooth with an electronic camera. Automatic control of the intensity of illumination is preferably provided to avoid saturation of the camera. The camera may include a charge-coupled-device and the resulting digital images are preferably enhanced by wavelet analysis. If a video camera is used, the images may be digitized and then enhanced. Current images of the tooth may be compared to prior images of the same tooth to monitor changes in the tooth over time. The images can be used to detect **dental caries** and other dental conditions. A handpiece for illuminating the tooth and receiving the light passing through the tooth for reception by the camera in a reproducible manner, is also described.

  Excerpt(s): A portion of the disclosure of this patent document contains material which is subject to copyright protection. The copyright owner has no objection to the facsimile reproduction by anyone of the patent document or the patent disclosure, as it appears in the Patent and Trademark Office patent file or records, but otherwise reserves all copyrights whatsoever. This invention relates to method and apparatus for imaging teeth. More particularly, the invention relates to illuminating a tooth with light and creating images of the illuminated tooth. The most commonly used clinical techniques for detecting **dental caries** are tactile examination and dental radiography, each of which has significant shortcomings. Tactile examination typically uses an explorer, which can accelerate the development of irreversible caries by causing traumatic changes to tooth structure. Radiography requires the use of x-ray radiation, which is an ionizing radiation dangerous to the health of the patient. The use of lower x-ray fluence with digital sensing of the x-ray transmission and computer enhancement of the image contrast, provides poorer resolution than that obtainable with x-ray film.

  Web site: http://www.delphion.com/details?pn=US06201880__

- **Method and apparatus for removing dental caries by using laser radiation**

  Inventor(s): Chou; Mau-Song (Rancho Palos Verdes, CA)

  Assignee(s): TRW Inc. (Redondo Beach, CA)

  Patent Number: 6,083,218

  Date filed: July 10, 1996

  Abstract: An apparatus (1) is provided for treating a target area (22) of a tooth (10). The apparatus (1) generally comprises a coolant delivery system (20) and an ultraviolet laser system (15). The coolant delivery system (20) delivers coolant (52) to the target area (22) while a light guide (44) focuses ultraviolet radiation thereon. The ultraviolet radiation

(18) and coolant (52) combine to ablate a desired material without generating excess heat which may otherwise char surface tissue or cause thermal damage.

Excerpt(s): The present invention generally relates to an apparatus and method for removing plaque and decay tissue, commonly known as **dental caries,** using laser radiation. More particularly, the present invention relates to an apparatus using ultraviolet radiation and a coolant to ablate a desired material from a tooth without generating excess heat at the target site or surrounding areas. As is generally known in the art of dentistry, conventional drilling machines for treating **dental caries** such as plaque and decay tissue can be inaccurate and painful. Therefore, it is desirable to replace or support conventional drilling machines with lasers in order to achieve a more accurate and painless treatment of caries. However, laser irradiation processes currently available often produce charring on the target surface and surrounding areas due to laser generated heat. The blackened char tissue effectively blocks the laser radiation thereby preventing it from reaching biological tissue thereunder. Thus, charring due to excess heat interrupts the ablation process. Excess heat may also produce cracks in the tooth surface and damage the nerve system and other pulp structure in the pulp chamber irreversibly. Accordingly, laser treatment of hard tissue, including caries removal, has not yet achieved practical dental application due to the thermal damage related to laser generated heat. Therefore, it is desirable to provide an apparatus and method for treating **dental caries** using laser irradiation which does not generate sufficient heat to cause thermal damage.

Web site: http://www.delphion.com/details?pn=US06083218__

- **Method for detection of dental caries and periodontal disease using optical imaging**

  Inventor(s): Kinney; John H. (Danville, CA), Nathel; Howard (Albany, CA), Otis; Linda L. (San Francisco, CA)

  Assignee(s): Regents of the University of California (Oakland, CA)

  Patent Number: 5,570,182

  Date filed: May 27, 1994

  Abstract: A method for detecting the presence of active and inactive caries in teeth and diagnosing periodontal disease uses non-ionizing radiation with techniques for reducing interference from scattered light. A beam of non-ionizing radiation is divided into sample and reference beams. The region to be examined is illuminated by the sample beam, and reflected or transmitted radiation from the sample is recombined with the reference beam to form an interference pattern on a detector. The length of the reference beam path is adjustable, allowing the operator to select the reflected or transmitted sample photons that recombine with the reference photons. Thus radiation scattered by the dental or periodontal tissue can be prevented from obscuring the interference pattern. A series of interference patterns may be generated and interpreted to locate **dental caries** and periodontal tissue interfaces.

  Excerpt(s): The invention relates to imaging of dental and periodontal tissue. More particularly, the invention relates to a method for detection of caries and periodontal disease by an optical imaging technique that is non-invasive and uses non-ionizing radiation. Dental caries, caused primarily by bacterial action on sugars, are a common disease that can be easily treated if detected early. If undetected and untreated, caries may progress through the outer enamel layer of a tooth into the softer dentin so far as to require extraction of the tooth or to cause inflammation of periodontal tissue

surrounding the tooth. The standard methods for detecting caries in teeth are by visual inspection or by the use dental x-rays. Both methods are unreliable for the detection of small caries (<1 mm) or caries between teeth. In addition, dental x-rays subject the patient to ionizing radiation, a known mutagen. Non-ionizing radiation has long been used for imaging the internal structures of soft tissue, and has shown promise in such applications as mammography, neonatal brain scanning and imaging of some tumors. Generally, however, it is unsatisfactory for tissue imaging because scattering of the lower-energy non-ionizing radiation by the tissue severely compromises the resolution of the image. Although resolution of optical images may be improved by the use of polarizing filters or phase conjugated mirrors, or by collimation of the incident and transmitted beams to reduce interference from scattered radiation, x-ray images still produce superior resolution. Optical imaging with non-ionizing radiation requires sophisticated techniques such as photon time-of-flight range gating to achieve image resolution comparable to x-ray techniques.

Web site: http://www.delphion.com/details?pn=US05570182__

- **Method of preventing dental caries and other oral lesions**

  Inventor(s): Blackshear; Perry J. (Chapel Hill, NC)

  Assignee(s): Duke University (Durham, NC)

  Patent Number: 5,972,311

  Date filed: January 26, 1998

  Abstract: The present invention relates to a method of preventing caries and other sugar-dependent dental and oral lesions and to a carbohydrate binding protein-based composition suitable for use therein.

  Excerpt(s): The present invention relates to a method of preventing caries and other sugar-dependent dental and oral lesions, and to a carbohydrate-binding protein-based composition suitable for use therein. It is widely agreed that there is a direct relationship between sugar consumption and caries. Both total sugar consumption and between meal consumption have been shown to be important factors in cary development. Sugar is also thought to be an important pathogenic determinant for other oral lesions, including dental plaque and calculus, and gingival disease. While caries have declined in frequency in most industrialized counties during the past 20 years, about 25% of the population of even those countries continues to be at high risk for caries (J. Am. Dent. Ass. 123:68 (1992)). Numerous measures have been used to control **dental caries.** These include fluoride treatment (of drinking water and teeth), pit and fissure sealants, vaccines, and "substrate modification". This last category includes non-sucrose sweeteners that are purported to have a specific anti-cariogenic effect, such as xylitol, sorbitol, mannitol and glycerol. Xylitol in particular is used in dentifrices such as mouthwashes and chewing gum. However, at best, such non-sucrose sweeteners have a modest effect, since they do little to remove the sucrose and other cariogenic sugars present. The present invention, by contrast, provides for the removal of sugars from the oral cavity, thereby preventing the development of caries and various other oral lesions.

  Web site: http://www.delphion.com/details?pn=US05972311__

- **Methods and apparatus for the detection of dental caries**

  Inventor(s): Longbottom; Christopher (Fife, GB), Los; Przemyslaw (Wroclaw, PL), Pitts; Nigel Berry (Perth, GB)

  Assignee(s): The University Court of the University of Dundee (Dundee, GB)

  Patent Number: 6,230,050

  Date filed: August 5, 1999

  Abstract: The present invention is directed to a method and apparatus for the detection of **dental caries.** The method comprises the steps of placing at least one probe electrode in electrical contact with a surface of a patient's tooth, placing a second electrode in electrical contact with another part of the body of the patient, passing an alternating electrical current between said probe and second electrodes, and measuring the electrical impedance between the electrodes.

  Excerpt(s): This invention relates to methods and apparatus for use in detecting dental carious (i.e. dental decay, or "caries" or "carious lesions") by electrical and/or electronic means. Caries is defined as the progressive decay of tooth or bone, and **dental caries** is the most common ailment known world wide. **Dental caries** can be treated by either removing the decayed material in the tooth and filling the resultant space with a dental amalgam, or in severe cases, by removal of the entire tooth. The early diagnosis of **dental caries** is of utmost importance to any subsequent treatment since by the time pain is felt due to decay of the tooth, the treatment required to restore the tooth may be extensive and in some cases, the tooth may be lost.

  Web site: http://www.delphion.com/details?pn=US06230050__

- **NSAID/fluoride periodontal compositions and methods**

  Inventor(s): Aberg; Gunnar (Westborough, MA), Jerussi; Thomas Patrick (Framingham, MA), McCullough; John R. (Worcester, MA)

  Assignee(s): Sepracor, Inc. (Marlborough, MA)

  Patent Number: 5,807,541

  Date filed: April 22, 1996

  Abstract: A method for preventing **dental caries** by administering fluoride and, at the same time controlling periodontal bone loss precipitated by the fluoride, by providing a combination of fluoride and NSAID is disclosed. Topical medicament compositions including NSAIDS and fluoride are also disclosed.

  Excerpt(s): The invention relates to dental compositions. In another aspect this invention relates to methods and compositions for controlling periodontal bone loss. The role of topical and systemic fluoride in the inhibition of **dental caries** is well established. There is good evidence that professionally applied topical fluoride and the use of dentifrices and mouthwashes containing fluoride are effective in preventing **dental caries** among high risk patients. The amount of fluoride ion employed in most dentifrices and mouthwashes ranges from 0.05 to 0.15% weight-to-volume. Most commonly sodium fluoride, and sodium monofluorophosphate, less commonly, stannous fluoride and amine fluoride, are employed as sources of fluoride ion. It is also known that under certain circumstances sodium fluoride and fluoroaluminates can activate G proteins and thereby induce prostaglandin production in endothelial cells and leukotriene production in platelets, granulocytes and monocytes. The metabolites of arachidonic

acid have been implicated as important biochemical mediators of tissue destruction in various inflammatory diseases.

Web site: http://www.delphion.com/details?pn=US05807541__

- **Oral hygiene powder composition and method**

  Inventor(s): Anderson; Michael R. (1355 W. Palmetto Park Rd. #129, Boca Raton, FL 33486)

  Assignee(s): none reported

  Patent Number: 6,645,472

  Date filed: September 13, 2002

  Abstract: A anhydrous tooth and gum powdered dentifrice formulated of calcium or magnesium peroxide, sodium bicarbonate, methylsufonymethane, ascorbic acid, colostrum, and optionally menthol, flavoring agent, sweetening agent, sodium laurel sulfate and green tea extract that has a long shelf life but when activated by water or saliva, functions to effect a synergistic chemical and mechanical action to whiten, brighten, polish teeth and reduce bacteria so as to aid in the prevention and treatment of periodontal disease, **dental caries** and mouth odor.

  Excerpt(s): The invention relates to a storable, normally inactive, anhydrous oral dentifrice which promotes oral hygiene and which is activated by saliva and/or water, then applied onto the surface of teeth and adjacent gum tissues. The composition and method includes calcium or magnesium peroxide, sodium bicarbonate, ascorbic acid, methylsulfonymethane, and colostrum which are believed to function synergistically to cosmetically whiten, brighten, and bleach (to make whiter or lighter) teeth and therapeutically to cleanse the teeth and surrounding oral tissues and to kill the bacteria which contribute to the formation of dental plaque, caries, and mouth odor. Optionally green tea extract, sodium laurel sulfate, flavors, and sweeteners may be added. The desire of people to have white teeth has been present in our society for decades. This desire is heightened by the presence of stains on teeth caused from the food we eat, smoking tobacco, medications, and poor oral hygiene, just to name a few. Many materials, compositions and processes have been developed over the years in attempts to solve this problem. These approaches are not without drawbacks, the most common being product instability, cost, product harshness to teeth and gums, specially trained personnel being required for product application, necessity of wearing specially crafted dental appliances often referred to as "splints". Thus, it is clear that a need exists for a tooth whitener and cleanser that is stable until use, reasonably priced, safe, easy to use, requires no special apparatus or trained personnel to apply, is not harmful to teeth, gums, and other surrounding tissues, and combats tooth and gum diseases commonly caused by bacteria. To a large degree, **dental caries** and periodontal disease are connected closely to the formation of dental plaque. The literature has long reported that a majority of the world's population suffers from periodontal disease. According to the Merck Manual, 14th ed. 1982, P. 2104, the most common types of periodontal disease are gingivitis and periodontitis. Gingivitis (early stage gum disease) is an inflammation of the gums, characterized by swelling, redness, change in normal contours, and bleeding. If gingivitis is allowed to progress, periodontitis (late, stage gum disease), characterized by loss of tooth-supporting bone, will follow. The greatest single source of periodontal disease is poor hygiene, indicated by the appearance of bacterial and calcified plaque.

  Web site: http://www.delphion.com/details?pn=US06645472__

- **Polypeptide fragments capable of competition with Streptococcus mutans antigen I/II**

  Inventor(s): Kelly; Charles (London, GB), Lehner; Thomas (London, GB)

  Assignee(s): The Council of Governors of the United Medical & Dental School of Guy's (GB)

  Patent Number: 6,024,958

  Date filed: October 20, 1997

  Abstract: Defined peptide subunits of Streptococcus mutans antigen I/II are useful as agents to prevent and treat **dental caries** either by eliciting an immunological response or by preventing adhesion of S. mutans to the tooth.

  Excerpt(s): This invention relates to polypeptide fragments of the Streptococcus mutans I/II antigen that are useful in treating and preventing **dental caries.** Streptococcus mutans is the main etiological agent of **dental caries,** a disease which affects mammals including humans. The S. mutans I/II antigen (SA I/II) is a cell surface protein with an M.sub.r of about 185 kDa. It is believed to comprise several antigenic epitopes and to be at least partly responsible for S. mutans adhesion to teeth.

  Web site: http://www.delphion.com/details?pn=US06024958__

- **Quantitative dental caries detection system and method**

  Inventor(s): Gakenheimer; David C. (Redondo Beach, CA), Manukian; Narbik (Glendale, CA), Neuhaus; Joseph A. (Marina del Ray, CA), Wilensky; Gregg D. (Venice, CA), Yoon; Douglas C. (Beverly Hills, CA)

  Assignee(s): Logicon, Inc. (Torrance, CA)

  Patent Number: 5,742,700

  Date filed: October 13, 1995

  Abstract: A caries detection system and method for quantifying a probability of lesions existing in tissues are presented. Digital X-ray images are segmented and further processed to generate feature statistics inputs for a neural network. The feature statistics include colinearity measurements of candidate lesions in different tissue segments. The neural network is trained by back propagation with an extensive data set of radiographs and histologic examinations and processes the statistics to determine the probability of lesions existing in the tissues.

  Excerpt(s): The present invention relates to a system and method for the digital detection of tissue lesions and, more particularly, pertains to a system and method for quantifying a probability of lesions existing in tissues. According to the Journal of the American Dental Association, Volume 108, May 1984, page 755, dentists fail to detect carious lesions in teeth a significant fraction of the time (up to 40%). Healthy teeth are misdiagnosed a significant fraction of the time as well (up to 20%). In part, this problem is due to the fact that dentists are unable to directly view carious lesions on proximal surfaces, i.e., between the teeth. The human eye is an imperfect tool for visually analyzing dental x-rays because of its tendency to smooth out intensity gradients. Furthermore, substantial variations in dental x-ray images are attributable to variations in film type, exposure level, tooth structure and shape, and location and extent of lesions. Another object is to provide a digital imaging method for quantifying a probability of lesions existing in tissues.

Web site: http://www.delphion.com/details?pn=US05742700__

- **Reductant rinse for use with ozone treatment of dental caries**

  Inventor(s): Lynch; Edward (Belfast, GB), Schemmer; Jurgen (King City, CA)

  Assignee(s): Curozone Ireland Limited (IE)

  Patent Number: 6,649,148

  Date filed: March 12, 2002

  Abstract: A reductant rinse including xylitol prevents buildup in ozone carrying lines in apparatus for the treatment of **dental caries.**

  Excerpt(s): This invention relates to the use of reductants in the ozone in the treatment of **dental caries.** The great destructive disease of teeth is **dental caries** which may be defined as the acid dissolution of enamel, dentine or cementum as a consequence of the metabolism of micro-organisms living within deposits on the teeth known a plaque. **Dental caries** is believed to be associated with specific micro-organisms, the principal ones being Streptococcus Mutans, Lactobacilli, Actinomyces Visosus Serovar 2, Actinomyces Naeslundii and "Intermediate" Actinomyces, other Streptococci and yeasts. These are acid producing micro-organisms which produce acids such as acetic and lactic acids from the dietary carbohydrates. The micro-organisms associated with **dental caries** are unique and are ecologically very different from those associated with, for example, infected root canals. (iii) the protection of any newly exposed non-carious dentine with restorative material.

  Web site: http://www.delphion.com/details?pn=US06649148__

- **Removal of dental caries with high speed water jet**

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  Assignee(s): Medjet, Inc. (Edison, NJ)

  Patent Number: 6,164,966

  Date filed: March 17, 1999

  Abstract: A method and device for the high speed fluid (preferably water) jet removal of **dental caries.** The water jet is of a controlled upper and lower speed and pressure with a low speed and pressure being of at least 5 to 10 kpsi, sufficient to pierce and flush decayed tissue of a caries with a small beam fluid jet diameter. A pulsed or continuous fluid jet is used to remove and completely flush caries material from a tooth in a time period of under a second with a maximum stagnation pressure of about 30 kpsi, at which point healthy dentin is affected. A coherent or pseudo-coherent water jet operating at high stagnation pressure (range 10,000 to 20,000-psi and no more than 30-kpsi), in a brief burst (.apprxeq.1 second) and small beam diameter (30 to 100-.mu.m) will cleanly remove caries without damage to the tooth structure in particular the sound dentin at the boundary of the caries. No anaesthetic is accordingly required in the absence of a possible exposed nerve.

  Excerpt(s): This invention relates to methods and devices for the removal of the **dental caries** and in particular those methods and devices with lessened damage to healthy

dentin and reduced pain for the patient. At present the method of choice for removing decayed dentin and other structure in a **dental caries** associated with a cavity, preparatory to filling the tooth, is a mechanical dental drill. The dental drill is guided by a dentist to drill into a tooth until all remnants of the caries are separated from the healthy dentin. Thereafter a low pressure water jet or air spray is used to wash or remove the caries material from the tooth. The process involved entails a certain degree of inevitable pain as a result of small portions of healthy dentin being removed as well. In addition, the high pitched whine of a dental drill is often accompanied by psychological trauma of the patient. In fact, fear of the dental drill is a major reason that people in need of dental care postpone visits to a dentist. Recently research has involved the use of lasers to selectively burn out the caries prior to filling of the tooth. Though the lasers are silent they nevertheless also inevitably remove a small portion of healthy dentin.

Web site: http://www.delphion.com/details?pn=US06164966__

- **Tooth surface treatment method**

  Inventor(s): Craig; Graham George (Balgowlah, AU), Knight; Geoffrey M. (Brighton, AU), Ngo; Hien (Athelstone, AU), Sekiguchi; Toshihiro (Tokyo, JP)

  Assignee(s): GC Corporation (Tokyo, JP)

  Patent Number: 6,461,161

  Date filed: May 25, 2001

  Abstract: There is provided a tooth surface treatment method, which enables one to effectively inhibit the progress of **dental caries** without impairing the aesthetics. The tooth surface treatment method of the invention includes applying a solution comprising a silver compound in an affected part of a tooth and then applying a solution comprising at least one compound selected from the group of sodium chloride, sodium bromide, sodium iodide, potassium chloride, potassium bromide, potassium iodide, magnesium chloride, magnesium bromide, magnesium iodide, calcium chloride, calcium bromide, calcium iodide thereto. It is preferred that a concentration of silver compound in the solution thereof is 2 to 75% by weight and that a concentration of at least one compound selected from the group of sodium chloride, sodium bromide, sodium iodide, potassium chloride, potassium bromide, potassium iodide, magnesium chloride, magnesium bromide, magnesium iodide, calcium chloride, calcium bromide, calcium iodide in the solution thereof is 1 to 50% by weight.

  Excerpt(s): The present invention relates to a tooth surface treatment method for the inhibition of the progress of **dental caries** without impairing aesthetics. It is considered that about a half of causes for which teeth are lost are because of **dental caries.** Therefore, it is important to remedy and prevent the **dental caries,** and various remedy methods have hitherto been developed. In recent years, there has been developed a remedy method in which, even in a state where dental remedy treatment equipments that have hitherto been considered to be necessary in the operative dentistry of the conventional art, such as tooth cutting turbines and electrical equipments, is not available, the remedy of a **dental caries** for conservation of the tooth can be performed, called "ART" (Atraumatic Restorative Treatment). In accordance with a basic remedy method of ART, a saliva in a diseased part is wiped out; a dental plaque is removed; a tooth surface is dried; an enamel is cut off by hand instruments such as an excavator, to form a cavity; an enamel piece in the cavity is removed; a dentin that has become soft by the **dental caries** is removed by using an excavator; the cavity is washed with water; if

desired, a tooth surface processing agent or the like is applied; and a glass ionomer cement having a high biocompatibility and a caries preventing function due to sustained fluorine-releasing properties, is filled, thereby completing the treatment. Since ART can be effected by using simple hand instruments and a dental filling material, it is possible to implement the remedy of **dental caries** even in an area where specific dental equipments are not provided, or electrical supply is not sufficient.

Web site: http://www.delphion.com/details?pn=US06461161__

Patent Applications on Dental Caries

As of December 2000, U.S. patent applications are open to public viewing.[9] Applications are patent requests which have yet to be granted. (The process to achieve a patent can take several years.) The following patent applications have been filed since December 2000 relating to dental caries:

- **Anticariogenic dairy product and its use**

  Inventor(s): Guggenheim, Bernhard; (Erlenbach, SZ), Nesser, Jean-Richard; (Savigny, SZ), Parmantier, Claude; (Glos, FR)

  Correspondence: Pennie And Edmonds; 1155 Avenue OF The Americas; New York; NY; 100362711

  Patent Application Number: 20010033887

  Date filed: February 5, 2001

  Abstract: The invention relates to a food composition containing an effective quantity of rennetted milk for preventing or treating **dental caries** or dental plaque. The invention also relates to a method of preparing the composition.

  Excerpt(s): This application is a continuation of the U.S. national stage designation of International Application No. PCT/EP99/05335, filed Jul. 20, 1999, the content of which is expressly incorporated herein by reference thereto. The present invention relates to a dairy product possessing anticariogenic properties as well as food compositions prepared from the product. Some products derived from milk are of great interest for dentiboccal health. Thus, anticariogenic properties are recognized for casein in certain forms and for some of its derivatives. A few cheeses, for example, are known for their anti-caries activity (Nutrition Reviews, 46, 215-217, 1988; Pause, B. and Lembke, J., Milchwissenschaft, 47, 697-700, 1992; Pause, B. and Lernbke, J., Milchwisssenschaft, 48, 137-141, 1993).

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

[9] This has been a common practice outside the United States prior to December 2000.

- **Combination of IgY against dental caries**

  Inventor(s): Paau, Shing; (Causeway Bay, HK), Yang, Rong Jian; (Wan Chai, HK)

  Correspondence: Raymond Y. Chan; Suite 128; 108 N. Ynez Avenue; Monterey Park; CA; 91754; US

  Patent Application Number: 20040126384

  Date filed: December 15, 2003

  Abstract: For the purpose of preparing the immunoglobulin of yolk (IgY) against **dental caries** bacteria and the combination, Streptococcus mutans type c and type d are used as antigen bacteria, the antibody is purified by water dilution, DEAE-Sephadex A50 and Sephadex G200 chromatography. It is low cost of production, high titer, strong resistance to osmotic pressure, and high immune activity and wide range of cross-reaction to streptococcus mutans. Present invention provides the combination preventing **dental caries** wherein the effective components are IgY and antiseptic features in safe use and effective prevention; The combination is effectively preventing **dental caries.**

  Excerpt(s): This is a divisional application of a non-provisional application, application Ser. No. 09/684,794, filed Oct. 10, 2000. The present invention relates to preparation of immunoglobulin from hen yolk, and more particularly to IgY against **dental caries** bacteria and the combination preventing **dental caries** wherein the IgY and antiseptic are effective components. It is well known that streptococcus mutans are major **dental caries** bacteria. There are two measures of passive immunization to streptococcus mutans at this moment.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Composition and method for improving, altering, and treating teeth**

  Inventor(s): Cohen, Morton; (Elkins Park, PA)

  Correspondence: Frank J. Bonini JR.; 86 The Commons AT Valley Forge East; 1288 Valley Forge Road; P.O. Box 750; Valley Forge; PA; 19482-0750; US

  Patent Application Number: 20020006600

  Date filed: February 22, 2001

  Abstract: A composition and method for administering a treatment agent to a tooth, such as fluoride to improve the tooth's resistance to **dental caries** with a composition which can be selectively removed, the composition comprising a lac based compound with a treatment agent such as fluoride for applying to a tooth, and a method including selecting the color to be applied, preparing the colorized compound with the treatment agent to be applied to a tooth, exposing the tooth to be covered, applying the treatment containing a colorized compound to the enamel surface of the tooth, and allowing the compound to dry on the tooth, and selectively removing the compound from the tooth. Stencil apparatus can be used to create a design on the tooth using a covering compound.

  Excerpt(s): This application is a continuation-in-part of U.S. application Ser. No. 09/370,325 filed on Aug. 9, 1999 which is a continuation-in-part of U.S. application Ser. No. 09/054,898, filed on Apr. 3, 1998, now U.S. Pat. No. 6,036,494. The present invention relates to the field of applying a composition to a tooth to alter the appearance thereof or provide a treatment to the tooth. Many procedures are done to improve the appearance

of teeth. Teeth are filled to replace dentin and enamel invaded by bacteria, and can be capped to replicate a removed or abraded portion of a tooth.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Composition for remineralization of a tooth**

  Inventor(s): Hirota, Kazuo; (Itabashi-ku, JP), Ishihara, Yoko; (Itabashi-ku, JP), Yoshii, Eiichi; (Itabashi-ku, JP)

  Correspondence: Oblon Spivak Mcclelland Maier & Neustadt PC; Fourth Floor; 1755 Jefferson Davis Highway; Arlington; VA; 22202; US

  Patent Application Number: 20020044912

  Date filed: July 5, 2001

  Abstract: A composition for remineralization of a tooth, adapting to a tooth surface demineralized due to **dental caries** and forming a compound within the tooth to gradually release a phosphate ion and a calcium ion therein, is comprised of a solution A to be first applied to a tooth surface, containing 1 to 30% by weight of a calcium salt, with the remainder being a volatile solvent; and a solution B that is an aqueous solution containing 1 to 30% by weight of a phosphate and preferably a fluoride in an amount of 0.0001 to 5% by weight, where at least one of the solution A and the solution B preferably further contains a surfactant in an amount of 0.0005 to 1 % by weight.

  Excerpt(s): The present invention relates to a composition for remineralization of a tooth, which is aimed to accelerate remineralization of a tooth by applying it to a tooth surface demineralized due to **dental caries** and forming a compound within the tooth, from which a phosphate ion and a calcium ion are then gradually released. In an oral cavity, a tooth repeats demineralization and remineralization. A **dental caries** refers to a disease resulted from the matter that a balance between demineralization and remineralization is lost, whereby the balance is greatly inclined to the demineralization side. Thus, if an intraoral circumstance were regulated such that the balance is inclined to the remineralization side, it would become possible that the tooth is again mineralized to stop the progress of the **dental caries** and apply a remedy. As factors for introducing this remineralization, are enumerated the amount of saliva and the presence of a fluoride ion. But, first of all, it is important that sufficient amounts of a phosphate ion and a calcium ion as constitutional substances of a tooth is present in a demineralized site.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Detection material for initial dental caries**

  Inventor(s): Ishihara, Yoko; (Tokyo, JP), Okada, Akane; (Tokyo, JP), Yoshii, Eiichi; (Tokyo, JP)

  Correspondence: Oblon Spivak Mcclelland Maier & Neustadt PC; Fourth Floor; 1755 Jefferson Davis Highway; Arlington; VA; 22202; US

  Patent Application Number: 20020119100

  Date filed: December 18, 2001

  Abstract: To simply and accurately detect initial **dental caries** without impairing the aesthetics, the detection material for initial **dental caries** contains 0.001 to 5% by weight

of at least one dye selected from fluorescein sodium, fluorescein potassium, dibromofluorescein sodium, and dibromofluorescein potassium compounded in a solvent. It is preferred that the solvent is one member selected from water, ethanol, glycerin, isobutyl alcohol, ethyleneglycol, diethyleneglycol, triethyleneglycol, acetone, and propylene glycol, or a mixed solution of two or more of these members.

Excerpt(s): About a half of the causes of losing teeth is considered to be **dental caries,** and hence, it is important to prevent the **dental caries.** However, with respect to the **dental caries,** demineralization gradually proceeds in an unseen portion under a surface layer of a tooth, and as a result, when a subjective symptom such as one that can be observed with naked eye has appeared, the **dental caries** often proceeds to such an extent that the conservation remedy is needed. In other words, what is important in preventing the **dental caries** is to find out the demineralization proceeding under the surface layer of the tooth at an initial stage as far as possible, thereby giving a person a guidance for brushing the subject portion or subjecting to a treatment for stopping the progress of the demineralization by applying a fluoride. At the initial stage of the **dental caries,** even if the conservation remedy were needed, the remedy could be simple, so that a risk of the secondary **dental caries** can be minimized. The demineralization under the surface layer as initial **dental caries** of a tooth is non-cavitation-forming **dental caries** that is free from substantial defects, formed due to the matter that during long-term repetition of demineralization wherein calcium ions and phosphate ions elute out from teeth due to plaque bacteria-producing acids and remineralization as a phenomenon wherein the calcium ions and phosphate ions are again taken into the teeth, a balance of the both is broken, and the environment is inclined towards the demineralization side over a long period of time. Thereafter, when the symptoms proceeds to some extent, it is confirmed as a white spot on an enamel from the clinical standpoint. It is considered that so far as the plaque is eliminated, and the surface of the teeth is brought into contact with saliva over a long period of time as far as possible, the initial **dental caries** up to the presence of a white spot does not proceed to the **dental caries** accompanied by substantial defects. In addition, it is already confirmed that when a fluoride is applied to an diseased part, the remineralization is promoted, whereby the initial **dental caries** can be restored to an original sound teeth to some extent. Accordingly, the detection for the initial **dental caries** has become important more and more in preventing the **dental caries.** As a method for detecting the initial **dental caries,** a method in which a site from which the plaque has been eliminated is dried and inspected using a dental explorer and a dental mirror is the main current. However, it is very difficult to confirm the initial **dental caries** before the presence of a white spot. Further, there may be present a white spot portion generated by other causes than the demineralization such as one seen in the case of enamel hypoplasia. Accordingly, its diagnosis relied on the experiences and lacked in accuracy. Besides, as the detection and diagnosis techniques for the initial **dental caries,** there is hitherto known a method for measuring an electric resistance value of a tooth. However, this method involved a problem from the standpoint of the practical use because the measured values are scattered according to the measurement conditions and differences among individuals. Further, there are disclosed methods using devices, for example, a method in which a laser light having a specific wavelength is irradiated, and a reflected light from the irradiated site is quantitated, whereby the degree of progress of the **dental caries** is evaluated (see Japanese Patent Laid-Open No. 337142/1993); a method using an infrared camera (see Japanese Patent Laid-Open No. 233758/1996; and a method in which the water content in an initial **dental caries** site is quantitated by an infrared light (see Japanese Patent Laid-Open No. 71092/1996). The devices to be used in these methods

are each required to use a large-sized and expensive detector, and therefore, have not been generally spreaded.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Diagnostic assays for determination of dental caries susceptibility**

  Inventor(s): Gregory, Richard L.; (Carmel, IN)

  Correspondence: Fullbright & Jaworski L.L.P.; 600 Congress AVE.; Suite 2400; Austin; TX; 78701; US

  Patent Application Number: 20030113823

  Date filed: October 9, 2002

  Abstract: The invention overcomes the limitations of the prior art by providing rapid assays for predicting the likelihood of caries development in patients. The assays allow implementation of appropriate dental care measures during a patient visit depending on the results of the assay. The assay utilizes the finding that caries-free children and adults have significantly higher levels of naturally occurring protective salivary IgA antibody to S. mutans than caries-active subjects. The assays are carried out using patient saliva. The speed and ease of use of the assay allows dental practitioners to assess at an early stage the relative risk of future caries formation. With this information, preventive methods may be applied only to those determined to be at risk.

  Excerpt(s): This application claims the priority of U.S. Provisional Patent Application Ser. No. 60/328,537, filed Oct. 11, 2001. The government may own rights in the present invention pursuant to grant number DE007125-20 from the National Institute of Dental and Cranialfacial Research. The present invention relates generally to the field of dentistry. More particularly, it concerns assays for the identification of individuals susceptible to future caries development. Streptococcus mutans has been established to be the main etiologic factor in the development of **dental caries** (Loesche, 1986). Like other bacterial cells, S. mutans has surface antigens which are unique and enable the cell to adhere to the smooth surfaces of teeth. The most important cell attachment antigens include glucosyltransferase, antigen I/II, and fimbriae present on the cell surface. Glucosyltranferase (GTF) is a complex of enzymes on the cell surface which are responsible for adherence of the cell to enamel through a mechanism which involves cleaving sucrose into insoluble and soluble glucose polymers called glucans. These glucans bind to the pellicle on the tooth, enabling the cell to attach to the tooth surface. In addition, the glucans serve to promote inter-bacterial binding. Antigen I/II is present on the surface of the bacterial cell and promotes binding of the cell to the tooth surface (reviewed in Gregory, 1994a). Fimbriae are small hairlike appendages which extend from the cell surface, allowing the cell to adhere to pellicle-coated tooth surfaces in a sucrose-independent manner.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Edible candy compositions and methods of using same**

  Inventor(s): Finnegan, Sarah; (Mays Landing, NJ), Kligerman, Alan E.; (Egg Harbor Township, NJ)

  Correspondence: Akin, Gump, Strauss, Hauer & Feld, L.L.P.; One Commerce Square; 2005 Market Street, Suite 2200; Philadelphia; PA; 19103; US

  Patent Application Number: 20020064550

  Date filed: September 7, 2001

  Abstract: Candy food, a piece of confectionery, which is a small, hard, chewy, or soft piece of food made from sugar and other ingredients or flavorings, such as chocolate, nuts, fruit, or peppermint is provided with enhanced refreshing properties of deacidifying the mouth and a stomach from the food or drink just consumed as well as reducing mouth, throat, esophageal, or other gastrointestinal irritation, together with reducing the incidence of **dental caries** and delivering absorbable calcium and phosphorus, wherein said candy food comprises combining a candy component with an effective amount of calcium glycerophosphate.

  Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/230,650 filed Sep. 7, 2000. Candy is defined as a piece of confectionery which is a small hard, chewy, or soft piece of food made from sugar and other ingredients or flavorings such as chocolate, nuts, fruit, or peppermint. Candy may also be called confectionery in the United States and sweets in the United Kingdom. Soft, or crystalline, candy is smooth, creamy, and easily chewed. Typical soft candies are fondants (the basis of chocolate creams) and fudge. Typical hard, or noncrystalline candies include toffees and caramels. Other favorite candies include nougats, marshmallows, the various forms of chocolate (bars or molded pieces, sometimes filled), pastes and marzipan (based on crushed almonds or almond paste), cotton candy (spun sugar), popcorn, licorice, and chewing gum. Mint or other flavored candies, hard, soft or filled, chocolate covered or otherwise are very popular and widely enjoyed by many people as an after meal refreshment. Although not traditionally marketed as candies, cough drops and other medicated lozenges are a type of confection which contains sugar and other flavorings, such as fruit. "Confections" also describes foods such as cake and pastry icing, jellied pastry filling, ice cream, and all baked goods containing sugar, such as, but not limited to, cakes, cookies, buns, pastries, and ice cream cones. Candies are usually high in sugar content, and therefore, known to cause **dental caries** in humans as well as in animals. While the high sugar content and high calorie content of candy foods, chocolate foods, beverages and confections (hereinafter collectively referred to as "candy foods") have been known for some time, neither property of these candy foods has been much of a deterrent to their widespread consumption. However, there are people who experience some physical discomfort when consuming edible, chocolate foods, and thus, do not experience the same enjoyment as others when consuming these foods.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Effect of electrolyzed solutions on acidogenesis of plaque**

  Inventor(s): Morisawa, Shinkatsu; (Kyoto, JP), Wang, Xiao Bing; (Lutherville, MD)

  Correspondence: Troutman Sanders Llp; Bank OF America Plaza, Suite 5200; 600 Peachtree Street , NE; Atlanta; GA; 30308-2216; US

  Patent Application Number: 20030175220

  Date filed: December 11, 2002

  Abstract: The present invention provides compositions and methods for inhibiting, reducing, preventing or controlling **dental caries** formation. Electrolyzed water having an oxidation-reduction potential from about -150 to 0 mV measured against a platinum electrode, also known as "Trim water" can reduce, inhibit, prevent, or control caries in part by neutralizing dental plaque acid by increasing the pH in the area surrounding dental plaque. One embodiment provides contacting a tooth with electrolyzed water, typically after the tooth has been challenged with a sugar, to neutralize dental plaque acid and thereby reduce the formation of **dental caries.** Electrolyzed water and compositions comprising electrolyzed water can be formulated as palatable beverages, gels, candy, or other foodstuffs that are safely digested by individuals such as young children.

  Excerpt(s): This application claims benefit of priority to provisional patent application serial No. 60/340,769 entitled "The Effect of a Buffer on Acidogenesis of Plaque" filed on Dec. 11, 2001. Dental caries occur in teeth where microbial plaques exists. Dental plaque is a soft deposit that accumulates on the teeth. Plaque can be defined as a complex microbial community, with greater than 10.sup.10 bacteria per milligram. It has been estimated that as many as 400 distinct bacterial species may be found in plaque. In addition to the bacterial cells, plaque contains a small number of epithelial cells, leukocytes, and macrophages. The cells are contained within an extracellular matrix, which is formed from bacterial products and saliva. The extracellular matrix contains protein, polysaccharide and lipids. Streptococcus sanguis, Streptococcus mutans, and Actinomyces viscosus are examples of primary microbial colonizers of dental plaque. Secondary colonizers include Gram-negative species such as Fusobacterium nucleatum, Prevotella intermedia, and Capnocytophaga species. Other microbial colonizers include Porphyromonas gingivalis, Campylobacter rectus, Eikenella corrodens, Actinobacillus actinomycetemcomitans, and the oral spirochetes (Treponema species). Fermentable carbohydrates such as sugars in the diet are metabolized to acids such as lactic acid by plaque bacteria causing a pH change at the tooth surface. If the pH is sufficiently acidic and is not neutralized, the tooth, which is comprised mainly of calcium phosphate crystals such as hydroxylapatite will dissolve or decalcify producing a carious lesion. A pH at or below 5.5 is generally accepted as the threshold at which decalcification can proceed.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Immunogenicity of glucan binding protein**

  Inventor(s): Smith, Daniel J.; (Natick, MA), Taubman, Martin A.; (Newtonville, MA)

  Correspondence: Ingrid A. Beattie, PH.D.; Mintz, Levin, Cohn, Ferris, Glovsky And POPEO,P.C.; One Financial Center; Boston; MA; 02111; US

  Patent Application Number: 20040127400

  Date filed: March 7, 2003

Abstract: Immunogenic compositions and subunit vaccines for **dental caries** are described which comprise peptide subunits of glucan binding protein-B and peptide subunits of glucan binding protein-B in combination with peptide subunits of glucosyltransferase. Methods of provoking an immune response to S. mutans glucan binding protein-B or glucosyltransferase. Methods of immunizing a mammal against **dental caries** are also described, along with antibodies which bind particular epitopes of glucan binding protein-B or glucosyltransferase.

Excerpt(s): This application claims the benefit of U.S. Provisional Application No. 60/363,209, filed Mar. 7, 2002 and U.S. Provisional Application 60/402,483, filed Aug. 8, 2002, the entire contents of which are hereby incorporated by reference. Mutans streptococci have been implicated in the initiation of **dental caries** in humans. Streptococcus mutans have several virulence factors that allow the bacteria to accumulate within the dental biofilm and produce and tolerate the acids that cause **dental caries.** The ability of cariogenic mutans streptococci to accumulate in the dental biofilm is thought to be a consequence of the synthesis of glucans by glucosyltransferases, followed by the binding of the bacteria to these polymers via the cell-associated glucan binding proteins (Gbps). Biofilm development occurs in two distinct phases. During the first phase, bacterial surface proteins interact with host or bacterial products adsorbed on the tooth surface. In the second phase, a biofilm forms as bacteria accumulate by aggregation with the same or other species and produce an extracellular polysaccharide matrix. Epitopes associated with these functions are thought to be primary targets for immunogenic attack, provided that the relevant sequences are located in molecular areas that can be accessible to antibody. Several mutans streptococcal proteins with glucan binding activity have been described (Russell, R. R., J. Gen. Microbiol., 112:197-201 (1979); Smith D. J. et al., Infect. Immun. 62:2545-2552 (1994); Sato, Y., et al., Infect. Immun., 65:668-675 (1997)). One of these components, glucan-binding protein-B (GbpB), has been shown to induce protective immune responses against experimental **dental caries** following systemic or mucosal immunization (Smith D. J. et al., Infect. Immun. 64:3069-3073 (1996) and Smith D. J. et al., Oral Microbiol. Immunol. 13:278-285(1998)). Furthermore, there is evidence that the expression of GbpB is directly related to biofilm formation (Mattos-Graner, R.O., et al., Infect. and Immun. 69(11) 6931-6941(2001)). However, use of the intact GbpB protein in a vaccine may induce immunity to irrelevant or unwanted epitopes.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Inspection of teeth using stress wave time non-destructive methods**

  Inventor(s): Johnson, Kenneth; (Corvallis, OR), Tingley, Daniel A.; (Corvallis, OR)

  Correspondence: Charles D. Mcclung; Chrnoff, Vilhauer, Mcclung & Stenzel, Llp; 1600 Ods Tower; 601 S.W. Second Avenue; Portland; OR; 97204-3157; US

  Patent Application Number: 20020012897

  Date filed: July 18, 2001

  Abstract: A method and device using stress waves for dental examination. According to the method, the dental structure (such as a tooth) under examination is subjected to a stress (acoustic) wave. The stress wave propagates through the dental structure and is received on the other side. From the analysis of the transmission time and/or the resulting waveform, diagnostic information results as to the presence of dental disease such as **dental caries** that may be present on the tooth surface under dental restorations such as fillings or metal crowns. According to the invention, the stress wave is generated

by a suitable transducer, coupled to the dental structure through a transmission medium, propagates through the dental structure, coupled through another transmission medium, received by a acousto-electric transducer, and analyzed by suitable electronic means.

Excerpt(s): The invention relates to the non-invasive ultrasonic diagnosis of lesions on tooth surfaces or under dental restorations such as gold crowns and other dental restorations. The invention further relates to the non-invasive ultrasonic diagnosis of lesions on interproximal tooth surfaces and/or interproximal areas of dental restorations such as gold crowns and other dental restorations. The invention also relates to the non-invasive ultrasonic diagnosis of periodontal disease. Tooth lesions diagnosed could be enamel caries, dentinal caries and cracks in the tooth. Similarly, periodontal disease diagnosed could be gingivitis and periodontitis. In particular, the invention relates to ultrasonic stress waves imparted through the tooth (transmitted from one transducer through the tooth, and/or gum and bone to a second receiving transducer) or through a dental restoration for the detection of said lesions. Non-destructive material evaluation is the identification of physical and mechanical properties of a piece of material without altering its end-use capabilities. One effective technique used to provide accurate information pertaining to the material properties is ultrasonic Stress Wave Timing. Stress waves, for the purpose of this patent, are the propagation of stresses distributed longitudinally through material. Wavelength can encompass any range. The preferred embodiment is between ten and thirty megahertz. As indicated, stress wave can be an ultrasonic wave pulse. The basic principle of stress wave timing is to use a stress wave to measure the speed of sound transmission by recording the time it takes to pass through material and/or attenuation of induced stress wave. The speed with which sound waves travel through a material is dependent upon the materials properties. The transmission of sound through materials and the related rates of travel and attenuations is a well-understood art. All of the above cited U.S. patents, other than one (U.S. Pat. No. 5,570,182), have used a related but different method of evaluating materials with ultrasound. They have looked at the ultrasound Pulse-Echo that is returned from structures or boundaries in the tooth being evaluated, that is they use an ultrasonic transducer to transmitted a ultrasound pulse into the tooth and then used the same transducer, or another very close to it, to receive the reflected energy, the echo of that pulse, off internal layers or other structures within the tooth they are looking into. U.S. Pat. Nos. 5,874,677, 6,162,177 and 6,190,318 transmit surface (Rayleigh) waves and these patents only look for the pulse-echo from this surface wave. They do not look through the tooth; they look around the outer surface of the tooth, to diagnose carious lesions. U.S. Pat. No. 5,570,182 uses light instead of sound as a medium to evaluate materials. Many articles have been published on the use of Pulse-Echo ultrasound in teeth also. (Ultrasonic Pulse-Echo Measurements in Teeth. FE. Barber, S. Lees, R. R. Lobene. Archs oral Biol., Vol. 14, 745-760, 1969), (Observation of Internal Structures of Teeth by Ultrasonography. G. Baum, I. Greenwood, S. Slawski, R. Smirnow. Science, Vol. 139, 495-496, 1962. According to prior art, sound in dental materials travels at different speeds according to the material it is passing through. The slowest is the tooths pulp section, which has sound transmission characteristics very similar to water (Examination of the Contents of the Pulp Cavity in Teeth. G. Kossoff, C. J. Sharpe. Ultrasonic, 77-83, 1966), next is dentine at approximately four times faster. The fastest is in enamel at about six times faster than water (Determination of Ultrasonic Velocity in Human Enamel and Dentine. S. Y Ng, P. A. Payne, N. A. Cartledge, M. W. J. Ferguson. Archs oral Biol., Vol. 34, No. 5, 341-345, 1988). **Dental caries,** in general, would have a different transmission time, the time it takes for the stress (acoustic) wave to travel from the transmitting transducer to the receiving transducer, so the location

and severity of material change (caries) can be found easily and quickly by recording multiple transmission times over an area. By using oscilloscopes, or other measuring or recording devices, transmission time, wave attenuation, transit times and wave shape, thus time and speed, can be recorded and evaluated. The sequence of transit times can be mapped onto the path taken by the receive and transmit transducer pairs as they are mechanically or electronically translated about the tooth. The resulting map can be thought of as an image of the shortest times taken by the stress wave through that region of the tooth defined by the transducer locations. Regions of anomalous transit times are interpreted as regions of **dental caries** or some other defect in the tooth structure. Mapping is the preferred embodiment of imaging, of the material (tooth and gums) that can be used to diagnose lesions such as enamel caries, dentinal caries and cracks in the tooth. (Development and Application of an Ultrasonic Imaging System for Dental Diagnosis. H. Fukukita, T. Yanco, A. Fukumoto, K. Sawada, T. Fujimasa, and I. Sciaenidae. Journal Of Clinical Ultrasound No. 13, 597-600, October 1985).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Luminescence assisted caries excavation**

  Inventor(s): Buchalla, Wolfgang; (Indianapolis, IN), Lennon, Aine M.; (Indianapolis, IN)

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  Patent Application Number: 20030022126

  Date filed: April 16, 2001

  Abstract: The present invention provides an improved method and apparatus for detecting **dental caries** (including residual caries) during treatment thereof. A dental handpiece in accordance with the present invention includes both an integral drill head (or other apparatus for excavating caries) and an integral light source operable to cause tooth luminescence. The light source is configured whereby tooth luminescence is caused when the dental handpiece is placed in operable position to treat the tooth with the drill head. During treatment, an observer can differentiate carious tooth substance from non-carious tooth substance due to the luminescent characteristics of each. Specifically, it has been found that when illuminated with a blue-violet light, the carious region of a tooth will appear as a red-orange central region surrounded by an intensely luminescent region of green color. The aforementioned intensely luminescent region is positioned intermediate the red-orange central region and a dark outer ring. According to the method of the present invention, the red-orange centered region is identified as the bacterially invaded zone of the carious lesion and is removed.

  Excerpt(s): The present invention relates to a method and apparatus for facilitating the removal of substantially all the bacterially invaded tooth substance in a carious region, e.g., prior to placing a restoration in an affected area (i.e., enamel and dentin) of a tooth. More particularly, the present invention relates to an improved method and apparatus for the luminescent detection of the bacterially invaded tooth substance in a carious region during removal thereof to facilitate removal of substantially all of the bacterially invaded tooth substance, while providing maximum preservation of healthy tooth structure. To effect caries excavation, e.g., prior to positioning a restoration, the dentist must differentiate between carious tooth substance which will be removed and sound tooth substance which will be conserved. Currently several methods of differentiating between carious and non-carious tooth substance are available. One available method utilizes the hardness differential between carious and non-carious tooth substance. A sharp dental explorer is utilized to probe the tooth substance and to determine if the

tissue is soft or hard. Generally the soft tissue is thought to be carious, while the hard tissue is considered to be non-carious. Utilizing this technique is relatively time consuming to implement. Furthermore, this process is inaccurate (due, e.g., to the subjective analysis employed) and can therefore lead to removal of healthy (i.e., non-carious) tooth substance and can also lead to carious substance being overlooked. Additionally, probing the dentin region of the tooth close to the pulp chamber can disadvantageously lead to exposure of the pulp chamber.

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- **Material for evaluating dental caries activity**

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  Patent Application Number: 20030113266

  Date filed: November 20, 2002

  Abstract: A material for evaluating **dental caries** activity that is capable of evaluating **dental caries** activity, i.e., the released amount of an acid from dental plaque, which is important in dental health, by a simple manner in a short period of time, contains an absorptive material having carried thereon a pH indicator having an indicator range of pH 3.5 to 8.0 and a sugar, and has been adjusted to have a pH value higher than the indicator range of the pH indicator, in which dental plaque taken from a subject is directly applied on the material to evaluate **dental caries** activity by change in color.

  Excerpt(s): The present invention relates to a material for evaluating **dental caries** activity, which is capable of evaluating activity of **dental caries** in an oral cavity of a subject by a simple manner in a short period of time. Evaluation of **dental caries** activity in dental surgery is to estimate and determine activity of **dental caries,** i.e., as to whether or not **dental caries** of teeth currently developed further proceeds, and as to whether or not there is a possibility of future development of **dental caries** due to activity of **dental caries** although no **dental caries** is currently developed. Therefore, it has great significance in dental health. It is considered that development and progress of **dental caries** of teeth are caused in such mechanisms referred to as a decalcifying phenomenon that cariogenic bacteria present in dental plaque attached to the teeth metabolize carbohydrate to produce an acid, and calcium ions and phosphoric ions in the teeth are eluted by the acid. Therefore, a method of measuring a released amount of an acid from dental plaque is studied as a method for evaluating **dental caries** activity. Because it is considered that the released amount of an acid from dental plaque depends on the number of cariogenic bacteria present in the dental plaque, such a method is carried out by a measuring test for the number of mutans streptococcus in the dental plaque and a measuring test for the number of lactobacilli in the dental plaque. However, these methods have such disadvantages that expensive culturing equipments, sophisticated operation techniques and prolonged culturing periods are required.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method and means for caries prevention and susceptibility detection**

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  Patent Application Number: 20020177171

  Date filed: July 29, 2002

  Abstract: A method for identifying the susceptibility of a person to **dental caries** comprises the assay of one or several of: an agent having high binding capacity to Streptococcus mutans but low binding capacity to Actinomyces naeslundii, an agent having high binding capacity to S. mutans-binding agglutinin, an agent having high binding capacity to A. naeslundii. The agent having high binding capacity to Streptococcus mutans but low binding capacity to A. naeslundii comprises an allelic Db type of salivary acidic proline-rich molecules (acidic PRPs), a biologically active fragment or a genetic precursor thereof. A corresponding reagent is also identified. Also disclosed are a method and an agent for the prevention of caries, as well as labelled S. mutans and A. naeslundii and their use.

  Excerpt(s): This is a division of application Ser. No. 09/701,407, filed Dec. 22, 2000. The present invention relates to a method for determining the susceptibility of individuals to **dental caries** and a corresponding means. The present invention also relates to a method for preventing caries and a corresponding means. The two major dental diseases, **dental caries** and periodontitis, are chronic polymicrobial infectious diseases [1,2,3]. Two principal mechanisms, adhesion and metabolism, account for the oral polymicrobial societies. Acid proline-rich proteins (acidic PRPs: PRP-1; PRP-2; Db; PIF; Pa) from the PRH1 and PRH2 gene loci on chromosome 12p13.2, act at the tooth-saliva interface (4,5]. Acidic PRPs regulate calcium phosphate precipitation, crystal formation and attach commensal Actinomyces and streptococci over pathogenic S. mutans and lactobacilli. The acidic PRPs are polymorphic proteins displaying both allelic (large PRP-1, PRP-2 PIF-s, Db-s and Pa-s) and post-translatory (small PRP-3, PRP-4, PIF-f and DB-f) variation.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Method for reducing the viability of detrimental oral microorganisms in an individual, and for prevention and/or treatment of diseases caused by such microorganisms; and whitening and/or cleaning of an individual's teeth**

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  Patent Application Number: 20020114768

  Date filed: December 7, 2001

  Abstract: The invention relates to a method for reducing the viability of detrimental oral microorganisms in an individual, said method comprising subjecting the individual's oral cavity to a bioactive glass, the average particle size of which is less than 100.mu.m.Furthermore, this invention concerns a method for the prevention of **dental caries** and/or gingivitis in an individual, said caries being caused by a cariogenic

bacteria; or for prevention or treatment of periapical infections.Further the invention relates to a method for the whitening and/or mechanical cleaning of an individual's teeth.

Excerpt(s): This invention relates to a method for reducing the viability of detrimental oral microorganisms in an individual, and for prevention of **dental caries** and gingivitis, and for prevention or treatment of periapical infections, and whithening and/or mechanical cleaning of an individual's teeth. The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference. Bioactive glasses have been tested as substitutes for reconstruction of defects of the facial bones (1), rehabilitation of the dentoalveolar complex (2), regeneration of periodontal pockets (3), and recently also for treatment of hypersensitive teeth (4). The surface reactive bioactive glass contains SiO.sub.2, Na.sub.2O, CaO and P.sub.2O.sub.5. The chemical bond with bone in vivo is reported to result from the leaching of Na.sup.+-ions and the congruent dissolution of calcium, phosphate and silica from the glass in an aqueous environment, giving rise to an Si-rich layer on the material. The Si-rich layer acts as a templet for a calcium phosphate precipitation, which then binds to the bone (5). Bioactive glass has been successfully used for reconstructions of closed bone defects, which are not exposed to the external environment after the clinical procedure (1). However, there are a number of conditions for which bioactive glasses are used as therapeutic materials but that, at the same time, are imminently prone to microbial infections. These include clinical conditions such as infected frontal sinuses (6), periodontal pockets (3) and hypersensitive teeth as a complication of periodontal treatment or tooth wear that has resulted in the exposure of dentin and dentinal tubules (4). Obviously, the demonstration of any antibacterial activity of the biactive glass would add to the therapeutic value of the material in the clinical conditions described. Earlier studies have shown that P. gingivalis is agglutinated in the presence of granules (315-500.mu.m) of the bioactive glass S53P4 in an aqueous environment due to Ca.sup.+2-ions released from the granules (19, 7). The minimum Ca.sup.2+-concentration needed to induce agglutination of P. gingivalis was found to be 0.04 g/l (7). In these studies, however, no reduction of the viability of the bacteria was noticed.

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- **METHOD FOR THE TREATMENT AND THE PREVENTION OF DENTAL CARIES AND PERIDONTAL DISEASES USING BACTERIO PHAGE-ENCODED ENZYMES**

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  Patent Application Number: 20010014463

  Date filed: June 30, 1997

  Abstract: A method for the treatment and prevention of **dental caries** and periodontal diseases using bacteriophages and phage-encoded anti-bacterial enzymes to inhibit establishment of bacteria in the oral cavity is provided. Also provided are methods for studying the cell wall of an oral bacterium, a method for preventing spoilage of perishable items and a method for removing dextrans from surfaces utilized in sugar manufacture. Purified enzymes and the isolated DNA fragments encoding them are also provided.

Excerpt(s): This invention relates to bacteriophage-encoded enzymes useful in preventing **dental caries** and periodontal diseases. More specifically, this invention relates to lysozyme-like enzymes isolated from bacteriophages which are capable of killing cariogenic bacteria and other periodontal disease-causing organisms. The invention also relates to dextranase-like enzymes suitable for dental treatments (i.e., loosening plaque) and other applications where it is desired to remove dextran and other bacterial polysaccharides (i.e., mutan) synthesized from sucrose. With regard to their function in dental plaque, phages are likely to influence the plaque flora in several potentially significant ways. Prophages, for example, provide immunity to super-infection by homoimmune phages and would presumably assist lysogens which carry them in competing with other bacteria in plaque by killing phage-sensitive competitors in a manner analogous to bacteriocinogenic cells. The semi-solid nature of dental plaque provides an especially favorable environment for this type of competition. Alternatively, lytic phage would be expected to select for phage-resistant mutants of sensitive strains and for mucoid mutants (phenotypically phage-resistant), which could well have altered colonizing and pathogenic properties. Actinophage-resistant mutants have in fact already been used to study cell surface structures that appear to be involved in specific, intergeneric oral bacterial coagreggation reactions (Delisle, A. L. et al (1988) Infect. Immun. 56:54-59; Tylenda, C. A. et al (1985) Infect. Immun. 48:228-233), which are believed to play an important role in colonization of dental plaque (Kolenbrander, P. E. et al (1985) In, S. E. Murgenhagen and B. Rosan (eds) pp. 164-171, American Society for Microbiology, Washington, D.C.). The literature on S. mutans phages dates back to 1970, when Greer first claimed to be able to induce phages, by treatment with mitomycin C, from oral streptococcal strains AHT, BHT and HHT (Greer, S. W., et al (1970) IADR Abstr. 160; J. Dent. Res, 48A:88) and subsequently claimed that the same virus was present in all of eight cariogenic streptococci he examined, but not in non-cariogenic strains (Greer, S. W., et al (1971) J. Dent. Res. 50:1594-1604). He then reported that lysogens could be cured of their prophages by treatment with acridine orange (Greer, S. W., et al (1971) IADR Abstr. 57: J. Dent. Res. 49:67) and nitrosoguanidine (Greer, S. W., et al (1972) IADR Abstr. 68: J. Dent. Res. 50:65). The latter was used to isolate temperature-sensitive mutants, one of which was heat-inducible and could be used to obtain cured cells by brief heating. Greer also proposed a curing procedure based on radiosensitization of DNA by incorporating 5-bromodeoxyuridine lysogens (Ramberg, E. et al (1973) IADR Abstr. 113: J. Dent. Res. 52a), but its application to S. mutans was never subsequently reported. Greer never reported the successful isolation of an infectious phage which could be grown in S. mutans. Difficulties in repeating Greer's induction experiments led many microbiologists to assume that he was really working with enterococci, which were common contaminants in the oral streptococcal cultures being exchanged among various laboratories during this time.

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- **Method for the treatment of dental caries caused by streptococci mutans infection by inhibiting energy storage and utilization**

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  Patent Application Number: 20030232021

  Date filed: April 11, 2003

Abstract: A method and pharmaceutical composition for inhibiting infections of S. mutans by the addition of said composition to toothpaste or mouthwash, by inhibiting the production of ADP-glucose, particularly by inhibiting the activity of ADP-glucose pyrophosphorylase or glycogen synthase.

Excerpt(s): This application claims priority on provisional Application No. 60/372,307 filed on Apr. 12, 2002, the entire contents of which are hereby incorporated by reference. The present invention is directed to the use of bacterial enzymes as targets for antibiotic therapy and the treatment of **dental caries** caused by S. mutans infection, particularly by inhibiting enzymes involved in energy storage and utilization. Starch, a complex polymer of glucose, is present in most green plants in practically every type of tissue and is the major intracellular reserve polysaccharide in photosynthetic organisms. The glucan accumulates during development of storage or seed tissues and is catabolized to serve as a source of energy. In the animal kingdom, as well as in fungi, yeast and bacteria, the primary reserve polysaccharide is glycogen. Glycogen is a polysaccharide containing linear molecules with.alpha.-1,4 glucosyl linkages and is branched via.alpha.-1,6-glucosyl linkages. Although glycogen is analogous to starch with regard to linkages, glycogen exhibits a different chain length and a different degree of polymerization.

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- **Method of treating dental caries and remineralizing lesions**

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  Patent Application Number: 20040022744

  Date filed: July 17, 2003

  Abstract: A method of treating dental carries and remineralizing lesions, provides for directing a stream comprising an oxidizing gas onto a carious lesions for a period of time sufficient to kill microorganisms within the carious lesion; and thereafter, applying to the lesion a remineralization formulation.

  Excerpt(s): This invention relates to the use of ozone in the treatment of **dental caries** and subsequent remineralization of teeth. The great destructive disease of teeth is **dental caries** which may be defined as the acid dissolution of enamel, dentine or cementum as a consequence of the metabolism of micro-organisms living within deposits on the teeth known a plaque. **Dental caries** is believed to be associated with specific micro-organisms, the principal ones being Streptococcus Mutans, Lactobacilli, Actinomyces Visosus Serovar 2, Actinomyces Naeslundii and "Intermediate" Actinomyces, other Streptococci and yeasts. These are acid producing micro-organisms which produce acids such as acetic and lactic acids from the dietary carbohydrates. The micro-organisms associated with **dental caries** are unique and are ecologically very different from those associated with, for example, infected root canals. (iii) the protection of any newly exposed non-carious dentine with restorative material.

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- **Model of dental caries**

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  Patent Application Number: 20040067477

  Date filed: July 11, 2003

  Abstract: A model of **dental caries** may include simulated decay material in a cavity in an artificial tooth. The artificial tooth may be made of resin. The cavity may include an opening that extends from a simulated enamel surface to, e.g., at least the dentinoenamel junction of the tooth. The model may include at least one groove that extends from the opening (e.g., along the dentinoenamel junction). The cavity may contain simulated decay material in a groove and/or the opening. The simulated decay material is a homogenous substance that may include a curable resin, a porous substance, and/or coloring. The simulated decay material may be detectable with caries detecting stain. An etching solution and/or a curable bonding substance may be applied to the cavity before the simulated decay material is applied. The simulated decay material may simulate **dental caries** in color, texture, and/or tenacity.

  Excerpt(s): This application claims priority to U.S. Provisional Application No. 60/395,432 entitled "MODEL OF DENTAL CARIES" filed Jul. 11, 2002. The above-referenced provisional application is hereby incorporated by reference as if fully set forth herein. The present invention generally relates to a model of **dental caries.** Embodiments of the invention relate to a model of **dental caries** that simulates dental decay in color, texture, and/or tenacity. Traditionally, pre-clinical dental students learn to treat various classifications of decayed teeth by working on pristine resin teeth (teeth without defects) arranged in simulated upper and lower resin jaws. In some cases, students may work with resin teeth with defects. These defects may include various defects caused by human dental decay (caries). Some resin teeth have defects but contain no simulated decay material. Other resin teeth for pre-clinical use contain simulated decay material. Currently, simulated carious resin teeth are produced by cutting away the outer layer of a resin crown, cutting defects into the prepared tooth, inserting simulated carious material into the defects, and then covering the prepared tooth with a resin crown. No opening is provided into the dental cavity. Furthermore, the simulated carious material may be a heterogeneous substance with unrealistic color, texture, and/or tenacity.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **MOUTHWASH COMPOSITIONS**

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  Patent Application Number: 20020044910

  Date filed: July 9, 1999

  Abstract: Aqueous solutions are disclosed which are supersaturated with respect to calcium phosphate(s) and which further comprise a stabilising agent in an amount

sufficient to enable the calcium ions and phosphate ions to remain in supersaturated solution so that it may be used as a dental rinse or mouthwash. Such solutions are suitable for treating patients having **dental caries** or other conditions of the oral cavity.

Excerpt(s): The present invention relates to calcium- and phosphate-containing compositions for use as mouthwashes or dental rinses. In particular, it relates to solutions supersaturated with calcium and phosphate, their preparation and use. By "supersaturated" with calcium and phosphate is herein meant that higher concentration of calcium ions and orthophosphate ions is present in the solution than would be present in a saturated solution of those ions. British patent specification no. GB 1 090 340, published in 1967, discloses compositions for rehardening dental enamel comprising fluoride, calcium, phosphate and sodium chloride which yield, on contact with saliva, supersaturated solutions to form hydroxyapatite. Because saliva is required to form the supersaturated solution, the preferred compositions are in the form of confectionery such as chewing gum. However, it is known that, under most circumstances, saliva is already supersaturated with calcium and phosphate. No disclosure is given of how to make a supersaturated solution ab initio which can then be used effectively in the form of a mouthwash or dental rinse. Furthermore, no mention is made of the possibility of excluding fluoride; or of the formation of octacalcium phosphate by the supersaturated solution in the saliva. In any case, in the absence of or where there is a significantly reduced amount of saliva, these compositions would not work as described.

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- **Oral compositions and use thereof**

  Inventor(s): Bowen, William H.; (Victor, NY), Cury, Jaime Aparecido; (Piracicaba, BR), Koo, Hyun; (Rochester, NY), Park, Yong Kun; (Campinas, BR), Rosalen, Pedro Luiz; (Piracicaba, BR)

  Correspondence: Edwin V Merkel; Nixon Peabody; Clinton Square; P O Box 31051; Rochester; NY; 14603; US

  Patent Application Number: 20040057908

  Date filed: October 1, 2003

  Abstract: The present invention relates to an oral composition which includes an organoleptically suitable carrier and an amount of a terpenoid and a flavonoid, dispersed in the carrier, which is effective to prevent or treat **dental caries,** dental plaque formation, gingivitis, candidiasis, dental stomatitis, aphthous ulceration, or fungal infection. The invention also relates to various uses of oral compositions, containing a terpenoid, a flavonoid, or both, such uses include: inhibiting the activity of surface-bound glusosyltransferase; treating or inhibiting **dental caries,** gingivitis, candidiasis, denture stomatitis; inhibiting the accumulation of microorganisms on an oral surface; and/or treating or inhibiting aphthous ulcerations on an oral surface.

  Excerpt(s): This application claims the priority benefit of U.S. Provisional Patent Application Serial No. 60/255,304 filed Dec. 13, 2001, which is hereby incorporated by reference in its entirety. The present invention relates to oral compositions and their use for inhibiting the activity of surface-bound glucosyltransferase; treating or inhibiting **dental caries,** gingivitis, candidiasis, and/or denture stomatitis; inhibiting the accumulation of microorganisms on an oral surface; and treating or inhibiting aphthous ulcerations on an oral surface. Colonization of tooth surfaces by mutans streptococci is

associated with the etiology and pathogenesis of **dental caries** in animals and humans (Fitzgerald and Keyes, 1960; Loesche, 1986). Glucosyltransferase enzymes ("GTFs") produced by Streptococcus mutans have been recognized as virulence factors in the pathogenesis of **dental caries** (De Stoppelaar et al., 1971; Tanzer et al., 1985; Yamashita et al., 1993). GTFs catalyze the formation of soluble and insoluble.alpha.-linked glucans from sucrose and contribute significantly to the polysaccharide composition of dental plaque matrix (Rolla et al., 1983). Dental plaque is essentially a biofilm. Glucans promote the adherence and accumulation of cariogenic streptococci on the tooth surface, and play an essential role in the development of pathogenic dental plaque related to caries activity (Hamada and Slade, 1980; Schilling and Bowen, 1992; Yamashita et al., 1993). Streptococcus mutans produces at least three GTFs: GTF B, which synthesizes a polymer of mostly insoluble.alpha.1,3-linked glucan; GTF C, which synthesizes a mixture of insoluble.alpha.1,3-linked glucan and soluble.alpha.1,6-linked glucan; and GTF D which synthesizes.alpha.1,6-linked soluble glucan (Aoki et al., 1986; Hanada and Kuramitsu, 1988; Hanada and Kuramitsu, 1989). An additional enzyme, GTF from S. sanguinis (GTF Ss), may also be involved in the development of dental plaque (Nyvad and Kilian, 1987; Vacca-Smith et al., 2000). S. sanguinis colonizes tooth surface early in plaque formation, and its GTF catalyzes predominantly.alpha.1,6-linked soluble glucan (Ceska et al., 1972). Enzymatically active GTFs are present in the soluble fraction of whole human saliva and are also incorporated into salivary pellicle that is formed on tooth surfaces (Rolla et al., 1983; Scheie et al., 1987). Furthermore, the GTFs incorporated into an experimental pellicle demonstrate distinct physical and kinetic properties when compared to the same enzymes in solution; GTF C and D express enhanced enzymatic activity (Schilling and Bowen, 1988; Vacca-Smith et al., 1996; Venkitaraman et al., 1995). A large proportion of the glucans synthesized by these surface-adsorbed GTFs is retained on the pellicle and may provide binding sites for mutans streptococci, contributing to the in situ formation of dental plaque (Schilling and Bowen, 1988; Schilling and Bowen, 1992; Vacca-Smith and Bowen, 1998). Therefore, inhibition of GTFs both in solution and adsorbed to the pellicle of tooth surface is one of the strategies to prevent **dental caries** and other plaque related diseases.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Risk check sheet for dental caries**

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  Patent Application Number: 20030011191

  Date filed: June 14, 2002

  Abstract: To enables a technician for dental care to grasp the risk of **dental caries** of a patient and show its state to the patient in an easily understandable way, a risk check sheet for **dental caries** is constituted of a list sheet provided with three kinds of risk items consisting of a risk of **dental caries** caused by a resistance, a risk of **dental caries** caused by intra-oral bacteria, and a risk of **dental caries** caused by eating habit, each having a plurality of check items, as to each of which one from a plurality of selection items having different ranks is to be alternatively selected, and numericalizing data of the risks of **dental caries** from by summing up evaluation scores given in the selection items for each risk item; and a chart sheet provided with a standard circle centering

around an origin and having indicator circles provided radially with a distance of 120 degree centering around the origin from each other and allocated for data of the three kinds of risks of **dental caries** based on the numerical data by the list sheet.

Excerpt(s): The present invention relates to a risk check sheet for **dental caries,** which enables a technician for dental care to grasp the risk of **dental caries** of a patient and to show its state to the patient in an easily understandable way. In order to consider a measure for inhibiting the progress of "dental caries" as a condition-pluricausal disease caused by the intra-oral state or life habit and to plan for treating it, a movement in which a technician for dental care confirms the intra-oral state and life habit of a patient through inquiries or inspections and grasps "whether easily or hardly to be attacked by the dental caries", that is, "a risk of dental caries", of the patient per se starts to occur. To make the patient per se understand the risk of **dental caries** is necessary in giving a motivation against the maintenance and continuation of oral care. For example, the caries risk radar chart as disclosed in Clinical Cariology (published by Ishiyaku Publishers, Inc.) is concerned with a method in which among the results obtained by checking the amount of dental plaque, the level of Mutans streptococci, the level of Lactobacilli, the number of eating and drinking per day, the amount and quality of saliva, the buffer capacity of saliva, DMFT (an index showing the caries experience of permanent teeth, which is expressed by a value obtained by dividing the sum of caries-experienced teeth of permanent teeth of a subject by the number of subjects), the shape of fissure in enamel, the fluoride mouth wash, the fluoride application, the family make-up, the level of bacteria of the family, and the like by using a "Caries Risk Questionnaire", the eight major factors, i.e., the buffer capacity of saliva, the level of Mutans stroptococci, the level of Lactobacilli, the number of eating and drinking, the accumulated amount of dental plaque, the use status of fluoride, the DMFT, and the amount and quality of saliva, are selected as parameters related to the risk of **dental caries** and plotted in the radar chart, and the risk of **dental caries** is confirmed from the size and shape of a graph thus drawn. Accordingly, the risk of **dental caries** can be simply shown in a visual form. However, not only the number of the parameters related to the risk of **dental caries** is high and the procedures are complicated, but also each of the parameters uses technical terminologies, which is difficult for a general patient to understand. Therefore, it has been difficult to make the patient per se understand the risk of **dental caries** and give a motivation for the maintenance and continuation of oral care.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Sialagogue, and food composition and oral composition containing thereof**

  Inventor(s): Hirose, Kazuo; (Osaka, JP), Matsumura, Shinichi; (Osaka, JP), Nakasugi, Tohru; (Osaka, JP)

  Correspondence: S. Alex Liao; Suite 905; 12 South First ST.; San Jose; CA; 95113; US

  Patent Application Number: 20030039706

  Date filed: March 13, 2002

  Abstract: This invention is to provide sialagogue wherein one or more kind of plant and/or extract thereof selected from the group of the plant belonging to Capparidaceae and the plant belonging to Umbelliferae are contained, and food composition and oral composition containing thereof. The sialagogue, and the food composition and the oral composition containing thereof, which cure dryness of a mouth by promoting salivary

secretion having more than fixed quantity consecutively for a long time, and which can prevent generating **dental caries** by raising the self-cleansing action in the mouth.

Excerpt(s): This invention relates to sialagogue, and food composition and oral composition containing thereof, and the object thereof is to provide the sialagogue, and the food composition and the oral composition containing thereof, which cure dryness of a mouth by promoting salivary secretion having more than fixed quantity consecutively for a long time, and which can prevent generating **dental caries** by raising the self-cleansing action in the mouth. The saliva secreted from the salivary gland has a lot of functions: digestion, assertive action for mastication, solvent action, smooth action for chatting and vocalizing, cleaning operation, pH buffering action and so on, whereas, it is well-known that the secretion quantity of the saliva is declined because of an emotional disorder, a neurosis, an internal organ derangement, encephalitis, a neoplasm, a cerebral vascular accident, hypertension, all kinds of diseases such as the diabetes, adverse reaction of medicine, radiotherapy and so on. There are many people complaining the dryness in the mouth, in particular, the aged people, since the secretion quantity of the saliva is decreased by aging, a plurality of chronic disease or their cure medicine. Dryness in a mouth with decreasing secretion quantity of the saliva will cause indisposition, the occurrence of the halitosis and so on, and further progressive of the disease will cause periodontal disease, infection disease and so on. Thus, it is desired to increase the secretion quantity of the saliva of the patient having the symptom as the above by some means.

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **SYNTHETIC PEPTIDE VACCINES FOR DENTAL CARIES**

  Inventor(s): SMITH, DANIEL J.; (NATICK, MA), TAUBMAN, MARTIN A.; (NEWTONVILLE, MA)

  Correspondence: Patricia Granahan; Hamilton Brook Smith And Reynolds; Two Militia Drive; Lexington; MA; 02173

  Patent Application Number: 20010048926

  Date filed: November 10, 1997

  Abstract: Vaccine compositions and immunogenic compositions are described which are glucosyltransferase subunit vaccines for **dental caries** and which contain at least one peptide which corresponds to a sequence of glucosyltransferase containing aspartate 413, aspartate 415 or both aspartate 413 and aspartate 415. These subunit vaccines elicit antibodies which protect an immunized mammal from **dental caries.** Methods of provoking an immune response to intact glucosyltransferase are also described.

  Excerpt(s): This application is a continuation-in-part of U.S. application Ser. No. 08/057,162, filed Apr. 30, 1993, which is a continuation-in-part of U.S. application Ser. No. 07/877,295, filed May 1, 1992. The entire teachings of these priority applications are incorporated herein by reference. Mutans streptococci have been convincingly implicated in the initiation of **dental caries** in humans. The ability of these organisms to accumulate and colonize on the tooth surface has been associated with the synthesis of glucans from sucrose. Glucans are synthesized by constitutively secreted glucosyltransferase (GTF) enzymes. These enzymes have been considered as potential components of a **dental caries** vaccine because of their role in the pathogenicity of Mutans streptococci. However, vaccines based on intact GTF have a variety of disadvantages such as the presence of inappropriate epitopes and excess molecular

material that does not possess appropriate immunogenic features. Although the exact basis for experimental protection with GTF-type vaccines is unclear, it is quite likely that protection involves functional inhibition of the catalytic and/or the glucan-binding activities of GTF. Epitopes associated with these functions would theoretically be primary targets for immunological attack, provided that the relevant sequences are located in molecular areas that are accessible to antibody. Subunit vaccines provide a method to block functional domains without inducing immunity to irrelevant or unwanted epitopes. It has been reported that synthetic peptide vaccines associated with catalytic or glucan-binding domains of GTF could protect rats from experimental **dental caries** (Taubman et al., Infect. Immun. 63:3088-3093 (1995)). One of the peptides that was successfully used as a vaccine (Smith et al., Infect. Immun. 62:5470-5476 (1994)) demonstrated a sequence containing an aspartic acid (aspartate 451 in S. mutans GTF-B) to which the glucosyl moiety of sucrose was covalently bound (Mooser et al., J. Biol. Chem. 266:8916-8922 (1991)).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **System for the controlled delivery of an active material to a dental site**

  Inventor(s): Jodaikin, Ahron; (Kiryat Telstone, IL), Jodaikin, Hilary; (Kiryat Telstone, IL)

  Correspondence: Lerner, David, Littenberg,; Krumholz & Mentlik; 600 South Avenue West; Westfield; NJ; 07090; US

  Patent Application Number: 20030165792

  Date filed: January 6, 2003

  Abstract: A system for the strategic controlled delivery of materials to the dental surfaces of the intraoral cavity, in particular materials having a desired or predetermined activity with respect to such dental surfaces. In particular, the system enables delivery of fluoridising and other agents to interproximal sites among others, specially to contact points/areas (aproximal sites), to enable inter alia the prevention, treatment, diagnosis, elimination or retardation of **dental caries.**

  Excerpt(s): The present invention relates generally to the strategic delivery of materials to the dental surfaces of the intraoral cavity, in particular materials having a desired or predetermined activity with respect to such dental surfaces. More particularly, the present invention is directed at the delivery of fluoridising and other agents to interproximal sites among others, specially to contact points/areas (aproximal sites), to enable inter alia the prevention, treatment, diagnosis, elimination or retardation of **dental caries.** Dental caries (demineralisation,decay) ranks among the most significant of human diseases simply because of its frequency of occurrence in the modem world where over 90% of the population is affected, ranking **dental caries** first amongst the chronic diseases affecting humans in terms of the numbers of people involved.(see Poole, D. F. G. and Silverstone,L. M. in Hard Tissue Growth,Repair and Remineralisation pp 35-52 Ciba Foundation Symposium No. 11, Elsevier Scientific Publishing Company, 1973; Legler D. W. and Menaker, L. in The Biological Basis of **Dental Caries;** Menaker,L. pp 211-225, Harper & Row, 1980; Winston, A. E. and Bhaskar S. N. JADA 129:1579-1587, 1998, Achievements in (US) Public Health, 48(41):933, 1999). Although the seventy of this disease in terms of its life threatening potential is limited to rare instances, certain important consequences exist. **Dental caries** treatment is costly (requiring highly skilled and exacting manpower as well as complex biomaterials), it is time consuming, it often involves pain and discomfort (both because of sequellae and treatment); it affects aesthetics and furthermore there is a need to avoid or limit

restorative dentistry because of the potential hazards of radiation, treatment and dental materials slowly degrading in the oral cavity over many years (see Nathanson, D. et al. JADA 128:1517-1523, 1997; Berry, T. C. et al. JADA 129:1547-1556,1998; Saxe, S. R. et al. JADA 130:191-199, 1999; Soderholm, K. J. and Marlott, A. JADA 130:201-209, 1999).

Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

- **Use of bacterial phage associated lysing proteins for treating bacterial dental caries**

  Inventor(s): Fischetti, Vincent; (West Hempstead, NY), Loomis, Lawrence; (Columbia, MD)

  Correspondence: Jonathan E. Grant; 2120 L Street, N.W.; Suite 210; Washington; DC; 20037; US

  Patent Application Number: 20030082110

  Date filed: June 21, 2002

  Abstract: A composition and method for treating bacterial **dental caries** by the use of an effective amount of at least one lytic specific for the bacteria causing **dental caries.** The lytic enzyme is genetically coded for by a bacteriophage which may be specific for said bacteria. The enzyme may be at least one lytic protein or peptides in a natural or modified form

  Excerpt(s): This is a continuation-in-part of U.S. patent application Ser. No. 09/671,881, filed Sep. 28, 2000, which is a continuation in part of application Ser. No. 09/497,495, filed Apr. 14, 2000, which is a continuation of U.S. patent application Ser. No. 09/395,636, filed Sep. 14, 1999, now U.S. Pat. No. 6,056,954 which is a continuation of U.S. patent application Ser. No. 08/962,523, filed Oct. 3, 1997, now U.S. Pat. No. 5,997,862. The present invention relates to methods and compositions for the treatment of bacterial infections by the use of bacteria-associated phage proteins, or peptides and peptide fragments thereof. More specifically, the invention pertains to phage lytic and/or holin proteins, or peptides and peptide fragments thereof, blended with a carrier for the treatment and prophylaxis of bacterial infection. In the past, antibiotics have been used to treat various infections. The work of Selman Waksman in the introduction and production of Streptomycetes, and Dr. Fleming's discovery of penicillin, as well as the work of numerous others in the field of antibiotics, are well known. Over the years, there have been additions and chemical modifications to the "basic" antibiotics in attempts to make them more powerful, or to treat people allergic to these antibiotics.

  Web site: http://appft1.uspto.gov/netahtml/PTO/search-bool.html

Keeping Current

In order to stay informed about patents and patent applications dealing with dental caries, you can access the U.S. Patent Office archive via the Internet at the following Web address: **http://www.uspto.gov/patft/index.html**. You will see two broad options: (1) Issued Patent, and (2) Published Applications. To see a list of issued patents, perform the following steps: Under “Issued Patents,” click “Quick Search.” Then, type “dental caries” (or synonyms) into the “Term 1” box. After clicking on the search button, scroll down to see the various patents which have been granted to date on dental caries.

You can also use this procedure to view pending patent applications concerning dental caries. Simply go back to **http://www.uspto.gov/patft/index.html**. Select "Quick Search" under "Published Applications." Then proceed with the steps listed above.

CHAPTER 6. BOOKS ON DENTAL CARIES

Overview

This chapter provides bibliographic book references relating to dental caries. In addition to online booksellers such as **www.amazon.com** and **www.bn.com**, excellent sources for book titles on dental caries include the Combined Health Information Database and the National Library of Medicine. Your local medical library also may have these titles available for loan.

Book Summaries: Federal Agencies

The Combined Health Information Database collects various book abstracts from a variety of healthcare institutions and federal agencies. To access these summaries, go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. You will need to use the "Detailed Search" option. To find book summaries, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer. For the format option, select "Monograph/Book." Now type "dental caries" (or synonyms) into the "For these words:" box. You should check back periodically with this database which is updated every three months. The following is a typical result when searching for books on dental caries:

- **Diagnosis and Risk Prediction of Dental Caries, Volume 2**

  Source: Chicago, IL: Quintessence Publishing Co, Inc. 2000. 315 p.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $118.00 plus shipping and handling. ISBN: 0867153628.

  Summary: This lengthy textbook, the second in a series of five, provides up to date information about the etiology (cause), modifying factors, risk evaluation, development, diagnosis, and epidemiology of **dental caries** (cavities). Specific topics covered in the six chapters include the role of dental plaque, the role of the oral environment, specific cariogenic microflora (such as bacteria), prediction of caries risk (how to know who will get dental cavities), the role of dietary factors, socioeconomic and behavioral factors, the role of saliva, chronic systemic diseases as risk factors, the role of tooth size,

morphology, and composition, the development of carious lesions, the diagnosis and registration of carious lesions, limitations of epidemiologic surveys, the prevalence and incidence of caries, caries treatment needs, and reasons for changes in caries prevalence. The text is illustrated with full color graphics and photographs. The text concludes with a list of references, a list of abbreviations, and a subject index. 362 references.

- **NIH Consensus Development Conference on Diagnosis and Management of Dental Caries Throughout Life: Program and abstracts**

  Source: Bethesda, MD: National Institute of Dental and Craniofacial Research. 2001. 190 pp.

  Contact: Available from National Institute of Dental and Craniofacial Research, Building 45, Room 4AS19, Bethesda, MD 20892-2290 / e-mail: nidcrinfo@mail.nih.gov / Web site: http://www.nidcr.nih.gov. Available at no charge.

  Summary: This publication provides the program and abstracts from the Consensus Development Conference on Diagnosis and Management of **Dental Caries** Throughout Life, which was sponsored by the National Institute of Dental and Craniofacial Research and the National Institutes of Health Office of Medical Applications of Research. The program provides abstracts for the following key issues: (1) methods for reviewing diagnosis and management methods for caries, (2) detecting early and advanced **dental caries,** (3) indicators for risk of **dental caries,** (4) the primary prevention of **dental caries,** (5) methods of stopping or reversing early carious lesions, and (6) clinical decisions in caries management. The program also identifies panel participants, speakers, planning committee members, and sponsoring agencies are provided. Most abstracts contain tables, figures, charts, and/or references.

Book Summaries: Online Booksellers

Commercial Internet-based booksellers, such as Amazon.com and Barnes&Noble.com, offer summaries which have been supplied by each title's publisher. Some summaries also include customer reviews. Your local bookseller may have access to in-house and commercial databases that index all published books (e.g. Books in Print®). **IMPORTANT NOTE:** Online booksellers typically produce search results for medical and non-medical books. When searching for "dental caries" at online booksellers' Web sites, you may discover non-medical books that use the generic term "dental caries" (or a synonym) in their titles. The following is indicative of the results you might find when searching for "dental caries" (sorted alphabetically by title; follow the hyperlink to view more details at Amazon.com):

- **Cost and Benefit of Fluoride in the Prevention of Dental Caries (WHO offset publication; no. 9)** by G.N. Davies; ISBN: 9241700092; http://www.amazon.com/exec/obidos/ASIN/9241700092/icongroupinterna
- **Diet, Nutrition and Dental Caries (Journal : Caries Research, Supplement 1, 1990 : Vol 1)** by M.E.; Ten Cate, J.M., Editors Curzon; ISBN: 3805553056; http://www.amazon.com/exec/obidos/ASIN/3805553056/icongroupinterna
- **Early detection of dental caries II: Proceedings of the 4th Annual Indiana Conference, Indianapolis, Indiana**; ISBN: 0965514927; http://www.amazon.com/exec/obidos/ASIN/0965514927/icongroupinterna

- **Nutrition Counseling for Dental Caries Prevention** by Ae Nizel; ISBN: 0721698417; http://www.amazon.com/exec/obidos/ASIN/0721698417/icongroupinterna
- **Phosphates and dental caries (Monographs in oral science)** by Bernard Lilienthal; ISBN: 3805526776; http://www.amazon.com/exec/obidos/ASIN/3805526776/icongroupinterna
- **Risk Markers for Oral Diseases: Dental Caries : Markers of High and Low Risk Groups and Individuals** by N.W. Johnson; ISBN: 0521375630; http://www.amazon.com/exec/obidos/ASIN/0521375630/icongroupinterna
- **Strategy for Dental Caries Prevention in European Countries According to Their Laws and Regulations: Proceedings** by R.M. Frank, S. O'Hickey; ISBN: 1852210087; http://www.amazon.com/exec/obidos/ASIN/1852210087/icongroupinterna
- **WHO Study of Dental Caries Etiology in Papua New Guinea (WHO Offset Publications)** by R.G. Schamschula; ISBN: 9241700408; http://www.amazon.com/exec/obidos/ASIN/9241700408/icongroupinterna

Chapters on Dental Caries

In order to find chapters that specifically relate to dental caries, an excellent source of abstracts is the Combined Health Information Database. You will need to limit your search to book chapters and dental caries using the "Detailed Search" option. Go to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find book chapters, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Book Chapter." Type "dental caries" (or synonyms) into the "For these words:" box. The following is a typical result when searching for book chapters on dental caries:

- **Tooth Loss, Dental Caries, and Quality of Life: A Public Health Perspective**

  Source: in Inglehart, M.R.; Bagramian, R.A., eds. Oral Health-Related Quality of Life. Chicago, IL: Quintessence Publishing Co, Inc. 2002. p.65-78.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $42.00 plus shipping and handling. ISBN: 0867154217.

  Summary: Oral conditions can have a significant impact, whether positive or negative, both on an individual's sense of personal well-being and on the function of a society as a whole. This chapter on tooth loss, dental cares, and quality of life is from a book on oral health-related quality of life. The authors offer a public health perspective on this topic. They first define quality of life (QOL) and public health and the interplay between these two concepts. Next, they discuss improved oral health in adults, changes in oral health among children, traditional measures of oral health (e.g., volume of dental visits, third molar extractions, professional applied topical fluoride), quantifiable comparison of QOL among individuals, and determining what should be covered by dental insurance. The authors conclude that better oral health does lead to better QOL; when oral health is evaluated using basic measures such as tooth retention or the severity of caries (cavities), the connection seems obvious. However, the issue becomes complicated when making decisions on how to best direct resources toward improving the oral health, and therefore the QOL, of the population. 13 figures. 16 references.

- **External Modifying Factors Involved in Dental Caries**

  Source: in Axelsson, P. Diagnosis and Risk Prediction of Dental Caries, Volume 2. Chicago, IL: Quintessence Publishing Co, Inc. 2000. p. 43-90.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $118.00 plus shipping and handling. ISBN: 0867153628.

  Summary: This chapter is from a lengthy textbook, the second in a series of five, that provides up to date information about the etiology (cause), modifying factors, risk evaluation, development, diagnosis, and epidemiology of **dental caries** (cavities). This chapter focuses on external modifying factors involved in **dental caries.** Specific topics include the role of dietary, socioeconomic and behavioral factors in **dental caries.** The author focuses on external modifying risk factors including fermentable carbohydrates (sugars), poor socioeconomic status, systemic disease, the use of medication that impairs salivary function, and irregular dental care attendance habits. For each topic, the author reviews research studies that offer data on the risk factors and how to modify its impact on dental health. The text is illustrated with full color graphics and photographs. References are provided at the end of the textbook. 79 figures. 11 tables.

- **Dental Caries: Characteristics of Lesions And Pulpal Reactions**

  Source: in Mjor, I.A. Pulp-Dentin Biology in Restorative Dentistry. Chicago, IL: Quintessence Publishing Co, Inc. 2002. p. 55-75.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail: quintpub@aol.com. Website: www.quintpub.com. PRICE: $59.00 plus shipping and handling. ISBN: 0867154128.

  Summary: This chapter on **dental caries** (cavities) is from a textbook that reviews pulp-dentin biology as it applies to restorative dentistry. The textbook focuses on applying the knowledge gained from the basic science component of the dental curriculum to the clinical practice of restorative dentistry. The dental pulp is the central, living core of the tooth, composed of blood vessels and nerves. Dentin is the mineralized substance that forms the bulk of the tooth underneath the harder enamel outer coat. The infectious disease **dental caries** results in lesions that affect enamel, dentin, and pulp, and cementum if the root portion of the tooth is involved. This chapter focuses on primary lesions. Topics include primary enamel lesions, enamel-dentin lesions, pulpal reactions, clinical diagnostic strategies, and removal of carious tissue. The assessment of lesion progression is an essential part of caries diagnosis and management. If caries lesions progress to the stage at which they require restorative intervention, it is important to understand the tissue changes in the dentin that are likely to have taken place during lesion development. Evaluation of such tissue responses should enter into the treatment planning. 42 figures. 108 references.

- **Prevention of Dental Caries**

  Source: in Wilson, N.H.F.; Roulet, J.; Fuzzi, M., eds. Advances in Operative Dentistry: Challenges of the Future. Volume 2. Chicago, IL: Quintessence Publishing Co, Inc. 2001. p. 19-28.

  Contact: Available from Quintessence Publishing Co, Inc. 551 Kimberly Drive, Carol Stream, IL 60188-9981. (800) 621-0387 or (630) 682-3223. Fax (630) 682-3288. E-mail:

quintpub@aol.com. Website: www.quintpub.com. PRICE: $98.00 plus shipping and handling. ISBN: 0867154039.

Summary: This chapter on the prevention of **dental caries** (cavities) is from a book that captures the state of the art views and approaches of European opinion leaders in the field of operative dentistry. The authors note that since **dental caries** is an avoidable disease, all dentists are called upon to show their patients how to achieve good oral health and to accompany them on the road to this goal. The chapter covers three aspects of prevention: preventive programs for the community, preventive programs for the dental office, and preventive programs for home care. Specific topics include fluoridation of the water supply, dental prophylaxis, patient education, home oral hygiene, chemical plaque control, the relationship between diet and dental health, fluoride prophylaxis, sealing of fissures (in children and adolescents), and quality management in the areas of diagnosis, documentation, individual prophylaxis, and cooperation of the patient. The authors conclude that prevention is an integral and indispensable part of the dental care of every individual. However, patients are ultimately responsible for their dental health. 2 figures. 22 references.

- **Dental Caries, Pulpitis, and Apical Inflammation**

  Source: in Miller, R.L., et al. General and Oral Pathology for the Dental Hygienist. St. Louis, MO: Mosby-Year Book, Inc. 1995. p. 198-214.

  Contact: Available from Mosby-Year Book, Inc. 11830 Westline Industrial Drive, St. Louis, MO 63146-9934. (800) 426-4545 or (314) 872-8370; Fax (800) 535-9935 or (314) 432-1380; E-mail: customer.support@mosby.com; http://www.mosby.com. PRICE: $43.00 plus shipping and handling. ISBN: 0801670241. Stock Number 07024.

  Summary: This chapter, from a textbook on pathology for dental hygiene students, presents a discussion of **dental caries,** pulpitis, and apical inflammation. Topics covered include the epidemiology of the U.S. **dental caries** rate; common etiologic factors that contribute to **dental caries;** the relationship of the quality and quantity of dental plaque to the caries process; preventive procedures and practices that can reduce the caries rate; the pathogenesis of enamel, dentin, and cemental caries; the role of saliva in caries control; the clinical signs and symptoms of reversible and irreversible pulpitis; the pathogenesis of periapical abscesses, cysts, and granulomas; and tissue infections subsequent to periapical infection, including parulis, acute osteomyelitis, cellulitis (Ludwig's angina), and cavernous sinus thrombosis. The chapter includes a list of learning objectives; illustrative case studies; and recommended readings. 8 figures.

Directories

In addition to the references and resources discussed earlier in this chapter, a number of directories relating to dental caries have been published that consolidate information across various sources. The Combined Health Information Database lists the following, which you may wish to consult in your local medical library:[10]

[10] You will need to limit your search to "Directory" and "dental caries" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find directories, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Select your preferred language and the format option "Directory." Type "dental caries" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months.

- **S.T.O.P. Guide: The Smokeless Tobacco Outreach and Prevention Guide. A Comprehensive Directory of Smokeless Tobacco Prevention and Cessation Resources**

  Source: Point Richmond, CA: Applied Behavior Science Press. 1997. 252 p.

  Contact: Available from Applied Behavior Science Press. 114 Washington Avenue, Point Richmond, CA 94801. (888) 222-7347 or (510) 236-9400. Fax (510) 236-1979. E-mail: khnow@aol.com. PRICE: $89.00 plus $10.00 for shipping and handling. ISBN: 0963955780.

  Summary: This directory provides a broad array of information regarding smokeless or spit tobacco use, focusing on cessation and prevention programs. Although titled a directory, the looseleaf notebook contains a variety of information materials, including published articles, essays, and statistics. Topics include the prevalence of snuff and chewing tobacco use in the U.S.; legislation and litigation issues; tobacco industry marketing, sales and promotion; ingredients in smokeless tobacco products; health problems associated with spit tobacco use, including **dental caries,** periodontal effects, soft tissue alterations, leukoplakia, cancer of the oral cavity and pharynx, and cardiovascular effects; school-based prevention of spit tobacco use; spit tobacco cessation; and resources, including Internet resources and resource organizations. The directory concludes with an extensive bibliography of materials on prevalence, health effects and physiology, use patterns, attitudes and perceptions, prevention, assessment, addiction and withdrawal, cessation, marketing, production and content, and public policy. The directory also includes a glossary of terms, a list of recommended alternatives to spit tobacco, and a series of article reprints.

CHAPTER 7. MULTIMEDIA ON DENTAL CARIES

Overview

In this chapter, we show you how to keep current on multimedia sources of information on dental caries. We start with sources that have been summarized by federal agencies, and then show you how to find bibliographic information catalogued by the National Library of Medicine.

Video Recordings

An excellent source of multimedia information on dental caries is the Combined Health Information Database. You will need to limit your search to "Videorecording" and "dental caries" using the "Detailed Search" option. Go directly to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. To find video productions, use the drop boxes at the bottom of the search page where "You may refine your search by." Select the dates and language you prefer, and the format option "Videorecording (videotape, videocassette, etc.)." Type "dental caries" (or synonyms) into the "For these words:" box. The following is a typical result when searching for video recordings on dental caries:

- **What You Should Know About Xerostomia (Dry Mouth)**

  Source: Fairburn, GA: National Oral Cancer Awareness (NOCAP). 199x. (videocassette).

  Contact: Available from American Dental Hygienists' Association (ADHA). 444 North Michigan Avenue, Suite 3400, Chicago, IL 60611. (800) 243-2342 (press 2) or (312) 440-8900. Fax (312) 467-1806. Website: www.adha.org. PRICE: $18.00. Item Number 3917 COM.

  Summary: This videocassette program describes the problem of xerostomia (dry mouth). The introduction stresses that the health impact of saliva goes far beyond the mouth and includes eating, talking, tooth maintenance, and tasting. The program then features a person with xerostomia describing how it feels to have problems with dry mouth. A brief description of the chemical makeup of salivary and the anatomy of the salivary glands follow. The next section discusses the potential causes of xerostomia, including radiation therapy, especially for cancer of the head and neck; drug effects, particularly from antihistamines, tranquilizers, and some blood pressure medications;

anxiety or depression, even without drug therapy; dehydration; and systemic diseases, including Sjogren's syndrome, lupus, cystic fibrosis, rheumatoid arthritis, and scleroderma. The narrator stresses that aging itself is not necessarily the cause of xerostomia. Complications of xerostomia include dry lips, burning mouth or tongue, constant thirst, difficulty talking or swallowing, impaired taste, **dental caries** (cavities), candidiasis (a fungal infection), and problems related to dehydration. Viewers are encouraged to work closely with health care providers to obtain an accurate diagnosis and employ strategies to cope with xerostomia. Treatment encompasses three options: eliminating the cause of the xerostomia, if possible; stimulating the salivary glands with sugar-free chewing gum, oral moisturizers, or the prescription drug pilocarpine; and using other measures to get relief, including saliva substitutes, frequent sips of water, room humidifiers (especially during winter), and lip balm. The program concludes with a reminder that xerostomia results in the need for increased attention to dental hygiene, including increased dental visits, limiting sugar intake, the use of fluoride, and the prevention of candidiasis. The program encourages viewers to learn about xerostomia, seek help, and improve the quality of their lives.

- **Dental Care in the 20th Century: How Your Teeth Affect Your Health**

  Source: Calhoun, KY: NIMCO. 1994. (videocassette).

  Contact: Available from National Center for Health Care Advances. NIMCO, Inc., P.O. Box 9, 117 Highway 815, Calhoun, KY 42327-0009. (800) 962-6662 or (502) 273-5050; Fax (502) 273-5844; http://nimcoinc.com. PRICE: $89.95 plus shipping and handling. Number NIM-SM-DC20-V52.

  Summary: This videotape program presents an overview of dental health concerns and how the teeth and their problems affect general health. Topics include taking better care of one's teeth, recognizing gum disease, different types of dentistry and dental specialties (including orthodontics, restorative dentistry, pediatrics, and oral surgery), anatomy and physiology of the teeth, role of nutrition, recommended dental care for infants and children, dietary concerns for children, preventing baby bottle tooth decay, toothbrushing and flossing, fluoride, **dental caries** (four types of cavities: pit and fissure, smooth surface, gum line, and root), problems of the temporomandibular joint (TMJ), problems and sequelae of tooth loss, and types of periodontal disease. The program features interviews with a variety of dentists and patients who have undergone different types of dental procedures. The program also includes some graphics, including diagrams of the dentition and anatomy of a tooth.

- **Smile on All Faces**

  Source: Geneva, Switzerland: World Health Organization (WHO). 1993. (videocassette).

  Contact: Available from World Health Organization (WHO). WHO Publications Center USA, 49 Sheridan Avenue, Albany, NY 12210. (518) 436-9686; Fax (518) 436-7433. PRICE: $36.00 plus shipping and handling. Order Number 1650077.

  Summary: Using scenes from different countries, this videotape program shows the World Health Organization's (WHO) three-pronged approach to oral health. The three facets involve improved oral hygiene, the use of fluorides, and nutritious diets. Implementation of these three aspects could lead to the elimination of today's most common oral health problems, **dental caries** and periodontal disease. The video also shows what can be done to combat the more severe problems of oral cancer, noma, and the oral symptoms of HIV infection. Since oral health problems affect rich and poor

countries alike, other scenes show how WHO is using simple but effective technologies to extend oral care to poor populations and remote rural areas. (AA-M).

CHAPTER 8. PERIODICALS AND NEWS ON DENTAL CARIES

Overview

In this chapter, we suggest a number of news sources and present various periodicals that cover dental caries.

News Services and Press Releases

One of the simplest ways of tracking press releases on dental caries is to search the news wires. In the following sample of sources, we will briefly describe how to access each service. These services only post recent news intended for public viewing.

PR Newswire

To access the PR Newswire archive, simply go to **http://www.prnewswire.com/**. Select your country. Type "dental caries" (or synonyms) into the search box. You will automatically receive information on relevant news releases posted within the last 30 days. The search results are shown by order of relevance.

Reuters Health

The Reuters' Medical News and Health eLine databases can be very useful in exploring news archives relating to dental caries. While some of the listed articles are free to view, others are available for purchase for a nominal fee. To access this archive, go to **http://www.reutershealth.com/en/index.html** and search by "dental caries" (or synonyms). The following was recently listed in this archive for dental caries:

- **Consensus panel calls for innovative research into dental caries management**
  Source: Reuters Medical News
  Date: March 28, 2001
- **Vaccine protects against dental caries in mice**
  Source: Reuters Medical News
  Date: December 28, 1999

The NIH

Within MEDLINEplus, the NIH has made an agreement with the New York Times Syndicate, the AP News Service, and Reuters to deliver news that can be browsed by the public. Search news releases at **http://www.nlm.nih.gov/medlineplus/alphanews_a.html**. MEDLINEplus allows you to browse across an alphabetical index. Or you can search by date at the following Web page: **http://www.nlm.nih.gov/medlineplus/newsbydate.html**. Often, news items are indexed by MEDLINEplus within its search engine.

Business Wire

Business Wire is similar to PR Newswire. To access this archive, simply go to **http://www.businesswire.com/**. You can scan the news by industry category or company name.

Market Wire

Market Wire is more focused on technology than the other wires. To browse the latest press releases by topic, such as alternative medicine, biotechnology, fitness, healthcare, legal, nutrition, and pharmaceuticals, access Market Wire's Medical/Health channel at **http://www.marketwire.com/mw/release_index?channel=MedicalHealth**. Or simply go to Market Wire's home page at **http://www.marketwire.com/mw/home**, type "dental caries" (or synonyms) into the search box, and click on "Search News." As this service is technology oriented, you may wish to use it when searching for press releases covering diagnostic procedures or tests.

Search Engines

Medical news is also available in the news sections of commercial Internet search engines. See the health news page at Yahoo (**http://dir.yahoo.com/Health/News_and_Media/**), or you can use this Web site's general news search page at **http://news.yahoo.com/**. Type in "dental caries" (or synonyms). If you know the name of a company that is relevant to dental caries, you can go to any stock trading Web site (such as **http://www.etrade.com/**) and search for the company name there. News items across various news sources are reported on indicated hyperlinks. Google offers a similar service at **http://news.google.com/**.

BBC

Covering news from a more European perspective, the British Broadcasting Corporation (BBC) allows the public free access to their news archive located at **http://www.bbc.co.uk/**. Search by "dental caries" (or synonyms).

Newsletter Articles

Use the Combined Health Information Database, and limit your search criteria to "newsletter articles." Again, you will need to use the "Detailed Search" option. Go directly

to the following hyperlink: **http://chid.nih.gov/detail/detail.html**. Go to the bottom of the search page where "You may refine your search by." Select the dates and language that you prefer. For the format option, select "Newsletter Article." Type "dental caries" (or synonyms) into the "For these words:" box. You should check back periodically with this database as it is updated every three months. The following is a typical result when searching for newsletter articles on dental caries:

- **Smoking and Periodontal Disease, Tooth Loss, and Dental Caries**

  Source: Oral Care Report. 13(1): 4,8. 2003.

  Contact: Available from Oral Care Report. c/o Dr. Chester W. Douglass, Department of Oral Health Policy, Harvard School of Dental Medicine, 188 Longwood Avenue, Boston, MA 02115. Fax (617) 432-0047. E-mail: colgateoralcarereport@hms.harvard.edu. Website: www.colgateprofessional.com (full-text available online).

  Summary: Apart from the established associations between smoking and serious illnesses such as cancer, heart disease and lung disease, oral health problems are also linked to smoking. Numerous studies report an increased risk for periodontal disease, tooth loss, and **dental caries** in smokers as compared to nonsmokers. This brief article explores this association, focusing on tooth loss, probing attachment loss, and **dental caries** in smokers. The authors consider the potential mechanisms by which smoking affects dental status, noting that said mechanisms are not well understood. 1 table. 3 references.

- **Tooth Decay and Sjogren's Syndrome: Recognizing the Risk, Preventing and Managing Dental Caries**

  Source: Moisture Seekers Newsletter. 13(2): 1, 3-4. February 1995.

  Contact: Available from Sjogren's Syndrome Foundation, Inc. 8120 Woodmont Avenue, Suite 530, Bethesda MD 20814-1437. (301) 718-0300 or (800) 475-6473. Fax (301) 718-0322. Website: www.sjogrens.org.

  Summary: This newsletter article presents information about tooth decay and Sjogren's syndrome (SS). The author emphasizes the need for readers to understand the nature of tooth decay and its relation to the flow of saliva, to the diet, and to the bacteria that live on the surfaces of the teeth. Specific topics covered include why SS patients are at particular risk for **dental caries** (cavities); tooth decay as an infectious disease; the role of mutans streptococci (MS) and how MS is transmitted by mothers to their children; the life cycle of the bacteria in the mouth; and the role of saliva in protecting the mucous membranes and the teeth. The article is part of a series of articles on this topic.

Academic Periodicals covering Dental Caries

Numerous periodicals are currently indexed within the National Library of Medicine's PubMed database that are known to publish articles relating to dental caries. In addition to these sources, you can search for articles covering dental caries that have been published by any of the periodicals listed in previous chapters. To find the latest studies published, go to **http://www.ncbi.nlm.nih.gov/pubmed**, type the name of the periodical into the search box, and click "Go."

If you want complete details about the historical contents of a journal, you can also visit the following Web site: **http://www.ncbi.nlm.nih.gov/entrez/jrbrowser.cgi**. Here, type in the name of the journal or its abbreviation, and you will receive an index of published articles. At **http://locatorplus.gov/**, you can retrieve more indexing information on medical periodicals (e.g. the name of the publisher). Select the button "Search LOCATORplus." Then type in the name of the journal and select the advanced search option "Journal Title Search."

CHAPTER 9. RESEARCHING MEDICATIONS

Overview

While a number of hard copy or CD-ROM resources are available for researching medications, a more flexible method is to use Internet-based databases. Broadly speaking, there are two sources of information on approved medications: public sources and private sources. We will emphasize free-to-use public sources.

U.S. Pharmacopeia

Because of historical investments by various organizations and the emergence of the Internet, it has become rather simple to learn about the medications recommended for dental caries. One such source is the United States Pharmacopeia. In 1820, eleven physicians met in Washington, D.C. to establish the first compendium of standard drugs for the United States. They called this compendium the U.S. Pharmacopeia (USP). Today, the USP is a non-profit organization consisting of 800 volunteer scientists, eleven elected officials, and 400 representatives of state associations and colleges of medicine and pharmacy. The USP is located in Rockville, Maryland, and its home page is located at **http://www.usp.org/**. The USP currently provides standards for over 3,700 medications. The resulting USP DI® Advice for the Patient® can be accessed through the National Library of Medicine of the National Institutes of Health. The database is partially derived from lists of federally approved medications in the Food and Drug Administration's (FDA) Drug Approvals database, located at **http://www.fda.gov/cder/da/da.htm**.

While the FDA database is rather large and difficult to navigate, the Phamacopeia is both user-friendly and free to use. It covers more than 9,000 prescription and over-the-counter medications. To access this database, simply type the following hyperlink into your Web browser: **http://www.nlm.nih.gov/medlineplus/druginformation.html**. To view examples of a given medication (brand names, category, description, preparation, proper use, precautions, side effects, etc.), simply follow the hyperlinks indicated within the United States Pharmacopeia (USP).

Below, we have compiled a list of medications associated with dental caries. If you would like more information on a particular medication, the provided hyperlinks will direct you to ample documentation (e.g. typical dosage, side effects, drug-interaction risks, etc.). The

following drugs have been mentioned in the Pharmacopeia and other sources as being potentially applicable to dental caries:

Sodium Fluoride

- **Systemic - U.S. Brands:** Fluoritab; Fluorodex; Flura; Flura-Drops; Flura-Loz; Karidium; Luride; Luride Lozi-Tabs; Luride-SF Lozi-Tabs; Pediaflor; Pharmaflur; Pharmaflur 1.1; Pharmaflur df; Phos-Flur
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202527.html

Vitamins and Fluoride

- **Systemic - U.S. Brands:** Adeflor; Cari-Tab; Mulvidren-F; Poly-Vi-Flor; Tri-Vi-Flor; Vi-Daylin/F
  http://www.nlm.nih.gov/medlineplus/druginfo/uspdi/202600.html

Commercial Databases

In addition to the medications listed in the USP above, a number of commercial sites are available by subscription to physicians and their institutions. Or, you may be able to access these sources from your local medical library.

Mosby's Drug Consult™

Mosby's Drug Consult™ database (also available on CD-ROM and book format) covers 45,000 drug products including generics and international brands. It provides prescribing information, drug interactions, and patient information. Subscription information is available at the following hyperlink: **http://www.mosbysdrugconsult.com/**.

PDR*health*

The PDR*health* database is a free-to-use, drug information search engine that has been written for the public in layman's terms. It contains FDA-approved drug information adapted from the Physicians' Desk Reference (PDR) database. PDR*health* can be searched by brand name, generic name, or indication. It features multiple drug interactions reports. Search PDR*health* at **http://www.pdrhealth.com/drug_info/index.html**.

Other Web Sites

Drugs.com (**www.drugs.com**) reproduces the information in the Pharmacopeia as well as commercial information. You may also want to consider the Web site of the Medical Letter, Inc. (**http://www.medletter.com/**) which allows users to download articles on various drugs and therapeutics for a nominal fee.

Researching Orphan Drugs

Although the list of orphan drugs is revised on a daily basis, you can quickly research orphan drugs that might be applicable to dental caries by using the database managed by the National Organization for Rare Disorders, Inc. (NORD), at **http://www.rarediseases.org/**. Scroll down the page, and on the left toolbar, click on "Orphan Drug Designation Database." On this page (**http://www.rarediseases.org/search/noddsearch.html**), type "dental caries" (or synonyms) into the search box, and click "Submit Query." When you receive your results, note that not all of the drugs may be relevant, as some may have been withdrawn from orphan status. Write down or print out the name of each drug and the relevant contact information. From there, visit the Pharmacopeia Web site and type the name of each orphan drug into the search box at **http://www.nlm.nih.gov/medlineplus/druginformation.html**. You may need to contact the sponsor or NORD for further information.

NORD conducts "early access programs for investigational new drugs (IND) under the Food and Drug Administration's (FDA's) approval 'Treatment INDs' programs which allow for a limited number of individuals to receive investigational drugs before FDA marketing approval." If the orphan product about which you are seeking information is approved for marketing, information on side effects can be found on the product's label. If the product is not approved, you may need to contact the sponsor.

The following is a list of orphan drugs currently listed in the NORD Orphan Drug Designation Database for dental caries:

- **intraoral fluoride releasing system (trade name: IFRS)**
  http://www.rarediseases.org/nord/search/nodd_full?code=1175

If you have any questions about a medical treatment, the FDA may have an office near you. Look for their number in the blue pages of the phone book. You can also contact the FDA through its toll-free number, 1-888-INFO-FDA (1-888-463-6332), or on the World Wide Web at **www.fda.gov**.

APPENDICES

APPENDIX A. PHYSICIAN RESOURCES

Overview

In this chapter, we focus on databases and Internet-based guidelines and information resources created or written for a professional audience.

NIH Guidelines

Commonly referred to as "clinical" or "professional" guidelines, the National Institutes of Health publish physician guidelines for the most common diseases. Publications are available at the following by relevant Institute[11]:

- Office of the Director (OD); guidelines consolidated across agencies available at **http://www.nih.gov/health/consumer/conkey.htm**
- National Institute of General Medical Sciences (NIGMS); fact sheets available at **http://www.nigms.nih.gov/news/facts/**
- National Library of Medicine (NLM); extensive encyclopedia (A.D.A.M., Inc.) with guidelines: **http://www.nlm.nih.gov/medlineplus/healthtopics.html**
- National Cancer Institute (NCI); guidelines available at **http://www.cancer.gov/cancerinfo/list.aspx?viewid=5f35036e-5497-4d86-8c2c-714a9f7c8d25**
- National Eye Institute (NEI); guidelines available at **http://www.nei.nih.gov/order/index.htm**
- National Heart, Lung, and Blood Institute (NHLBI); guidelines available at **http://www.nhlbi.nih.gov/guidelines/index.htm**
- National Human Genome Research Institute (NHGRI); research available at **http://www.genome.gov/page.cfm?pageID=10000375**
- National Institute on Aging (NIA); guidelines available at **http://www.nia.nih.gov/health/**

[11] These publications are typically written by one or more of the various NIH Institutes.

- National Institute on Alcohol Abuse and Alcoholism (NIAAA); guidelines available at **http://www.niaaa.nih.gov/publications/publications.htm**
- National Institute of Allergy and Infectious Diseases (NIAID); guidelines available at **http://www.niaid.nih.gov/publications/**
- National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS); fact sheets and guidelines available at **http://www.niams.nih.gov/hi/index.htm**
- National Institute of Child Health and Human Development (NICHD); guidelines available at **http://www.nichd.nih.gov/publications/pubskey.cfm**
- National Institute on Deafness and Other Communication Disorders (NIDCD); fact sheets and guidelines at **http://www.nidcd.nih.gov/health/**
- National Institute of Dental and Craniofacial Research (NIDCR); guidelines available at **http://www.nidr.nih.gov/health/**
- National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK); guidelines available at **http://www.niddk.nih.gov/health/health.htm**
- National Institute on Drug Abuse (NIDA); guidelines available at **http://www.nida.nih.gov/DrugAbuse.html**
- National Institute of Environmental Health Sciences (NIEHS); environmental health information available at **http://www.niehs.nih.gov/external/facts.htm**
- National Institute of Mental Health (NIMH); guidelines available at **http://www.nimh.nih.gov/practitioners/index.cfm**
- National Institute of Neurological Disorders and Stroke (NINDS); neurological disorder information pages available at **http://www.ninds.nih.gov/health_and_medical/disorder_index.htm**
- National Institute of Nursing Research (NINR); publications on selected illnesses at **http://www.nih.gov/ninr/news-info/publications.html**
- National Institute of Biomedical Imaging and Bioengineering; general information at **http://grants.nih.gov/grants/becon/becon_info.htm**
- Center for Information Technology (CIT); referrals to other agencies based on keyword searches available at **http://kb.nih.gov/www_query_main.asp**
- National Center for Complementary and Alternative Medicine (NCCAM); health information available at **http://nccam.nih.gov/health/**
- National Center for Research Resources (NCRR); various information directories available at **http://www.ncrr.nih.gov/publications.asp**
- Office of Rare Diseases; various fact sheets available at **http://rarediseases.info.nih.gov/html/resources/rep_pubs.html**
- Centers for Disease Control and Prevention; various fact sheets on infectious diseases available at **http://www.cdc.gov/publications.htm**

NIH Databases

In addition to the various Institutes of Health that publish professional guidelines, the NIH has designed a number of databases for professionals.[12] Physician-oriented resources provide a wide variety of information related to the biomedical and health sciences, both past and present. The format of these resources varies. Searchable databases, bibliographic citations, full-text articles (when available), archival collections, and images are all available. The following are referenced by the National Library of Medicine:[13]

- **Bioethics:** Access to published literature on the ethical, legal, and public policy issues surrounding healthcare and biomedical research. This information is provided in conjunction with the Kennedy Institute of Ethics located at Georgetown University, Washington, D.C.: **http://www.nlm.nih.gov/databases/databases_bioethics.html**
- **HIV/AIDS Resources:** Describes various links and databases dedicated to HIV/AIDS research: **http://www.nlm.nih.gov/pubs/factsheets/aidsinfs.html**
- **NLM Online Exhibitions:** Describes "Exhibitions in the History of Medicine": **http://www.nlm.nih.gov/exhibition/exhibition.html**. Additional resources for historical scholarship in medicine: **http://www.nlm.nih.gov/hmd/hmd.html**
- **Biotechnology Information:** Access to public databases. The National Center for Biotechnology Information conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information for the better understanding of molecular processes affecting human health and disease: **http://www.ncbi.nlm.nih.gov/**
- **Population Information:** The National Library of Medicine provides access to worldwide coverage of population, family planning, and related health issues, including family planning technology and programs, fertility, and population law and policy: **http://www.nlm.nih.gov/databases/databases_population.html**
- **Cancer Information:** Access to cancer-oriented databases: **http://www.nlm.nih.gov/databases/databases_cancer.html**
- **Profiles in Science:** Offering the archival collections of prominent twentieth-century biomedical scientists to the public through modern digital technology: **http://www.profiles.nlm.nih.gov/**
- **Chemical Information:** Provides links to various chemical databases and references: **http://sis.nlm.nih.gov/Chem/ChemMain.html**
- **Clinical Alerts:** Reports the release of findings from the NIH-funded clinical trials where such release could significantly affect morbidity and mortality: **http://www.nlm.nih.gov/databases/alerts/clinical_alerts.html**
- **Space Life Sciences:** Provides links and information to space-based research (including NASA): **http://www.nlm.nih.gov/databases/databases_space.html**
- **MEDLINE:** Bibliographic database covering the fields of medicine, nursing, dentistry, veterinary medicine, the healthcare system, and the pre-clinical sciences: **http://www.nlm.nih.gov/databases/databases_medline.html**

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[12] Remember, for the general public, the National Library of Medicine recommends the databases referenced in MEDLINE*plus* (**http://medlineplus.gov/** or **http://www.nlm.nih.gov/medlineplus/databases.html**).

[13] See **http://www.nlm.nih.gov/databases/databases.html**.

- **Toxicology and Environmental Health Information (TOXNET):** Databases covering toxicology and environmental health: **http://sis.nlm.nih.gov/Tox/ToxMain.html**
- **Visible Human Interface:** Anatomically detailed, three-dimensional representations of normal male and female human bodies: **http://www.nlm.nih.gov/research/visible/visible_human.html**

The NLM Gateway[14]

The NLM (National Library of Medicine) Gateway is a Web-based system that lets users search simultaneously in multiple retrieval systems at the U.S. National Library of Medicine (NLM). It allows users of NLM services to initiate searches from one Web interface, providing one-stop searching for many of NLM's information resources or databases.[15] To use the NLM Gateway, simply go to the search site at **http://gateway.nlm.nih.gov/gw/Cmd**. Type "dental caries" (or synonyms) into the search box and click "Search." The results will be presented in a tabular form, indicating the number of references in each database category.

Results Summary

Category	Items Found
Journal Articles	29882
Books / Periodicals / Audio Visual	627
Consumer Health	400
Meeting Abstracts	21
Other Collections	83
Total	31013

HSTAT[16]

HSTAT is a free, Web-based resource that provides access to full-text documents used in healthcare decision-making.[17] These documents include clinical practice guidelines, quick-reference guides for clinicians, consumer health brochures, evidence reports and technology assessments from the Agency for Healthcare Research and Quality (AHRQ), as well as AHRQ's Put Prevention Into Practice.[18] Simply search by "dental caries" (or synonyms) at the following Web site: **http://text.nlm.nih.gov**.

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[14] Adapted from NLM: **http://gateway.nlm.nih.gov/gw/Cmd?Overview.x**.

[15] The NLM Gateway is currently being developed by the Lister Hill National Center for Biomedical Communications (LHNCBC) at the National Library of Medicine (NLM) of the National Institutes of Health (NIH).

[16] Adapted from HSTAT: **http://www.nlm.nih.gov/pubs/factsheets/hstat.html**.

[17] The HSTAT URL is **http://hstat.nlm.nih.gov/**.

[18] Other important documents in HSTAT include: the National Institutes of Health (NIH) Consensus Conference Reports and Technology Assessment Reports; the HIV/AIDS Treatment Information Service (ATIS) resource documents; the Substance Abuse and Mental Health Services Administration's Center for Substance Abuse Treatment (SAMHSA/CSAT) Treatment Improvement Protocols (TIP) and Center for Substance Abuse Prevention (SAMHSA/CSAP) Prevention Enhancement Protocols System (PEPS); the Public Health Service (PHS) Preventive Services Task Force's *Guide to Clinical Preventive Services*; the independent, nonfederal Task Force on Community Services' *Guide to Community Preventive Services*; and the Health Technology Advisory Committee (HTAC) of the Minnesota Health Care Commission (MHCC) health technology evaluations.

Coffee Break: Tutorials for Biologists[19]

Coffee Break is a general healthcare site that takes a scientific view of the news and covers recent breakthroughs in biology that may one day assist physicians in developing treatments. Here you will find a collection of short reports on recent biological discoveries. Each report incorporates interactive tutorials that demonstrate how bioinformatics tools are used as a part of the research process. Currently, all Coffee Breaks are written by NCBI staff.[20] Each report is about 400 words and is usually based on a discovery reported in one or more articles from recently published, peer-reviewed literature.[21] This site has new articles every few weeks, so it can be considered an online magazine of sorts. It is intended for general background information. You can access the Coffee Break Web site at the following hyperlink: **http://www.ncbi.nlm.nih.gov/Coffeebreak/**.

Other Commercial Databases

In addition to resources maintained by official agencies, other databases exist that are commercial ventures addressing medical professionals. Here are some examples that may interest you:

- **CliniWeb International:** Index and table of contents to selected clinical information on the Internet; see **http://www.ohsu.edu/cliniweb/**.
- **Medical World Search:** Searches full text from thousands of selected medical sites on the Internet; see **http://www.mwsearch.com/**.

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[19] Adapted from **http://www.ncbi.nlm.nih.gov/Coffeebreak/Archive/FAQ.html**.

[20] The figure that accompanies each article is frequently supplied by an expert external to NCBI, in which case the source of the figure is cited. The result is an interactive tutorial that tells a biological story.

[21] After a brief introduction that sets the work described into a broader context, the report focuses on how a molecular understanding can provide explanations of observed biology and lead to therapies for diseases. Each vignette is accompanied by a figure and hypertext links that lead to a series of pages that interactively show how NCBI tools and resources are used in the research process.

APPENDIX B. PATIENT RESOURCES

Overview

Official agencies, as well as federally funded institutions supported by national grants, frequently publish a variety of guidelines written with the patient in mind. These are typically called "Fact Sheets" or "Guidelines." They can take the form of a brochure, information kit, pamphlet, or flyer. Often they are only a few pages in length. Since new guidelines on dental caries can appear at any moment and be published by a number of sources, the best approach to finding guidelines is to systematically scan the Internet-based services that post them.

Patient Guideline Sources

The remainder of this chapter directs you to sources which either publish or can help you find additional guidelines on topics related to dental caries. Due to space limitations, these sources are listed in a concise manner. Do not hesitate to consult the following sources by either using the Internet hyperlink provided, or, in cases where the contact information is provided, contacting the publisher or author directly.

The National Institutes of Health

The NIH gateway to patients is located at **http://health.nih.gov/**. From this site, you can search across various sources and institutes, a number of which are summarized below.

Topic Pages: MEDLINEplus

The National Library of Medicine has created a vast and patient-oriented healthcare information portal called MEDLINEplus. Within this Internet-based system are "health topic pages" which list links to available materials relevant to dental caries. To access this system, log on to **http://www.nlm.nih.gov/medlineplus/healthtopics.html**. From there you can either search using the alphabetical index or browse by broad topic areas. Recently, MEDLINEplus listed the following when searched for "dental caries":

Child Dental Health
http://www.nlm.nih.gov/medlineplus/childdentalhealth.html

Cosmetic Dentistry
http://www.nlm.nih.gov/medlineplus/cosmeticdentistry.html

Dental Health
http://www.nlm.nih.gov/medlineplus/dentalhealth.html

Gum Disease
http://www.nlm.nih.gov/medlineplus/gumdisease.html

Tooth Disorders
http://www.nlm.nih.gov/medlineplus/toothdisorders.html

You may also choose to use the search utility provided by MEDLINEplus at the following Web address: **http://www.nlm.nih.gov/medlineplus/**. Simply type a keyword into the search box and click "Search." This utility is similar to the NIH search utility, with the exception that it only includes materials that are linked within the MEDLINEplus system (mostly patient-oriented information). It also has the disadvantage of generating unstructured results. We recommend, therefore, that you use this method only if you have a very targeted search.

The Combined Health Information Database (CHID)

CHID Online is a reference tool that maintains a database directory of thousands of journal articles and patient education guidelines on dental caries. CHID offers summaries that describe the guidelines available, including contact information and pricing. CHID's general Web site is **http://chid.nih.gov/**. To search this database, go to **http://chid.nih.gov/detail/detail.html**. In particular, you can use the advanced search options to look up pamphlets, reports, brochures, and information kits. The following was recently posted in this archive:

- **Is your child at risk for dental caries (tooth decay)?**

  Source: Minneapolis, MN: Center for Health Promotion, HealthPartners. 2000. 2 pp.

  Contact: Available from Susan Hahn, susan.h.hahn@healthpartners.com, HealthPartners, Center for Health Promotion, 8100 34th Avenue South, P.O. Box 1309, Minneapolis, MN 55440-1309. Telephone: (952) 967-6795 / fax: (952) 883-6767 / Web site: http://www.healthpartners.com. Available at no charge.

  Summary: This fact sheet is a check-off form dental health professionals can use to provide information to parents and caregivers about a child's risk for **dental caries** and ways to reduce the risk of future tooth decay. It also gives anticipatory guidance on actions to take to ensure good oral health in children at ages 3, 4, 6, 8, 10, and adolescence.

- **Preventing dental caries**

  Source: Atlanta, GA: Centers for Disease Control and Prevention. [2002]. 2 pp.

  Contact: Available from Centers for Disease Control and Prevention, 1600 Clifton Road, N.E, Atlanta, GA 30333. Telephone: (404) 639-3311 or (404) 639-3312 TTY / Web site: http://www.cdc.gov. Available from the Web site at no charge.

Summary: This fact sheet presents a snapshot of efforts to reduce **dental caries** in children in the United States. A brief statistical overview of **dental caries** is provided along with an outline of community-based strategies to prevent tooth decay such as water fluoridation and school-based dental sealant programs. Additional information is provided on efforts in Ohio, how these strategies help save money, samples of other effective prevention strategies, and a review of oral health objectives in Healthy People 2010.

The National Guideline Clearinghouse™

The National Guideline Clearinghouse™ offers hundreds of evidence-based clinical practice guidelines published in the United States and other countries. You can search this site located at **http://www.guideline.gov/** by using the keyword "dental caries" (or synonyms). The following was recently posted:

- **Diagnosis and management of dental caries throughout life**

  Source: National Institute on Dental and Craniofacial Research - Federal Government Agency [U.S.]; 2001 March; 24 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2792&nbr=2018&string=dental+AND+caries

- **Preventing dental caries in children at high caries risk. Targeted prevention of dental caries in the permanent teeth of 6 to 16 year olds presenting for dental care. A national clinical guideline**

  Source: Scottish Intercollegiate Guidelines Network - National Government Agency [Non-U.S.]; 2000 December; 39 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2913&nbr=2139&string=dental+AND+caries

- **Prevention of dental caries in preschool children: recommendations and rationale**

  Source: United States Preventive Services Task Force - Independent Expert Panel; 1989 (revised 2004 April 8); 9 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=4156&nbr=3184&string=dental+AND+caries

- **Recommendations for using fluoride to prevent and control dental caries in the United States**

  Source: Centers for Disease Control and Prevention - Federal Government Agency [U.S.]; 2001 August; 59 pages

  http://www.guideline.gov/summary/summary.aspx?doc_id=2919&nbr=2145&string=dental+AND+caries

Healthfinder™

Healthfinder™ is sponsored by the U.S. Department of Health and Human Services and offers links to hundreds of other sites that contain healthcare information. This Web site is located at **http://www.healthfinder.gov**. Again, keyword searches can be used to find guidelines. The following was recently found in this database:

- **Diagnosis and Management of Dental Caries Throughout Life: NIH Consensus Statement**

  Summary: This consensus statement covers the methods for detecting dental caries, indications for the risk of cavities, and prevention, research, and treatment activities in relation to dental caries.

  Source: National Institutes of Health, U.S. Department of Health and Human Services

  http://www.healthfinder.gov/scripts/recordpass.asp?RecordType=0&RecordID=6379

The NIH Search Utility

The NIH search utility allows you to search for documents on over 100 selected Web sites that comprise the NIH-WEB-SPACE. Each of these servers is "crawled" and indexed on an ongoing basis. Your search will produce a list of various documents, all of which will relate in some way to dental caries. The drawbacks of this approach are that the information is not organized by theme and that the references are often a mix of information for professionals and patients. Nevertheless, a large number of the listed Web sites provide useful background information. We can only recommend this route, therefore, for relatively rare or specific disorders, or when using highly targeted searches. To use the NIH search utility, visit the following Web page: **http://search.nih.gov/index.html**.

Additional Web Sources

A number of Web sites are available to the public that often link to government sites. These can also point you in the direction of essential information. The following is a representative sample:

- AOL: **http://search.aol.com/cat.adp?id=168&layer=&from=subcats**
- Family Village: **http://www.familyvillage.wisc.edu/specific.htm**
- Google: **http://directory.google.com/Top/Health/Conditions_and_Diseases/**
- Med Help International: **http://www.medhelp.org/HealthTopics/A.html**
- Open Directory Project: **http://dmoz.org/Health/Conditions_and_Diseases/**
- Yahoo.com: **http://dir.yahoo.com/Health/Diseases_and_Conditions/**
- WebMD®Health: **http://my.webmd.com/health_topics**

Finding Associations

There are several Internet directories that provide lists of medical associations with information on or resources relating to dental caries. By consulting all of associations listed

in this chapter, you will have nearly exhausted all sources for patient associations concerned with dental caries.

The National Health Information Center (NHIC)

The National Health Information Center (NHIC) offers a free referral service to help people find organizations that provide information about dental caries. For more information, see the NHIC's Web site at **http://www.health.gov/NHIC/** or contact an information specialist by calling 1-800-336-4797.

Directory of Health Organizations

The Directory of Health Organizations, provided by the National Library of Medicine Specialized Information Services, is a comprehensive source of information on associations. The Directory of Health Organizations database can be accessed via the Internet at **http://www.sis.nlm.nih.gov/Dir/DirMain.html**. It is composed of two parts: DIRLINE and Health Hotlines.

The DIRLINE database comprises some 10,000 records of organizations, research centers, and government institutes and associations that primarily focus on health and biomedicine. To access DIRLINE directly, go to the following Web site: **http://dirline.nlm.nih.gov/**. Simply type in "dental caries" (or a synonym), and you will receive information on all relevant organizations listed in the database.

Health Hotlines directs you to toll-free numbers to over 300 organizations. You can access this database directly at **http://www.sis.nlm.nih.gov/hotlines/**. On this page, you are given the option to search by keyword or by browsing the subject list. When you have received your search results, click on the name of the organization for its description and contact information.

The Combined Health Information Database

Another comprehensive source of information on healthcare associations is the Combined Health Information Database. Using the "Detailed Search" option, you will need to limit your search to "Organizations" and "dental caries". Type the following hyperlink into your Web browser: **http://chid.nih.gov/detail/detail.html**. To find associations, use the drop boxes at the bottom of the search page where "You may refine your search by." For publication date, select "All Years." Then, select your preferred language and the format option "Organization Resource Sheet." Type "dental caries" (or synonyms) into the "For these words:" box. You should check back periodically with this database since it is updated every three months.

The National Organization for Rare Disorders, Inc.

The National Organization for Rare Disorders, Inc. has prepared a Web site that provides, at no charge, lists of associations organized by health topic. You can access this database at the following Web site: **http://www.rarediseases.org/search/orgsearch.html**. Type "dental caries" (or a synonym) into the search box, and click "Submit Query."

APPENDIX C. FINDING MEDICAL LIBRARIES

Overview

In this Appendix, we show you how to quickly find a medical library in your area.

Preparation

Your local public library and medical libraries have interlibrary loan programs with the National Library of Medicine (NLM), one of the largest medical collections in the world. According to the NLM, most of the literature in the general and historical collections of the National Library of Medicine is available on interlibrary loan to any library. If you would like to access NLM medical literature, then visit a library in your area that can request the publications for you.[22]

Finding a Local Medical Library

The quickest method to locate medical libraries is to use the Internet-based directory published by the National Network of Libraries of Medicine (NN/LM). This network includes 4626 members and affiliates that provide many services to librarians, health professionals, and the public. To find a library in your area, simply visit **http://nnlm.gov/members/adv.html** or call 1-800-338-7657.

Medical Libraries in the U.S. and Canada

In addition to the NN/LM, the National Library of Medicine (NLM) lists a number of libraries with reference facilities that are open to the public. The following is the NLM's list and includes hyperlinks to each library's Web site. These Web pages can provide information on hours of operation and other restrictions. The list below is a small sample of

[22] Adapted from the NLM: **http://www.nlm.nih.gov/psd/cas/interlibrary.html**.

libraries recommended by the National Library of Medicine (sorted alphabetically by name of the U.S. state or Canadian province where the library is located)[23]:

- **Alabama:** Health InfoNet of Jefferson County (Jefferson County Library Cooperative, Lister Hill Library of the Health Sciences), **http://www.uab.edu/infonet/**
- **Alabama:** Richard M. Scrushy Library (American Sports Medicine Institute)
- **Arizona:** Samaritan Regional Medical Center: The Learning Center (Samaritan Health System, Phoenix, Arizona), **http://www.samaritan.edu/library/bannerlibs.htm**
- **California:** Kris Kelly Health Information Center (St. Joseph Health System, Humboldt), **http://www.humboldt1.com/~kkhic/index.html**
- **California:** Community Health Library of Los Gatos, **http://www.healthlib.org/orgresources.html**
- **California:** Consumer Health Program and Services (CHIPS) (County of Los Angeles Public Library, Los Angeles County Harbor-UCLA Medical Center Library) - Carson, CA, **http://www.colapublib.org/services/chips.html**
- **California:** Gateway Health Library (Sutter Gould Medical Foundation)
- **California:** Health Library (Stanford University Medical Center), **http://www-med.stanford.edu/healthlibrary/**
- **California:** Patient Education Resource Center - Health Information and Resources (University of California, San Francisco), **http://sfghdean.ucsf.edu/barnett/PERC/default.asp**
- **California:** Redwood Health Library (Petaluma Health Care District), **http://www.phcd.org/rdwdlib.html**
- **California:** Los Gatos PlaneTree Health Library, **http://planetreesanjose.org/**
- **California:** Sutter Resource Library (Sutter Hospitals Foundation, Sacramento), **http://suttermedicalcenter.org/library/**
- **California:** Health Sciences Libraries (University of California, Davis), **http://www.lib.ucdavis.edu/healthsci/**
- **California:** ValleyCare Health Library & Ryan Comer Cancer Resource Center (ValleyCare Health System, Pleasanton), **http://gaelnet.stmarys-ca.edu/other.libs/gbal/east/vchl.html**
- **California:** Washington Community Health Resource Library (Fremont), **http://www.healthlibrary.org/**
- **Colorado:** William V. Gervasini Memorial Library (Exempla Healthcare), **http://www.saintjosephdenver.org/yourhealth/libraries/**
- **Connecticut:** Hartford Hospital Health Science Libraries (Hartford Hospital), **http://www.harthosp.org/library/**
- **Connecticut:** Healthnet: Connecticut Consumer Health Information Center (University of Connecticut Health Center, Lyman Maynard Stowe Library), **http://library.uchc.edu/departm/hnet/**

[23] Abstracted from **http://www.nlm.nih.gov/medlineplus/libraries.html**.

- **Connecticut:** Waterbury Hospital Health Center Library (Waterbury Hospital, Waterbury), **http://www.waterburyhospital.com/library/consumer.shtml**
- **Delaware:** Consumer Health Library (Christiana Care Health System, Eugene du Pont Preventive Medicine & Rehabilitation Institute, Wilmington), **http://www.christianacare.org/health_guide/health_guide_pmri_health_info.cfm**
- **Delaware:** Lewis B. Flinn Library (Delaware Academy of Medicine, Wilmington), **http://www.delamed.org/chls.html**
- **Georgia:** Family Resource Library (Medical College of Georgia, Augusta), **http://cmc.mcg.edu/kids_families/fam_resources/fam_res_lib/frl.htm**
- **Georgia:** Health Resource Center (Medical Center of Central Georgia, Macon), **http://www.mccg.org/hrc/hrchome.asp**
- **Hawaii:** Hawaii Medical Library: Consumer Health Information Service (Hawaii Medical Library, Honolulu), **http://hml.org/CHIS/**
- **Idaho:** DeArmond Consumer Health Library (Kootenai Medical Center, Coeur d'Alene), **http://www.nicon.org/DeArmond/index.htm**
- **Illinois:** Health Learning Center of Northwestern Memorial Hospital (Chicago), **http://www.nmh.org/health_info/hlc.html**
- **Illinois:** Medical Library (OSF Saint Francis Medical Center, Peoria), **http://www.osfsaintfrancis.org/general/library/**
- **Kentucky:** Medical Library - Services for Patients, Families, Students & the Public (Central Baptist Hospital, Lexington), **http://www.centralbap.com/education/community/library.cfm**
- **Kentucky:** University of Kentucky - Health Information Library (Chandler Medical Center, Lexington), **http://www.mc.uky.edu/PatientEd/**
- **Louisiana:** Alton Ochsner Medical Foundation Library (Alton Ochsner Medical Foundation, New Orleans), **http://www.ochsner.org/library/**
- **Louisiana:** Louisiana State University Health Sciences Center Medical Library-Shreveport, **http://lib-sh.lsuhsc.edu/**
- **Maine:** Franklin Memorial Hospital Medical Library (Franklin Memorial Hospital, Farmington), **http://www.fchn.org/fmh/lib.htm**
- **Maine:** Gerrish-True Health Sciences Library (Central Maine Medical Center, Lewiston), **http://www.cmmc.org/library/library.html**
- **Maine:** Hadley Parrot Health Science Library (Eastern Maine Healthcare, Bangor), **http://www.emh.org/hll/hpl/guide.htm**
- **Maine:** Maine Medical Center Library (Maine Medical Center, Portland), **http://www.mmc.org/library/**
- **Maine:** Parkview Hospital (Brunswick), **http://www.parkviewhospital.org/**
- **Maine:** Southern Maine Medical Center Health Sciences Library (Southern Maine Medical Center, Biddeford), **http://www.smmc.org/services/service.php3?choice=10**
- **Maine:** Stephens Memorial Hospital's Health Information Library (Western Maine Health, Norway), **http://www.wmhcc.org/Library/**

- **Manitoba, Canada:** Consumer & Patient Health Information Service (University of Manitoba Libraries), **http://www.umanitoba.ca/libraries/units/health/reference/chis.html**
- **Manitoba, Canada:** J.W. Crane Memorial Library (Deer Lodge Centre, Winnipeg), **http://www.deerlodge.mb.ca/crane_library/about.asp**
- **Maryland:** Health Information Center at the Wheaton Regional Library (Montgomery County, Dept. of Public Libraries, Wheaton Regional Library), **http://www.mont.lib.md.us/healthinfo/hic.asp**
- **Massachusetts:** Baystate Medical Center Library (Baystate Health System), **http://www.baystatehealth.com/1024/**
- **Massachusetts:** Boston University Medical Center Alumni Medical Library (Boston University Medical Center), **http://med-libwww.bu.edu/library/lib.html**
- **Massachusetts:** Lowell General Hospital Health Sciences Library (Lowell General Hospital, Lowell), **http://www.lowellgeneral.org/library/HomePageLinks/WWW.htm**
- **Massachusetts:** Paul E. Woodard Health Sciences Library (New England Baptist Hospital, Boston), **http://www.nebh.org/health_lib.asp**
- **Massachusetts:** St. Luke's Hospital Health Sciences Library (St. Luke's Hospital, Southcoast Health System, New Bedford), **http://www.southcoast.org/library/**
- **Massachusetts:** Treadwell Library Consumer Health Reference Center (Massachusetts General Hospital), **http://www.mgh.harvard.edu/library/chrcindex.html**
- **Massachusetts:** UMass HealthNet (University of Massachusetts Medical School, Worchester), **http://healthnet.umassmed.edu/**
- **Michigan:** Botsford General Hospital Library - Consumer Health (Botsford General Hospital, Library & Internet Services), **http://www.botsfordlibrary.org/consumer.htm**
- **Michigan:** Helen DeRoy Medical Library (Providence Hospital and Medical Centers), **http://www.providence-hospital.org/library/**
- **Michigan:** Marquette General Hospital - Consumer Health Library (Marquette General Hospital, Health Information Center), **http://www.mgh.org/center.html**
- **Michigan:** Patient Education Resouce Center - University of Michigan Cancer Center (University of Michigan Comprehensive Cancer Center, Ann Arbor), **http://www.cancer.med.umich.edu/learn/leares.htm**
- **Michigan:** Sladen Library & Center for Health Information Resources - Consumer Health Information (Detroit), **http://www.henryford.com/body.cfm?id=39330**
- **Montana:** Center for Health Information (St. Patrick Hospital and Health Sciences Center, Missoula)
- **National:** Consumer Health Library Directory (Medical Library Association, Consumer and Patient Health Information Section), **http://caphis.mlanet.org/directory/index.html**
- **National:** National Network of Libraries of Medicine (National Library of Medicine) - provides library services for health professionals in the United States who do not have access to a medical library, **http://nnlm.gov/**
- **National:** NN/LM List of Libraries Serving the Public (National Network of Libraries of Medicine), **http://nnlm.gov/members/**

- **Nevada:** Health Science Library, West Charleston Library (Las Vegas-Clark County Library District, Las Vegas), **http://www.lvccld.org/special_collections/medical/index.htm**
- **New Hampshire:** Dartmouth Biomedical Libraries (Dartmouth College Library, Hanover), **http://www.dartmouth.edu/~biomed/resources.htmld/conshealth.htmld/**
- **New Jersey:** Consumer Health Library (Rahway Hospital, Rahway), **http://www.rahwayhospital.com/library.htm**
- **New Jersey:** Dr. Walter Phillips Health Sciences Library (Englewood Hospital and Medical Center, Englewood), **http://www.englewoodhospital.com/links/index.htm**
- **New Jersey:** Meland Foundation (Englewood Hospital and Medical Center, Englewood), **http://www.geocities.com/ResearchTriangle/9360/**
- **New York:** Choices in Health Information (New York Public Library) - NLM Consumer Pilot Project participant, **http://www.nypl.org/branch/health/links.html**
- **New York:** Health Information Center (Upstate Medical University, State University of New York, Syracuse), **http://www.upstate.edu/library/hic/**
- **New York:** Health Sciences Library (Long Island Jewish Medical Center, New Hyde Park), **http://www.lij.edu/library/library.html**
- **New York:** ViaHealth Medical Library (Rochester General Hospital), **http://www.nyam.org/library/**
- **Ohio:** Consumer Health Library (Akron General Medical Center, Medical & Consumer Health Library), **http://www.akrongeneral.org/hwlibrary.htm**
- **Oklahoma:** The Health Information Center at Saint Francis Hospital (Saint Francis Health System, Tulsa), **http://www.sfh-tulsa.com/services/healthinfo.asp**
- **Oregon:** Planetree Health Resource Center (Mid-Columbia Medical Center, The Dalles), **http://www.mcmc.net/phrc/**
- **Pennsylvania:** Community Health Information Library (Milton S. Hershey Medical Center, Hershey), **http://www.hmc.psu.edu/commhealth/**
- **Pennsylvania:** Community Health Resource Library (Geisinger Medical Center, Danville), **http://www.geisinger.edu/education/commlib.shtml**
- **Pennsylvania:** HealthInfo Library (Moses Taylor Hospital, Scranton), **http://www.mth.org/healthwellness.html**
- **Pennsylvania:** Hopwood Library (University of Pittsburgh, Health Sciences Library System, Pittsburgh), **http://www.hsls.pitt.edu/guides/chi/hopwood/index_html**
- **Pennsylvania:** Koop Community Health Information Center (College of Physicians of Philadelphia), **http://www.collphyphil.org/kooppg1.shtml**
- **Pennsylvania:** Learning Resources Center - Medical Library (Susquehanna Health System, Williamsport), **http://www.shscares.org/services/lrc/index.asp**
- **Pennsylvania:** Medical Library (UPMC Health System, Pittsburgh), **http://www.upmc.edu/passavant/library.htm**
- **Quebec, Canada:** Medical Library (Montreal General Hospital), **http://www.mghlib.mcgill.ca/**

- **South Dakota:** Rapid City Regional Hospital Medical Library (Rapid City Regional Hospital), **http://www.rcrh.org/Services/Library/Default.asp**
- **Texas:** Houston HealthWays (Houston Academy of Medicine-Texas Medical Center Library), **http://hhw.library.tmc.edu/**
- **Washington:** Community Health Library (Kittitas Valley Community Hospital), **http://www.kvch.com/**
- **Washington:** Southwest Washington Medical Center Library (Southwest Washington Medical Center, Vancouver), **http://www.swmedicalcenter.com/body.cfm?id=72**

ONLINE GLOSSARIES

The Internet provides access to a number of free-to-use medical dictionaries. The National Library of Medicine has compiled the following list of online dictionaries:

- ADAM Medical Encyclopedia (A.D.A.M., Inc.), comprehensive medical reference: **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**
- MedicineNet.com Medical Dictionary (MedicineNet, Inc.): **http://www.medterms.com/Script/Main/hp.asp**
- Merriam-Webster Medical Dictionary (Inteli-Health, Inc.): **http://www.intelihealth.com/IH/**
- Multilingual Glossary of Technical and Popular Medical Terms in Eight European Languages (European Commission) - Danish, Dutch, English, French, German, Italian, Portuguese, and Spanish: **http://allserv.rug.ac.be/~rvdstich/eugloss/welcome.html**
- On-line Medical Dictionary (CancerWEB): **http://cancerweb.ncl.ac.uk/omd/**
- Rare Diseases Terms (Office of Rare Diseases): **http://ord.aspensys.com/asp/diseases/diseases.asp**
- Technology Glossary (National Library of Medicine) - Health Care Technology: **http://www.nlm.nih.gov/nichsr/ta101/ta10108.htm**

Beyond these, MEDLINEplus contains a very patient-friendly encyclopedia covering every aspect of medicine (licensed from A.D.A.M., Inc.). The ADAM Medical Encyclopedia can be accessed at **http://www.nlm.nih.gov/medlineplus/encyclopedia.html**. ADAM is also available on commercial Web sites such as drkoop.com (**http://www.drkoop.com/**) and Web MD (**http://my.webmd.com/adam/asset/adam_disease_articles/a_to_z/a**). The NIH suggests the following Web sites in the ADAM Medical Encyclopedia when searching for information on dental caries:

- **Basic Guidelines for Dental Caries**

  Dental caries
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001055.htm

- **Signs & Symptoms for Dental Caries**

  Toothache
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003067.htm

- **Diagnostics and Tests for Dental Caries**

  Dental X-rays
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003801.htm

  X-ray
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/003337.htm

- **Nutrition for Dental Caries**

  Carbohydrate
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002469.htm

  Carbohydrates
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002469.htm

  Starches
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002469.htm

  Sugars
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/002469.htm

- **Background Topics for Dental Caries**

  Oral hygiene
  Web site: http://www.nlm.nih.gov/medlineplus/ency/article/001957.htm

Online Dictionary Directories

The following are additional online directories compiled by the National Library of Medicine, including a number of specialized medical dictionaries:

- Medical Dictionaries: Medical & Biological (World Health Organization): **http://www.who.int/hlt/virtuallibrary/English/diction.htm#Medical**
- MEL-Michigan Electronic Library List of Online Health and Medical Dictionaries (Michigan Electronic Library): **http://mel.lib.mi.us/health/health-dictionaries.html**
- Patient Education: Glossaries (DMOZ Open Directory Project): **http://dmoz.org/Health/Education/Patient_Education/Glossaries/**
- Web of Online Dictionaries (Bucknell University): **http://www.yourdictionary.com/diction5.html#medicine**

DENTAL CARIES DICTIONARY

The definitions below are derived from official public sources, including the National Institutes of Health [NIH] and the European Union [EU].

3-dimensional: 3-D. A graphic display of depth, width, and height. Three-dimensional radiation therapy uses computers to create a 3-dimensional picture of the tumor. This allows doctors to give the highest possible dose of radiation to the tumor, while sparing the normal tissue as much as possible. [NIH]

Abdomen: That portion of the body that lies between the thorax and the pelvis. [NIH]

Ablate: In surgery, is to remove. [NIH]

Ablation: The removal of an organ by surgery. [NIH]

Acceptor: A substance which, while normally not oxidized by oxygen or reduced by hydrogen, can be oxidized or reduced in presence of a substance which is itself undergoing oxidation or reduction. [NIH]

Acetone: A colorless liquid used as a solvent and an antiseptic. It is one of the ketone bodies produced during ketoacidosis. [NIH]

Acidity: The quality of being acid or sour; containing acid (hydrogen ions). [EU]

Acidulated Phosphate Fluoride: A sodium fluoride solution, paste or powder, which has been acidulated to pH 3 to 4 and buffered with a phosphate. It is used in the prevention of dental caries. [NIH]

Acne: A disorder of the skin marked by inflammation of oil glands and hair glands. [NIH]

Acoustic: Having to do with sound or hearing. [NIH]

Acremonium: A mitosporic fungal genus with many reported ascomycetous teleomorphs. Cephalosporin antibiotics are derived from this genus. [NIH]

Acridine Orange: Cationic cytochemical stain specific for cell nuclei, especially DNA. It is used as a supravital stain and in fluorescence cytochemistry. It may cause mutations in microorganisms. [NIH]

Acute renal: A condition in which the kidneys suddenly stop working. In most cases, kidneys can recover from almost complete loss of function. [NIH]

Adaptation: 1. The adjustment of an organism to its environment, or the process by which it enhances such fitness. 2. The normal ability of the eye to adjust itself to variations in the intensity of light; the adjustment to such variations. 3. The decline in the frequency of firing of a neuron, particularly of a receptor, under conditions of constant stimulation. 4. In dentistry, (a) the proper fitting of a denture, (b) the degree of proximity and interlocking of restorative material to a tooth preparation, (c) the exact adjustment of bands to teeth. 5. In microbiology, the adjustment of bacterial physiology to a new environment. [EU]

Adenosine: A nucleoside that is composed of adenine and d-ribose. Adenosine or adenosine derivatives play many important biological roles in addition to being components of DNA and RNA. Adenosine itself is a neurotransmitter. [NIH]

Adenylate Cyclase: An enzyme of the lyase class that catalyzes the formation of cyclic AMP and pyrophosphate from ATP. EC 4.6.1.1. [NIH]

Adhesives: Substances that cause the adherence of two surfaces. They include glues (properly collagen-derived adhesives), mucilages, sticky pastes, gums, resins, or latex. [NIH]

Adjustment: The dynamic process wherein the thoughts, feelings, behavior, and biophysiological mechanisms of the individual continually change to adjust to the environment. [NIH]

Adjuvant: A substance which aids another, such as an auxiliary remedy; in immunology, nonspecific stimulator (e.g., BCG vaccine) of the immune response. [EU]

Adolescence: The period of life beginning with the appearance of secondary sex characteristics and terminating with the cessation of somatic growth. The years usually referred to as adolescence lie between 13 and 18 years of age. [NIH]

Adrenal Medulla: The inner part of the adrenal gland; it synthesizes, stores and releases catecholamines. [NIH]

Adverse Effect: An unwanted side effect of treatment. [NIH]

Aerosol: A solution of a drug which can be atomized into a fine mist for inhalation therapy. [EU]

Affinity: 1. Inherent likeness or relationship. 2. A special attraction for a specific element, organ, or structure. 3. Chemical affinity; the force that binds atoms in molecules; the tendency of substances to combine by chemical reaction. 4. The strength of noncovalent chemical binding between two substances as measured by the dissociation constant of the complex. 5. In immunology, a thermodynamic expression of the strength of interaction between a single antigen-binding site and a single antigenic determinant (and thus of the stereochemical compatibility between them), most accurately applied to interactions among simple, uniform antigenic determinants such as haptens. Expressed as the association constant (K litres mole -1), which, owing to the heterogeneity of affinities in a population of antibody molecules of a given specificity, actually represents an average value (mean intrinsic association constant). 6. The reciprocal of the dissociation constant. [EU]

Affinity Chromatography: In affinity chromatography, a ligand attached to a column binds specifically to the molecule to be purified. [NIH]

Agar: A complex sulfated polymer of galactose units, extracted from Gelidium cartilagineum, Gracilaria confervoides, and related red algae. It is used as a gel in the preparation of solid culture media for microorganisms, as a bulk laxative, in making emulsions, and as a supporting medium for immunodiffusion and immunoelectrophoresis. [NIH]

Age Groups: Persons classified by age from birth (infant, newborn) to octogenarians and older (aged, 80 and over). [NIH]

Age of Onset: The age or period of life at which a disease or the initial symptoms or manifestations of a disease appear in an individual. [NIH]

Aged, 80 and Over: A person 80 years of age and older. [NIH]

Agonist: In anatomy, a prime mover. In pharmacology, a drug that has affinity for and stimulates physiologic activity at cell receptors normally stimulated by naturally occurring substances. [EU]

Airway: A device for securing unobstructed passage of air into and out of the lungs during general anesthesia. [NIH]

Albumin: 1. Any protein that is soluble in water and moderately concentrated salt solutions and is coagulable by heat. 2. Serum albumin; the major plasma protein (approximately 60 per cent of the total), which is responsible for much of the plasma colloidal osmotic pressure and serves as a transport protein carrying large organic anions, such as fatty acids, bilirubin, and many drugs, and also carrying certain hormones, such as cortisol and thyroxine, when their specific binding globulins are saturated. Albumin is synthesized in the liver. Low serum levels occur in protein malnutrition, active inflammation and serious hepatic and

renal disease. [EU]

Algorithms: A procedure consisting of a sequence of algebraic formulas and/or logical steps to calculate or determine a given task. [NIH]

Alimentary: Pertaining to food or nutritive material, or to the organs of digestion. [EU]

Alkaline: Having the reactions of an alkali. [EU]

Alkaline Phosphatase: An enzyme that catalyzes the conversion of an orthophosphoric monoester and water to an alcohol and orthophosphate. EC 3.1.3.1. [NIH]

Alleles: Mutually exclusive forms of the same gene, occupying the same locus on homologous chromosomes, and governing the same biochemical and developmental process. [NIH]

Allergen: An antigenic substance capable of producing immediate-type hypersensitivity (allergy). [EU]

Allergic Rhinitis: Inflammation of the nasal mucous membrane associated with hay fever; fits may be provoked by substances in the working environment. [NIH]

Allo: A female hormone. [NIH]

Alloys: A mixture of metallic elements or compounds with other metallic or metalloid elements in varying proportions. [NIH]

Allylamine: Possesses an unusual and selective cytotoxicity for vascular smooth muscle cells in dogs and rats. Useful for experiments dealing with arterial injury, myocardial fibrosis or cardiac decompensation. [NIH]

Alpha Particles: Positively charged particles composed of two protons and two neutrons, i.e., helium nuclei, emitted during disintegration of very heavy isotopes; a beam of alpha particles or an alpha ray has very strong ionizing power, but weak penetrability. [NIH]

Alpha-Amylase: An enzyme that catalyzes the endohydrolysis of 1,4-alpha-glycosidic linkages in starch, glycogen, and related polysaccharides and oligosaccharides containing 3 or more 1,4-alpha-linked D-glucose units. EC 3.2.1.1. [NIH]

Alternative medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used instead of standard treatments. Alternative medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Alveolar Bone Loss: The resorption of bone in the supporting structures of the maxilla or mandible as a result of periodontal disease. [NIH]

Alveoli: Tiny air sacs at the end of the bronchioles in the lungs. [NIH]

Amelogenesis Imperfecta: Either hereditary enamel hypoplasia or hypocalcification. [NIH]

Amine: An organic compound containing nitrogen; any member of a group of chemical compounds formed from ammonia by replacement of one or more of the hydrogen atoms by organic (hydrocarbon) radicals. The amines are distinguished as primary, secondary, and tertiary, according to whether one, two, or three hydrogen atoms are replaced. The amines include allylamine, amylamine, ethylamine, methylamine, phenylamine, propylamine, and many other compounds. [EU]

Amino acid: Any organic compound containing an amino (-NH2 and a carboxyl (- COOH) group. The 20 a-amino acids listed in the accompanying table are the amino acids from which proteins are synthesized by formation of peptide bonds during ribosomal translation of messenger RNA; all except glycine, which is not optically active, have the L configuration. Other amino acids occurring in proteins, such as hydroxyproline in collagen, are formed by

posttranslational enzymatic modification of amino acids residues in polypeptide chains. There are also several important amino acids, such as the neurotransmitter y-aminobutyric acid, that have no relation to proteins. Abbreviated AA. [EU]

Amino Acid Sequence: The order of amino acids as they occur in a polypeptide chain. This is referred to as the primary structure of proteins. It is of fundamental importance in determining protein conformation. [NIH]

Ammonia: A colorless alkaline gas. It is formed in the body during decomposition of organic materials during a large number of metabolically important reactions. [NIH]

Amoxicillin: A broad-spectrum semisynthetic antibiotic similar to ampicillin except that its resistance to gastric acid permits higher serum levels with oral administration. [NIH]

Ampicillin: Semi-synthetic derivative of penicillin that functions as an orally active broad-spectrum antibiotic. [NIH]

Amylase: An enzyme that helps the body digest starches. [NIH]

Anaesthesia: Loss of feeling or sensation. Although the term is used for loss of tactile sensibility, or of any of the other senses, it is applied especially to loss of the sensation of pain, as it is induced to permit performance of surgery or other painful procedures. [EU]

Anaesthetic: 1. Pertaining to, characterized by, or producing anaesthesia. 2. A drug or agent that is used to abolish the sensation of pain. [EU]

Anal: Having to do with the anus, which is the posterior opening of the large bowel. [NIH]

Analogous: Resembling or similar in some respects, as in function or appearance, but not in origin or development;. [EU]

Anatomical: Pertaining to anatomy, or to the structure of the organism. [EU]

Anemia: A reduction in the number of circulating erythrocytes or in the quantity of hemoglobin. [NIH]

Anesthesia: A state characterized by loss of feeling or sensation. This depression of nerve function is usually the result of pharmacologic action and is induced to allow performance of surgery or other painful procedures. [NIH]

Angina: Chest pain that originates in the heart. [NIH]

Angiogenesis: Blood vessel formation. Tumor angiogenesis is the growth of blood vessels from surrounding tissue to a solid tumor. This is caused by the release of chemicals by the tumor. [NIH]

Anhydrous: Deprived or destitute of water. [EU]

Animal model: An animal with a disease either the same as or like a disease in humans. Animal models are used to study the development and progression of diseases and to test new treatments before they are given to humans. Animals with transplanted human cancers or other tissues are called xenograft models. [NIH]

Anions: Negatively charged atoms, radicals or groups of atoms which travel to the anode or positive pole during electrolysis. [NIH]

Anisotropy: A physical property showing different values in relation to the direction in or along which the measurement is made. The physical property may be with regard to thermal or electric conductivity or light refraction. In crystallography, it describes crystals whose index of refraction varies with the direction of the incident light. It is also called acolotropy and colotropy. The opposite of anisotropy is isotropy wherein the same values characterize the object when measured along axes in all directions. [NIH]

Annealing: The spontaneous alignment of two single DNA strands to form a double helix. [NIH]

Anomalies: Birth defects; abnormalities. [NIH]

Anthocyanins: Glycosidic pigments in blue, red, and purple flowers and also found as metabolic byproducts in blood and urine. [NIH]

Antibacterial: A substance that destroys bacteria or suppresses their growth or reproduction. [EU]

Antibiotic: A drug used to treat infections caused by bacteria and other microorganisms. [NIH]

Antibodies: Immunoglobulin molecules having a specific amino acid sequence by virtue of which they interact only with the antigen that induced their synthesis in cells of the lymphoid series (especially plasma cells), or with an antigen closely related to it. [NIH]

Antibody: A type of protein made by certain white blood cells in response to a foreign substance (antigen). Each antibody can bind to only a specific antigen. The purpose of this binding is to help destroy the antigen. Antibodies can work in several ways, depending on the nature of the antigen. Some antibodies destroy antigens directly. Others make it easier for white blood cells to destroy the antigen. [NIH]

Anticoagulant: A drug that helps prevent blood clots from forming. Also called a blood thinner. [NIH]

Antidote: A remedy for counteracting a poison. [EU]

Antigen: Any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T-lymphocytes, or both. Antigens may be soluble substances, such as toxins and foreign proteins, or particulate, such as bacteria and tissue cells; however, only the portion of the protein or polysaccharide molecule known as the antigenic determinant (q.v.) combines with antibody or a specific receptor on a lymphocyte. Abbreviated Ag. [EU]

Anti-infective: An agent that so acts. [EU]

Antimetabolite: A chemical that is very similar to one required in a normal biochemical reaction in cells. Antimetabolites can stop or slow down the reaction. [NIH]

Antimicrobial: Killing microorganisms, or suppressing their multiplication or growth. [EU]

Antimycotic: Suppressing the growth of fungi. [EU]

Antineoplastic: Inhibiting or preventing the development of neoplasms, checking the maturation and proliferation of malignant cells. [EU]

Antioxidant: A substance that prevents damage caused by free radicals. Free radicals are highly reactive chemicals that often contain oxygen. They are produced when molecules are split to give products that have unpaired electrons. This process is called oxidation. [NIH]

Antiseptic: A substance that inhibits the growth and development of microorganisms without necessarily killing them. [EU]

Antiserum: The blood serum obtained from an animal after it has been immunized with a particular antigen. It will contain antibodies which are specific for that antigen as well as antibodies specific for any other antigen with which the animal has previously been immunized. [NIH]

Antiviral: Destroying viruses or suppressing their replication. [EU]

Anus: The opening of the rectum to the outside of the body. [NIH]

Anxiety: Persistent feeling of dread, apprehension, and impending disaster. [NIH]

Aplasia: Lack of development of an organ or tissue, or of the cellular products from an

organ or tissue. [EU]

Approximate: Approximal [EU]

Aqueous: Having to do with water. [NIH]

Arachidonic Acid: An unsaturated, essential fatty acid. It is found in animal and human fat as well as in the liver, brain, and glandular organs, and is a constituent of animal phosphatides. It is formed by the synthesis from dietary linoleic acid and is a precursor in the biosynthesis of prostaglandins, thromboxanes, and leukotrienes. [NIH]

Archaea: One of the three domains of life (the others being bacteria and Eucarya), formerly called Archaebacteria under the taxon Bacteria, but now considered separate and distinct. They are characterized by: 1) the presence of characteristic tRNAs and ribosomal RNAs; 2) the absence of peptidoglycan cell walls; 3) the presence of ether-linked lipids built from branched-chain subunits; and 4) their occurrence in unusual habitats. While archaea resemble bacteria in morphology and genomic organization, they resemble eukarya in their method of genomic replication. The domain contains at least three kingdoms: crenarchaeota, euryarchaeota, and korarchaeota. [NIH]

Arginine: An essential amino acid that is physiologically active in the L-form. [NIH]

Arterial: Pertaining to an artery or to the arteries. [EU]

Arteries: The vessels carrying blood away from the heart. [NIH]

Arterioles: The smallest divisions of the arteries located between the muscular arteries and the capillaries. [NIH]

Artery: Vessel-carrying blood from the heart to various parts of the body. [NIH]

Ascorbic Acid: A six carbon compound related to glucose. It is found naturally in citrus fruits and many vegetables. Ascorbic acid is an essential nutrient in human diets, and necessary to maintain connective tissue and bone. Its biologically active form, vitamin C, functions as a reducing agent and coenzyme in several metabolic pathways. Vitamin C is considered an antioxidant. [NIH]

Aspartate: A synthetic amino acid. [NIH]

Aspartic: The naturally occurring substance is L-aspartic acid. One of the acidic-amino-acids is obtained by the hydrolysis of proteins. [NIH]

Aspartic Acid: One of the non-essential amino acids commonly occurring in the L-form. It is found in animals and plants, especially in sugar cane and sugar beets. It may be a neurotransmitter. [NIH]

Assay: Determination of the amount of a particular constituent of a mixture, or of the biological or pharmacological potency of a drug. [EU]

Astringent: Causing contraction, usually locally after topical application. [EU]

Attenuated: Strain with weakened or reduced virulence. [NIH]

Attenuation: Reduction of transmitted sound energy or its electrical equivalent. [NIH]

Autoimmune disease: A condition in which the body recognizes its own tissues as foreign and directs an immune response against them. [NIH]

Avidity: The strength of the interaction of an antiserum with a multivalent antigen. [NIH]

Bacteria: Unicellular prokaryotic microorganisms which generally possess rigid cell walls, multiply by cell division, and exhibit three principal forms: round or coccal, rodlike or bacillary, and spiral or spirochetal. [NIH]

Bacterial Adhesion: Physicochemical property of fimbriated and non-fimbriated bacteria of attaching to cells, tissue, and nonbiological surfaces. It is a factor in bacterial colonization

and pathogenicity. [NIH]

Bacterial Infections: Infections by bacteria, general or unspecified. [NIH]

Bacterial Physiology: Physiological processes and activities of bacteria. [NIH]

Bactericidal: Substance lethal to bacteria; substance capable of killing bacteria. [NIH]

Bacteriophage: A virus whose host is a bacterial cell; A virus that exclusively infects bacteria. It generally has a protein coat surrounding the genome (DNA or RNA). One of the coliphages most extensively studied is the lambda phage, which is also one of the most important. [NIH]

Bacteriostatic: 1. Inhibiting the growth or multiplication of bacteria. 2. An agent that inhibits the growth or multiplication of bacteria. [EU]

Bacterium: Microscopic organism which may have a spherical, rod-like, or spiral unicellular or non-cellular body. Bacteria usually reproduce through asexual processes. [NIH]

Basement Membrane: Ubiquitous supportive tissue adjacent to epithelium and around smooth and striated muscle cells. This tissue contains intrinsic macromolecular components such as collagen, laminin, and sulfated proteoglycans. As seen by light microscopy one of its subdivisions is the basal (basement) lamina. [NIH]

Basophils: Granular leukocytes characterized by a relatively pale-staining, lobate nucleus and cytoplasm containing coarse dark-staining granules of variable size and stainable by basic dyes. [NIH]

Benign: Not cancerous; does not invade nearby tissue or spread to other parts of the body. [NIH]

Benzoic Acid: A fungistatic compound that is widely used as a food preservative. It is conjugated to glycine in the liver and excreted as hippuric acid. [NIH]

Beta-Galactosidase: A group of enzymes that catalyzes the hydrolysis of terminal, non-reducing beta-D-galactose residues in beta-galactosides. Deficiency of beta-Galactosidase A1 may cause gangliodisosis GM1. EC 3.2.1.23. [NIH]

Bilateral: Affecting both the right and left side of body. [NIH]

Bilirubin: A bile pigment that is a degradation product of heme. [NIH]

Binding Sites: The reactive parts of a macromolecule that directly participate in its specific combination with another molecule. [NIH]

Bioassay: Determination of the relative effective strength of a substance (as a vitamin, hormone, or drug) by comparing its effect on a test organism with that of a standard preparation. [NIH]

Bioavailable: The ability of a drug or other substance to be absorbed and used by the body. Orally bioavailable means that a drug or other substance that is taken by mouth can be absorbed and used by the body. [NIH]

Biochemical: Relating to biochemistry; characterized by, produced by, or involving chemical reactions in living organisms. [EU]

Bioengineering: The application of engineering principles to the solution of biological problems, for example, remote-handling devices, life-support systems, controls, and displays. [NIH]

Biofilms: Films of bacteria or other microbial organisms, usually embedded in extracellular polymers such as implanted medical devices, which adhere to surfaces submerged in, or subjected to, aquatic environments (From Singleton & Sainsbury, Dictionary of Microbiology and Molecular Biology, 2d ed). Biofilms consist of multilayers of microbial cells glued together to form microbial communities which are highly resistant to both

phagocytes and antibiotics. [NIH]

Biogenesis: The origin of life. It includes studies of the potential basis for life in organic compounds but excludes studies of the development of altered forms of life through mutation and natural selection, which is evolution. [NIH]

Biological Assay: A method of measuring the effects of a biologically active substance using an intermediate in vivo or in vitro tissue or cell model under controlled conditions. It includes virulence studies in animal fetuses in utero, mouse convulsion bioassay of insulin, quantitation of tumor-initiator systems in mouse skin, calculation of potentiating effects of a hormonal factor in an isolated strip of contracting stomach muscle, etc. [NIH]

Biological Factors: Compounds made by living organisms that contribute to or influence a phenomenon or process. They have biological or physiological activities. [NIH]

Biological therapy: Treatment to stimulate or restore the ability of the immune system to fight infection and disease. Also used to lessen side effects that may be caused by some cancer treatments. Also known as immunotherapy, biotherapy, or biological response modifier (BRM) therapy. [NIH]

Biological Transport: The movement of materials (including biochemical substances and drugs) across cell membranes and epithelial layers, usually by passive diffusion. [NIH]

Bioluminescence: The emission of light by living organisms such as the firefly, certain mollusks, beetles, fish, bacteria, fungi and protozoa. [NIH]

Biomarkers: Substances sometimes found in an increased amount in the blood, other body fluids, or tissues and that may suggest the presence of some types of cancer. Biomarkers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and GI tract cancers), and PSA (prostate cancer). Also called tumor markers. [NIH]

Biosynthesis: The building up of a chemical compound in the physiologic processes of a living organism. [EU]

Biotechnology: Body of knowledge related to the use of organisms, cells or cell-derived constituents for the purpose of developing products which are technically, scientifically and clinically useful. Alteration of biologic function at the molecular level (i.e., genetic engineering) is a central focus; laboratory methods used include transfection and cloning technologies, sequence and structure analysis algorithms, computer databases, and gene and protein structure function analysis and prediction. [NIH]

Bladder: The organ that stores urine. [NIH]

Blood Coagulation: The process of the interaction of blood coagulation factors that results in an insoluble fibrin clot. [NIH]

Blood pressure: The pressure of blood against the walls of a blood vessel or heart chamber. Unless there is reference to another location, such as the pulmonary artery or one of the heart chambers, it refers to the pressure in the systemic arteries, as measured, for example, in the forearm. [NIH]

Blood vessel: A tube in the body through which blood circulates. Blood vessels include a network of arteries, arterioles, capillaries, venules, and veins. [NIH]

Blood Volume: Volume of circulating blood. It is the sum of the plasma volume and erythrocyte volume. [NIH]

Blot: To transfer DNA, RNA, or proteins to an immobilizing matrix such as nitrocellulose. [NIH]

Body Burden: The total amount of a chemical, metal or radioactive substance present at any time after absorption in the body of man or animal. [NIH]

Body Fluids: Liquid components of living organisms. [NIH]

Bolus: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus infusion. [NIH]

Bolus infusion: A single dose of drug usually injected into a blood vessel over a short period of time. Also called bolus. [NIH]

Bone Marrow: The soft tissue filling the cavities of bones. Bone marrow exists in two types, yellow and red. Yellow marrow is found in the large cavities of large bones and consists mostly of fat cells and a few primitive blood cells. Red marrow is a hematopoietic tissue and is the site of production of erythrocytes and granular leukocytes. Bone marrow is made up of a framework of connective tissue containing branching fibers with the frame being filled with marrow cells. [NIH]

Bone Marrow Transplantation: The transference of bone marrow from one human or animal to another. [NIH]

Bone scan: A technique to create images of bones on a computer screen or on film. A small amount of radioactive material is injected into a blood vessel and travels through the bloodstream; it collects in the bones and is detected by a scanner. [NIH]

Bottle Feeding: Use of nursing bottles for feeding. Applies to humans and animals. [NIH]

Brachytherapy: A collective term for interstitial, intracavity, and surface radiotherapy. It uses small sealed or partly-sealed sources that may be placed on or near the body surface or within a natural body cavity or implanted directly into the tissues. [NIH]

Bradykinin: A nonapeptide messenger that is enzymatically produced from kallidin in the blood where it is a potent but short-lived agent of arteriolar dilation and increased capillary permeability. Bradykinin is also released from mast cells during asthma attacks, from gut walls as a gastrointestinal vasodilator, from damaged tissues as a pain signal, and may be a neurotransmitter. [NIH]

Broad-spectrum: Effective against a wide range of microorganisms; said of an antibiotic. [EU]

Bromodeoxyuridine: A nucleoside that substitutes for thymidine in DNA and thus acts as an antimetabolite. It causes breaks in chromosomes and has been proposed as an antiviral and antineoplastic agent. It has been given orphan drug status for use in the treatment of primary brain tumors. [NIH]

Bronchi: The larger air passages of the lungs arising from the terminal bifurcation of the trachea. [NIH]

Bronchitis: Inflammation (swelling and reddening) of the bronchi. [NIH]

Buccal: Pertaining to or directed toward the cheek. In dental anatomy, used to refer to the buccal surface of a tooth. [EU]

Buffers: A chemical system that functions to control the levels of specific ions in solution. When the level of hydrogen ion in solution is controlled the system is called a pH buffer. [NIH]

Calcification: Deposits of calcium in the tissues of the breast. Calcification in the breast can be seen on a mammogram, but cannot be detected by touch. There are two types of breast calcification, macrocalcification and microcalcification. Macrocalcifications are large deposits and are usually not related to cancer. Microcalcifications are specks of calcium that may be found in an area of rapidly dividing cells. Many microcalcifications clustered together may be a sign of cancer. [NIH]

Calcium: A basic element found in nearly all organized tissues. It is a member of the alkaline earth family of metals with the atomic symbol Ca, atomic number 20, and atomic weight 40. Calcium is the most abundant mineral in the body and combines with

phosphorus to form calcium phosphate in the bones and teeth. It is essential for the normal functioning of nerves and muscles and plays a role in blood coagulation (as factor IV) and in many enzymatic processes. [NIH]

Calcium Chloride: A salt used to replenish calcium levels, as an acid-producing diuretic, and as an antidote for magnesium poisoning. [NIH]

Candidiasis: Infection with a fungus of the genus Candida. It is usually a superficial infection of the moist cutaneous areas of the body, and is generally caused by C. albicans; it most commonly involves the skin (dermatocandidiasis), oral mucous membranes (thrush, def. 1), respiratory tract (bronchocandidiasis), and vagina (vaginitis). Rarely there is a systemic infection or endocarditis. Called also moniliasis, candidosis, oidiomycosis, and formerly blastodendriosis. [EU]

Candidosis: An infection caused by an opportunistic yeasts that tends to proliferate and become pathologic when the environment is favorable and the host resistance is weakened. [NIH]

Capillary: Any one of the minute vessels that connect the arterioles and venules, forming a network in nearly all parts of the body. Their walls act as semipermeable membranes for the interchange of various substances, including fluids, between the blood and tissue fluid; called also vas capillare. [EU]

Capping: A 7-methyl guanosine cap attached to the 5'-end of eucaryotic mRNAs by a phosphodiester linkage. The cap is believed to increase the stability of the message, since most nucleases require a 5'-3'or 3'-5'bond in order to cleave the RNA. [NIH]

Capsules: Hard or soft soluble containers used for the oral administration of medicine. [NIH]

Carbohydrate: An aldehyde or ketone derivative of a polyhydric alcohol, particularly of the pentahydric and hexahydric alcohols. They are so named because the hydrogen and oxygen are usually in the proportion to form water, (CH2O)n. The most important carbohydrates are the starches, sugars, celluloses, and gums. They are classified into mono-, di-, tri-, poly- and heterosaccharides. [EU]

Carbon Dioxide: A colorless, odorless gas that can be formed by the body and is necessary for the respiration cycle of plants and animals. [NIH]

Carcinogenic: Producing carcinoma. [EU]

Cardiac: Having to do with the heart. [NIH]

Cardiovascular: Having to do with the heart and blood vessels. [NIH]

Cardiovascular disease: Any abnormal condition characterized by dysfunction of the heart and blood vessels. CVD includes atherosclerosis (especially coronary heart disease, which can lead to heart attacks), cerebrovascular disease (e.g., stroke), and hypertension (high blood pressure). [NIH]

Carrier Proteins: Transport proteins that carry specific substances in the blood or across cell membranes. [NIH]

Case report: A detailed report of the diagnosis, treatment, and follow-up of an individual patient. Case reports also contain some demographic information about the patient (for example, age, gender, ethnic origin). [NIH]

Case series: A group or series of case reports involving patients who were given similar treatment. Reports of case series usually contain detailed information about the individual patients. This includes demographic information (for example, age, gender, ethnic origin) and information on diagnosis, treatment, response to treatment, and follow-up after treatment. [NIH]

Caseins: A mixture of related phosphoproteins occurring in milk and cheese. The group is

characterized as one of the most nutritive milk proteins, containing all of the common amino acids and rich in the essential ones. [NIH]

Catabolism: Any destructive metabolic process by which organisms convert substances into excreted compounds. [EU]

Catalytic Domain: The region of an enzyme that interacts with its substrate to cause the enzymatic reaction. [NIH]

Catecholamine: A group of chemical substances manufactured by the adrenal medulla and secreted during physiological stress. [NIH]

Catheters: A small, flexible tube that may be inserted into various parts of the body to inject or remove liquids. [NIH]

Cathode: An electrode, usually an incandescent filament of tungsten, which emits electrons in an X-ray tube. [NIH]

Cations: Postively charged atoms, radicals or groups of atoms which travel to the cathode or negative pole during electrolysis. [NIH]

Causal: Pertaining to a cause; directed against a cause. [EU]

Cavernous Sinus: An irregularly shaped venous space in the dura mater at either side of the sphenoid bone. [NIH]

Cell: The individual unit that makes up all of the tissues of the body. All living things are made up of one or more cells. [NIH]

Cell Cycle: The complex series of phenomena, occurring between the end of one cell division and the end of the next, by which cellular material is divided between daughter cells. [NIH]

Cell Division: The fission of a cell. [NIH]

Cell Survival: The span of viability of a cell characterized by the capacity to perform certain functions such as metabolism, growth, reproduction, some form of responsiveness, and adaptability. [NIH]

Cellulitis: An acute, diffuse, and suppurative inflammation of loose connective tissue, particularly the deep subcutaneous tissues, and sometimes muscle, which is most commonly seen as a result of infection of a wound, ulcer, or other skin lesions. [NIH]

Cellulose: A polysaccharide with glucose units linked as in cellobiose. It is the chief constituent of plant fibers, cotton being the purest natural form of the substance. As a raw material, it forms the basis for many derivatives used in chromatography, ion exchange materials, explosives manufacturing, and pharmaceutical preparations. [NIH]

Cephalosporins: A group of broad-spectrum antibiotics first isolated from the Mediterranean fungus Acremonium (Cephalosporium acremonium). They contain the beta-lactam moiety thia-azabicyclo-octenecarboxylic acid also called 7-aminocephalosporanic acid. [NIH]

Cerebral: Of or pertaining of the cerebrum or the brain. [EU]

Cerebral Cortex: The thin layer of gray matter on the surface of the cerebral hemisphere that develops from the telencephalon and folds into gyri. It reaches its highest development in man and is responsible for intellectual faculties and higher mental functions. [NIH]

Cerebral Palsy: Refers to a motor disability caused by a brain dysfunction. [NIH]

Cerebrovascular: Pertaining to the blood vessels of the cerebrum, or brain. [EU]

Cerebrum: The largest part of the brain. It is divided into two hemispheres, or halves, called the cerebral hemispheres. The cerebrum controls muscle functions of the body and also

controls speech, emotions, reading, writing, and learning. [NIH]

Cervical: Relating to the neck, or to the neck of any organ or structure. Cervical lymph nodes are located in the neck; cervical cancer refers to cancer of the uterine cervix, which is the lower, narrow end (the "neck") of the uterus. [NIH]

Cervix: The lower, narrow end of the uterus that forms a canal between the uterus and vagina. [NIH]

Character: In current usage, approximately equivalent to personality. The sum of the relatively fixed personality traits and habitual modes of response of an individual. [NIH]

Chin: The anatomical frontal portion of the mandible, also known as the mentum, that contains the line of fusion of the two separate halves of the mandible (symphysis menti). This line of fusion divides inferiorly to enclose a triangular area called the mental protuberance. On each side, inferior to the second premolar tooth, is the mental foramen for the passage of blood vessels and a nerve. [NIH]

Chlorhexidine: Disinfectant and topical anti-infective agent used also as mouthwash to prevent oral plaque. [NIH]

Cholera: An acute diarrheal disease endemic in India and Southeast Asia whose causative agent is vibrio cholerae. This condition can lead to severe dehydration in a matter of hours unless quickly treated. [NIH]

Cholera Toxin: The enterotoxin from Vibrio cholerae. It is a protein that consists of two major components, the heavy (H) or A peptide and the light (L) or B peptide or choleragenoid. The B peptide anchors the protein to intestinal epithelial cells, while the A peptide, enters the cytoplasm, and activates adenylate cyclase, and production of cAMP. Increased levels of cAMP are thought to modulate release of fluid and electrolytes from intestinal crypt cells. [NIH]

Cholesterol: The principal sterol of all higher animals, distributed in body tissues, especially the brain and spinal cord, and in animal fats and oils. [NIH]

Chromosomal: Pertaining to chromosomes. [EU]

Chromosome: Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes. [NIH]

Chronic: A disease or condition that persists or progresses over a long period of time. [NIH]

Chronic Disease: Disease or ailment of long duration. [NIH]

Chronic Obstructive Pulmonary Disease: Collective term for chronic bronchitis and emphysema. [NIH]

CIS: Cancer Information Service. The CIS is the National Cancer Institute's link to the public, interpreting and explaining research findings in a clear and understandable manner, and providing personalized responses to specific questions about cancer. Access the CIS by calling 1-800-4-CANCER, or by using the Web site at http://cis.nci.nih.gov. [NIH]

Cleave: A double-stranded cut in DNA with a restriction endonuclease. [NIH]

Clinical Medicine: The study and practice of medicine by direct examination of the patient. [NIH]

Clinical Protocols: Precise and detailed plans for the study of a medical or biomedical problem and/or plans for a regimen of therapy. [NIH]

Clinical study: A research study in which patients receive treatment in a clinic or other medical facility. Reports of clinical studies can contain results for single patients (case reports) or many patients (case series or clinical trials). [NIH]

Clinical trial: A research study that tests how well new medical treatments or other

interventions work in people. Each study is designed to test new methods of screening, prevention, diagnosis, or treatment of a disease. [NIH]

Clone: The term "clone" has acquired a new meaning. It is applied specifically to the bits of inserted foreign DNA in the hybrid molecules of the population. Each inserted segment originally resided in the DNA of a complex genome amid millions of other DNA segment. [NIH]

Cloning: The production of a number of genetically identical individuals; in genetic engineering, a process for the efficient replication of a great number of identical DNA molecules. [NIH]

Coenzyme: An organic nonprotein molecule, frequently a phosphorylated derivative of a water-soluble vitamin, that binds with the protein molecule (apoenzyme) to form the active enzyme (holoenzyme). [EU]

Cofactor: A substance, microorganism or environmental factor that activates or enhances the action of another entity such as a disease-causing agent. [NIH]

Cohort Studies: Studies in which subsets of a defined population are identified. These groups may or may not be exposed to factors hypothesized to influence the probability of the occurrence of a particular disease or other outcome. Cohorts are defined populations which, as a whole, are followed in an attempt to determine distinguishing subgroup characteristics. [NIH]

Coliphages: Viruses whose host is Escherichia coli. [NIH]

Collagen: A polypeptide substance comprising about one third of the total protein in mammalian organisms. It is the main constituent of skin, connective tissue, and the organic substance of bones and teeth. Different forms of collagen are produced in the body but all consist of three alpha-polypeptide chains arranged in a triple helix. Collagen is differentiated from other fibrous proteins, such as elastin, by the content of proline, hydroxyproline, and hydroxylysine; by the absence of tryptophan; and particularly by the high content of polar groups which are responsible for its swelling properties. [NIH]

Collagenases: Enzymes that catalyze the degradation of collagen by acting on the peptide bonds. EC 3.4.24.-. [NIH]

Colloidal: Of the nature of a colloid. [EU]

Colon: The long, coiled, tubelike organ that removes water from digested food. The remaining material, solid waste called stool, moves through the colon to the rectum and leaves the body through the anus. [NIH]

Colostrum: The thin, yellow, serous fluid secreted by the mammary glands during pregnancy and immediately postpartum before lactation begins. It consists of immunologically active substances, white blood cells, water, protein, fat, and carbohydrates. [NIH]

Commensal: 1. Living on or within another organism, and deriving benefit without injuring or benefiting the other individual. 2. An organism living on or within another, but not causing injury to the host. [EU]

Complement: A term originally used to refer to the heat-labile factor in serum that causes immune cytolysis, the lysis of antibody-coated cells, and now referring to the entire functionally related system comprising at least 20 distinct serum proteins that is the effector not only of immune cytolysis but also of other biologic functions. Complement activation occurs by two different sequences, the classic and alternative pathways. The proteins of the classic pathway are termed 'components of complement' and are designated by the symbols C1 through C9. C1 is a calcium-dependent complex of three distinct proteins C1q, C1r and C1s. The proteins of the alternative pathway (collectively referred to as the properdin

system) and complement regulatory proteins are known by semisystematic or trivial names. Fragments resulting from proteolytic cleavage of complement proteins are designated with lower-case letter suffixes, e.g., C3a. Inactivated fragments may be designated with the suffix 'i', e.g. C3bi. Activated components or complexes with biological activity are designated by a bar over the symbol e.g. C1 or C4b,2a. The classic pathway is activated by the binding of C1 to classic pathway activators, primarily antigen-antibody complexes containing IgM, IgG1, IgG3; C1q binds to a single IgM molecule or two adjacent IgG molecules. The alternative pathway can be activated by IgA immune complexes and also by nonimmunologic materials including bacterial endotoxins, microbial polysaccharides, and cell walls. Activation of the classic pathway triggers an enzymatic cascade involving C1, C4, C2 and C3; activation of the alternative pathway triggers a cascade involving C3 and factors B, D and P. Both result in the cleavage of C5 and the formation of the membrane attack complex. Complement activation also results in the formation of many biologically active complement fragments that act as anaphylatoxins, opsonins, or chemotactic factors. [EU]

Complementary and alternative medicine: CAM. Forms of treatment that are used in addition to (complementary) or instead of (alternative) standard treatments. These practices are not considered standard medical approaches. CAM includes dietary supplements, megadose vitamins, herbal preparations, special teas, massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementary medicine: Practices not generally recognized by the medical community as standard or conventional medical approaches and used to enhance or complement the standard treatments. Complementary medicine includes the taking of dietary supplements, megadose vitamins, and herbal preparations; the drinking of special teas; and practices such as massage therapy, magnet therapy, spiritual healing, and meditation. [NIH]

Complementation: The production of a wild-type phenotype when two different mutations are combined in a diploid or a heterokaryon and tested in trans-configuration. [NIH]

Compliance: Distensibility measure of a chamber such as the lungs (lung compliance) or bladder. Compliance is expressed as a change in volume per unit change in pressure. [NIH]

Compomers: Composite materials composed of an ion-leachable glass embedded in a polymeric matrix. They differ from glass-ionomer cements in that partially silanized glass particles are used to provide a direct bond to the resin matrix and the matrix is primarily formed by a light-activated, radical polymerization reaction. [NIH]

Composite Resins: Synthetic resins, containing an inert filler, that are widely used in dentistry. [NIH]

Computational Biology: A field of biology concerned with the development of techniques for the collection and manipulation of biological data, and the use of such data to make biological discoveries or predictions. This field encompasses all computational methods and theories applicable to molecular biology and areas of computer-based techniques for solving biological problems including manipulation of models and datasets. [NIH]

Computed tomography: CT scan. A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called computerized tomography and computerized axial tomography (CAT) scan. [NIH]

Computer Simulation: Computer-based representation of physical systems and phenomena such as chemical processes. [NIH]

Computerized axial tomography: A series of detailed pictures of areas inside the body, taken from different angles; the pictures are created by a computer linked to an x-ray machine. Also called CAT scan, computed tomography (CT scan), or computerized

tomography. [NIH]

Conduction: The transfer of sound waves, heat, nervous impulses, or electricity. [EU]

Cones: One type of specialized light-sensitive cells (photoreceptors) in the retina that provide sharp central vision and color vision. [NIH]

Confounding: Extraneous variables resulting in outcome effects that obscure or exaggerate the "true" effect of an intervention. [NIH]

Conjugated: Acting or operating as if joined; simultaneous. [EU]

Conjunctivitis: Inflammation of the conjunctiva, generally consisting of conjunctival hyperaemia associated with a discharge. [EU]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Connective Tissue: Tissue that supports and binds other tissues. It consists of connective tissue cells embedded in a large amount of extracellular matrix. [NIH]

Constitutional: 1. Affecting the whole constitution of the body; not local. 2. Pertaining to the constitution. [EU]

Constriction: The act of constricting. [NIH]

Consultation: A deliberation between two or more physicians concerning the diagnosis and the proper method of treatment in a case. [NIH]

Contamination: The soiling or pollution by inferior material, as by the introduction of organisms into a wound, or sewage into a stream. [EU]

Contraindications: Any factor or sign that it is unwise to pursue a certain kind of action or treatment, e. g. giving a general anesthetic to a person with pneumonia. [NIH]

Control group: In a clinical trial, the group that does not receive the new treatment being studied. This group is compared to the group that receives the new treatment, to see if the new treatment works. [NIH]

Convulsion: A violent involuntary contraction or series of contractions of the voluntary muscles. [EU]

Coronary: Encircling in the manner of a crown; a term applied to vessels; nerves, ligaments, etc. The term usually denotes the arteries that supply the heart muscle and, by extension, a pathologic involvement of them. [EU]

Coronary heart disease: A type of heart disease caused by narrowing of the coronary arteries that feed the heart, which needs a constant supply of oxygen and nutrients carried by the blood in the coronary arteries. When the coronary arteries become narrowed or clogged by fat and cholesterol deposits and cannot supply enough blood to the heart, CHD results. [NIH]

Coronary Thrombosis: Presence of a thrombus in a coronary artery, often causing a myocardial infarction. [NIH]

Cortex: The outer layer of an organ or other body structure, as distinguished from the internal substance. [EU]

Cortisol: A steroid hormone secreted by the adrenal cortex as part of the body's response to stress. [NIH]

Cost Savings: Reductions in all or any portion of the costs of providing goods or services. Savings may be incurred by the provider or the consumer. [NIH]

Cross-Sectional Studies: Studies in which the presence or absence of disease or other health-related variables are determined in each member of the study population or in a

representative sample at one particular time. This contrasts with longitudinal studies which are followed over a period of time. [NIH]

Crowns: A prosthetic restoration that reproduces the entire surface anatomy of the visible natural crown of a tooth. It may be partial (covering three or more surfaces of a tooth) or complete (covering all surfaces). It is made of gold or other metal, porcelain, or resin. [NIH]

Cryptosporidiosis: Parasitic intestinal infection with severe diarrhea caused by a protozoan, Cryptosporidium. It occurs in both animals and humans. [NIH]

Cues: Signals for an action; that specific portion of a perceptual field or pattern of stimuli to which a subject has learned to respond. [NIH]

Curative: Tending to overcome disease and promote recovery. [EU]

Cutaneous: Having to do with the skin. [NIH]

Cysteine: A thiol-containing non-essential amino acid that is oxidized to form cystine. [NIH]

Cystine: A covalently linked dimeric nonessential amino acid formed by the oxidation of cysteine. Two molecules of cysteine are joined together by a disulfide bridge to form cystine. [NIH]

Cytogenetics: A branch of genetics which deals with the cytological and molecular behavior of genes and chromosomes during cell division. [NIH]

Cytokines: Non-antibody proteins secreted by inflammatory leukocytes and some non-leukocytic cells, that act as intercellular mediators. They differ from classical hormones in that they are produced by a number of tissue or cell types rather than by specialized glands. They generally act locally in a paracrine or autocrine rather than endocrine manner. [NIH]

Cytoplasm: The protoplasm of a cell exclusive of that of the nucleus; it consists of a continuous aqueous solution (cytosol) and the organelles and inclusions suspended in it (phaneroplasm), and is the site of most of the chemical activities of the cell. [EU]

Cytotoxic: Cell-killing. [NIH]

Cytotoxicity: Quality of being capable of producing a specific toxic action upon cells of special organs. [NIH]

Data Collection: Systematic gathering of data for a particular purpose from various sources, including questionnaires, interviews, observation, existing records, and electronic devices. The process is usually preliminary to statistical analysis of the data. [NIH]

Deamination: The removal of an amino group (NH2) from a chemical compound. [NIH]

Degenerative: Undergoing degeneration : tending to degenerate; having the character of or involving degeneration; causing or tending to cause degeneration. [EU]

Dehydration: The condition that results from excessive loss of body water. [NIH]

Denaturation: Rupture of the hydrogen bonds by heating a DNA solution and then cooling it rapidly causes the two complementary strands to separate. [NIH]

Density: The logarithm to the base 10 of the opacity of an exposed and processed film. [NIH]

Dental Abutments: Natural teeth or teeth roots used as anchorage for a fixed or removable denture or other prosthesis (such as an implant) serving the same purpose. [NIH]

Dental Amalgam: An alloy used in restorative dentistry that contains mercury, silver, tin, copper, and possibly zinc. [NIH]

Dental Care: The total of dental diagnostic, preventive, and restorative services provided to meet the needs of a patient (from Illustrated Dictionary of Dentistry, 1982). [NIH]

Dental Health Services: Services designed to promote, maintain, or restore dental health. [NIH]

Dental Hygienists: Persons trained in an accredited school or dental college and licensed by the state in which they reside to provide dental prophylaxis under the direction of a licensed dentist. [NIH]

Dental Materials: Materials used in the production of dental bases, restorations, impressions, prostheses, etc. [NIH]

Dental Plaque: A film that attaches to teeth, often causing dental caries and gingivitis. It is composed of mucins, secreted from salivary glands, and microorganisms. [NIH]

Dental Polishing: Creation of a smooth and glossy surface finish on a denture or amalgam. [NIH]

Dental Prophylaxis: Treatment for the prevention of periodontal diseases or other dental diseases by the cleaning of the teeth in the dental office using the procedures of dental scaling and dental polishing. The treatment may include plaque detection, removal of supra- and subgingival plaque and calculus, application of caries-preventing agents, checking of restorations and prostheses and correcting overhanging margins and proximal contours of restorations, and checking for signs of food impaction. [NIH]

Dental Scaling: Removal of dental plaque and dental calculus from the surface of a tooth, from the surface of a tooth apical to the gingival margin accumulated in periodontal pockets, or from the surface coronal to the gingival margin. [NIH]

Dentifrices: Any preparations used for cleansing teeth; they usually contain an abrasive, detergent, binder and flavoring agent and may exist in the form of liquid, paste or powder; may also contain medicaments and caries preventives. [NIH]

Dentists: Individuals licensed to practice dentistry. [NIH]

Dentition: The teeth in the dental arch; ordinarily used to designate the natural teeth in position in their alveoli. [EU]

Dentures: An appliance used as an artificial or prosthetic replacement for missing teeth and adjacent tissues. It does not include crowns, dental abutments, nor artificial teeth. [NIH]

Deprivation: Loss or absence of parts, organs, powers, or things that are needed. [EU]

Dermal: Pertaining to or coming from the skin. [NIH]

Desensitization: The prevention or reduction of immediate hypersensitivity reactions by administration of graded doses of allergen; called also hyposensitization and immunotherapy. [EU]

Detoxification: Treatment designed to free an addict from his drug habit. [EU]

Developing Countries: Countries in the process of change directed toward economic growth, that is, an increase in production, per capita consumption, and income. The process of economic growth involves better utilization of natural and human resources, which results in a change in the social, political, and economic structures. [NIH]

Dextrans: A group of glucose polymers made by certain bacteria. Dextrans are used therapeutically as plasma volume expanders and anticoagulants. They are also commonly used in biological experimentation and in industry for a wide variety of purposes. [NIH]

Diabetes Mellitus: A heterogeneous group of disorders that share glucose intolerance in common. [NIH]

Diagnostic procedure: A method used to identify a disease. [NIH]

Diarrhea: Passage of excessively liquid or excessively frequent stools. [NIH]

Diastolic: Of or pertaining to the diastole. [EU]

Dietary Sucrose: Sucrose present in the diet. It is added to food and drinks as a sweetener. [NIH]

Diffusion: The tendency of a gas or solute to pass from a point of higher pressure or concentration to a point of lower pressure or concentration and to distribute itself throughout the available space; a major mechanism of biological transport. [NIH]

Digestion: The process of breakdown of food for metabolism and use by the body. [NIH]

Dilution: A diluted or attenuated medicine; in homeopathy, the diffusion of a given quantity of a medicinal agent in ten or one hundred times the same quantity of water. [NIH]

Diploid: Having two sets of chromosomes. [NIH]

Direct: 1. Straight; in a straight line. 2. Performed immediately and without the intervention of subsidiary means. [EU]

Discrete: Made up of separate parts or characterized by lesions which do not become blended; not running together; separate. [NIH]

Disinfectant: An agent that disinfects; applied particularly to agents used on inanimate objects. [EU]

Disparity: Failure of the two retinal images of an object to fall on corresponding retinal points. [NIH]

Dissociation: 1. The act of separating or state of being separated. 2. The separation of a molecule into two or more fragments (atoms, molecules, ions, or free radicals) produced by the absorption of light or thermal energy or by solvation. 3. In psychology, a defense mechanism in which a group of mental processes are segregated from the rest of a person's mental activity in order to avoid emotional distress, as in the dissociative disorders (q.v.), or in which an idea or object is segregated from its emotional significance; in the first sense it is roughly equivalent to splitting, in the second, to isolation. 4. A defect of mental integration in which one or more groups of mental processes become separated off from normal consciousness and, thus separated, function as a unitary whole. [EU]

Distal: Remote; farther from any point of reference; opposed to proximal. In dentistry, used to designate a position on the dental arch farther from the median line of the jaw. [EU]

Diuretic: A drug that increases the production of urine. [NIH]

Dominance: In genetics, the full phenotypic expression of a gene in both heterozygotes and homozygotes. [EU]

Drive: A state of internal activity of an organism that is a necessary condition before a given stimulus will elicit a class of responses; e.g., a certain level of hunger (drive) must be present before food will elicit an eating response. [NIH]

Dross: Residue remaining in an opium pipe which has been smoked; contains 50 % of the morphine present in the original drug. [NIH]

Drug Interactions: The action of a drug that may affect the activity, metabolism, or toxicity of another drug. [NIH]

Drug Tolerance: Progressive diminution of the susceptibility of a human or animal to the effects of a drug, resulting from its continued administration. It should be differentiated from drug resistance wherein an organism, disease, or tissue fails to respond to the intended effectiveness of a chemical or drug. It should also be differentiated from maximum tolerated dose and no-observed-adverse-effect level. [NIH]

Duct: A tube through which body fluids pass. [NIH]

Duodenum: The first part of the small intestine. [NIH]

Dura mater: The outermost, toughest, and most fibrous of the three membranes (meninges) covering the brain and spinal cord; called also pachymeninx. [EU]

Dysentery: Any of various disorders marked by inflammation of the intestines, especially of

the colon, and attended by pain in the abdomen, tenesmus, and frequent stools containing blood and mucus. Causes include chemical irritants, bacteria, protozoa, or parasitic worms. [EU]

Ecosystem: A dynamic complex of plant, animal and micro-organism communities and their non-living environment interacting as a functional unit. [NIH]

Effector: It is often an enzyme that converts an inactive precursor molecule into an active second messenger. [NIH]

Efficacy: The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions. Ideally, the determination of efficacy is based on the results of a randomized control trial. [NIH]

Egg Yolk: Cytoplasm stored in an egg that contains nutritional reserves for the developing embryo. It is rich in polysaccharides, lipids, and proteins. [NIH]

Elastic: Susceptible of resisting and recovering from stretching, compression or distortion applied by a force. [EU]

Elasticity: Resistance and recovery from distortion of shape. [NIH]

Elastin: The protein that gives flexibility to tissues. [NIH]

Electric Conductivity: The ability of a substrate to allow the passage of electrons. [NIH]

Electrode: Component of the pacing system which is at the distal end of the lead. It is the interface with living cardiac tissue across which the stimulus is transmitted. [NIH]

Electrolysis: Destruction by passage of a galvanic electric current, as in disintegration of a chemical compound in solution. [NIH]

Electrolyte: A substance that dissociates into ions when fused or in solution, and thus becomes capable of conducting electricity; an ionic solute. [EU]

Electron microscope: A microscope (device used to magnify small objects) that uses electrons (instead of light) to produce an enlarged image. An electron microscopes shows tiny details better than any other type of microscope. [NIH]

Electrons: Stable elementary particles having the smallest known negative charge, present in all elements; also called negatrons. Positively charged electrons are called positrons. The numbers, energies and arrangement of electrons around atomic nuclei determine the chemical identities of elements. Beams of electrons are called cathode rays or beta rays, the latter being a high-energy biproduct of nuclear decay. [NIH]

Electrophoresis: An electrochemical process in which macromolecules or colloidal particles with a net electric charge migrate in a solution under the influence of an electric current. [NIH]

Embryo: The prenatal stage of mammalian development characterized by rapid morphological changes and the differentiation of basic structures. [NIH]

Emollient: Softening or soothing; called also malactic. [EU]

Emphysema: A pathological accumulation of air in tissues or organs. [NIH]

Emulsion: A preparation of one liquid distributed in small globules throughout the body of a second liquid. The dispersed liquid is the discontinuous phase, and the dispersion medium is the continuous phase. When oil is the dispersed liquid and an aqueous solution is the continuous phase, it is known as an oil-in-water emulsion, whereas when water or aqueous solution is the dispersed phase and oil or oleaginous substance is the continuous phase, it is known as a water-in-oil emulsion. Pharmaceutical emulsions for which official standards have been promulgated include cod liver oil emulsion, cod liver oil emulsion with malt, liquid petrolatum emulsion, and phenolphthalein in liquid petrolatum emulsion. [EU]

Enamel: A very hard whitish substance which covers the dentine of the anatomical crown of a tooth. [NIH]

Encephalitis: Inflammation of the brain due to infection, autoimmune processes, toxins, and other conditions. Viral infections (see encephalitis, viral) are a relatively frequent cause of this condition. [NIH]

Encephalitis, Viral: Inflammation of brain parenchymal tissue as a result of viral infection. Encephalitis may occur as primary or secondary manifestation of Togaviridae infections; Herpesviridae infections; Adenoviridae infections; Flaviviridae infections; Bunyaviridae infections; Picornaviridae infections; Paramyxoviridae infections; Orthomyxoviridae infections; Retroviridae infections; and Arenaviridae infections. [NIH]

Endemic: Present or usually prevalent in a population or geographical area at all times; said of a disease or agent. Called also endemial. [EU]

Endocarditis: Exudative and proliferative inflammatory alterations of the endocardium, characterized by the presence of vegetations on the surface of the endocardium or in the endocardium itself, and most commonly involving a heart valve, but sometimes affecting the inner lining of the cardiac chambers or the endocardium elsewhere. It may occur as a primary disorder or as a complication of or in association with another disease. [EU]

Endocardium: The innermost layer of the heart, comprised of endothelial cells. [NIH]

Endothelial cell: The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart. [NIH]

Environmental Health: The science of controlling or modifying those conditions, influences, or forces surrounding man which relate to promoting, establishing, and maintaining health. [NIH]

Enzymatic: Phase where enzyme cuts the precursor protein. [NIH]

Enzyme: A protein that speeds up chemical reactions in the body. [NIH]

Enzyme Inhibitors: Compounds or agents that combine with an enzyme in such a manner as to prevent the normal substrate-enzyme combination and the catalytic reaction. [NIH]

Eosinophils: Granular leukocytes with a nucleus that usually has two lobes connected by a slender thread of chromatin, and cytoplasm containing coarse, round granules that are uniform in size and stainable by eosin. [NIH]

Epidemiologic Studies: Studies designed to examine associations, commonly, hypothesized causal relations. They are usually concerned with identifying or measuring the effects of risk factors or exposures. The common types of analytic study are case-control studies, cohort studies, and cross-sectional studies. [NIH]

Epidemiological: Relating to, or involving epidemiology. [EU]

Epidermal: Pertaining to or resembling epidermis. Called also epidermic or epidermoid. [EU]

Epidermis: Nonvascular layer of the skin. It is made up, from within outward, of five layers: 1) basal layer (stratum basale epidermidis); 2) spinous layer (stratum spinosum epidermidis); 3) granular layer (stratum granulosum epidermidis); 4) clear layer (stratum lucidum epidermidis); and 5) horny layer (stratum corneum epidermidis). [NIH]

Epithelial: Refers to the cells that line the internal and external surfaces of the body. [NIH]

Epithelial Cells: Cells that line the inner and outer surfaces of the body. [NIH]

Epitopes: Sites on an antigen that interact with specific antibodies. [NIH]

Erythrocytes: Red blood cells. Mature erythrocytes are non-nucleated, biconcave disks containing hemoglobin whose function is to transport oxygen. [NIH]

Esophageal: Having to do with the esophagus, the muscular tube through which food passes from the throat to the stomach. [NIH]

Esophagus: The muscular tube through which food passes from the throat to the stomach. [NIH]

Ethanol: A clear, colorless liquid rapidly absorbed from the gastrointestinal tract and distributed throughout the body. It has bactericidal activity and is used often as a topical disinfectant. It is widely used as a solvent and preservative in pharmaceutical preparations as well as serving as the primary ingredient in alcoholic beverages. [NIH]

Eukaryotic Cells: Cells of the higher organisms, containing a true nucleus bounded by a nuclear membrane. [NIH]

Evoke: The electric response recorded from the cerebral cortex after stimulation of a peripheral sense organ. [NIH]

Exfoliation: A falling off in scales or layers. [EU]

Exogenous: Developed or originating outside the organism, as exogenous disease. [EU]

Expander: Any of several colloidal substances of high molecular weight. used as a blood or plasma substitute in transfusion for increasing the volume of the circulating blood. called also extender. [NIH]

Expectorant: 1. Promoting the ejection, by spitting, of mucus or other fluids from the lungs and trachea. 2. An agent that promotes the ejection of mucus or exudate from the lungs, bronchi, and trachea; sometimes extended to all remedies that quiet cough (antitussives). [EU]

External-beam radiation: Radiation therapy that uses a machine to aim high-energy rays at the cancer. Also called external radiation. [NIH]

Extracellular: Outside a cell or cells. [EU]

Extracellular Matrix: A meshwork-like substance found within the extracellular space and in association with the basement membrane of the cell surface. It promotes cellular proliferation and provides a supporting structure to which cells or cell lysates in culture dishes adhere. [NIH]

Extracellular Matrix Proteins: Macromolecular organic compounds that contain carbon, hydrogen, oxygen, nitrogen, and usually, sulfur. These macromolecules (proteins) form an intricate meshwork in which cells are embedded to construct tissues. Variations in the relative types of macromolecules and their organization determine the type of extracellular matrix, each adapted to the functional requirements of the tissue. The two main classes of macromolecules that form the extracellular matrix are: glycosaminoglycans, usually linked to proteins (proteoglycans), and fibrous proteins (e.g., collagen, elastin, fibronectins and laminin). [NIH]

Extracellular Space: Interstitial space between cells, occupied by fluid as well as amorphous and fibrous substances. [NIH]

Extraction: The process or act of pulling or drawing out. [EU]

Facial: Of or pertaining to the face. [EU]

Facial Nerve: The 7th cranial nerve. The facial nerve has two parts, the larger motor root which may be called the facial nerve proper, and the smaller intermediate or sensory root. Together they provide efferent innervation to the muscles of facial expression and to the lacrimal and salivary glands, and convey afferent information for taste from the anterior two-thirds of the tongue and for touch from the external ear. [NIH]

Family Planning: Programs or services designed to assist the family in controlling reproduction by either improving or diminishing fertility. [NIH]

Fat: Total lipids including phospholipids. [NIH]

Fathers: Male parents, human or animal. [NIH]

Fermentation: An enzyme-induced chemical change in organic compounds that takes place in the absence of oxygen. The change usually results in the production of ethanol or lactic acid, and the production of energy. [NIH]

Fertilizers: Substances or mixtures that are added to the soil to supply nutrients or to make available nutrients already present in the soil, in order to increase plant growth and productivity. [NIH]

Fetus: The developing offspring from 7 to 8 weeks after conception until birth. [NIH]

Fibril: Most bacterial viruses have a hollow tail with specialized fibrils at its tip. The tail fibers attach to the cell wall of the host. [NIH]

Fibrinogen: Plasma glycoprotein clotted by thrombin, composed of a dimer of three non-identical pairs of polypeptide chains (alpha, beta, gamma) held together by disulfide bonds. Fibrinogen clotting is a sol-gel change involving complex molecular arrangements: whereas fibrinogen is cleaved by thrombin to form polypeptides A and B, the proteolytic action of other enzymes yields different fibrinogen degradation products. [NIH]

Fibronectin: An adhesive glycoprotein. One form circulates in plasma, acting as an opsonin; another is a cell-surface protein which mediates cellular adhesive interactions. [NIH]

Fibrosis: Any pathological condition where fibrous connective tissue invades any organ, usually as a consequence of inflammation or other injury. [NIH]

Filler: An inactive substance used to make a product bigger or easier to handle. For example, fillers are often used to make pills or capsules because the amount of active drug is too small to be handled conveniently. [NIH]

Fissure: Any cleft or groove, normal or otherwise; especially a deep fold in the cerebral cortex which involves the entire thickness of the brain wall. [EU]

Flatus: Gas passed through the rectum. [NIH]

Flexor: Muscles which flex a joint. [NIH]

Fluorescence: The property of emitting radiation while being irradiated. The radiation emitted is usually of longer wavelength than that incident or absorbed, e.g., a substance can be irradiated with invisible radiation and emit visible light. X-ray fluorescence is used in diagnosis. [NIH]

Fluoridation: The addition of fluorine usually as a fluoride to something, as the adding of a fluoride to drinking water or public water supplies for prevention of tooth decay in children. [NIH]

Fluorine: A nonmetallic, diatomic gas that is a trace element and member of the halogen family. It is used in dentistry as flouride to prevent dental caries. [NIH]

Fluorosis: Discoloration of the tooth enamel due to fluorine. [NIH]

Flush: Transient, episodic redness of the face and neck caused by certain diseases, ingestion of certain drugs or other substances, heat, emotional factors, or physical exertion. [EU]

Focus Groups: A method of data collection and a qualitative research tool in which a small group of individuals are brought together and allowed to interact in a discussion of their opinions about topics, issues, or questions. [NIH]

Fold: A plication or doubling of various parts of the body. [NIH]

Food Preservatives: Substances capable of inhibiting, retarding or arresting the process of fermentation, acidification or other deterioration of foods. [NIH]

Forearm: The part between the elbow and the wrist. [NIH]

Fractionation: Dividing the total dose of radiation therapy into several smaller, equal doses delivered over a period of several days. [NIH]

Free Radicals: Highly reactive molecules with an unsatisfied electron valence pair. Free radicals are produced in both normal and pathological processes. They are proven or suspected agents of tissue damage in a wide variety of circumstances including radiation, damage from environment chemicals, and aging. Natural and pharmacological prevention of free radical damage is being actively investigated. [NIH]

Frontal Sinus: One of the paired, but seldom symmetrical, air spaces located between the inner and outer compact layers of the frontal bone. [NIH]

Fructans: Polysaccharides composed of D-fructose units. [NIH]

Fungi: A kingdom of eukaryotic, heterotrophic organisms that live as saprobes or parasites, including mushrooms, yeasts, smuts, molds, etc. They reproduce either sexually or asexually, and have life cycles that range from simple to complex. Filamentous fungi refer to those that grow as multicelluar colonies (mushrooms and molds). [NIH]

Fungus: A general term used to denote a group of eukaryotic protists, including mushrooms, yeasts, rusts, moulds, smuts, etc., which are characterized by the absence of chlorophyll and by the presence of a rigid cell wall composed of chitin, mannans, and sometimes cellulose. They are usually of simple morphological form or show some reversible cellular specialization, such as the formation of pseudoparenchymatous tissue in the fruiting body of a mushroom. The dimorphic fungi grow, according to environmental conditions, as moulds or yeasts. [EU]

Galactosides: Glycosides formed by the reaction of the hydroxyl group on the anomeric carbon atom of galactose with an alcohol to form an acetal. They include both alpha- and beta-galactosides. [NIH]

Gamma Rays: Very powerful and penetrating, high-energy electromagnetic radiation of shorter wavelength than that of x-rays. They are emitted by a decaying nucleus, usually between 0.01 and 10 MeV. They are also called nuclear x-rays. [NIH]

Ganglia: Clusters of multipolar neurons surrounded by a capsule of loosely organized connective tissue located outside the central nervous system. [NIH]

Gangrenous: A circumscribed, deep-seated, suppurative inflammation of the subcutaneous tissue of the eyelid discharging pus from several points. [NIH]

Gas: Air that comes from normal breakdown of food. The gases are passed out of the body through the rectum (flatus) or the mouth (burp). [NIH]

Gastrectomy: An operation to remove all or part of the stomach. [NIH]

Gastric: Having to do with the stomach. [NIH]

Gastric Acid: Hydrochloric acid present in gastric juice. [NIH]

Gastritis: Inflammation of the stomach. [EU]

Gastroenteritis: An acute inflammation of the lining of the stomach and intestines, characterized by anorexia, nausea, diarrhoea, abdominal pain, and weakness, which has various causes, including food poisoning due to infection with such organisms as Escherichia coli, Staphylococcus aureus, and Salmonella species; consumption of irritating food or drink; or psychological factors such as anger, stress, and fear. Called also enterogastritis. [EU]

Gastrointestinal: Refers to the stomach and intestines. [NIH]

Gastrointestinal tract: The stomach and intestines. [NIH]

Gels: Colloids with a solid continuous phase and liquid as the dispersed phase; gels may be unstable when, due to temperature or other cause, the solid phase liquifies; the resulting colloid is called a sol. [NIH]

Gene: The functional and physical unit of heredity passed from parent to offspring. Genes are pieces of DNA, and most genes contain the information for making a specific protein. [NIH]

Gene Expression: The phenotypic manifestation of a gene or genes by the processes of gene action. [NIH]

Gene Expression Profiling: The determination of the pattern of genes expressed i.e., transcribed, under specific circumstances or in a specific cell. [NIH]

Gene Fusion: Fusion of structural genes to analyze protein behavior or fusion of regulatory sequences with structural genes to determine mechanisms of regulation. [NIH]

Gene Therapy: The introduction of new genes into cells for the purpose of treating disease by restoring or adding gene expression. Techniques include insertion of retroviral vectors, transfection, homologous recombination, and injection of new genes into the nuclei of single cell embryos. The entire gene therapy process may consist of multiple steps. The new genes may be introduced into proliferating cells in vivo (e.g., bone marrow) or in vitro (e.g., fibroblast cultures) and the modified cells transferred to the site where the gene expression is required. Gene therapy may be particularly useful for treating enzyme deficiency diseases, hemoglobinopathies, and leukemias and may also prove useful in restoring drug sensitivity, particularly for leukemia. [NIH]

Genetic Code: The specifications for how information, stored in nucleic acid sequence (base sequence), is translated into protein sequence (amino acid sequence). The start, stop, and order of amino acids of a protein is specified by consecutive triplets of nucleotides called codons (codon). [NIH]

Genetic Engineering: Directed modification of the gene complement of a living organism by such techniques as altering the DNA, substituting genetic material by means of a virus, transplanting whole nuclei, transplanting cell hybrids, etc. [NIH]

Genetic Markers: A phenotypically recognizable genetic trait which can be used to identify a genetic locus, a linkage group, or a recombination event. [NIH]

Genetic Techniques: Chromosomal, biochemical, intracellular, and other methods used in the study of genetics. [NIH]

Genetic testing: Analyzing DNA to look for a genetic alteration that may indicate an increased risk for developing a specific disease or disorder. [NIH]

Genetics: The biological science that deals with the phenomena and mechanisms of heredity. [NIH]

Genomics: The systematic study of the complete DNA sequences (genome) of organisms. [NIH]

Genotype: The genetic constitution of the individual; the characterization of the genes. [NIH]

Germfree: Free from all living micro-organisms. [NIH]

Gingivitis: Inflammation of the gingivae. Gingivitis associated with bony changes is referred to as periodontitis. Called also oulitis and ulitis. [EU]

Gland: An organ that produces and releases one or more substances for use in the body. Some glands produce fluids that affect tissues or organs. Others produce hormones or participate in blood production. [NIH]

Glomerular: Pertaining to or of the nature of a glomerulus, especially a renal glomerulus. [EU]

Glomerular Filtration Rate: The volume of water filtered out of plasma through glomerular capillary walls into Bowman's capsules per unit of time. It is considered to be equivalent to inulin clearance. [NIH]

Glucans: Polysaccharides composed of repeating glucose units. They can consist of branched or unbranched chains in any linkages. [NIH]

Glucose: D-Glucose. A primary source of energy for living organisms. It is naturally occurring and is found in fruits and other parts of plants in its free state. It is used therapeutically in fluid and nutrient replacement. [NIH]

Glucose Intolerance: A pathological state in which the fasting plasma glucose level is less than 140 mg per deciliter and the 30-, 60-, or 90-minute plasma glucose concentration following a glucose tolerance test exceeds 200 mg per deciliter. This condition is seen frequently in diabetes mellitus but also occurs with other diseases. [NIH]

Glucosyltransferases: Enzymes that catalyze the transfer of glucose from a nucleoside diphosphate glucose to an acceptor molecule which is frequently another carbohydrate. EC 2.4.1.-. [NIH]

Glutamic Acid: A non-essential amino acid naturally occurring in the L-form. Glutamic acid (glutamate) is the most common excitatory neurotransmitter in the central nervous system. [NIH]

Glycerol: A trihydroxy sugar alcohol that is an intermediate in carbohydrate and lipid metabolism. It is used as a solvent, emollient, pharmaceutical agent, and sweetening agent. [NIH]

Glycine: A non-essential amino acid. It is found primarily in gelatin and silk fibroin and used therapeutically as a nutrient. It is also a fast inhibitory neurotransmitter. [NIH]

Glycogen: A sugar stored in the liver and muscles. It releases glucose into the blood when cells need it for energy. Glycogen is the chief source of stored fuel in the body. [NIH]

Glycogen Synthase: An enzyme that catalyzes the transfer of D-glucose from UDPglucose into 1,4-alpha-D-glucosyl chains. EC 2.4.1.11. [NIH]

Glycoprotein: A protein that has sugar molecules attached to it. [NIH]

Glycosidic: Formed by elimination of water between the anomeric hydroxyl of one sugar and a hydroxyl of another sugar molecule. [NIH]

Goniometer: An instrument for measuring angles, such as those of crystals and prisms. [NIH]

Governing Board: The group in which legal authority is vested for the control of health-related institutions and organizations. [NIH]

Grade: The grade of a tumor depends on how abnormal the cancer cells look under a microscope and how quickly the tumor is likely to grow and spread. Grading systems are different for each type of cancer. [NIH]

Grading: A system for classifying cancer cells in terms of how abnormal they appear when examined under a microscope. The objective of a grading system is to provide information about the probable growth rate of the tumor and its tendency to spread. The systems used to grade tumors vary with each type of cancer. Grading plays a role in treatment decisions. [NIH]

Graft: Healthy skin, bone, or other tissue taken from one part of the body and used to replace diseased or injured tissue removed from another part of the body. [NIH]

Graft vs Host Reaction: An immunological attack mounted by a graft against the host because of tissue incompatibility when immunologically competent cells are transplanted to an immunologically incompetent host; the resulting clinical picture is that of graft vs host disease. [NIH]

Grafting: The operation of transfer of tissue from one site to another. [NIH]

Gram-negative: Losing the stain or decolorized by alcohol in Gram's method of staining, a primary characteristic of bacteria having a cell wall composed of a thin layer of peptidoglycan covered by an outer membrane of lipoprotein and lipopolysaccharide. [EU]

Gram-Negative Bacteria: Bacteria which lose crystal violet stain but are stained pink when treated by Gram's method. [NIH]

Gram-positive: Retaining the stain or resisting decolorization by alcohol in Gram's method of staining, a primary characteristic of bacteria whose cell wall is composed of a thick layer of peptidologlycan with attached teichoic acids. [EU]

Granulocytes: Leukocytes with abundant granules in the cytoplasm. They are divided into three groups: neutrophils, eosinophils, and basophils. [NIH]

Granulomas: Small lumps in tissues caused by inflammation. [NIH]

Growth factors: Substances made by the body that function to regulate cell division and cell survival. Some growth factors are also produced in the laboratory and used in biological therapy. [NIH]

Halitosis: An offensive, foul breath odor resulting from a variety of causes such as poor oral hygiene, dental or oral infections, or the ingestion of certain foods. [NIH]

Haploid: An organism with one basic chromosome set, symbolized by n; the normal condition of gametes in diploids. [NIH]

Haptens: Small antigenic determinants capable of eliciting an immune response only when coupled to a carrier. Haptens bind to antibodies but by themselves cannot elicit an antibody response. [NIH]

Hay Fever: A seasonal variety of allergic rhinitis, marked by acute conjunctivitis with lacrimation and itching, regarded as an allergic condition triggered by specific allergens. [NIH]

Health Behavior: Behaviors expressed by individuals to protect, maintain or promote their health status. For example, proper diet, and appropriate exercise are activities perceived to influence health status. Life style is closely associated with health behavior and factors influencing life style are socioeconomic, educational, and cultural. [NIH]

Health Education: Education that increases the awareness and favorably influences the attitudes and knowledge relating to the improvement of health on a personal or community basis. [NIH]

Health Status: The level of health of the individual, group, or population as subjectively assessed by the individual or by more objective measures. [NIH]

Health Surveys: A systematic collection of factual data pertaining to health and disease in a human population within a given geographic area. [NIH]

Heart attack: A seizure of weak or abnormal functioning of the heart. [NIH]

Hemoglobin: One of the fractions of glycosylated hemoglobin A1c. Glycosylated hemoglobin is formed when linkages of glucose and related monosaccharides bind to hemoglobin A and its concentration represents the average blood glucose level over the previous several weeks. HbA1c levels are used as a measure of long-term control of plasma glucose (normal, 4 to 6 percent). In controlled diabetes mellitus, the concentration of glycosylated hemoglobin A is within the normal range, but in uncontrolled cases the level may be 3 to 4 times the normal conentration. Generally, complications are substantially lower among patients with Hb levels of 7 percent or less than in patients with HbA1c levels of 9 percent or more. [NIH]

Hemoglobinopathies: A group of inherited disorders characterized by structural alterations within the hemoglobin molecule. [NIH]

Hemolytic: A disease that affects the blood and blood vessels. It destroys red blood cells, cells that cause the blood to clot, and the lining of blood vessels. HUS is often caused by the Escherichia coli bacterium in contaminated food. People with HUS may develop acute renal failure. [NIH]

Hemorrhage: Bleeding or escape of blood from a vessel. [NIH]

Hepatic: Refers to the liver. [NIH]

Hereditary: Of, relating to, or denoting factors that can be transmitted genetically from one generation to another. [NIH]

Heredity: 1. The genetic transmission of a particular quality or trait from parent to offspring. 2. The genetic constitution of an individual. [EU]

Heterogeneity: The property of one or more samples or populations which implies that they are not identical in respect of some or all of their parameters, e. g. heterogeneity of variance. [NIH]

Heterotrophic: Pertaining to organisms that are consumers and dependent on other organisms for their source of energy (food). [NIH]

Heterozygotes: Having unlike alleles at one or more corresponding loci on homologous chromosomes. [NIH]

Histology: The study of tissues and cells under a microscope. [NIH]

Homeostasis: The processes whereby the internal environment of an organism tends to remain balanced and stable. [NIH]

Homologous: Corresponding in structure, position, origin, etc., as (a) the feathers of a bird and the scales of a fish, (b) antigen and its specific antibody, (c) allelic chromosomes. [EU]

Homozygotes: An individual having a homozygous gene pair. [NIH]

Hormonal: Pertaining to or of the nature of a hormone. [EU]

Hormone: A substance in the body that regulates certain organs. Hormones such as gastrin help in breaking down food. Some hormones come from cells in the stomach and small intestine. [NIH]

Humoral: Of, relating to, proceeding from, or involving a bodily humour - now often used of endocrine factors as opposed to neural or somatic. [EU]

Hybrid: Cross fertilization between two varieties or, more usually, two species of vines, see also crossing. [NIH]

Hybridomas: Cells artificially created by fusion of activated lymphocytes with neoplastic cells. The resulting hybrid cells are cloned and produce pure or "monoclonal" antibodies or T-cell products, identical to those produced by the immunologically competent parent, and continually grow and divide as the neoplastic parent. [NIH]

Hydrogel: A network of cross-linked hydrophilic macromolecules used in biomedical applications. [NIH]

Hydrogen: The first chemical element in the periodic table. It has the atomic symbol H, atomic number 1, and atomic weight 1. It exists, under normal conditions, as a colorless, odorless, tasteless, diatomic gas. Hydrogen ions are protons. Besides the common H1 isotope, hydrogen exists as the stable isotope deuterium and the unstable, radioactive isotope tritium. [NIH]

Hydrolysis: The process of cleaving a chemical compound by the addition of a molecule of

water. [NIH]

Hydroxylysine: A hydroxylated derivative of the amino acid lysine that is present in certain collagens. [NIH]

Hydroxyproline: A hydroxylated form of the imino acid proline. A deficiency in ascorbic acid can result in impaired hydroxyproline formation. [NIH]

Hygienic: Pertaining to hygiene, or conducive to health. [EU]

Hyperplasia: An increase in the number of cells in a tissue or organ, not due to tumor formation. It differs from hypertrophy, which is an increase in bulk without an increase in the number of cells. [NIH]

Hyperreflexia: Exaggeration of reflexes. [EU]

Hypersensitivity: Altered reactivity to an antigen, which can result in pathologic reactions upon subsequent exposure to that particular antigen. [NIH]

Hypertension: Persistently high arterial blood pressure. Currently accepted threshold levels are 140 mm Hg systolic and 90 mm Hg diastolic pressure. [NIH]

Hypoplasia: Incomplete development or underdevelopment of an organ or tissue. [EU]

Ice Cream: A frozen dairy food made from cream or butterfat, milk, sugar, and flavorings. Frozen custard and French-type ice creams also contain eggs. [NIH]

Idiopathic: Describes a disease of unknown cause. [NIH]

Immune function: Production and action of cells that fight disease or infection. [NIH]

Immune response: The activity of the immune system against foreign substances (antigens). [NIH]

Immune Sera: Serum that contains antibodies. It is obtained from an animal that has been immunized either by antigen injection or infection with microorganisms containing the antigen. [NIH]

Immune system: The organs, cells, and molecules responsible for the recognition and disposal of foreign ("non-self") material which enters the body. [NIH]

Immunization: Deliberate stimulation of the host's immune response. Active immunization involves administration of antigens or immunologic adjuvants. Passive immunization involves administration of immune sera or lymphocytes or their extracts (e.g., transfer factor, immune RNA) or transplantation of immunocompetent cell producing tissue (thymus or bone marrow). [NIH]

Immunocompromised: Having a weakened immune system caused by certain diseases or treatments. [NIH]

Immunogen: A substance that is capable of causing antibody formation. [NIH]

Immunogenetics: A branch of genetics which deals with the genetic basis of the immune response. [NIH]

Immunogenic: Producing immunity; evoking an immune response. [EU]

Immunoglobulin: A protein that acts as an antibody. [NIH]

Immunologic: The ability of the antibody-forming system to recall a previous experience with an antigen and to respond to a second exposure with the prompt production of large amounts of antibody. [NIH]

Immunologic Diseases: Disorders caused by abnormal or absent immunologic mechanisms, whether humoral, cell-mediated or both. [NIH]

Immunology: The study of the body's immune system. [NIH]

Immunosuppression: Deliberate prevention or diminution of the host's immune response. It may be nonspecific as in the administration of immunosuppressive agents (drugs or radiation) or by lymphocyte depletion or may be specific as in desensitization or the simultaneous administration of antigen and immunosuppressive drugs. [NIH]

Immunotherapy: Manipulation of the host's immune system in treatment of disease. It includes both active and passive immunization as well as immunosuppressive therapy to prevent graft rejection. [NIH]

Impaction: The trapping of an object in a body passage. Examples are stones in the bile duct or hardened stool in the colon. [NIH]

Implant radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called [NIH]

In situ: In the natural or normal place; confined to the site of origin without invasion of neighbouring tissues. [EU]

In Situ Hybridization: A technique that localizes specific nucleic acid sequences within intact chromosomes, eukaryotic cells, or bacterial cells through the use of specific nucleic acid-labeled probes. [NIH]

In vitro: In the laboratory (outside the body). The opposite of in vivo (in the body). [NIH]

In vivo: In the body. The opposite of in vitro (outside the body or in the laboratory). [NIH]

Incision: A cut made in the body during surgery. [NIH]

Induction: The act or process of inducing or causing to occur, especially the production of a specific morphogenetic effect in the developing embryo through the influence of evocators or organizers, or the production of anaesthesia or unconsciousness by use of appropriate agents. [EU]

Infancy: The period of complete dependency prior to the acquisition of competence in walking, talking, and self-feeding. [NIH]

Infant, Newborn: An infant during the first month after birth. [NIH]

Infarction: A pathological process consisting of a sudden insufficient blood supply to an area, which results in necrosis of that area. It is usually caused by a thrombus, an embolus, or a vascular torsion. [NIH]

Infection: 1. Invasion and multiplication of microorganisms in body tissues, which may be clinically unapparent or result in local cellular injury due to competitive metabolism, toxins, intracellular replication, or antigen-antibody response. The infection may remain localized, subclinical, and temporary if the body's defensive mechanisms are effective. A local infection may persist and spread by extension to become an acute, subacute, or chronic clinical infection or disease state. A local infection may also become systemic when the microorganisms gain access to the lymphatic or vascular system. 2. An infectious disease. [EU]

Infection Control: Programs of disease surveillance, generally within health care facilities, designed to investigate, prevent, and control the spread of infections and their causative microorganisms. [NIH]

Infiltration: The diffusion or accumulation in a tissue or cells of substances not normal to it or in amounts of the normal. Also, the material so accumulated. [EU]

Inflammation: A pathological process characterized by injury or destruction of tissues caused by a variety of cytologic and chemical reactions. It is usually manifested by typical signs of pain, heat, redness, swelling, and loss of function. [NIH]

Ingestion: Taking into the body by mouth [NIH]

Initiation: Mutation induced by a chemical reactive substance causing cell changes; being a step in a carcinogenic process. [NIH]

Initiator: A chemically reactive substance which may cause cell changes if ingested, inhaled or absorbed into the body; the substance may thus initiate a carcinogenic process. [NIH]

Inorganic: Pertaining to substances not of organic origin. [EU]

Insight: The capacity to understand one's own motives, to be aware of one's own psychodynamics, to appreciate the meaning of symbolic behavior. [NIH]

Insulin: A protein hormone secreted by beta cells of the pancreas. Insulin plays a major role in the regulation of glucose metabolism, generally promoting the cellular utilization of glucose. It is also an important regulator of protein and lipid metabolism. Insulin is used as a drug to control insulin-dependent diabetes mellitus. [NIH]

Insulin-dependent diabetes mellitus: A disease characterized by high levels of blood glucose resulting from defects in insulin secretion, insulin action, or both. Autoimmune, genetic, and environmental factors are involved in the development of type I diabetes. [NIH]

Intermittent: Occurring at separated intervals; having periods of cessation of activity. [EU]

Internal radiation: A procedure in which radioactive material sealed in needles, seeds, wires, or catheters is placed directly into or near the tumor. Also called brachytherapy, implant radiation, or interstitial radiation therapy. [NIH]

Interstitial: Pertaining to or situated between parts or in the interspaces of a tissue. [EU]

Intervention Studies: Epidemiologic investigations designed to test a hypothesized cause-effect relation by modifying the supposed causal factor(s) in the study population. [NIH]

Intestinal: Having to do with the intestines. [NIH]

Intestine: A long, tube-shaped organ in the abdomen that completes the process of digestion. There is both a large intestine and a small intestine. Also called the bowel. [NIH]

Intoxication: Poisoning, the state of being poisoned. [EU]

Intracellular: Inside a cell. [NIH]

Intramuscular: IM. Within or into muscle. [NIH]

Intravenous: IV. Into a vein. [NIH]

Intrinsic: Situated entirely within or pertaining exclusively to a part. [EU]

Invasive: 1. Having the quality of invasiveness. 2. Involving puncture or incision of the skin or insertion of an instrument or foreign material into the body; said of diagnostic techniques. [EU]

Invertebrates: Animals that have no spinal column. [NIH]

Iodine: A nonmetallic element of the halogen group that is represented by the atomic symbol I, atomic number 53, and atomic weight of 126.90. It is a nutritionally essential element, especially important in thyroid hormone synthesis. In solution, it has anti-infective properties and is used topically. [NIH]

Ionization: 1. Any process by which a neutral atom gains or loses electrons, thus acquiring a net charge, as the dissociation of a substance in solution into ions or ion production by the passage of radioactive particles. 2. Iontophoresis. [EU]

Ionizing: Radiation comprising charged particles, e. g. electrons, protons, alpha-particles, etc., having sufficient kinetic energy to produce ionization by collision. [NIH]

Ions: An atom or group of atoms that have a positive or negative electric charge due to a gain (negative charge) or loss (positive charge) of one or more electrons. Atoms with a positive charge are known as cations; those with a negative charge are anions. [NIH]

Irradiation: The use of high-energy radiation from x-rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Irradiation is also called radiation therapy, radiotherapy, and x-ray therapy. [NIH]

Irritants: Drugs that act locally on cutaneous or mucosal surfaces to produce inflammation; those that cause redness due to hyperemia are rubefacients; those that raise blisters are vesicants and those that penetrate sebaceous glands and cause abscesses are pustulants; tear gases and mustard gases are also irritants. [NIH]

Isoenzymes: One of various structurally related forms of an enzyme, each having the same mechanism but with differing chemical, physical, or immunological characteristics. [NIH]

Kb: A measure of the length of DNA fragments, 1 Kb = 1000 base pairs. The largest DNA fragments are up to 50 kilobases long. [NIH]

Keratolytic: An agent that promotes keratolysis. [EU]

Ketoacidosis: Acidosis accompanied by the accumulation of ketone bodies (ketosis) in the body tissues and fluids, as in diabetic acidosis. [EU]

Ketone Bodies: Chemicals that the body makes when there is not enough insulin in the blood and it must break down fat for its energy. Ketone bodies can poison and even kill body cells. When the body does not have the help of insulin, the ketones build up in the blood and then "spill" over into the urine so that the body can get rid of them. The body can also rid itself of one type of ketone, called acetone, through the lungs. This gives the breath a fruity odor. Ketones that build up in the body for a long time lead to serious illness and coma. [NIH]

Kidney Failure: The inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake. In the acute form (kidney failure, acute), it is marked by uremia and usually by oliguria or anuria, with hyperkalemia and pulmonary edema. The chronic form (kidney failure, chronic) is irreversible and requires hemodialysis. [NIH]

Kinetic: Pertaining to or producing motion. [EU]

Labyrinth: The internal ear; the essential part of the organ of hearing. It consists of an osseous and a membranous portion. [NIH]

Laceration: 1. The act of tearing. 2. A torn, ragged, mangled wound. [EU]

Lactation: The period of the secretion of milk. [EU]

Lactobacillus: A genus of gram-positive, microaerophilic, rod-shaped bacteria occurring widely in nature. Its species are also part of the many normal flora of the mouth, intestinal tract, and vagina of many mammals, including humans. Pathogenicity from this genus is rare. [NIH]

Laminin: Large, noncollagenous glycoprotein with antigenic properties. It is localized in the basement membrane lamina lucida and functions to bind epithelial cells to the basement membrane. Evidence suggests that the protein plays a role in tumor invasion. [NIH]

Large Intestine: The part of the intestine that goes from the cecum to the rectum. The large intestine absorbs water from stool and changes it from a liquid to a solid form. The large intestine is 5 feet long and includes the appendix, cecum, colon, and rectum. Also called colon. [NIH]

Laxative: An agent that acts to promote evacuation of the bowel; a cathartic or purgative. [EU]

Lenses: Pieces of glass or other transparent materials used for magnification or increased visual acuity. [NIH]

Lesion: An area of abnormal tissue change. [NIH]

Leukemia: Cancer of blood-forming tissue. [NIH]

Leukocytes: White blood cells. These include granular leukocytes (basophils, eosinophils, and neutrophils) as well as non-granular leukocytes (lymphocytes and monocytes). [NIH]

Leukoplakia: A white patch that may develop on mucous membranes such as the cheek, gums, or tongue and may become cancerous. [NIH]

Lichen Planus: An inflammatory, pruritic disease of the skin and mucous membranes, which can be either generalized or localized. It is characterized by distinctive purplish, flat-topped papules having a predilection for the trunk and flexor surfaces. The lesions may be discrete or coalesce to form plaques. Histologically, there is a "saw-tooth" pattern of epidermal hyperplasia and vacuolar alteration of the basal layer of the epidermis along with an intense upper dermal inflammatory infiltrate composed predominantly of T-cells. Etiology is unknown. [NIH]

Life cycle: The successive stages through which an organism passes from fertilized ovum or spore to the fertilized ovum or spore of the next generation. [NIH]

Ligaments: Shiny, flexible bands of fibrous tissue connecting together articular extremities of bones. They are pliant, tough, and inextensile. [NIH]

Linkage: The tendency of two or more genes in the same chromosome to remain together from one generation to the next more frequently than expected according to the law of independent assortment. [NIH]

Linkage Disequilibrium: Nonrandom association of linked genes. This is the tendency of the alleles of two separate but already linked loci to be found together more frequently than would be expected by chance alone. [NIH]

Lip: Either of the two fleshy, full-blooded margins of the mouth. [NIH]

Lipid: Fat. [NIH]

Lipid Peroxidation: Peroxidase catalyzed oxidation of lipids using hydrogen peroxide as an electron acceptor. [NIH]

Lipopolysaccharide: Substance consisting of polysaccaride and lipid. [NIH]

Lipoprotein: Any of the lipid-protein complexes in which lipids are transported in the blood; lipoprotein particles consist of a spherical hydrophobic core of triglycerides or cholesterol esters surrounded by an amphipathic monolayer of phospholipids, cholesterol, and apolipoproteins; the four principal classes are high-density, low-density, and very-low-density lipoproteins and chylomicrons. [EU]

Liver: A large, glandular organ located in the upper abdomen. The liver cleanses the blood and aids in digestion by secreting bile. [NIH]

Liver scan: An image of the liver created on a computer screen or on film. A radioactive substance is injected into a blood vessel and travels through the bloodstream. It collects in the liver, especially in abnormal areas, and can be detected by the scanner. [NIH]

Localization: The process of determining or marking the location or site of a lesion or disease. May also refer to the process of keeping a lesion or disease in a specific location or site. [NIH]

Localized: Cancer which has not metastasized yet. [NIH]

Locomotion: Movement or the ability to move from one place or another. It can refer to humans, vertebrate or invertebrate animals, and microorganisms. [NIH]

Longitudinal Studies: Studies in which variables relating to an individual or group of individuals are assessed over a period of time. [NIH]

Longitudinal study: Also referred to as a "cohort study" or "prospective study"; the analytic method of epidemiologic study in which subsets of a defined population can be identified who are, have been, or in the future may be exposed or not exposed, or exposed in different degrees, to a factor or factors hypothesized to influence the probability of occurrence of a given disease or other outcome. The main feature of this type of study is to observe large numbers of subjects over an extended time, with comparisons of incidence rates in groups that differ in exposure levels. [NIH]

Long-Term Care: Care over an extended period, usually for a chronic condition or disability, requiring periodic, intermittent, or continuous care. [NIH]

Lucida: An instrument, invented by Wollaton, consisting essentially of a prism or a mirror through which an object can be viewed so as to appear on a plane surface seen in direct view and on which the outline of the object may be traced. [NIH]

Luciferase: Any one of several enzymes that catalyze the bioluminescent reaction in certain marine crustaceans, fish, bacteria, and insects. The enzyme is a flavoprotein; it oxidizes luciferins to an electronically excited compound that emits energy in the form of light. The color of light emitted varies with the organism. The firefly enzyme is a valuable reagent for measurement of ATP concentration. (Dorland, 27th ed) EC 1.13.12.-. [NIH]

Luminescence: The property of giving off light without emitting a corresponding degree of heat. It includes the luminescence of inorganic matter or the bioluminescence of human matter, invertebrates and other living organisms. For the luminescence of bacteria, bacterial luminescence is available. [NIH]

Lupus: A form of cutaneous tuberculosis. It is seen predominantly in women and typically involves the nasal, buccal, and conjunctival mucosa. [NIH]

Lymph: The almost colorless fluid that travels through the lymphatic system and carries cells that help fight infection and disease. [NIH]

Lymph node: A rounded mass of lymphatic tissue that is surrounded by a capsule of connective tissue. Also known as a lymph gland. Lymph nodes are spread out along lymphatic vessels and contain many lymphocytes, which filter the lymphatic fluid (lymph). [NIH]

Lymphatic: The tissues and organs, including the bone marrow, spleen, thymus, and lymph nodes, that produce and store cells that fight infection and disease. [NIH]

Lymphatic system: The tissues and organs that produce, store, and carry white blood cells that fight infection and other diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and a network of thin tubes that carry lymph and white blood cells. These tubes branch, like blood vessels, into all the tissues of the body. [NIH]

Lymphocyte: A white blood cell. Lymphocytes have a number of roles in the immune system, including the production of antibodies and other substances that fight infection and diseases. [NIH]

Lymphoid: Referring to lymphocytes, a type of white blood cell. Also refers to tissue in which lymphocytes develop. [NIH]

Lymphokines: Soluble protein factors generated by activated lymphocytes that affect other cells, primarily those involved in cellular immunity. [NIH]

Lytic: 1. Pertaining to lysis or to a lysin. 2. Producing lysis. [EU]

Magnesium Chloride: Magnesium chloride. An inorganic compound consisting of one magnesium and two chloride ions. The compound is used in medicine as a source of magnesium ions, which are essential for many cellular activities. It has also been used as a cathartic and in alloys. [NIH]

Magnetic Resonance Imaging: Non-invasive method of demonstrating internal anatomy based on the principle that atomic nuclei in a strong magnetic field absorb pulses of radiofrequency energy and emit them as radiowaves which can be reconstructed into computerized images. The concept includes proton spin tomographic techniques. [NIH]

Malignant: Cancerous; a growth with a tendency to invade and destroy nearby tissue and spread to other parts of the body. [NIH]

Malnutrition: A condition caused by not eating enough food or not eating a balanced diet. [NIH]

Mammary: Pertaining to the mamma, or breast. [EU]

Mammogram: An x-ray of the breast. [NIH]

Mammography: Radiographic examination of the breast. [NIH]

Mandible: The largest and strongest bone of the face constituting the lower jaw. It supports the lower teeth. [NIH]

Manifest: Being the part or aspect of a phenomenon that is directly observable : concretely expressed in behaviour. [EU]

Mannitol: A diuretic and renal diagnostic aid related to sorbitol. It has little significant energy value as it is largely eliminated from the body before any metabolism can take place. It can be used to treat oliguria associated with kidney failure or other manifestations of inadequate renal function and has been used for determination of glomerular filtration rate. Mannitol is also commonly used as a research tool in cell biological studies, usually to control osmolarity. [NIH]

Mastication: The act and process of chewing and grinding food in the mouth. [NIH]

Masticatory: 1. subserving or pertaining to mastication; affecting the muscles of mastication. 2. a remedy to be chewed but not swallowed. [EU]

Mastitis: Inflammatory disease of the breast, or mammary gland. [NIH]

Matrix metalloproteinase: A member of a group of enzymes that can break down proteins, such as collagen, that are normally found in the spaces between cells in tissues (i.e., extracellular matrix proteins). Because these enzymes need zinc or calcium atoms to work properly, they are called metalloproteinases. Matrix metalloproteinases are involved in wound healing, angiogenesis, and tumor cell metastasis. [NIH]

Mediate: Indirect; accomplished by the aid of an intervening medium. [EU]

Mediator: An object or substance by which something is mediated, such as (1) a structure of the nervous system that transmits impulses eliciting a specific response; (2) a chemical substance (transmitter substance) that induces activity in an excitable tissue, such as nerve or muscle; or (3) a substance released from cells as the result of the interaction of antigen with antibody or by the action of antigen with a sensitized lymphocyte. [EU]

Medicament: A medicinal substance or agent. [EU]

MEDLINE: An online database of MEDLARS, the computerized bibliographic Medical Literature Analysis and Retrieval System of the National Library of Medicine. [NIH]

Melanoma: A form of skin cancer that arises in melanocytes, the cells that produce pigment. Melanoma usually begins in a mole. [NIH]

Membrane: A very thin layer of tissue that covers a surface. [NIH]

Memory: Complex mental function having four distinct phases: (1) memorizing or learning, (2) retention, (3) recall, and (4) recognition. Clinically, it is usually subdivided into immediate, recent, and remote memory. [NIH]

Mental: Pertaining to the mind; psychic. 2. (L. mentum chin) pertaining to the chin. [EU]

Mental Disorders: Psychiatric illness or diseases manifested by breakdowns in the adaptational process expressed primarily as abnormalities of thought, feeling, and behavior producing either distress or impairment of function. [NIH]

Mental Health: The state wherein the person is well adjusted. [NIH]

Menthol: An alcohol produced from mint oils or prepared synthetically. [NIH]

Mentors: Senior professionals who provide guidance, direction and support to those persons desirous of improvement in academic positions, administrative positions or other career development situations. [NIH]

Mercury: A silver metallic element that exists as a liquid at room temperature. It has the atomic symbol Hg (from hydrargyrum, liquid silver), atomic number 80, and atomic weight 200.59. Mercury is used in many industrial applications and its salts have been employed therapeutically as purgatives, antisyphilitics, disinfectants, and astringents. It can be absorbed through the skin and mucous membranes which leads to mercury poisoning. Because of its toxicity, the clinical use of mercury and mercurials is diminishing. [NIH]

Meta-Analysis: A quantitative method of combining the results of independent studies (usually drawn from the published literature) and synthesizing summaries and conclusions which may be used to evaluate therapeutic effectiveness, plan new studies, etc., with application chiefly in the areas of research and medicine. [NIH]

Metastasis: The spread of cancer from one part of the body to another. Tumors formed from cells that have spread are called "secondary tumors" and contain cells that are like those in the original (primary) tumor. The plural is metastases. [NIH]

MI: Myocardial infarction. Gross necrosis of the myocardium as a result of interruption of the blood supply to the area; it is almost always caused by atherosclerosis of the coronary arteries, upon which coronary thrombosis is usually superimposed. [NIH]

Micelles: Electrically charged colloidal particles or ions consisting of oriented molecules; aggregates of a number of molecules held loosely together by secondary bonds. [NIH]

Microbe: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microbiology: The study of microorganisms such as fungi, bacteria, algae, archaea, and viruses. [NIH]

Microcalcifications: Tiny deposits of calcium in the breast that cannot be felt but can be detected on a mammogram. A cluster of these very small specks of calcium may indicate that cancer is present. [NIH]

Microorganism: An organism that can be seen only through a microscope. Microorganisms include bacteria, protozoa, algae, and fungi. Although viruses are not considered living organisms, they are sometimes classified as microorganisms. [NIH]

Micro-organism: An organism which cannot be observed with the naked eye; e. g. unicellular animals, lower algae, lower fungi, bacteria. [NIH]

Microradiography: Production of a radiographic image of a small or very thin object on fine-grained photographic film under conditions which permit subsequent microscopic examination or enlargement of the radiograph at linear magnifications of up to several hundred and with a resolution approaching the resolving power of the photographic

emulsion (about 1000 lines per millimeter). [NIH]

Microspheres: Small uniformly-sized spherical particles frequently labeled with radioisotopes or various reagents acting as tags or markers. [NIH]

Migration: The systematic movement of genes between populations of the same species, geographic race, or variety. [NIH]

Milligram: A measure of weight. A milligram is approximately 450,000-times smaller than a pound and 28,000-times smaller than an ounce. [NIH]

Millimeter: A measure of length. A millimeter is approximately 26-times smaller than an inch. [NIH]

Mineralization: The action of mineralizing; the state of being mineralized. [EU]

Miotic: 1. Pertaining to, characterized by, or producing miosis : contraction of the pupil. 2. An agent that causes the pupil to contract. 3. Meiotic: characterized by cell division. [EU]

Modeling: A treatment procedure whereby the therapist presents the target behavior which the learner is to imitate and make part of his repertoire. [NIH]

Modification: A change in an organism, or in a process in an organism, that is acquired from its own activity or environment. [NIH]

Molecular: Of, pertaining to, or composed of molecules : a very small mass of matter. [EU]

Molecular Structure: The location of the atoms, groups or ions relative to one another in a molecule, as well as the number, type and location of covalent bonds. [NIH]

Molecule: A chemical made up of two or more atoms. The atoms in a molecule can be the same (an oxygen molecule has two oxygen atoms) or different (a water molecule has two hydrogen atoms and one oxygen atom). Biological molecules, such as proteins and DNA, can be made up of many thousands of atoms. [NIH]

Monitor: An apparatus which automatically records such physiological signs as respiration, pulse, and blood pressure in an anesthetized patient or one undergoing surgical or other procedures. [NIH]

Monoclonal: An antibody produced by culturing a single type of cell. It therefore consists of a single species of immunoglobulin molecules. [NIH]

Monoclonal antibodies: Laboratory-produced substances that can locate and bind to cancer cells wherever they are in the body. Many monoclonal antibodies are used in cancer detection or therapy; each one recognizes a different protein on certain cancer cells. Monoclonal antibodies can be used alone, or they can be used to deliver drugs, toxins, or radioactive material directly to a tumor. [NIH]

Monocytes: Large, phagocytic mononuclear leukocytes produced in the vertebrate bone marrow and released into the blood; contain a large, oval or somewhat indented nucleus surrounded by voluminous cytoplasm and numerous organelles. [NIH]

Mononuclear: A cell with one nucleus. [NIH]

Morphology: The science of the form and structure of organisms (plants, animals, and other forms of life). [NIH]

Mucins: A secretion containing mucopolysaccharides and protein that is the chief constituent of mucus. [NIH]

Mucosa: A mucous membrane, or tunica mucosa. [EU]

Mucus: The viscous secretion of mucous membranes. It contains mucin, white blood cells, water, inorganic salts, and exfoliated cells. [NIH]

Multivalent: Pertaining to a group of 5 or more homologous or partly homologous

chromosomes during the zygotene stage of prophase to first metaphasis in meiosis. [NIH]

Mustard Gas: Severe irritant and vesicant of skin, eyes, and lungs. It may cause blindness and lethal lung edema and was formerly used as a war gas. The substance has been proposed as a cytostatic and for treatment of psoriasis. It has been listed as a known carcinogen in the Fourth Annual Report on Carcinogens (NTP-85-002, 1985) (Merck, 11th ed). [NIH]

Mutagen: Any agent, such as X-rays, gamma rays, mustard gas, TCDD, that can cause abnormal mutation in living cells; having the power to cause mutations. [NIH]

Mutagenesis: Process of generating genetic mutations. It may occur spontaneously or be induced by mutagens. [NIH]

Myocardium: The muscle tissue of the heart composed of striated, involuntary muscle known as cardiac muscle. [NIH]

Natural selection: A part of the evolutionary process resulting in the survival and reproduction of the best adapted individuals. [NIH]

NCI: National Cancer Institute. NCI, part of the National Institutes of Health of the United States Department of Health and Human Services, is the federal government's principal agency for cancer research. NCI conducts, coordinates, and funds cancer research, training, health information dissemination, and other programs with respect to the cause, diagnosis, prevention, and treatment of cancer. Access the NCI Web site at http://cancer.gov. [NIH]

Necrosis: A pathological process caused by the progressive degradative action of enzymes that is generally associated with severe cellular trauma. It is characterized by mitochondrial swelling, nuclear flocculation, uncontrolled cell lysis, and ultimately cell death. [NIH]

Neonatal: Pertaining to the first four weeks after birth. [EU]

Neoplasia: Abnormal and uncontrolled cell growth. [NIH]

Neoplasm: A new growth of benign or malignant tissue. [NIH]

Neoplastic: Pertaining to or like a neoplasm (= any new and abnormal growth); pertaining to neoplasia (= the formation of a neoplasm). [EU]

Nephropathy: Disease of the kidneys. [EU]

Nerve: A cordlike structure of nervous tissue that connects parts of the nervous system with other tissues of the body and conveys nervous impulses to, or away from, these tissues. [NIH]

Nervous System: The entire nerve apparatus composed of the brain, spinal cord, nerves and ganglia. [NIH]

Neural: 1. Pertaining to a nerve or to the nerves. 2. Situated in the region of the spinal axis, as the neutral arch. [EU]

Neuropathy: A problem in any part of the nervous system except the brain and spinal cord. Neuropathies can be caused by infection, toxic substances, or disease. [NIH]

Neurosis: Functional derangement due to disorders of the nervous system which does not affect the psychic personality of the patient. [NIH]

Neurotransmitter: Any of a group of substances that are released on excitation from the axon terminal of a presynaptic neuron of the central or peripheral nervous system and travel across the synaptic cleft to either excite or inhibit the target cell. Among the many substances that have the properties of a neurotransmitter are acetylcholine, norepinephrine, epinephrine, dopamine, glycine, y-aminobutyrate, glutamic acid, substance P, enkephalins, endorphins, and serotonin. [EU]

Neutralization: An act or process of neutralizing. [EU]

Neutrons: Electrically neutral elementary particles found in all atomic nuclei except light hydrogen; the mass is equal to that of the proton and electron combined and they are unstable when isolated from the nucleus, undergoing beta decay. Slow, thermal, epithermal, and fast neutrons refer to the energy levels with which the neutrons are ejected from heavier nuclei during their decay. [NIH]

Neutrophils: Granular leukocytes having a nucleus with three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine inconspicuous granules and stainable by neutral dyes. [NIH]

Nitrogen: An element with the atomic symbol N, atomic number 7, and atomic weight 14. Nitrogen exists as a diatomic gas and makes up about 78% of the earth's atmosphere by volume. It is a constituent of proteins and nucleic acids and found in all living cells. [NIH]

Nuclei: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nucleic acid: Either of two types of macromolecule (DNA or RNA) formed by polymerization of nucleotides. Nucleic acids are found in all living cells and contain the information (genetic code) for the transfer of genetic information from one generation to the next. [NIH]

Nucleus: A body of specialized protoplasm found in nearly all cells and containing the chromosomes. [NIH]

Nutritional Status: State of the body in relation to the consumption and utilization of nutrients. [NIH]

Odds Ratio: The ratio of two odds. The exposure-odds ratio for case control data is the ratio of the odds in favor of exposure among cases to the odds in favor of exposure among noncases. The disease-odds ratio for a cohort or cross section is the ratio of the odds in favor of disease among the exposed to the odds in favor of disease among the unexposed. The prevalence-odds ratio refers to an odds ratio derived cross-sectionally from studies of prevalent cases. [NIH]

Oligosaccharides: Carbohydrates consisting of between two and ten monosaccharides connected by either an alpha- or beta-glycosidic link. They are found throughout nature in both the free and bound form. [NIH]

Oliguria: Clinical manifestation of the urinary system consisting of a decrease in the amount of urine secreted. [NIH]

Opacity: Degree of density (area most dense taken for reading). [NIH]

Operon: The genetic unit consisting of a feedback system under the control of an operator gene, in which a structural gene transcribes its message in the form of mRNA upon blockade of a repressor produced by a regulator gene. Included here is the attenuator site of bacterial operons where transcription termination is regulated. [NIH]

Opportunistic Infections: An infection caused by an organism which becomes pathogenic under certain conditions, e.g., during immunosuppression. [NIH]

Oral Health: The optimal state of the mouth and normal functioning of the organs of the mouth without evidence of disease. [NIH]

Oral Hygiene: The practice of personal hygiene of the mouth. It includes the maintenance of oral cleanliness, tissue tone, and general preservation of oral health. [NIH]

Organelles: Specific particles of membrane-bound organized living substances present in eukaryotic cells, such as the mitochondria; the golgi apparatus; endoplasmic reticulum; lysomomes; plastids; and vacuoles. [NIH]

Orofacial: Of or relating to the mouth and face. [EU]

Orthodontics: A dental specialty concerned with the prevention and correction of dental and oral anomalies (malocclusion). [NIH]

Orthopaedic: Pertaining to the correction of deformities of the musculoskeletal system; pertaining to orthopaedics. [EU]

Osmolarity: The concentration of osmotically active particles expressed in terms of osmoles of solute per litre of solution. [EU]

Osmoles: The standard unit of osmotic pressure. [NIH]

Osmosis: Tendency of fluids (e.g., water) to move from the less concentrated to the more concentrated side of a semipermeable membrane. [NIH]

Osmotic: Pertaining to or of the nature of osmosis (= the passage of pure solvent from a solution of lesser to one of greater solute concentration when the two solutions are separated by a membrane which selectively prevents the passage of solute molecules, but is permeable to the solvent). [EU]

Ossicles: The hammer, anvil and stirrup, the small bones of the middle ear, which transmit the vibrations from the tympanic membrane to the oval window. [NIH]

Osteomyelitis: Inflammation of bone caused by a pyogenic organism. It may remain localized or may spread through the bone to involve the marrow, cortex, cancellous tissue, and periosteum. [EU]

Osteoporosis: Reduction of bone mass without alteration in the composition of bone, leading to fractures. Primary osteoporosis can be of two major types: postmenopausal osteoporosis and age-related (or senile) osteoporosis. [NIH]

Otitis: Inflammation of the ear, which may be marked by pain, fever, abnormalities of hearing, hearing loss, tinnitus, and vertigo. [EU]

Otitis Media: Inflammation of the middle ear. [NIH]

Otosclerosis: The formation of spongy bone in the labyrinth capsule. The ossicles can become fixed and unable to transmit sound vibrations, thereby causing deafness. [NIH]

Ovum: A female germ cell extruded from the ovary at ovulation. [NIH]

Oxidation: The act of oxidizing or state of being oxidized. Chemically it consists in the increase of positive charges on an atom or the loss of negative charges. Most biological oxidations are accomplished by the removal of a pair of hydrogen atoms (dehydrogenation) from a molecule. Such oxidations must be accompanied by reduction of an acceptor molecule. Univalent o. indicates loss of one electron; divalent o., the loss of two electrons. [EU]

Oxidation-Reduction: A chemical reaction in which an electron is transferred from one molecule to another. The electron-donating molecule is the reducing agent or reductant; the electron-accepting molecule is the oxidizing agent or oxidant. Reducing and oxidizing agents function as conjugate reductant-oxidant pairs or redox pairs (Lehninger, Principles of Biochemistry, 1982, p471). [NIH]

Oxidative Stress: A disturbance in the prooxidant-antioxidant balance in favor of the former, leading to potential damage. Indicators of oxidative stress include damaged DNA bases, protein oxidation products, and lipid peroxidation products (Sies, Oxidative Stress, 1991, pxv-xvi). [NIH]

Palate: The structure that forms the roof of the mouth. It consists of the anterior hard palate and the posterior soft palate. [NIH]

Palliative: 1. Affording relief, but not cure. 2. An alleviating medicine. [EU]

Palsy: Disease of the peripheral nervous system occurring usually after many years of increased lead absorption. [NIH]

Pancreas: A mixed exocrine and endocrine gland situated transversely across the posterior abdominal wall in the epigastric and hypochondriac regions. The endocrine portion is comprised of the Islets of Langerhans, while the exocrine portion is a compound acinar gland that secretes digestive enzymes. [NIH]

Parasite: An animal or a plant that lives on or in an organism of another species and gets at least some of its nutrition from that other organism. [NIH]

Parasitic: Having to do with or being a parasite. A parasite is an animal or a plant that lives on or in an organism of another species and gets at least some of its nutrients from it. [NIH]

Parenteral: Not through the alimentary canal but rather by injection through some other route, as subcutaneous, intramuscular, intraorbital, intracapsular, intraspinal, intrasternal, intravenous, etc. [EU]

Parotid: The space that contains the parotid gland, the facial nerve, the external carotid artery, and the retromandibular vein. [NIH]

Particle: A tiny mass of material. [EU]

Patch: A piece of material used to cover or protect a wound, an injured part, etc.: a patch over the eye. [NIH]

Pathogen: Any disease-producing microorganism. [EU]

Pathogenesis: The cellular events and reactions that occur in the development of disease. [NIH]

Pathologic: 1. Indicative of or caused by a morbid condition. 2. Pertaining to pathology (= branch of medicine that treats the essential nature of the disease, especially the structural and functional changes in tissues and organs of the body caused by the disease). [EU]

Pathologies: The study of abnormality, especially the study of diseases. [NIH]

Patient Compliance: Voluntary cooperation of the patient in following a prescribed regimen. [NIH]

Patient Education: The teaching or training of patients concerning their own health needs. [NIH]

Pediatrics: A medical specialty concerned with maintaining health and providing medical care to children from birth to adolescence. [NIH]

Penicillin: An antibiotic drug used to treat infection. [NIH]

Peptide: Any compound consisting of two or more amino acids, the building blocks of proteins. Peptides are combined to make proteins. [NIH]

Peptide Fragments: Partial proteins formed by partial hydrolysis of complete proteins. [NIH]

Perception: The ability quickly and accurately to recognize similarities and differences among presented objects, whether these be pairs of words, pairs of number series, or multiple sets of these or other symbols such as geometric figures. [NIH]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontal disease: Disease involving the supporting structures of the teeth (as the gums and periodontal membranes). [NIH]

Periodontal Pocket: An abnormal extension of a gingival sulcus accompanied by the apical migration of the epithelial attachment and bone resorption. [NIH]

Periodontics: A dental specialty concerned with the histology, physiology, and pathology of

the tissues that support, attach, and surround the teeth, and of the treatment and prevention of disease affecting these tissues. [NIH]

Periodontitis: Inflammation of the periodontal membrane; also called periodontitis simplex. [NIH]

Peripheral Nervous System: The nervous system outside of the brain and spinal cord. The peripheral nervous system has autonomic and somatic divisions. The autonomic nervous system includes the enteric, parasympathetic, and sympathetic subdivisions. The somatic nervous system includes the cranial and spinal nerves and their ganglia and the peripheral sensory receptors. [NIH]

Peroxide: Chemical compound which contains an atom group with two oxygen atoms tied to each other. [NIH]

PH: The symbol relating the hydrogen ion (H+) concentration or activity of a solution to that of a given standard solution. Numerically the pH is approximately equal to the negative logarithm of H+ concentration expressed in molarity. pH 7 is neutral; above it alkalinity increases and below it acidity increases. [EU]

Pharmaceutical Preparations: Drugs intended for human or veterinary use, presented in their finished dosage form. Included here are materials used in the preparation and/or formulation of the finished dosage form. [NIH]

Pharmacologic: Pertaining to pharmacology or to the properties and reactions of drugs. [EU]

Pharmacotherapy: A regimen of using appetite suppressant medications to manage obesity by decreasing appetite or increasing the feeling of satiety. These medications decrease appetite by increasing serotonin or catecholamine—two brain chemicals that affect mood and appetite. [NIH]

Pharynx: The hollow tube about 5 inches long that starts behind the nose and ends at the top of the trachea (windpipe) and esophagus (the tube that goes to the stomach). [NIH]

Phenotype: The outward appearance of the individual. It is the product of interactions between genes and between the genotype and the environment. This includes the killer phenotype, characteristic of yeasts. [NIH]

Phosphorus: A non-metallic element that is found in the blood, muscles, nevers, bones, and teeth, and is a component of adenosine triphosphate (ATP; the primary energy source for the body's cells.) [NIH]

Photoreceptors: Cells specialized to detect and transduce light. [NIH]

Physiologic: Having to do with the functions of the body. When used in the phrase "physiologic age," it refers to an age assigned by general health, as opposed to calendar age. [NIH]

Physiology: The science that deals with the life processes and functions of organismus, their cells, tissues, and organs. [NIH]

Pigments: Any normal or abnormal coloring matter in plants, animals, or micro-organisms. [NIH]

Pilocarpine: A slowly hydrolyzed muscarinic agonist with no nicotinic effects. Pilocarpine is used as a miotic and in the treatment of glaucoma. [NIH]

Pilot study: The initial study examining a new method or treatment. [NIH]

Pit and Fissure Sealants: Agents used to occlude dental enamel pits and fissures in the prevention of dental caries. [NIH]

Plants: Multicellular, eukaryotic life forms of the kingdom Plantae. They are characterized by a mainly photosynthetic mode of nutrition; essentially unlimited growth at localized

regions of cell divisions (meristems); cellulose within cells providing rigidity; the absence of organs of locomotion; absense of nervous and sensory systems; and an alteration of haploid and diploid generations. [NIH]

Plaque: A clear zone in a bacterial culture grown on an agar plate caused by localized destruction of bacterial cells by a bacteriophage. The concentration of infective virus in a fluid can be estimated by applying the fluid to a culture and counting the number of. [NIH]

Plasma: The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. [NIH]

Plasma cells: A type of white blood cell that produces antibodies. [NIH]

Plasma protein: One of the hundreds of different proteins present in blood plasma, including carrier proteins (such albumin, transferrin, and haptoglobin), fibrinogen and other coagulation factors, complement components, immunoglobulins, enzyme inhibitors, precursors of substances such as angiotension and bradykinin, and many other types of proteins. [EU]

Plasma Volume: Volume of plasma in the circulation. It is usually measured by indicator dilution techniques. [NIH]

Plasmid: An autonomously replicating, extra-chromosomal DNA molecule found in many bacteria. Plasmids are widely used as carriers of cloned genes. [NIH]

Plasmin: A product of the lysis of plasminogen (profibrinolysin) by plasminogen activators. It is composed of two polypeptide chains, light (B) and heavy (A), with a molecular weight of 75,000. It is the major proteolytic enzyme involved in blood clot retraction or the lysis of fibrin and quickly inactivated by antiplasmins. EC 3.4.21.7. [NIH]

Plasminogen: Precursor of fibrinolysin (plasmin). It is a single-chain beta-globulin of molecular weight 80-90,000 found mostly in association with fibrinogen in plasma; plasminogen activators change it to fibrinolysin. It is used in wound debriding and has been investigated as a thrombolytic agent. [NIH]

Plasminogen Activators: A heterogeneous group of proteolytic enzymes that convert plasminogen to plasmin. They are concentrated in the lysosomes of most cells and in the vascular endothelium, particularly in the vessels of the microcirculation. EC 3.4.21.-. [NIH]

Platelets: A type of blood cell that helps prevent bleeding by causing blood clots to form. Also called thrombocytes. [NIH]

Platinum: Platinum. A heavy, soft, whitish metal, resembling tin, atomic number 78, atomic weight 195.09, symbol Pt. (From Dorland, 28th ed) It is used in manufacturing equipment for laboratory and industrial use. It occurs as a black powder (platinum black) and as a spongy substance (spongy platinum) and may have been known in Pliny's time as "alutiae". [NIH]

Pneumonia: Inflammation of the lungs. [NIH]

Poisoning: A condition or physical state produced by the ingestion, injection or inhalation of, or exposure to a deleterious agent. [NIH]

Pollen: The male fertilizing element of flowering plants analogous to sperm in animals. It is released from the anthers as yellow dust, to be carried by insect or other vectors, including wind, to the ovary (stigma) of other flowers to produce the embryo enclosed by the seed. The pollens of many plants are allergenic. [NIH]

Polymerase: An enzyme which catalyses the synthesis of DNA using a single DNA strand as a template. The polymerase copies the template in the 5'-3'direction provided that sufficient quantities of free nucleotides, dATP and dTTP are present. [NIH]

Polymerase Chain Reaction: In vitro method for producing large amounts of specific DNA

or RNA fragments of defined length and sequence from small amounts of short oligonucleotide flanking sequences (primers). The essential steps include thermal denaturation of the double-stranded target molecules, annealing of the primers to their complementary sequences, and extension of the annealed primers by enzymatic synthesis with DNA polymerase. The reaction is efficient, specific, and extremely sensitive. Uses for the reaction include disease diagnosis, detection of difficult-to-isolate pathogens, mutation analysis, genetic testing, DNA sequencing, and analyzing evolutionary relationships. [NIH]

Polymers: Compounds formed by the joining of smaller, usually repeating, units linked by covalent bonds. These compounds often form large macromolecules (e.g., polypeptides, proteins, plastics). [NIH]

Polymorphic: Occurring in several or many forms; appearing in different forms at different stages of development. [EU]

Polypeptide: A peptide which on hydrolysis yields more than two amino acids; called tripeptides, tetrapeptides, etc. according to the number of amino acids contained. [EU]

Polysaccharide: A type of carbohydrate. It contains sugar molecules that are linked together chemically. [NIH]

Postmenopausal: Refers to the time after menopause. Menopause is the time in a woman's life when menstrual periods stop permanently; also called "change of life." [NIH]

Postnatal: Occurring after birth, with reference to the newborn. [EU]

Potassium: An element that is in the alkali group of metals. It has an atomic symbol K, atomic number 19, and atomic weight 39.10. It is the chief cation in the intracellular fluid of muscle and other cells. Potassium ion is a strong electrolyte and it plays a significant role in the regulation of fluid volume and maintenance of the water-electrolyte balance. [NIH]

Potassium Chloride: Potassium chloride. A white crystal or crystalline powder used as an electrolyte replenisher, in the treatment of hypokalemia, in buffer solutions, and in fertilizers and explosives. [NIH]

Potentiating: A degree of synergism which causes the exposure of the organism to a harmful substance to worsen a disease already contracted. [NIH]

Povidone: A polyvinyl polymer of variable molecular weight; used as suspending and dispersing agent and vehicle for pharmaceuticals; also used as blood volume expander. [NIH]

Povidone-Iodine: An iodinated polyvinyl polymer used as topical antiseptic in surgery and for skin and mucous membrane infections, also as aerosol. The iodine may be radiolabeled for research purposes. [NIH]

Practice Guidelines: Directions or principles presenting current or future rules of policy for the health care practitioner to assist him in patient care decisions regarding diagnosis, therapy, or related clinical circumstances. The guidelines may be developed by government agencies at any level, institutions, professional societies, governing boards, or by the convening of expert panels. The guidelines form a basis for the evaluation of all aspects of health care and delivery. [NIH]

Precipitation: The act or process of precipitating. [EU]

Precipitins: Antibodies which elicit precipitation when combined with antigen. [NIH]

Preclinical: Before a disease becomes clinically recognizable. [EU]

Precursor: Something that precedes. In biological processes, a substance from which another, usually more active or mature substance is formed. In clinical medicine, a sign or symptom that heralds another. [EU]

Prenatal: Existing or occurring before birth, with reference to the fetus. [EU]

Prevalence: The total number of cases of a given disease in a specified population at a designated time. It is differentiated from incidence, which refers to the number of new cases in the population at a given time. [NIH]

Preventive Dentistry: The branch of dentistry concerned with the prevention of disease and the maintenance and promotion of oral health. [NIH]

Primary endpoint: The main result that is measured at the end of a study to see if a given treatment worked (e.g., the number of deaths or the difference in survival between the treatment group and the control group). What the primary endpoint will be is decided before the study begins. [NIH]

Primary Prevention: Prevention of disease or mental disorders in susceptible individuals or populations through promotion of health, including mental health, and specific protection, as in immunization, as distinguished from the prevention of complications or after-effects of existing disease. [NIH]

Private Sector: That distinct portion of the institutional, industrial, or economic structure of a country that is controlled or owned by non-governmental, private interests. [NIH]

Probe: An instrument used in exploring cavities, or in the detection and dilatation of strictures, or in demonstrating the potency of channels; an elongated instrument for exploring or sounding body cavities. [NIH]

Professional Practice: The use of one's knowledge in a particular profession. It includes, in the case of the field of biomedicine, professional activities related to health care and the actual performance of the duties related to the provision of health care. [NIH]

Progeny: The offspring produced in any generation. [NIH]

Progression: Increase in the size of a tumor or spread of cancer in the body. [NIH]

Progressive: Advancing; going forward; going from bad to worse; increasing in scope or severity. [EU]

Proline: A non-essential amino acid that is synthesized from glutamic acid. It is an essential component of collagen and is important for proper functioning of joints and tendons. [NIH]

Promoter: A chemical substance that increases the activity of a carcinogenic process. [NIH]

Prone: Having the front portion of the body downwards. [NIH]

Prophylaxis: An attempt to prevent disease. [NIH]

Propolis: Resinous substance obtained from beehives; contains many different substances which may have antimicrobial or antimycotic activity topically; its extracts are called propolis resin or balsam. Synonyms: bee bread; hive dross; bee glue. [NIH]

Propylene Glycol: A clear, colorless, viscous organic solvent and diluent used in pharmaceutical preparations. [NIH]

Prospective study: An epidemiologic study in which a group of individuals (a cohort), all free of a particular disease and varying in their exposure to a possible risk factor, is followed over a specific amount of time to determine the incidence rates of the disease in the exposed and unexposed groups. [NIH]

Prostaglandins: A group of compounds derived from unsaturated 20-carbon fatty acids, primarily arachidonic acid, via the cyclooxygenase pathway. They are extremely potent mediators of a diverse group of physiological processes. [NIH]

Prostate: A gland in males that surrounds the neck of the bladder and the urethra. It secretes a substance that liquifies coagulated semen. It is situated in the pelvic cavity behind the lower part of the pubic symphysis, above the deep layer of the triangular ligament, and rests upon the rectum. [NIH]

Protease: Proteinase (= any enzyme that catalyses the splitting of interior peptide bonds in a protein). [EU]

Protein C: A vitamin-K dependent zymogen present in the blood, which, upon activation by thrombin and thrombomodulin exerts anticoagulant properties by inactivating factors Va and VIIIa at the rate-limiting steps of thrombin formation. [NIH]

Protein Conformation: The characteristic 3-dimensional shape of a protein, including the secondary, supersecondary (motifs), tertiary (domains) and quaternary structure of the peptide chain. Quaternary protein structure describes the conformation assumed by multimeric proteins (aggregates of more than one polypeptide chain). [NIH]

Protein S: The vitamin K-dependent cofactor of activated protein C. Together with protein C, it inhibits the action of factors VIIIa and Va. A deficiency in protein S can lead to recurrent venous and arterial thrombosis. [NIH]

Proteins: Polymers of amino acids linked by peptide bonds. The specific sequence of amino acids determines the shape and function of the protein. [NIH]

Proteolytic: 1. Pertaining to, characterized by, or promoting proteolysis. 2. An enzyme that promotes proteolysis (= the splitting of proteins by hydrolysis of the peptide bonds with formation of smaller polypeptides). [EU]

Protocol: The detailed plan for a clinical trial that states the trial's rationale, purpose, drug or vaccine dosages, length of study, routes of administration, who may participate, and other aspects of trial design. [NIH]

Protons: Stable elementary particles having the smallest known positive charge, found in the nuclei of all elements. The proton mass is less than that of a neutron. A proton is the nucleus of the light hydrogen atom, i.e., the hydrogen ion. [NIH]

Protozoa: A subkingdom consisting of unicellular organisms that are the simplest in the animal kingdom. Most are free living. They range in size from submicroscopic to macroscopic. Protozoa are divided into seven phyla: Sarcomastigophora, Labyrinthomorpha, Apicomplexa, Microspora, Ascetospora, Myxozoa, and Ciliophora. [NIH]

Protozoan: 1. Any individual of the protozoa; protozoon. 2. Of or pertaining to the protozoa; protozoal. [EU]

Pruritic: Pertaining to or characterized by pruritus. [EU]

Psychiatric: Pertaining to or within the purview of psychiatry. [EU]

Psychiatry: The medical science that deals with the origin, diagnosis, prevention, and treatment of mental disorders. [NIH]

Psychic: Pertaining to the psyche or to the mind; mental. [EU]

Psychoactive: Those drugs which alter sensation, mood, consciousness or other psychological or behavioral functions. [NIH]

Public Health: Branch of medicine concerned with the prevention and control of disease and disability, and the promotion of physical and mental health of the population on the international, national, state, or municipal level. [NIH]

Public Health Practice: The activities and endeavors of the public health services in a community on any level. [NIH]

Public Policy: A course or method of action selected, usually by a government, from among alternatives to guide and determine present and future decisions. [NIH]

Publishing: "The business or profession of the commercial production and issuance of literature" (Webster's 3d). It includes the publisher, publication processes, editing and editors. Production may be by conventional printing methods or by electronic publishing.

[NIH]

Pulmonary: Relating to the lungs. [NIH]

Pulmonary Artery: The short wide vessel arising from the conus arteriosus of the right ventricle and conveying unaerated blood to the lungs. [NIH]

Pulse: The rhythmical expansion and contraction of an artery produced by waves of pressure caused by the ejection of blood from the left ventricle of the heart as it contracts. [NIH]

Pyogenic: Producing pus; pyopoietic (= liquid inflammation product made up of cells and a thin fluid called liquor puris). [EU]

Quality of Life: A generic concept reflecting concern with the modification and enhancement of life attributes, e.g., physical, political, moral and social environment. [NIH]

Quercetin: Aglucon of quercetrin, rutin, and other glycosides. It is widely distributed in the plant kingdom, especially in rinds and barks, clover blossoms, and ragweed pollen. [NIH]

Race: A population within a species which exhibits general similarities within itself, but is both discontinuous and distinct from other populations of that species, though not sufficiently so as to achieve the status of a taxon. [NIH]

Radar: A system using beamed and reflected radio signals to and from an object in such a way that range, bearing, and other characteristics of the object may be determined. [NIH]

Radiation: Emission or propagation of electromagnetic energy (waves/rays), or the waves/rays themselves; a stream of electromagnetic particles (electrons, neutrons, protons, alpha particles) or a mixture of these. The most common source is the sun. [NIH]

Radiation therapy: The use of high-energy radiation from x-rays, gamma rays, neutrons, and other sources to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body in the area near cancer cells (internal radiation therapy, implant radiation, or brachytherapy). Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. Also called radiotherapy. [NIH]

Radioactive: Giving off radiation. [NIH]

Radiography: Examination of any part of the body for diagnostic purposes by means of roentgen rays, recording the image on a sensitized surface (such as photographic film). [NIH]

Radioimmunotherapy: Radiotherapy where cytotoxic radionuclides are linked to antibodies in order to deliver toxins directly to tumor targets. Therapy with targeted radiation rather than antibody-targeted toxins (immunotoxins) has the advantage that adjacent tumor cells, which lack the appropriate antigenic determinants, can be destroyed by radiation cross-fire. Radioimmunotherapy is sometimes called targeted radiotherapy, but this latter term can also refer to radionuclides linked to non-immune molecules (radiotherapy). [NIH]

Radiolabeled: Any compound that has been joined with a radioactive substance. [NIH]

Radiology: A specialty concerned with the use of x-ray and other forms of radiant energy in the diagnosis and treatment of disease. [NIH]

Radiometry: The measurement of radiation by photography, as in x-ray film and film badge, by Geiger-Mueller tube, and by scintillation counting. [NIH]

Radiosensitization: The use of a drug that makes tumor cells more sensitive to radiation therapy. [NIH]

Radiotherapy: The use of ionizing radiation to treat malignant neoplasms and other benign conditions. The most common forms of ionizing radiation used as therapy are x-rays,

gamma rays, and electrons. A special form of radiotherapy, targeted radiotherapy, links a cytotoxic radionuclide to a molecule that targets the tumor. When this molecule is an antibody or other immunologic molecule, the technique is called radioimmunotherapy. [NIH]

Random Allocation: A process involving chance used in therapeutic trials or other research endeavor for allocating experimental subjects, human or animal, between treatment and control groups, or among treatment groups. It may also apply to experiments on inanimate objects. [NIH]

Randomization: Also called random allocation. Is allocation of individuals to groups, e.g., for experimental and control regimens, by chance. Within the limits of chance variation, random allocation should make the control and experimental groups similar at the start of an investigation and ensure that personal judgment and prejudices of the investigator do not influence allocation. [NIH]

Randomized: Describes an experiment or clinical trial in which animal or human subjects are assigned by chance to separate groups that compare different treatments. [NIH]

Randomized clinical trial: A study in which the participants are assigned by chance to separate groups that compare different treatments; neither the researchers nor the participants can choose which group. Using chance to assign people to groups means that the groups will be similar and that the treatments they receive can be compared objectively. At the time of the trial, it is not known which treatment is best. It is the patient's choice to be in a randomized trial. [NIH]

Reagent: A substance employed to produce a chemical reaction so as to detect, measure, produce, etc., other substances. [EU]

Receptor: A molecule inside or on the surface of a cell that binds to a specific substance and causes a specific physiologic effect in the cell. [NIH]

Receptors, Complement: Molecules on the surface of some B-lymphocytes and macrophages, that recognize and combine with the C3b, C3d, C1q, and C4b components of complement. [NIH]

Recombinant: A cell or an individual with a new combination of genes not found together in either parent; usually applied to linked genes. [EU]

Recombination: The formation of new combinations of genes as a result of segregation in crosses between genetically different parents; also the rearrangement of linked genes due to crossing-over. [NIH]

Rectal: By or having to do with the rectum. The rectum is the last 8 to 10 inches of the large intestine and ends at the anus. [NIH]

Rectum: The last 8 to 10 inches of the large intestine. [NIH]

Recur: To occur again. Recurrence is the return of cancer, at the same site as the original (primary) tumor or in another location, after the tumor had disappeared. [NIH]

Red blood cells: RBCs. Cells that carry oxygen to all parts of the body. Also called erythrocytes. [NIH]

Refer: To send or direct for treatment, aid, information, de decision. [NIH]

Refraction: A test to determine the best eyeglasses or contact lenses to correct a refractive error (myopia, hyperopia, or astigmatism). [NIH]

Regeneration: The natural renewal of a structure, as of a lost tissue or part. [EU]

Regimen: A treatment plan that specifies the dosage, the schedule, and the duration of treatment. [NIH]

Relative risk: The ratio of the incidence rate of a disease among individuals exposed to a

specific risk factor to the incidence rate among unexposed individuals; synonymous with risk ratio. Alternatively, the ratio of the cumulative incidence rate in the exposed to the cumulative incidence rate in the unexposed (cumulative incidence ratio). The term relative risk has also been used synonymously with odds ratio. This is because the odds ratio and relative risk approach each other if the disease is rare (5 percent of population) and the number of subjects is large. [NIH]

Reliability: Used technically, in a statistical sense, of consistency of a test with itself, i. e. the extent to which we can assume that it will yield the same result if repeated a second time. [NIH]

Repressor: Any of the specific allosteric protein molecules, products of regulator genes, which bind to the operator of operons and prevent RNA polymerase from proceeding into the operon to transcribe messenger RNA. [NIH]

Resorption: The loss of substance through physiologic or pathologic means, such as loss of dentin and cementum of a tooth, or of the alveolar process of the mandible or maxilla. [EU]

Respiration: The act of breathing with the lungs, consisting of inspiration, or the taking into the lungs of the ambient air, and of expiration, or the expelling of the modified air which contains more carbon dioxide than the air taken in (Blakiston's Gould Medical Dictionary, 4th ed.). This does not include tissue respiration (= oxygen consumption) or cell respiration (= cell respiration). [NIH]

Response rate: The percentage of patients whose cancer shrinks or disappears after treatment. [NIH]

Retina: The ten-layered nervous tissue membrane of the eye. It is continuous with the optic nerve and receives images of external objects and transmits visual impulses to the brain. Its outer surface is in contact with the choroid and the inner surface with the vitreous body. The outer-most layer is pigmented, whereas the inner nine layers are transparent. [NIH]

Retinal: 1. Pertaining to the retina. 2. The aldehyde of retinol, derived by the oxidative enzymatic splitting of absorbed dietary carotene, and having vitamin A activity. In the retina, retinal combines with opsins to form visual pigments. One isomer, 11-cis retinal combines with opsin in the rods (scotopsin) to form rhodopsin, or visual purple. Another, all-trans retinal (trans-r.); visual yellow; xanthopsin) results from the bleaching of rhodopsin by light, in which the 11-cis form is converted to the all-trans form. Retinal also combines with opsins in the cones (photopsins) to form the three pigments responsible for colour vision. Called also retinal, and retinene1. [EU]

Retinopathy: 1. Retinitis (= inflammation of the retina). 2. Retinosis (= degenerative, noninflammatory condition of the retina). [EU]

Retrospective: Looking back at events that have already taken place. [NIH]

Retroviral vector: RNA from a virus that is used to insert genetic material into cells. [NIH]

Rheumatism: A group of disorders marked by inflammation or pain in the connective tissue structures of the body. These structures include bone, cartilage, and fat. [NIH]

Rheumatoid: Resembling rheumatism. [EU]

Rheumatoid arthritis: A form of arthritis, the cause of which is unknown, although infection, hypersensitivity, hormone imbalance and psychologic stress have been suggested as possible causes. [NIH]

Rhinitis: Inflammation of the mucous membrane of the nose. [NIH]

Ribosome: A granule of protein and RNA, synthesized in the nucleolus and found in the cytoplasm of cells. Ribosomes are the main sites of protein synthesis. Messenger RNA attaches to them and there receives molecules of transfer RNA bearing amino acids. [NIH]

Rickettsiae: One of a group of obligate intracellular parasitic microorganisms, once regarded as intermediate in their properties between bacteria and viruses but now classified as bacteria in the order Rickettsiales, which includes 17 genera and 3 families: Rickettsiace. [NIH]

Risk factor: A habit, trait, condition, or genetic alteration that increases a person's chance of developing a disease. [NIH]

Risk patient: Patient who is at risk, because of his/her behaviour or because of the type of person he/she is. [EU]

Rod: A reception for vision, located in the retina. [NIH]

Root Caries: Dental caries involving the tooth root, cementum, or cervical area of the tooth. [NIH]

Rotavirus: A genus of Reoviridae, causing acute gastroenteritis in birds and mammals, including humans. Transmission is horizontal and by environmental contamination. [NIH]

Rural Population: The inhabitants of rural areas or of small towns classified as rural. [NIH]

Rutin: 3-((6-O-(6-Deoxy-alpha-L-mannopyranosyl)-beta-D-glucopyranosyl)oxy)-2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-4H-1-benzopyran-4-one. Found in many plants, including buckwheat, tobacco, forsythia, hydrangea, pansies, etc. It has been used therapeutically to decrease capillary fragility. [NIH]

Saliva: The clear, viscous fluid secreted by the salivary glands and mucous glands of the mouth. It contains mucins, water, organic salts, and ptylin. [NIH]

Salivary: The duct that convey saliva to the mouth. [NIH]

Salivary glands: Glands in the mouth that produce saliva. [NIH]

Salivary Proteins: Proteins found in saliva and the salivary glands. These proteins show some enzymatic activity, but their composition varies in different individuals. [NIH]

Satellite: Applied to a vein which closely accompanies an artery for some distance; in cytogenetics, a chromosomal agent separated by a secondary constriction from the main body of the chromosome. [NIH]

Scans: Pictures of structures inside the body. Scans often used in diagnosing, staging, and monitoring disease include liver scans, bone scans, and computed tomography (CT) or computerized axial tomography (CAT) scans and magnetic resonance imaging (MRI) scans. In liver scanning and bone scanning, radioactive substances that are injected into the bloodstream collect in these organs. A scanner that detects the radiation is used to create pictures. In CT scanning, an x-ray machine linked to a computer is used to produce detailed pictures of organs inside the body. MRI scans use a large magnet connected to a computer to create pictures of areas inside the body. [NIH]

Scatter: The extent to which relative success and failure are divergently manifested in qualitatively different tests. [NIH]

Schizoid: Having qualities resembling those found in greater degree in schizophrenics; a person of schizoid personality. [NIH]

Schizophrenia: A mental disorder characterized by a special type of disintegration of the personality. [NIH]

Schizotypal Personality Disorder: A personality disorder in which there are oddities of thought (magical thinking, paranoid ideation, suspiciousness), perception (illusions, depersonalization), speech (digressive, vague, overelaborate), and behavior (inappropriate affect in social interactions, frequently social isolation) that are not severe enough to characterize schizophrenia. [NIH]

Sclera: The tough white outer coat of the eyeball, covering approximately the posterior five-sixths of its surface, and continuous anteriorly with the cornea and posteriorly with the external sheath of the optic nerve. [EU]

Scleroderma: A chronic disorder marked by hardening and thickening of the skin. Scleroderma can be localized or it can affect the entire body (systemic). [NIH]

Sclerosis: A pathological process consisting of hardening or fibrosis of an anatomical structure, often a vessel or a nerve. [NIH]

Sclerotic: Pertaining to the outer coat of the eye; the sclera; hard, indurated or sclerosed. [NIH]

Screening: Checking for disease when there are no symptoms. [NIH]

Secretion: 1. The process of elaborating a specific product as a result of the activity of a gland; this activity may range from separating a specific substance of the blood to the elaboration of a new chemical substance. 2. Any substance produced by secretion. [EU]

Secretory: Secreting; relating to or influencing secretion or the secretions. [NIH]

Secular trends: A relatively long-term trend in a community or country. [NIH]

Segregation: The separation in meiotic cell division of homologous chromosome pairs and their contained allelomorphic gene pairs. [NIH]

Semisynthetic: Produced by chemical manipulation of naturally occurring substances. [EU]

Senile: Relating or belonging to old age; characteristic of old age; resulting from infirmity of old age. [NIH]

Septicaemia: A term originally used to denote a putrefactive process in the body, but now usually referring to infection with pyogenic micro-organisms; a genus of Diptera; the severe type of infection in which the blood stream is invaded by large numbers of the causal. [NIH]

Sequence Analysis: A multistage process that includes the determination of a sequence (protein, carbohydrate, etc.), its fragmentation and analysis, and the interpretation of the resulting sequence information. [NIH]

Sequencing: The determination of the order of nucleotides in a DNA or RNA chain. [NIH]

Serine: A non-essential amino acid occurring in natural form as the L-isomer. It is synthesized from glycine or threonine. It is involved in the biosynthesis of purines, pyrimidines, and other amino acids. [NIH]

Serotonin: A biochemical messenger and regulator, synthesized from the essential amino acid L-tryptophan. In humans it is found primarily in the central nervous system, gastrointestinal tract, and blood platelets. Serotonin mediates several important physiological functions including neurotransmission, gastrointestinal motility, hemostasis, and cardiovascular integrity. Multiple receptor families (receptors, serotonin) explain the broad physiological actions and distribution of this biochemical mediator. [NIH]

Serotypes: A cause of haemorrhagic septicaemia (in cattle, sheep and pigs), fowl cholera of birds, pasteurellosis of rabbits, and gangrenous mastitis of ewes. It is also commonly found in atrophic rhinitis of pigs. [NIH]

Serous: Having to do with serum, the clear liquid part of blood. [NIH]

Serum: The clear liquid part of the blood that remains after blood cells and clotting proteins have been removed. [NIH]

Sex Characteristics: Those characteristics that distinguish one sex from the other. The primary sex characteristics are the ovaries and testes and their related hormones. Secondary sex characteristics are those which are masculine or feminine but not directly related to reproduction. [NIH]

Shedding: Release of infectious particles (e. g., bacteria, viruses) into the environment, for example by sneezing, by fecal excretion, or from an open lesion. [NIH]

Shock: The general bodily disturbance following a severe injury; an emotional or moral upset occasioned by some disturbing or unexpected experience; disruption of the circulation, which can upset all body functions: sometimes referred to as circulatory shock. [NIH]

Side effect: A consequence other than the one(s) for which an agent or measure is used, as the adverse effects produced by a drug, especially on a tissue or organ system other than the one sought to be benefited by its administration. [EU]

Signs and Symptoms: Clinical manifestations that can be either objective when observed by a physician, or subjective when perceived by the patient. [NIH]

Skeletal: Having to do with the skeleton (boney part of the body). [NIH]

Skeleton: The framework that supports the soft tissues of vertebrate animals and protects many of their internal organs. The skeletons of vertebrates are made of bone and/or cartilage. [NIH]

Sneezing: Sudden, forceful, involuntary expulsion of air from the nose and mouth caused by irritation to the mucous membranes of the upper respiratory tract. [NIH]

Social Environment: The aggregate of social and cultural institutions, forms, patterns, and processes that influence the life of an individual or community. [NIH]

Sodium: An element that is a member of the alkali group of metals. It has the atomic symbol Na, atomic number 11, and atomic weight 23. With a valence of 1, it has a strong affinity for oxygen and other nonmetallic elements. Sodium provides the chief cation of the extracellular body fluids. Its salts are the most widely used in medicine. (From Dorland, 27th ed) Physiologically the sodium ion plays a major role in blood pressure regulation, maintenance of fluid volume, and electrolyte balance. [NIH]

Sodium Bicarbonate: A white, crystalline powder that is commonly used as a pH buffering agent, an electrolyte replenisher, systemic alkalizer and in topical cleansing solutions. [NIH]

Sodium Fluoride: A source of inorganic fluoride which is used topically to prevent dental caries. [NIH]

Sodium Iodide: Sodium iodide (NaI). A compound forming white, odorless deliquescent crystals and used as iodine supplement, expectorant or in its radioactive (I-131) form as an diagnostic aid, particularly for thyroid function determinants. [NIH]

Soft tissue: Refers to muscle, fat, fibrous tissue, blood vessels, or other supporting tissue of the body. [NIH]

Solvent: 1. Dissolving; effecting a solution. 2. A liquid that dissolves or that is capable of dissolving; the component of a solution that is present in greater amount. [EU]

Somatic: 1. Pertaining to or characteristic of the soma or body. 2. Pertaining to the body wall in contrast to the viscera. [EU]

Sorbitol: A polyhydric alcohol with about half the sweetness of sucrose. Sorbitol occurs naturally and is also produced synthetically from glucose. It was formerly used as a diuretic and may still be used as a laxative and in irrigating solutions for some surgical procedures. It is also used in many manufacturing processes, as a pharmaceutical aid, and in several research applications. [NIH]

Sound wave: An alteration of properties of an elastic medium, such as pressure, particle displacement, or density, that propagates through the medium, or a superposition of such alterations. [NIH]

Specialist: In medicine, one who concentrates on 1 special branch of medical science. [NIH]

Species: A taxonomic category subordinate to a genus (or subgenus) and superior to a subspecies or variety, composed of individuals possessing common characters distinguishing them from other categories of individuals of the same taxonomic level. In taxonomic nomenclature, species are designated by the genus name followed by a Latin or Latinized adjective or noun. [EU]

Specificity: Degree of selectivity shown by an antibody with respect to the number and types of antigens with which the antibody combines, as well as with respect to the rates and the extents of these reactions. [NIH]

Spectrum: A charted band of wavelengths of electromagnetic vibrations obtained by refraction and diffraction. By extension, a measurable range of activity, such as the range of bacteria affected by an antibiotic (antibacterial s.) or the complete range of manifestations of a disease. [EU]

Sperm: The fecundating fluid of the male. [NIH]

Sphenoid: An unpaired cranial bone with a body containing the sphenoid sinus and forming the posterior part of the medial walls of the orbits. [NIH]

Spinal cord: The main trunk or bundle of nerves running down the spine through holes in the spinal bone (the vertebrae) from the brain to the level of the lower back. [NIH]

Spirochetes: Lyme disease. [NIH]

Spleen: An organ that is part of the lymphatic system. The spleen produces lymphocytes, filters the blood, stores blood cells, and destroys old blood cells. It is located on the left side of the abdomen near the stomach. [NIH]

Staging: Performing exams and tests to learn the extent of the cancer within the body, especially whether the disease has spread from the original site to other parts of the body. [NIH]

Statistically significant: Describes a mathematical measure of difference between groups. The difference is said to be statistically significant if it is greater than what might be expected to happen by chance alone. [NIH]

Sterile: Unable to produce children. [NIH]

Stimulus: That which can elicit or evoke action (response) in a muscle, nerve, gland or other excitable issue, or cause an augmenting action upon any function or metabolic process. [NIH]

Stomach: An organ of digestion situated in the left upper quadrant of the abdomen between the termination of the esophagus and the beginning of the duodenum. [NIH]

Stomatitis: Inflammation of the oral mucosa, due to local or systemic factors which may involve the buccal and labial mucosa, palate, tongue, floor of the mouth, and the gingivae. [EU]

Strand: DNA normally exists in the bacterial nucleus in a helix, in which two strands are coiled together. [NIH]

Streptococcal: Caused by infection due to any species of streptococcus. [NIH]

Streptococcal Infections: Infections with bacteria of the genus Streptococcus. [NIH]

Streptococci: A genus of spherical Gram-positive bacteria occurring in chains or pairs. They are widely distributed in nature, being important pathogens but often found as normal commensals in the mouth, skin, and intestine of humans and other animals. [NIH]

Streptococcus: A genus of gram-positive, coccoid bacteria whose organisms occur in pairs or chains. No endospores are produced. Many species exist as commensals or parasites on man or animals with some being highly pathogenic. A few species are saprophytes and

occur in the natural environment. [NIH]

Streptococcus mutans: A polysaccharide-producing species of Streptococcus isolated from human dental plaque. [NIH]

Stress: Forcibly exerted influence; pressure. Any condition or situation that causes strain or tension. Stress may be either physical or psychologic, or both. [NIH]

Stroke: Sudden loss of function of part of the brain because of loss of blood flow. Stroke may be caused by a clot (thrombosis) or rupture (hemorrhage) of a blood vessel to the brain. [NIH]

Strontium: An element of the alkaline earth family of metals. It has the atomic symbol Sr, atomic number 38, and atomic weight 87.62. [NIH]

Students, Dental: Individuals enrolled a school of dentistry or a formal educational program in leading to a degree in dentistry. [NIH]

Subacute: Somewhat acute; between acute and chronic. [EU]

Subclinical: Without clinical manifestations; said of the early stage(s) of an infection or other disease or abnormality before symptoms and signs become apparent or detectable by clinical examination or laboratory tests, or of a very mild form of an infection or other disease or abnormality. [EU]

Subcutaneous: Beneath the skin. [NIH]

Subspecies: A category intermediate in rank between species and variety, based on a smaller number of correlated characters than are used to differentiate species and generally conditioned by geographical and/or ecological occurrence. [NIH]

Substance P: An eleven-amino acid neurotransmitter that appears in both the central and peripheral nervous systems. It is involved in transmission of pain, causes rapid contractions of the gastrointestinal smooth muscle, and modulates inflammatory and immune responses. [NIH]

Substrate: A substance upon which an enzyme acts. [EU]

Succinic Acids: A class of dicarboxylic acids with the general structure of butanedioic acid (succinic acid). They are used in perfumery and as a chemical intermediate in medicine. [NIH]

Supplementation: Adding nutrients to the diet. [NIH]

Suppurative: Consisting of, containing, associated with, or identified by the formation of pus. [NIH]

Surfactant: A fat-containing protein in the respiratory passages which reduces the surface tension of pulmonary fluids and contributes to the elastic properties of pulmonary tissue. [NIH]

Synergistic: Acting together; enhancing the effect of another force or agent. [EU]

Systemic: Affecting the entire body. [NIH]

Systemic disease: Disease that affects the whole body. [NIH]

Systolic: Indicating the maximum arterial pressure during contraction of the left ventricle of the heart. [EU]

Tenesmus: Straining, especially ineffectual and painful straining at stool or in urination. [EU]

Testosterone: A hormone that promotes the development and maintenance of male sex characteristics. [NIH]

Tetani: Causal agent of tetanus. [NIH]

Tetanic: Having the characteristics of, or relating to tetanus. [NIH]

Tetanus: A disease caused by tetanospasmin, a powerful protein toxin produced by

Clostridium tetani. Tetanus usually occurs after an acute injury, such as a puncture wound or laceration. Generalized tetanus, the most common form, is characterized by tetanic muscular contractions and hyperreflexia. Localized tetanus presents itself as a mild condition with manifestations restricted to muscles near the wound. It may progress to the generalized form. [NIH]

Therapeutics: The branch of medicine which is concerned with the treatment of diseases, palliative or curative. [NIH]

Thermal: Pertaining to or characterized by heat. [EU]

Threshold: For a specified sensory modality (e. g. light, sound, vibration), the lowest level (absolute threshold) or smallest difference (difference threshold, difference limen) or intensity of the stimulus discernible in prescribed conditions of stimulation. [NIH]

Thrombin: An enzyme formed from prothrombin that converts fibrinogen to fibrin. (Dorland, 27th ed) EC 3.4.21.5. [NIH]

Thrombocytes: Blood cells that help prevent bleeding by causing blood clots to form. Also called platelets. [NIH]

Thrombolytic: 1. Dissolving or splitting up a thrombus. 2. A thrombolytic agent. [EU]

Thrombomodulin: A cell surface glycoprotein of endothelial cells that binds thrombin and serves as a cofactor in the activation of protein C and its regulation of blood coagulation. [NIH]

Thrombosis: The formation or presence of a blood clot inside a blood vessel. [NIH]

Thromboxanes: Physiologically active compounds found in many organs of the body. They are formed in vivo from the prostaglandin endoperoxides and cause platelet aggregation, contraction of arteries, and other biological effects. Thromboxanes are important mediators of the actions of polyunsaturated fatty acids transformed by cyclooxygenase. [NIH]

Thrush: A disease due to infection with species of fungi of the genus Candida. [NIH]

Thymidine: A chemical compound found in DNA. Also used as treatment for mucositis. [NIH]

Thymus: An organ that is part of the lymphatic system, in which T lymphocytes grow and multiply. The thymus is in the chest behind the breastbone. [NIH]

Thyroid: A gland located near the windpipe (trachea) that produces thyroid hormone, which helps regulate growth and metabolism. [NIH]

Thyroxine: An amino acid of the thyroid gland which exerts a stimulating effect on thyroid metabolism. [NIH]

Tinnitus: Sounds that are perceived in the absence of any external noise source which may take the form of buzzing, ringing, clicking, pulsations, and other noises. Objective tinnitus refers to noises generated from within the ear or adjacent structures that can be heard by other individuals. The term subjective tinnitus is used when the sound is audible only to the affected individual. Tinnitus may occur as a manifestation of cochlear diseases; vestibulocochlear nerve diseases; intracranial hypertension; craniocerebral trauma; and other conditions. [NIH]

Tissue: A group or layer of cells that are alike in type and work together to perform a specific function. [NIH]

Tissue Plasminogen Activator: A proteolytic enzyme in the serine protease family found in many tissues which converts plasminogen to plasmin. It has fibrin-binding activity and is immunologically different from urinary plasminogen activator. The primary sequence, composed of 527 amino acids, is identical in both the naturally occurring and synthetic proteases. EC 3.4.21.68. [NIH]

Tobacco Industry: The aggregate business enterprise of agriculture, manufacture, and distribution related to tobacco and tobacco-derived products. [NIH]

Tolerance: 1. The ability to endure unusually large doses of a drug or toxin. 2. Acquired drug tolerance; a decreasing response to repeated constant doses of a drug or the need for increasing doses to maintain a constant response. [EU]

Tomography: Imaging methods that result in sharp images of objects located on a chosen plane and blurred images located above or below the plane. [NIH]

Tone: 1. The normal degree of vigour and tension; in muscle, the resistance to passive elongation or stretch; tonus. 2. A particular quality of sound or of voice. 3. To make permanent, or to change, the colour of silver stain by chemical treatment, usually with a heavy metal. [EU]

Tooth Loss: The failure to retain teeth as a result of disease or injury. [NIH]

Tooth Preparation: Procedures carried out with regard to the teeth or tooth structures preparatory to specified dental therapeutic and surgical measures. [NIH]

Topical: On the surface of the body. [NIH]

Toxic: Having to do with poison or something harmful to the body. Toxic substances usually cause unwanted side effects. [NIH]

Toxicity: The quality of being poisonous, especially the degree of virulence of a toxic microbe or of a poison. [EU]

Toxicology: The science concerned with the detection, chemical composition, and pharmacologic action of toxic substances or poisons and the treatment and prevention of toxic manifestations. [NIH]

Toxin: A poison; frequently used to refer specifically to a protein produced by some higher plants, certain animals, and pathogenic bacteria, which is highly toxic for other living organisms. Such substances are differentiated from the simple chemical poisons and the vegetable alkaloids by their high molecular weight and antigenicity. [EU]

Toxoid: The material resulting from the treatment of toxin in such a way that the toxic properties are inactivated whilst the antigenic potency remains intact. [NIH]

Trace element: Substance or element essential to plant or animal life, but present in extremely small amounts. [NIH]

Trachea: The cartilaginous and membranous tube descending from the larynx and branching into the right and left main bronchi. [NIH]

Transcription Factors: Endogenous substances, usually proteins, which are effective in the initiation, stimulation, or termination of the genetic transcription process. [NIH]

Transduction: The transfer of genes from one cell to another by means of a viral (in the case of bacteria, a bacteriophage) vector or a vector which is similar to a virus particle (pseudovirion). [NIH]

Transfection: The uptake of naked or purified DNA into cells, usually eukaryotic. It is analogous to bacterial transformation. [NIH]

Transfer Factor: Factor derived from leukocyte lysates of immune donors which can transfer both local and systemic cellular immunity to nonimmune recipients. [NIH]

Transgenes: Genes that are introduced into an organism using gene transfer techniques. [NIH]

Transillumination: Passage of light through body tissues or cavities for examination of internal structures. [NIH]

Translation: The process whereby the genetic information present in the linear sequence of ribonucleotides in mRNA is converted into a corresponding sequence of amino acids in a protein. It occurs on the ribosome and is unidirectional. [NIH]

Translocation: The movement of material in solution inside the body of the plant. [NIH]

Transmitter: A chemical substance which effects the passage of nerve impulses from one cell to the other at the synapse. [NIH]

Transplantation: Transference of a tissue or organ, alive or dead, within an individual, between individuals of the same species, or between individuals of different species. [NIH]

Transplantation Immunology: A general term for the complex phenomena involved in allo- and xenograft rejection by a host and graft vs host reaction. Although the reactions involved in transplantation immunology are primarily thymus-dependent phenomena of cellular immunity, humoral factors also play a part in late rejection. [NIH]

Trauma: Any injury, wound, or shock, must frequently physical or structural shock, producing a disturbance. [NIH]

Tryptophan: An essential amino acid that is necessary for normal growth in infants and for nitrogen balance in adults. It is a precursor serotonin and niacin. [NIH]

Tuberculosis: Any of the infectious diseases of man and other animals caused by species of Mycobacterium. [NIH]

Tumor marker: A substance sometimes found in an increased amount in the blood, other body fluids, or tissues and which may mean that a certain type of cancer is in the body. Examples of tumor markers include CA 125 (ovarian cancer), CA 15-3 (breast cancer), CEA (ovarian, lung, breast, pancreas, and gastrointestinal tract cancers), and PSA (prostate cancer). Also called biomarker. [NIH]

Type 2 diabetes: Usually characterized by a gradual onset with minimal or no symptoms of metabolic disturbance and no requirement for exogenous insulin. The peak age of onset is 50 to 60 years. Obesity and possibly a genetic factor are usually present. [NIH]

Ulcer: A localized necrotic lesion of the skin or a mucous surface. [NIH]

Ulceration: 1. The formation or development of an ulcer. 2. An ulcer. [EU]

Ultraviolet radiation: Invisible rays that are part of the energy that comes from the sun. UV radiation can damage the skin and cause melanoma and other types of skin cancer. UV radiation that reaches the earth's surface is made up of two types of rays, called UVA and UVB rays. UVB rays are more likely than UVA rays to cause sunburn, but UVA rays pass deeper into the skin. Scientists have long thought that UVB radiation can cause melanoma and other types of skin cancer. They now think that UVA radiation also may add to skin damage that can lead to skin cancer and cause premature aging. For this reason, skin specialists recommend that people use sunscreens that reflect, absorb, or scatter both kinds of UV radiation. [NIH]

Urea: A compound (CO(NH2)2), formed in the liver from ammonia produced by the deamination of amino acids. It is the principal end product of protein catabolism and constitutes about one half of the total urinary solids. [NIH]

Urease: An enzyme that catalyzes the conversion of urea and water to carbon dioxide and ammonia. EC 3.5.1.5. [NIH]

Urethra: The tube through which urine leaves the body. It empties urine from the bladder. [NIH]

Urinary: Having to do with urine or the organs of the body that produce and get rid of urine. [NIH]

Urinary Plasminogen Activator: A proteolytic enzyme that converts plasminogen to plasmin where the preferential cleavage is between arginine and valine. It was isolated originally from human urine, but is found in most tissues of most vertebrates. EC 3.4.21.73. [NIH]

Urine: Fluid containing water and waste products. Urine is made by the kidneys, stored in the bladder, and leaves the body through the urethra. [NIH]

Uterus: The small, hollow, pear-shaped organ in a woman's pelvis. This is the organ in which a fetus develops. Also called the womb. [NIH]

Vaccination: Administration of vaccines to stimulate the host's immune response. This includes any preparation intended for active immunological prophylaxis. [NIH]

Vaccines: Suspensions of killed or attenuated microorganisms (bacteria, viruses, fungi, protozoa, or rickettsiae), antigenic proteins derived from them, or synthetic constructs, administered for the prevention, amelioration, or treatment of infectious and other diseases. [NIH]

Vagina: The muscular canal extending from the uterus to the exterior of the body. Also called the birth canal. [NIH]

Vaginitis: Inflammation of the vagina characterized by pain and a purulent discharge. [NIH]

Vascular: Pertaining to blood vessels or indicative of a copious blood supply. [EU]

Vector: Plasmid or other self-replicating DNA molecule that transfers DNA between cells in nature or in recombinant DNA technology. [NIH]

Vegetative: 1. Concerned with growth and with nutrition. 2. Functioning involuntarily or unconsciously, as the vegetative nervous system. 3. Resting; denoting the portion of a cell cycle during which the cell is not involved in replication. 4. Of, pertaining to, or characteristic of plants. [EU]

Vein: Vessel-carrying blood from various parts of the body to the heart. [NIH]

Venous: Of or pertaining to the veins. [EU]

Ventricle: One of the two pumping chambers of the heart. The right ventricle receives oxygen-poor blood from the right atrium and pumps it to the lungs through the pulmonary artery. The left ventricle receives oxygen-rich blood from the left atrium and pumps it to the body through the aorta. [NIH]

Venules: The minute vessels that collect blood from the capillary plexuses and join together to form veins. [NIH]

Vertigo: An illusion of movement; a sensation as if the external world were revolving around the patient (objective vertigo) or as if he himself were revolving in space (subjective vertigo). The term is sometimes erroneously used to mean any form of dizziness. [EU]

Veterinary Medicine: The medical science concerned with the prevention, diagnosis, and treatment of diseases in animals. [NIH]

Vibrio: A genus of Vibrionaceae, made up of short, slightly curved, motile, gram-negative rods. Various species produce cholera and other gastrointestinal disorders as well as abortion in sheep and cattle. [NIH]

Viral: Pertaining to, caused by, or of the nature of virus. [EU]

Viral Proteins: Proteins found in any species of virus. [NIH]

Virulence: The degree of pathogenicity within a group or species of microorganisms or viruses as indicated by case fatality rates and/or the ability of the organism to invade the tissues of the host. [NIH]

Virus: Submicroscopic organism that causes infectious disease. In cancer therapy, some

viruses may be made into vaccines that help the body build an immune response to, and kill, tumor cells. [NIH]

Visual Acuity: Acuteness or clearness of vision, especially of form vision, which is dependent mainly on the sharpness of the retinal focus. [NIH]

Vitro: Descriptive of an event or enzyme reaction under experimental investigation occurring outside a living organism. Parts of an organism or microorganism are used together with artificial substrates and/or conditions. [NIH]

Vivo: Outside of or removed from the body of a living organism. [NIH]

War: Hostile conflict between organized groups of people. [NIH]

Wettability: The quality or state of being wettable or the degree to which something can be wet. This is also the ability of any solid surface to be wetted when in contact with a liquid whose surface tension is reduced so that the liquid spreads over the surface of the solid. [NIH]

White blood cell: A type of cell in the immune system that helps the body fight infection and disease. White blood cells include lymphocytes, granulocytes, macrophages, and others. [NIH]

Whole cell vaccine: Vaccine made from whole tumor cells that have been changed in the laboratory. [NIH]

Windpipe: A rigid tube, 10 cm long, extending from the cricoid cartilage to the upper border of the fifth thoracic vertebra. [NIH]

Withdrawal: 1. A pathological retreat from interpersonal contact and social involvement, as may occur in schizophrenia, depression, or schizoid avoidant and schizotypal personality disorders. 2. (DSM III-R) A substance-specific organic brain syndrome that follows the cessation of use or reduction in intake of a psychoactive substance that had been regularly used to induce a state of intoxication. [EU]

Wound Healing: Restoration of integrity to traumatized tissue. [NIH]

Xenograft: The cells of one species transplanted to another species. [NIH]

Xerostomia: Decreased salivary flow. [NIH]

X-ray: High-energy radiation used in low doses to diagnose diseases and in high doses to treat cancer. [NIH]

X-Ray Film: A film base coated with an emulsion designed for use with X-rays. [NIH]

X-ray therapy: The use of high-energy radiation from x-rays to kill cancer cells and shrink tumors. Radiation may come from a machine outside the body (external-beam radiation therapy) or from materials called radioisotopes. Radioisotopes produce radiation and can be placed in or near the tumor or in the area near cancer cells. This type of radiation treatment is called internal radiation therapy, implant radiation, interstitial radiation, or brachytherapy. Systemic radiation therapy uses a radioactive substance, such as a radiolabeled monoclonal antibody, that circulates throughout the body. X-ray therapy is also called radiation therapy, radiotherapy, and irradiation. [NIH]

Yeasts: A general term for single-celled rounded fungi that reproduce by budding. Brewers' and bakers' yeasts are Saccharomyces cerevisiae; therapeutic dried yeast is dried yeast. [NIH]

Zymogen: Inactive form of an enzyme which can then be converted to the active form, usually by excision of a polypeptide, e. g. trypsinogen is the zymogen of trypsin. [NIH]

INDEX

D

E

Q